Saudi J Kidney Dis Transpl 2018;29(1):63-70

Saudi Journal of Kidney Diseases and Transplantation

Original Article

Assessment of Prevalence and Clinical Outcome of Frailty in an Elderly Predialysis Cohort Using Simple Tools

Hatem Ali, Tarek Abdelaziz, Fatima Abdelaal, Jyoti Baharani

Department of Renal Medicine, Heart of England Teaching Hospitals NHS Foundation Trust, Birmingham, UK

ABSTRACT. The relationship between frailty and chronic kidney disease in elderly population has been recognized; however, studies concentrating on frailty in predialysis patients are limited. For nephrologists, the recognition of frailty is important as it has impact on decisions on the choice of dialysis modality and sometimes on whether dialysis is indeed in the patients' best interests. Many of the tools for routine assessment of frailty are not easily applicable to those clinicians not practicing elderly care medicine. A tool needs to be simple and applicable for daily routine practice. The aim of this study was to assess the prevalence and clinical outcome of frailty in an elderly predialysis population using simple tools. A nonrandomized prospective study was conducted in which, 104 patients aged 65 years or above with an estimated glomerular filtration rate of 25 mL or less were included. Data including age, sex, renal function, calcium, albumin, parathormone, and comorbidities were collected at baseline and at three months interval for one year. Functional performance was assessed using Karnofsky scale. The Charlson comorbidity index was used to assess comorbid status of each patient. Frailty was assessed using a combination of PRISMA questionnaire and Timed up and Go test. End points were death or start of dialysis at 20-month follow-up. A frail group (n = 58; males = 32, females = 26) and a nonfrail group (n = 46; males = 21, females = 25) were identified. Frailty was prevalent in 53.8% of the selected population. There was no significant difference between both groups in terms of age, gender, comorbidities, hemoglobin, inflammatory markers, or calcium hemostasis. Nine patients chose conservative management in the frail group and six in nonfrail group. Rate of death was significantly higher in the frail group (death = 14) compared to nonfrail group (death = 3; P = 0.01). There was no significant difference between both groups in terms of initiation of dialysis (P = 0.1). Frailty and Charlson comorbidity index were significantly associated with mortality (P = 0.023 and 0.032, respectively). Survival in frail patients who started peritoneal dialysis (PD) was slightly better than those started on hemodialysis (HD) with hazard ratio = 3.23 (P = 0.23). Our study shows that the prevalence of frailty and mortality rate is high among

Correspondence to:

Dr. Jyoti Baharani,
Heart of England Teaching Hospitals NHS Foundation Trust, Birmingham, UK.
E-mail: jyoti.baharani@heartofengland.nhs.uk

elderly predialysis patients. Frailty and Charlson comorbidity index are independent predictors of outcome in this population. PD might be a better option of dialysis modality compared to HD in the frail population.

Introduction

Frailty is a discrete health condition in which different body organs steadily lose their reserves with aging.[1] It is a progressively frequent goal of epidemiological research and more recently of intervention studies.[2-4] Complexity in its measurement, however, hinders the widespread use of reporting frailty in the literature. The specific definition of frailty as a measure is difficult due to the associated comorbidities and health conditions associated with it.

The definition that has gained popularity is the phenotypic definition by Fried et al.[5] This multifactorial model includes measures of weakness, slowness, low activity, exhaustion, and weight loss. Nonetheless, recognition of frailty using this phenotype model in routine practice has its impediments. It is a model based on a composite of five elements that are time-consuming and there is variation between individuals.[6-8] Therefore, a test which is applicable in daily routine practice and is highly accurate to indicate frailty is of great importance.

The relationship between frailty and chronic kidney disease (CKD) in elderly population has been recognized, although studies concentrating on frailty in predialysis patients are limited,[9] and this is a compelling gap knowing that CKD is associated with aging.[10] CKD leads to many physiological alterations, mineral bone diseases, chronic inflammation, and atherosclerosis which can end up with sarcopenia and weakness, both of which are the main realms of frailty. Contrarily, frailty can negatively influence adjustments to the various health conditions that CKD patients endure with time. Therefore, patients with coexisting CKD and frailty can have a collusive risk of facing detrimental clinical outcomes, especially when this population approaches end-stage renal disease. Frailty may expedite the eventual need for dialysis and affect the quality of life.[10-12] Early identification of frailty and individuals at risk is a vital target for two reasons; first, due to its high prevalence that is expected to increase more in the future and second, due to its prognostic importance and potential managements as there are potential measures which may retard or oppose frailty in its early presentation prior to irreversible stages and consequently improve the quality of life.[13] In addition, frailty in addition to other comorbidities should be taken into account when taking decisions about further management plans in this population.[14-18]

For nephrologists, the recognition of frailty is important as it has impact on decisions regarding choice of dialysis modality and sometimes on whether dialysis is indeed needed in the patients' best interests. Many of the tools for routine assessment of frailty are cumbersome and not easily applicable to those clinicians not practicing elderly care medicine. A tool needs to be simple and applicable for daily routine practice. The aim of this study was to assess prevalence status and clinical outcome of frailty in an elderly predialysis population using simple tools.

Methodology and Materials

A cross-observational study was conducted in which 103 patients aged 65 years or above with an estimated glomerular filtration rate (eGFR) of 25 mL or less were included. The date of recruitment was July 2015 and follow-up data were collected until July 2016. Data including age, sex, full blood count, C-reactive protein, ferritin, renal function, calcium, albumin, parathormone, and comorbidities were collected at baseline and at three months' interval for one year. The GFR was estimated using 4-variable Modification of Diet in Renal Disease equation. Functional performance was assessed using Karnofsky scale. The Charlson comorbidity index was used to assess the comorbid status of each patient. Frailty was assessed using a combination of PRISMA questionnaire and Timed up and Go test (TUGT).[19]

Table 1. PRISMA questionnaire.

1.	Are you more than 85 years old?
2.	Male?
3.	Do you have any health problems that require you to limit your activity?
4.	Do you need someone to help you on regular basis?
5.	Do you have any health problems that require you to stay at home?
6.	In case of need, can you count on someone close to you?
7.	Do you regularly use stick, walker or wheelchair to get about?

Components of PRISMA questionnaire are shown in Table 1. TUGT test was defined as the time needed to get up and walk for a distance of 3 m. A chronological age of 65 years was used to define elderly population.[20] PRISMA questionnaire was conducted in the predialysis clinic where each question gave a score of 1 point if it was answered yes. Frailty was identified when a score of 3 or more was recorded in PRISMA questionnaire and a time of 8 s or more was needed to perform the TUGT test.[16] End points were death or start of dialysis at 20-month follow-up.

Statistical Analysis

Quantitative variables were reported as a mean and standard deviation or median and interquartile range, depending on whether data were skewed. Categorical variables were reported as frequencies and percentages. Comparisons of quantitative variables were performed using the independent samples *t*-test and the Chi-square test was used for categorical variables. Cox hazard regression analysis was used to identify predictors of frailty. Kaplan–Meier test was used to assess survival.

Results

In the cohort of 104 predialysis patients, two groups were identified; frail group (n = 58, males = 32, females = 26) and nonfrail group (n = 46, males = 21, females = 25). There was no significant difference between both groups in terms of age, gender, ethnicity, comorbidities, baseline GFR, hemoglobin, inflammatory markers, and calcium homeostasis. Baseline demographic characteristics are shown in Table 2.

Seventeen patients died during follow-up; 14 in the frail group and three in the nonfrail group. Death rate was significantly higher in the frail group compared to the nonfrail one with P = 0.01 as shown in Figure 1. The average survival time was 518 days in the frail group and 599 days in the nonfrail group.

Twenty-one patients started dialysis in the frail

Table 2. Baseline demographic characteristics between frail and non-frail group.

Variable	Frail (n=58)	Nonfrail (n=46)	P
Age (range)	77.4 (65–92)	76.7 (65–87)	0.14
Male (%)	32 (55)	21 (45)	0.42
Ethnicity (%)			
European	34 (58)	35 (76)	0.09
Asian	21(36)	9 (19)	0.08
African	3 (5)	2 (4)	0.84
Charlson co-morbidity score (mean)	7.21	6.61	0.85
Baseline GFR	16	15	0.21
Hemoglobin (g/L) mean	108	112	0.76
White blood cells	8.3	7.5	0.18
CRP	25	26	0.79
Albumin	31.8	33.3	0.59
Calcium	2.4	2.3	0.9
PTH	25.9	26.8	0.81

GFR: Glomerular filtration rate, CRP: C-reactive protein, PTH: Parathormone.

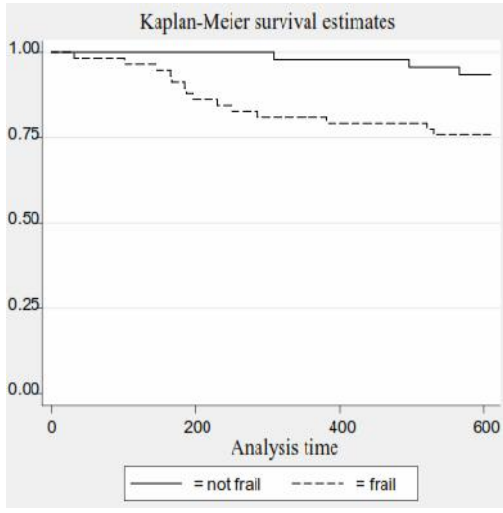

Figure 1. Kaplan-Meier survival curves (time to death).

Figure 3. Prevalence of frailty.

group [14 started hemodialysis (HD) and seven started peritoneal dialysis (PD)] and twenty patients started dialysis in the nonfrail group (14 started HD and six started PD). Mean time to initiation of dialysis was 265 days with no significant difference between both groups as shown in Figure 2. Mean GFR at initiation of dialysis was 7 mL/min in both groups.

Prevalence of frailty reached 53.8% in our elderly predialysis cohort (Figure 3). It was found that six patients in the nonfrail group and nine patients in the frail group chose conservative management.

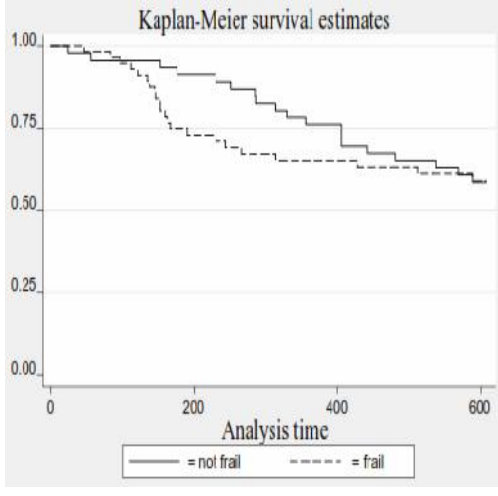

Figure 2. Kaplan–Meier survival curves (time to initiation of dialysis).

We used Cox hazard regression analysis to ascertain whether average calcium, average hemoglobin, baseline eGFR, Karnofsky grade, ethnicity, age, sex, average albumin, Charlson comorbidity score, and frailty can predict death. Univariate Cox hazard regression analysis showed that frailty, Charlson comorbidity index, and average serum albumin were independent risk factors for prediction of mortality in the predialysis population. On multivariate Cox hazard regression analysis, the same variables remained independent risk factors for estimation of mortality (Table 3).

Subgroup analysis showed that in the frail group, survival among patients who started PD was slightly better than in patients who started HD with hazard ratio (HR) of 3.32, although this was not statistically significant with P = 0.27 (Figure 4).

Discussion

In our study, frailty was found to be highly prevalent among elderly predialysis population and was associated with higher mortality. In the recent few years, the role of frailty as a prognostic factor of clinical outcome has been spotted. However, the data about its role in identifying

Table 3. Multivariate cox hazard regression analysis of patient survival

	Hazard ratio	Standard error (SE)	z	P>z	95% Confidence interval
Frailty					
Nonfrail	Base				
Frail	4.277949	2.735154	2.27	0.023	1.221829−14.97824
Average albumin	0.9177871	0.034872	−2.26	0.024	0.8519222−0.9887443
Charlson co-morbidity score	1.345426	0.1860121	2.15	0.032	1.02607−1.76418

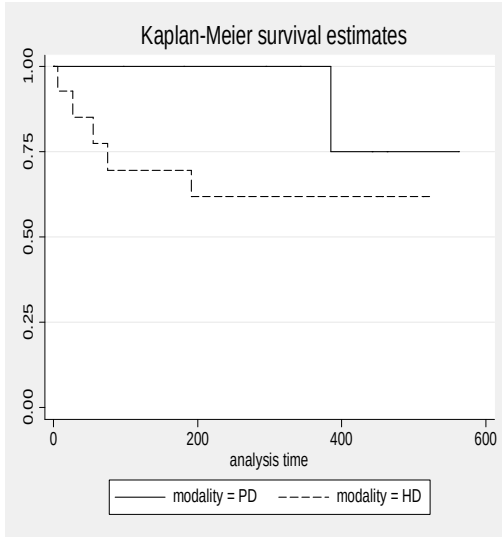

Figure 4. Survival among different dialysis modalities in the frail group.
PD: Peritoneal dialysis, HD: Hemodialysis.

clinical outcome of predialysis population are scarce. In the UK, many centers have incorporated multidisciplinary teams as part of predialysis assessment of the patients. Early identification of frailty would help both the patients and the multidisciplinary teams to better understand the possible clinical outcomes and in the complex decision-making.

In addition to the importance of informing the predialysis patients about their prognosis, our study highlighted that simple tools such as Charlson comorbidity index, PRISMA questionnaire, and TUGT test can be used for early identification of the frail population and earlier discussion of the different dialysis modalities and the estimated outcome.

So far, only one study has assessed frailty in elderly predialysis population. In 2016, in a retrospective study in the UK, Pugh et al assessed the effect of frailty on clinical outcome of either initiation of dialysis or death.[9] Sample size was 283 patients. In this population, CKD stage was IV–V. Frailty was evaluated using Clinical Frailty Score (CFS). It was found that rate of death or initiation of dialysis increased with higher CFS scores. Seventy-six percentage of patients with higher CFS scores died with 37% of them commenced on dialysis before death. Limitations of this study included its small sample size and single-center data covering catchment area that was one of the most socially deprived areas in the UK. Furthermore, the predominant ethnicity in the study population was Europeans. All these raise concerns about applicability of the results on other regions with more disparate ethnic groups. Finally, CFS could be used to assess the degree of frailty after a comprehensive geriatric assessment (CGS) and it was not validated to identify frailty without a detailed CGS.[18,21] This increases the complexity of the test and raises concerns about the applicability of CFS to identify frailty solely in daily routine care. Results in our study showed similar findings to that of Pugh et al in increasing risk of mortality in frail population. However, there was no significant difference in rate of initiation of dialysis in frail group compared to the nonfrail group.

Early identification of frailty is a vital target; first, due to its high prevalence, this is expected to increase more in the future,[22] second, due to its prognostic importance, knowing that frail population has higher risk of having detrimental health problems,[23,24] and also, because

there are potential managements which may retard or oppose frailty in its early presentation, ahead of the start of irreversible impairment.[25,26] Few studies showed prevalence of frailty among CKD population ranging between 14% and 20%.[16,27] However, the study population in these studies were middle aged and with various degrees of CKD. In our study, prevalence among elderly predialysis population was 53.8%. This shows that prevalence of frailty increases with older age and with increase in the severity of CKD.

Frailty should be taken into account when taking decisions about further management plans for patients in addition to their comorbidities.[28] Few studies used simple tools in assessing frailty in different populations. An Irish study on 1814 individuals was performed to assess the relationship between TUGT and frailty as defined using Fried criteria. The study found that TUGT is a sensitive (66%) and specific (77%) tool to assess frailty and can be used in the measurement of frailty where application of Fried criteria is not practical.[16] In the Netherlands, a study on 102 individuals older than 65 years was conducted to assess the accuracy of several instruments for the assessment of frailty against Fried criteria. Instruments included were PRISMA questionnaire, polypharmacy, the Groningen Frailty Indicator questionnaire, general practitioner assessment, and self-reported health. They concluded that the PRISMA questionnaire with a cutoff of three or more positive questions has the highest sensitivity (86%) and specificity (83%) when compared to other instruments.[27] In our study, a combination of PRISMA questionnaire and TUGT test was used to assess frailty. This combination was recognized to increase the accuracy of identifying frailty.[19]

In addition to frailty as an independent factor of predicting mortality, our study showed that simple tools of identifying comorbidities such as Charlson comorbidity score could predict similar outcome. Given the complexity of proper measurement of frailty, high scores of Charlson comorbidity index could be used as a marker of the ultimate start of proper assessment of frailty and discussion with the patients about possible outcomes. Lower serum albumin was shown to be associated with higher mortality in our study. Lower serum albumin could reflect lower muscle mass and sarcopenia associated with frailty and hence increased mortality.

Choosing the proper dialysis modality in this population is a complex decision. HD is associated with intradialytic hypotension and vascular access complications. PD could be a burden in this population, especially in the presence of associated cognitive problems. Our study, although did not show statistical significance in clinical outcome between HD and PD in the frail population, highlighted the possible favorable outcome with PD given the HR of 3.32. With larger sample size, these favorable outcomes could be more highlighted and magnified. The possible better survival with usage of PD could be explained by lesser associated cardiovascular complications with this dialysis modality.

Strengths of our study include the prospective design and using simple tools in identifying frailty that can be used in daily routine care. Limitations include the relatively small sample size and the nonrandomized selection of the patients. Finally, the subjective nature of the tools used to assess frailty could have affected the proper selection of the frail patients. This has been overcome by combining two methods; the PRISMA questionnaire and the TUGT test to identify frail patients.

In conclusion, the prevalence of frailty is high among elderly predialysis patients. Rate of death is significantly higher in the frail group compared to the nonfrail group. Frailty and Charlson comorbidity index are independent predictors of outcome in this population. As many of the frail patients will go on to have renal replacement and worsening of their physical parameters, it is important that frailty is recognized in these patients at the predialysis stage. Identifying a simple tool to recognize frailty and is applicable for daily routine practice is of utmost importance.

Acknowledgment

We would like to express our sincere gratitude to the low clearance team in Heartlands hospital for their help and support in this work.

Conflict of interest: None declared.

References

1. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 2004;59:255-63.
2. Srinivas-Shankar U, Roberts SA, Connolly MJ, et al. Effects of testosterone on muscle strength, physical function, body composition, and quality of life in intermediate-frail and frail elderly men: A randomized, double-blind, placebo-controlled study. J Clin Endocrinol Metab 2010;95:639-50.
3. Fairhall N, Aggar C, Kurrle SE, et al. Frailty intervention trial (FIT). BMC Geriatr 2008; 8:27.
4. Drey M, Pfeifer K, Sieber CC, Bauer JM. The fried frailty criteria as inclusion criteria for a randomized controlled trial: Personal experience and literature review. Gerontology 2011;57:11-8.
5. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
6. Alcalá MV, Puime AO, Santos MT, et al. Prevalence of frailty in an elderly Spanish urban population. Relationship with comorbidity and disability. Aten Primaria 2010;42: 520-7.
7. Santos-Eggimann B, Cuénoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. J Gerontol A Biol Sci Med Sci 2009;64:675-81.
8. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: A systematic review. Age Ageing 2015;44:148-52.
9. Pugh J, Aggett J, Goodland A, et al. Frailty and comorbidity are independent predictors of outcome in patients referred for pre-dialysis education. Clin Kidney J 2016;9:324-9.
10. Cook WL. The intersection of geriatrics and chronic kidney disease: Frailty and disability among older adults with kidney disease. Adv Chronic Kidney Dis 2009;16:420-9.
11. Abboud H, Henrich WL. Clinical practice. Stage IV chronic kidney disease. N Engl J Med 2010;362:56-65.
12. Shlipak MG, Stehman-Breen C, Fried LF, et al. The presence of frailty in elderly persons with chronic renal insufficiency. Am J Kidney Dis 2004;43:861-7.
13. Swidler MA, Uribarri J, Siu A, Viassara H. Characterization of frailty in older adults with chronic kidney disease (CKD): Correlations with biomarkers of inflammation. J Am Soc Nephrol 2005;6:813.
14. Fried LF, Lee JS, Shlipak M, et al. Chronic kidney disease and functional limitation in older people: Health, aging and body composition study. J Am Geriatr Soc 2006;54: 750-6.
15. Johansen KL, Chertow GM. Significance of frailty among dialysis patients. J Am Soc Nephrol 2007;18:2960-7.
16. Abizanda Soler P, López-Torres Hidalgo J, Romero Rizos L, et al. Frailty and dependence in albacete (FRADEA study): Reasoning, design and methodology. Rev Esp Geriatr Gerontol 2011;46:81-8.
17. Fit For Frailty: A Report by the British Geriatrics Society in Association with the Royal College of General Practitioners and Age UK; June, 2014.
18. "WHO Definition of an Older or Elderly Person". Available from: http://www.Who.int. [Last retrieved on 2016 Apr 04].
19. Raîche M, Hébert R, Dubois MF. PRISMA-7: A case-finding tool to identify older adults with moderate to severe disabilities. Arch Gerontol Geriatr 2008;47:9-18.
20. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-95.
21. Drey M, Wehr H, Wehr G, et al. The frailty syndrome in general practitioner care: A pilot study. Z Gerontol Geriatr 2011;44:48-54.
22. De Lepeleire J, Iliffe S, Mann E, Degryse JM. Frailty: An emerging concept for general practice. Br J Gen Pract 2009;59:e177-82.
23. Gómez Pavón J, Martín Lesende I, Baztán Cortés JJ, et al. Preventing dependency in the elderly. Rev Clin Esp 2008;208:361-2.
24. Wick JY. Understanding frailty in the geriatric population. Consult Pharm 2011;26:634-45.

25. Savva GM, Donoghue OA, Horgan F et al. Using timed up-and-go to identify frail members of the older population. J Gerontol A Biol Sci Med Sci 2013;68:441-6.
26. Hoogendijk EO, van der Horst HE, Deeg DJ, et al. The identification of frail older adults in primary care: Comparing the accuracy of five simple instruments. Age Ageing 2013;42:262-5.
27. Hoogendijk EO, van der Horst HE, Deeg DJ, et al. The identification of frail older adults in primary care: Comparing the accuracy of five simple instruments. Age Ageing 2013;42:262-5.
28. Hatem A. Assessment of frailty in elderly pre-dialysis population using simple tools. Saudi J Kidney Dis Transpl 2017;28:716-26.