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Association of Self-Reported Frailty with Falls and Fractures among Patients New to Dialysis

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Key Words
Fracture · Frailty · Hemodialysis

Abstract

Background: Although frailty has been linked to higher risk of falls and fracture in the general population, only few studies have examined the extent to which frailty is associated with these outcomes among patients with end-stage renal disease, who are at particularly high risk for these events. ***Methods:*** A total of 1,646 patients who were beginning maintenance hemodialysis in 297 dialysis units throughout the United States from September 2005 to June 2007 were enrolled in the Comprehensive Dialysis Study, and 1,053 Medicare beneficiaries were included in this study. Self-reported frailty was defined by the patients endorsing 2 or more of the following: poor physical functioning, exhaustion or low physical activity. Falls and fractures requiring medical attention were identified through Medicare claims data. We examined the association between frailty and the time to first fall or fracture using the Fine-Gray modification of Cox proportional hazards regression, adjusted for demographics, Quételet's body mass index, diabetes mellitus, heart failure and atherosclerosis. ***Results:*** Seventy-seven percent of patients were frail by self-report. The median length of follow-up was 2.5 (1.0–3.9) years. Crude rates of first medically urgent falls or fractures were 66 and 126 per 1,000 person-years in non-frail and self-reported frail participants, respectively. After accounting for demographic factors, comorbidities and the competing risk of death, self-reported frailty was associated with a higher risk of falls or fractures requiring medical attention (hazards ratio 1.60, 95% CI 1.16–2.20). ***Conclusion:*** Participants reporting frailty experienced nearly twice the risk of medically urgent falls or fractures compared to those who did not report frailty.

Introduction

In the general elderly population, falls and associated adverse outcomes, including fractures, are a substantial healthcare problem associated with a significant risk of death [1–3]. In the dialysis population, the 1-year risk of death following a fracture is nearly 4-fold higher compared to individuals with no fracture [4]. Even in the absence of fracture, falls carry a substantial risk of death in the end-stage renal disease (ESRD) population. Patients

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who fall have 60% higher 1-year risk of death compared to individuals who do not report a fall [5–7].

In the general population, frailty, a syndrome of decreased physiological reserve, has been linked to higher rates of falls and fracture [8, 9]. Frailty has been associated with adverse outcomes including hospitalization, disability and death among patients with chronic kidney disease (CKD) [10–13]. Although it is logical to expect that patients with ESRD who are frail should be prone to falls and subsequent fractures [14], only 1 study has evaluated self-reported falls among patients on dialysis from a single center [15]. Risk of fracture among patients with ESRD is related to serum parathyroid hormone concentrations [16], and recent data suggest that treatment of CKD–mineral and bone disorder (CKD-MBD) may affect fracture rates [17, 18]. Thus, it is possible that CKD-MBD is responsible for the higher rates of fracture observed among patients with ESRD and that the impact of frailty may be less important than among community-dwelling elders. On the other hand, if the risk of fall and fracture is higher among frail patients, early identification of frailty and intervention to address it could lead to a reduction in these events.

The purpose of this analysis was to examine the rates of falls or fractures requiring a medical visit or hospitalization in a diverse cohort of patients enrolled in the Comprehensive Dialysis Study (CDS), a United States Renal Data System Special Study [19]. We hypothesized that patients who were frail by self-report would be at higher risk for falls or fracture, even after accounting for the confounding effects of advanced age and other clinical factors.

Methods

Data Source

We used data from the CDS, a prospective cohort study in which information regarding physical activity, health-related quality of life and data on work and disability were collected among 1,678 incident patients receiving maintenance hemodialysis across 297 dialysis units throughout the United States from September 2005 to June 2007 [19]. Participants provided informed consent. The study was approved by institutional review boards at the US Renal Data System (USRDS) Coordinating Center (University of Minnesota), the USRDS Rehabilitation/Quality of Life Special Studies Center (Emory University) and the USRDS Nutrition Special Studies Center (University of California, San Francisco). For this analysis, the study sample was restricted to participants who were receiving hemodialysis and had Medicare part A and B as the primary payer prior to or within 60 days of the study start date and had Medicare claims data to allow us to identify fall and fracture events. Participants were followed for outcomes of interest until December 31, 2010.

Definition of Self-Reported Frailty

We defined self-reported frailty using questionnaire measures of physical function, exhaustion and physical activity as previously described [10]. This approach is an adaptation of the well-validated Fried frailty phenotype [9]. A similar adaptation has been shown to be predictive of hospitalization, disability and death among older women [20], and this definition was associated with higher mortality among patients with ESRD. We defined low self-reported function as a Medical Outcomes Study Short Form-12 Physical Function score <75 (1 point). We categorized 'exhaustion' as positive if participants answered either 'a little of the time' or 'none of the time' when asked how often they felt they had a lot of energy during the past 4 weeks (1 point). Participants met the low physical activity criterion if their score on the Adjusted Activity Score of the Human Activity Profile was in the lowest quintile of age- and sex-stratified normative data (1 point). If 2 or more of the criteria were met, the participant was considered to exhibit self-reported frailty [10].

Fall or Fracture Identification

We identified falls or fractures that were severe enough to require hospitalization or medical evaluation via Medicare claims data. We identified falls using the International Classification of Disease, Ninth revision, Clinical Modification (ICD-9-CM) codes and fractures using the ICD-9-CM diagnosis codes and Current Procedural Terminology codes for related procedures (online suppl. table A, see www.karger.com/doi/10.1159/000439000) [21]. Non-pathologic fractures of the leg, wrist, hip, vertebra and pelvis were included in the analysis. Pelvic fractures included fractures of the acetabulum, ilium and ischium. Hip fractures were primarily of the femur. If an individual had multiple admissions for fall or fracture over the time period of the analysis (n = 55 had more than 1 event), only the first event was considered in the analysis. The date of fall or fracture event was the date of the first documented physician, hospital or institutional claim. However, we required a hospital claim for hip and pelvic fracture to avoid capturing historical events.

Statistical Methods

We compared characteristics of CDS participants with and without self-reported frailty using the Mann–Whitney test for continuous variables and the Mantel–Haenszel test for categorical variables. We plotted cumulative incidence curves to examine the time to first fall or fracture in patients with and without self-reported frailty. For our primary analysis, we used the Fine-Gray modification of Cox proportional hazards regression, with time to first fall or fracture as the dependent variable, self-reported frailty as the primary explanatory variable, and adjusting for age, body mass index (BMI), sex, race, ethnicity, diabetes mellitus, heart failure and atherosclerotic disease (includes coronary heart disease, cerebrovascular disease, peripheral vascular disease or amputation) as covariates, thus accounting for the competing risk of death. We subsequently examined the associations of the individual components of self-reported frailty (poor physical function, exhaustion and low physical activity) with time to first fall or fracture using the Cox proportional hazards models adjusted for the same covariates. We considered a 2-tailed p value of <0.05 as statistically significant. We performed all analyses using the SAS version 9.4 (SAS Institute Inc., Cary, N.C., USA).

Table 1. Characteristics of the cohort according to self-reported frailty

Cohort characteristics	All (n = 1,053)	Frail (n = 808)	Not frail (n = 245)	p value
Sex, female, %	45 (472)	48.8 (394)	31.8 (78)	<0.001
Median age, years	63 (52–73)	62.5 (52–73)	65 (52–72)	0.80
Race, %				
African American	26.8 (282)	25.5 (206)	31 (76)	0.20
Caucasian	70.6 (743)	71.7 (579)	66.9 (167)	
Other	2.7 (28)	2.8 (23)	2.0 (5)	
Comorbidities				
Diabetes mellitus, %	58.5 (616)	63 (509)	43.7 (107)	<0.001
Heart failure, %	33.8 (356)	36.4 (294)	25.3 (62)	0.001
Atherosclerotic disease, %	37.9 (399)	40.1 (324)	30.6 (75)	0.007
BMI, kg/m^2	29.6 (8.2)	30.1 (8.26)	28.1 (7.72)	<0.001
Laboratory parameters, g/dl				
Serum albumin	3.14 (0.7)	3.13 (0.7)	3.20 (0.70)	0.30
Hemoglobin	10.1 (1.73)	10.2 (1.74)	9.94 (1.71)	0.12
Dialysis-related parameters				
Dialysis vintage, days	127 (111–148)	127 (112–149)	127 (112–149)	0.85
Self-reported frailty components, %				
Inactivity	94 (985)	99.6 (805)	73.5 (180)	<0.001
Poor physical function	70.8 (746)	91.5 (739)	2.9 (7)	
Exhaustion	51.1 (538)	65.3 (528)	4.1 (10)	

Displayed as mean (SD) for normally distributed variables, median (25th–75th percentile) for non-normally distributed variables and % (n) for categorical variables. Atherosclerotic disease includes coronary heart disease, cerebrovascular disease, peripheral vascular disease or amputation.

Results

Participant Characteristics

Of the 1,678 individuals in the original CDS cohort, 1,086 were Medicare beneficiaries, of whom 1,053 had complete data for assessment of self-reported frailty. The median age was 63 (25th–75th percentile 52–73) years, and 55% were men. Median dialysis vintage was 127 (111–148) days.

Prevalence of Self-Reported Frailty

The overall prevalence of self-reported frailty was 77%. A vast majority of individuals met the criterion for inactivity (94%). Seventy-eight percent of individuals met the definition for low self-reported function. The exhaustion component of frailty was endorsed by just over half (51%) the cohort. Table 1 lists the overall baseline participant characteristics and also according to the presence or absence of self-reported frailty. On an average, frail individuals had higher BMI than those who were not frail (30.0 ± 8.3 vs. 28.1 ± 7.7 kg/m^2 among the non-frail, $p < 0.01$). As expected, patients reporting frailty had a higher burden of comorbidity as compared to patients who did not.

Incidence of Fall or Fracture

During a median follow-up of 2.5 (1.0–3.9) years, 283 episodes of medical care for first fall or fracture were observed. The first event incidence rate was 66 per 1,000 person-years in non-frail participants as compared to 126 per 1,000 person years for those who reported frailty ($p < 0.001$; fig. 1a).

Association of Self-Reported Frailty with Time to First Fall or Fracture

In unadjusted analyses, self-reported frailty was associated with a higher risk of first fall or fracture (hazards ratio (HR) 1.66, 95% CI 1.22–2.26). Adjusting for demographics, BMI and select comorbidities did not attenuate the association of self-reported frailty with time to first fall or fracture (HR 1.60, 95% CI 1.16–2.20; table 2). As expected, older age, white race and female sex were associated with a higher risk of first fall or fracture.

In fully adjusted analyses of the separate components of frailty, poor self-reported functioning (HR 1.33, 95% CI 1.01–1.75) and exhaustion (HR 1.40, 95% CI 1.10–1.76) were significantly associated with risk of fall or fracture (fig. 1b and c, 2). Although the point estimate for low physical activity was similar, the association did not reach

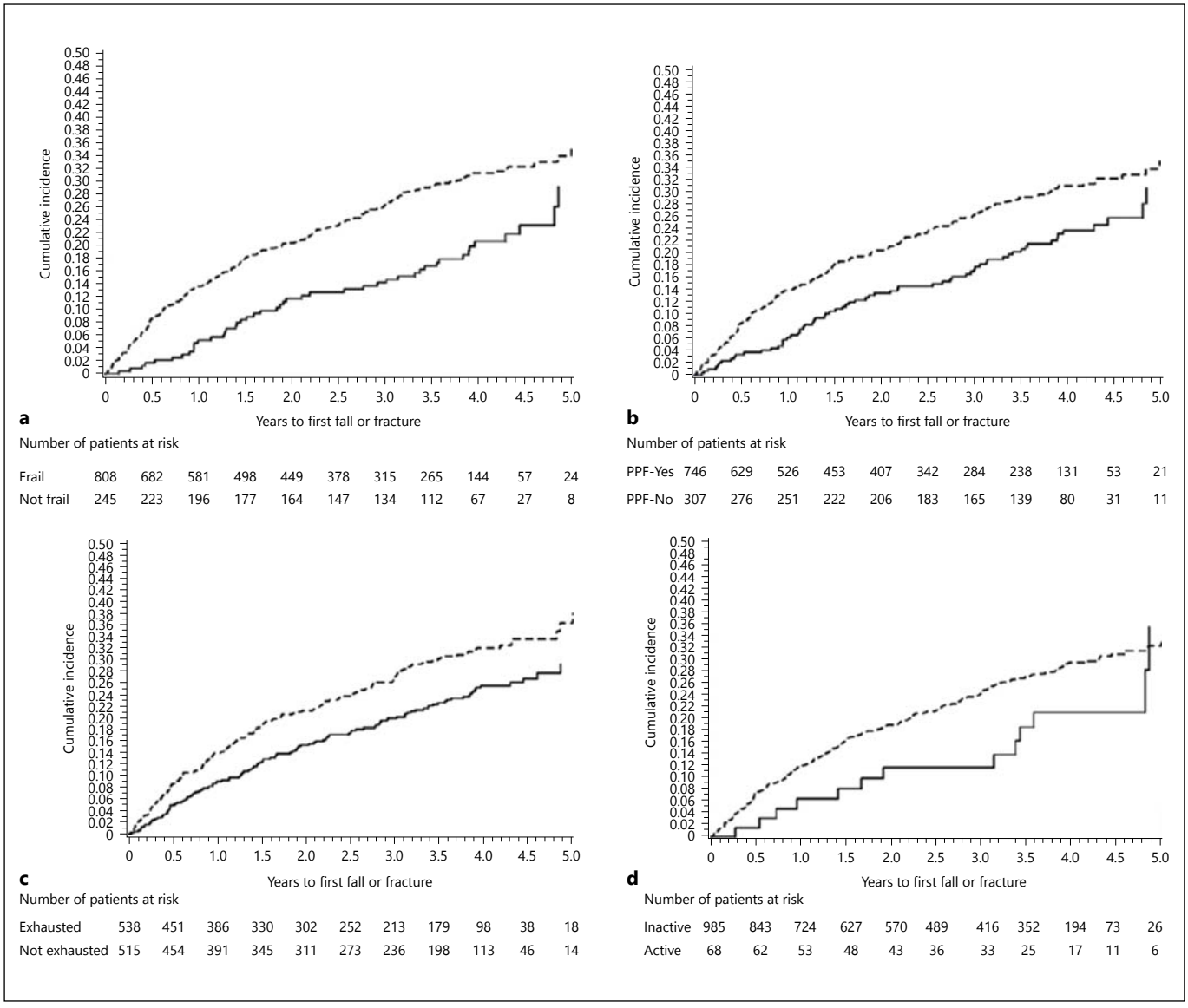

Fig. 1. Cumulative incidence plots of self-reported frailty and its components with time to first fall or fracture. **a** Frailty; **b** poor physical function (PPF); **c** exhaustion; **d** low physical activity. Dashed line represents individuals who endorsed frailty or component and solid line represents those who did not.

statistical significance (HR 1.36, 95% CI 0.78–2.37; fig. 1d, 2), perhaps because the proportion of patients without low physical activity was small.

Discussion

We found a strong association between self-reported frailty and first fall or fracture, which is severe enough to require medical attention in a cohort of patients new to dialysis. Patients reporting frailty had a higher risk of a fall or fracture compared to their non-frail counterparts. Although only poor self-reported functioning and exhaustion components of our frailty definition were significantly associated with medically urgent first fall or fracture, the association with low physical activity was of a similar magnitude.

The impact of falls and associated complications, including fracture and death, is well documented in the general elderly population [2, 6, 22, 23]. The overall rate of non-fatal falls requiring professional healthcare help was 43 per 1,000 person-years in 2010 [24]. Physiologic de-

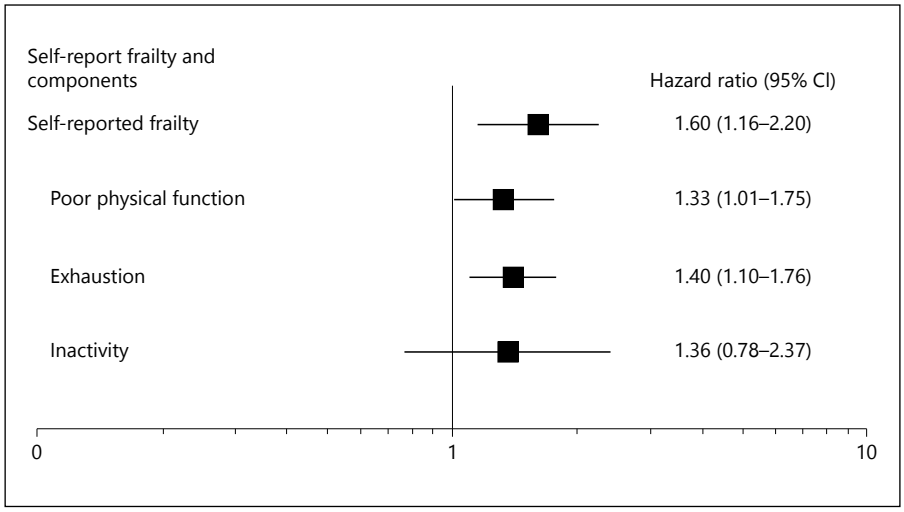

Fig. 2. The Forrest plot of the association of self-report frailty and its components with risk of fall or fracture adjusted for female sex, age per 10 years, Caucasian race, diabetes, atherosclerosis, heart failure and BMI.

Table 2. Multivariable Cox proportional hazards model examining the association of self-reported frailty with time to first fall or fracture requiring medical attention

Variables	HR (95% CI)	p value
Frail	1.60 (1.16–2.20)	<0.01
Female	1.70 (1.33–2.17)	<0.0001
Age, per 10 years	1.20 (1.10–1.33)	<0.0001
White (vs. other race)	1.36 (1.02–1.82)	<0.01
Diabetes mellitus	0.97 (0.76–1.25)	0.83
Atherosclerotic disease	0.96 (0.73–1.24)	0.74
Heart failure	0.88 (0.67–1.14)	0.32
BMI, kg/m^2	0.99 (0.97–1.00)	0.18

Atherosclerotic disease includes coronary heart disease, cerebrovascular disease, peripheral vascular disease or amputation.

rangements associated with CKD and ESRD heighten the risk of falls. In a prior study of 162 elderly patients receiving dialysis, 47% reported a fall during the 2.5-year study period, with a fall incidence of 1.60 falls per person-year based on patient report [25]. In the present study, we used Medicare claims to identify the fall events that were severe enough to require medical evaluation, which may account, at least in part, for the lower observed event rates compared to the aforementioned study. Data from a longitudinal pilot study found that the risk of death and hospitalization was 2-fold higher among patients receiving dialysis who had fallen over a 2-year follow-up period compared to those who had not [26]. Patients who reported even 1 accidental fall had a 78% percent higher risk of death over a 1-year follow-up period compared to 'non-fallers' [6].

Hip fracture has been most extensively studied, and patients on dialysis have been observed to have a 2- to 4-fold higher hip fracture rate than that of the general elderly population [17, 27]. For example, among Medicare beneficiaries, the adjusted hip fracture event rate for persons on hemodialysis was 21.9 per 1,000 person-years for patients receiving dialysis versus 10.6 per 1,000 person-years among patients not receiving dialysis [17]. Prior studies have suggested that the incidence of hip fracture may be increasing in the ESRD population. In a study of older dialysis patients, hip fracture rates were significantly higher in 2009 than in 1996 despite multiple advances in management of metabolic bone disease in CKD [28]. Even with high overall risk of hip fracture among patients with ESRD, the risk of death is twice as high among patients who experience a hip fracture compared with those who do not [29].

Based on observations showing the association between frailty and fracture in the general population, we hypothesized that rates of fracture would be higher in patients receiving dialysis who were frail by self-report, even given higher baseline rates in the ESRD population. Our study confirmed this expectation, with an event rate of 126 per 1,000 person-years in individuals who were frail compared to 66 per 1,000 person-years in those who were not frail. In addition, a single-center study of 115 prevalent patients receiving dialysis reported a 3-fold higher risk of patient-reported falls among patients who were frail based on the Frailty Index compared to those who were non-frail [15].

Our study had the advantage of capturing falls or fractures using claims data in an incident ESRD population from across the United States. However, we cannot extrapolate event rates in the CDS cohort to all patients on dialysis. Patients enrolled in the CDS were somewhat younger and less disabled than the general incident dialysis population in 2005 [19]. As for the outcome, we captured only falls or fractures that were severe enough to require hospitalization or emergency room evaluation, whereas other studies have used patients' report of fall events [5, 6, 15, 26]. Although less severe falls would have been missed with our approach, the use of Medicare claims abrogates a dependence on patient recollection (possibly a serious shortcoming of other studies), as few medical visits go unbilled.

In light of our findings, identification of frail dialysis patients who are at higher risk of fall and fracture could potentially improve outcomes. Frail individuals could be targeted for interventions beyond routine management of CKD-MBD, such as home safety fall risk assessment, referral to physical therapy for gait or strength training and careful evaluation for potential contribution of polypharmacy. Integrated secondary prevention measures of this type have been shown to significantly lower the risk of repeat falls [30, 31] and to reduce mortality by almost 50% in people over the age of 50 years diagnosed with a minimal trauma fracture [32].

Although we demonstrated a higher risk of fall or fracture among frail patients, a number of limitations must be acknowledged. Prevalence of self-reported frailty in this study was higher than in a previous evaluation of the full cohort using the same definition of frailty [10]. This is likely attributable to the need to restrict our analysis to the incident dialysis patients who were eligible for Medicare claims near the start of dialysis, a group that has been shown to have a higher burden of comorbidity than patients who were not eligible for Medicare claims at the start of dialysis [33]. Indeed, the prevalence, although high, was quite similar to the prevalence of self-reported frailty previously reported among patients in this age range in a cohort of incident dialysis patients in the US [11]. Although it would be of interest to the nephrology community to examine falls occurring on patients' dialysis days, we were unable to determine whether falls occurred on dialysis or non-dialysis days in this study. Because we were investigating events severe enough to require medical attention, there were a relatively small number of events, which restricted our ability to evaluate associations with falls and fractures separately.

Conclusion

Self-reported frailty was associated with higher risk of fall or fracture among patients new to dialysis. Further studies should examine potential interventions to reduce these rates.

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