Bachelor of Science in Medicine Degree Program
End of Term Final Report

Student Name: Blake Lerner **Date:** 08/04/17

Project Title: Frailty is associated with technique failure and mortality in prevalent home dialysis patients

Primary Supervisor Name: Dr. Navdeep Tangri
Department: Nephrology

Co-Supervisor Name: Dr. Paul Komenda and Dr.Claudio Rigatto
Department: Nephrology

Summary (250 words max single spaced):

Dialysis, while life preserving, is associated with poor quality of life and high healthcare costs. Home dialysis modalities offer equivalent survival to in-center dialysis but have quality of life advantages and reduced healthcare costs; however, nearly half of home dialysis patients experience technique failure within two years and transition to in-center dialysis.
Frailty has been associated with poor outcomes in kidney disease, but not study has evaluated its association with the outcomes of technique failure and mortality in those with kidney failure being treated with home dialysis. Furthermore, little research has been done in evaluating agreement between different constructs of frailty. In our prospective single center cohort study, we evaluated 109 peritoneal dialysis and home dialysis patients for frailty using the modified Fried criteria, the short physical performance batter (SPPB), and physician and nurse impressions. Over the course of the study 39 patients had technique failure and 38 died. Agreement between objective tools (modified Fried and SPPB) was found to be moderate (Cohen's kappa=0.55) and agreement between subjective tools (physician and nurse impressions) to be good (kappa=0.63). All assessment tools were associated with a two-fold increase in risk of technique failure or death independent of age, sex, and common comorbid conditions except for the SPPB with hazard ratios of 2.42-2.53.
Frailty is associated with adverse outcomes in home dialysis and is easy to assess at bedside. External validation followed by clinical implementation of frailty assessment as part of the home dialysis evaluation should be considered as the next steps.

Student Signature

Blake Lerner Digitally signed by Blake Lerner Date: 2017.08.04 17:57:42 -05'00'

Primary Supervisor Signature

Acknowledgments: I gratefully acknowledge the sole or partial funding support from the following sponsors;

H.T. Thorlakson Foundation
Dean, College of Medicine
Research Manitoba

Manitoba Medical Service Foundation (MMSF)
Vice-Dean, Research Rady FHS
Health Sciences Centre Research Foundation
Heart and Stroke Foundation

Sponsorship if different or additional to above;

INTRODUCTION

Kidney failure requiring dialysis affects nearly 680000 Americans, with most patients dialyzing thrice weekly in facilities.[1] Dialysis itself, while life preserving, is associated with a poor quality of life and high health care costs.[2,3] Home dialysis modalities, such as peritoneal dialysis (PD) and home-hemodialysis (HHD), have equivalent survival to in-center hemodialysis (HD), and offer increased independence, a more liberal diet, as well as reduced health care costs from a system perspective.[4-7]

Although home modalities may be preferred by patients and providers, there are many patient-specific factors, both physiologic and psychosocial, which prevent patients from staying on home dialysis.[8,9] Despite carefully selecting and training candidates for home based therapies, and providing support through nursing infrastructure, nearly half of patients on home dialysis experience technique failure within 2 years, and are transitioned to in-center HD .[10] Reasons for technique failure are complex, and often related to a functional decline in the patient or caregiver, rather than membrane or access failure itself. Nonetheless, technique failure events are traumatic, and often associated with morbidity and mortality.[11]

Frailty, as described by Fried, is a multidimensional clinical phenotype consisting of three or more of unintentional weight loss, exhaustion, slow gait speed, muscle weakness, and low levels of activity.[12] Frailty, as a general construct, has been associated with an increased risk of adverse health outcomes including disability, dependency, falls, and mortality.[13] In addition to the Fried definition of frailty, there are other operational definitions which may include measurement of physical performance, combination of clinical conditions, and a healthcare professional's general impression.[14,15]

Several studies have demonstrated a correlation between frailty and outcomes in CKD, but none yet have looked at its possible association with outcomes including technique failure and death in those with kidney failure being treated with home dialysis modalities.[16-19] As such, we sought to investigate the impact of frailty on technique failure and mortality in this vulnerable population.

MATERIALS AND METHODS

Design and Population

The Canadian Frailty Observation and Interventions Trial (CanFIT) is a prospective cohort study of frailty, physical function, and cognition in patients with advanced CKD.[18] The home dialysis arm of the study included prevalent patients in either the Peritoneal Dialysis or Home Hemodialysis programs at Seven Oaks General Hospital in Winnipeg, Manitoba, Canada. Patients were assessed in the manner described below at the first clinic appointment following consent (usually within 3-6 months). They were then assessed annually thereafter until reaching an endpoint of technique failure, death, opting out, or loss to follow-up. Patients with technique failure were subsequently followed until death without further assessment. Patients were excluded if they were unfit to provide consent, unable to speak English, blind or deaf, or commenced in-center dialysis prior to their baseline assessment. Ethics approval was obtained and renewed annually until the end of the study.

Data Collection

Demographic data (date of birth, sex, and race) were collected from the patient when consenting them and confirmed through chart review. Laboratory values and information on comorbid conditions where collected through chart review at each assessment. Comorbid

conditions were also collected via questionnaire during each assessment. The comorbid conditions collected include previous myocardial infarction, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, hypertension, arthritis, diabetes, peripheral vascular disease, cirrhosis, gastrointestinal disease, weight loss, and depression.[20,21]

Frailty Assessment

Frailty measures were assessed by a research coordinator at baseline and subsequent study visits by questionnaire and various physical tests. modified Fried criteria and short physical performance battery (SPPB), objective frailty criteria, were assessed. Subjective physician and nurse impressions of frailty were also collected.

Modified Fried Criteria: The modified Fried criteria looks are five domains of frailty, being slow gait speed, muscle weakness, unintentional weight loss, exhaustion, and low levels of activity.[12,18] A patient testing positive for any three or more of these domains are considered frail. Gait speed was assessed by a 4 meter walk test. Speeds less than 0.8 m/s are considered slow. Muscle weakness was assessed by testing hand grip strength using a Jamar Hydraulic Dynamometer (Model J00105, LaFayette Instrument Company Inc.). Grip strength less than or equal to 30 kg in males and 20 kg in females was scored as frail. Unintentional weight loss was assessed by asking the study participant if they had unintentionally lost weight in the previous 12 months and how much. Unintentional weight loss of 10 lbs (4.54 kg) was scored as frail. Activity levels were ascertained using the Physical Activity Scale for the Elderly. Results from the questionnaire were reported in kcal/week consistent with the Paffenbarger Physical activity questionnaire.[22] Activity less than 383 kcal/week in males and 270 kcal/week in females was scored as frail. Exhaustion was evaluated using the two exhaustion related questions in the Center for Epidemiologic Studies Depression (CES-D) scale.[23] Answering "occasionally" or "most or all of the time" to either question was scored as frail.

Short Physical Performance Battery: The SPPB consists of a series of balance tests, a gait speed test, and a chair stand test.[14] The SPPB is scored according to Guralnik et al., but in brief, patients receive points for being able to stand unassisted with their feet side-by-side, off set, and heel to toe for ten seconds. They receive points for their gait speed, with faster times receiving higher scores. Participants are also timed for how long it takes to stand unassisted from a seated position 5 times in a row. Again, higher scores are awarded for faster times. Scores in the SPPB correspond inversely with degree of frailty.

Physician and Nurse Impressions: Physician and nurse impressions of frailty were ascertained by first asking "Do you think this patient is frail?" followed by asking them to rate the patient on a five-point Likert scale where 1 is "very fit" and 5 is "very frail." A score of 3 or higher on this scale was considered frail.

Statistical Analysis

For baseline descriptive statistics, the study cohort was stratified and analyzed by modified Fried frailty status. Continuous variables were reported as median and interquartile range due to non-normal distribution. The Mann Whitney U test was used to compare continuous variables. Categorical variables were presented as frequency and percentage and were compared using the Chi Square Test. The prevalence of frailty as a function of assessments, not patients, was reported for the different assessment tools (modified Fried, SPPB, physician and nurse impression ratings). Cohen's Kappa was used to measure agreement between the tools.

The association between different frailty assessment tools and outcomes of technique failure, mortality, and a composite of the two were evaluated with Cox proportional hazards

models. Each frailty assessment tool, as well as the individual components of the modified Fried, were evaluated separately as predictors of the study outcomes in two models. The first is an unadjusted model, and the second adjusted for age, sex and a comorbidity index as described above. Patients who had received a transplant were removed from analysis for technique failure, but not mortality or composite outcome. All analyses were done using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Study Population

109 patients had complete data permitting inclusion in the analysis. Table 1 summarizes the clinical characteristics of the included patients. Patients deemed frail were 13 years older and had lower diastolic blood pressures, hemoglobin and serum albumin values. There was no significant difference in eGFR. Both groups had similar rates of most common comorbid conditions such as congestive heart failure and arthritis; however, the prevalence of diabetes was higher in frail patients.

Comparison of Frailty Assessment Tools

The prevalence of frailty varied depending on the assessment tool used, with as little as 18.3% of assessment yielding a frail result based on nurse impression, or as high as 42.2% based on the SPPB (Table 3). Agreement between objective measures (modified Fried and SPPB) was moderate (Cohen's Kappa: κ=0.55) and agreement between objective measures (physician and nurse impressions) was good(κ=0.63).

Association with Frailty Assessment Tools and Outcomes

Of the 109 included patients, 39 had technique failure, 38 died, and 59 had technique failure or death.

Association with Technique Failure

The associations between individual frailty measures, as well as components of the modified Fried criteria, and technique failure are presented in Table 3. Before and after adjusting for age, sex, and the comorbid conditions described above, the subjective physician impression of frailty as well as the objective Fried frailty criteria were both associated with greater than a two-fold increase in the risk of technique failure (HR 2.01 [95% CI: 1.04-3.88] and HR 2.46 [95% CI: 1.15-5.25], respectively). When the subcomponents of the Fried criteria were examined, weight loss and weakness remained strongly and consistently associated, whereas the other measures were not related to the outcome (Table 4).

Association with Mortality

All four assessment tools, before and after adjustment, were associated with mortality, with both unadjusted physician and nurse impressions being the best predictors (HR 3.84 [95% CI: 2.03-7.28] and HR 3.83 [95% CI: 1.97-7.42], respectively). Of the components of the modified Fried criteria, unadjusted weakness and slowness were the two best predictors of mortality (HR 3.72 [95% CI 1.84-7.52] and HR 2.76 [95% CI 1.44-5.28], respectively). Neither exhaustion, nor weight loss were significantly associated with mortality (HR 1.63 [95% CI: 0.86-3.09] and HR 1.39 [95% CI: 0.65-2.94], respectively).

Association with Composite Outcomes

Of objective frailty assessment tools, the modified Fried criteria was associated with greater than a two-fold increase in risk of poor outcome (HR 2.41 [95% CI: 1.42-4.11], adjusted HR 2.46 [95% CI 1.36-4.45]). The SPPB was also associated with poor outcome (HR 1.83 [95%

CI 1.10-3.07]); however, statistical significance was lost after adjusting for age, sex, and common comorbidities (HR 1.87 [95% CI 0.99-3.53]).

Both subjective assessment tools were associated with greater than a two-fold increase in risk of poor outcome before and after adjustment (Physician HR 2.50 [95% CI: 1.48-4.20], nurse HR 2.50 [95% CI: 1.41-4.42]).

Of the modified Fried Criteria components, weakness and weight loss were both associated with an increased risk of poor outcome (HR 2.18 [95% CI: 1.30-3.66] and HR 2.15 [95% CI 1.14-4.05]), whereas exhaustion, slowness, and low-activity level were not.

DISCUSSION

In our prospective cohort study of more than 100 individuals on home dialysis, frailty as defined by subjective or objective criteria was associated with a more than two-fold risk of death and technique failure. These findings were independent of age and comorbidity, suggesting that the operational definitions of frailty capture non-traditional risk factors for adverse outcomes in this population. Together, these findings suggest that frailty, as defined in our study, can be easily operationalized at bedside, and could be used to identify high risk home dialysis patients for additional support and intervention.

To our knowledge, this is the first paper to investigate association between frailty and outcomes including technique failure in patients on home dialysis. Previous studies have examined the association between frailty and mortality in in center dialysis patients. One such study, by Alfaadhel et al, looked at the association between physician ascertained Clinical Frailty Scale (CFS), essentially a Likert scale with each of the nine points being defined with respect to physical function, and mortality in 390 incident hemodialysis patients.[24] In an adjusted Cox proportional hazards model, their study found that each point increase in CFS was associated with an increase in risk of mortality (HR 1.22 [95% CI: 1.04-1.43]). These findings are consistent with our findings for the predictive power of physician impression of frailty, but also suggested a "frailty dose response." A similar study of 146 prevalent hemodialysis patients in Baltimore, MD, USA, found that frailty as defined by Fried et al was associated with a 2.60-fold higher risk of death (HR 2.60 [95% CI: 1.04-6.49) which was similar to the risk we found in home dialysis patients.[25] Our study findings are consistent with these previous studies, but demonstrate a novel association in the home dialysis population. In addition, we were also able to measure multiple definitions of frailty and determine their agreement. While our findings corroborate frailty as determined by physician impression and Fried criteria is associated with mortality, we found the agreement between the two to be only moderate (κ=0.46) suggesting that the two assessment tools are capturing different patients. As such, both subjective and objective assessment tools may have a place in clinical practice.

A study by Salter et al sought to evaluate the agreement between objective and subjective measures of frailty in in-center hemodialysis patients.[26] In contrast to our own study finding moderate agreement between subjective and objective assessment tools to be moderate (κ=0.36-0.46), this study found agreement to be poor (κ=0.24-0.27). Furthermore, agreement between subjective measures (physician and nurse practitioner) was also poor (κ=0.21), whereas our study showed agreement between subjective measures (physician and nurse) to be good (κ=0.63). It is worth noting, however, that the Salter study used 3-categories (frail, intermediately frail, and not frail) whereas ours only used two. As well, they used a weighted kappa. These two difference may account for the different results. Nevertheless, our findings still support the notion that objective and subjective measures of frailty classify different patients as frail. That being said, our

study demonstrates that both objective and subjective measures of frailty are associated with outcomes of technique failure and mortality in home dialysis patients.

There are clinical, research and health policy findings from our work. From a research perspective, we believe that our single center study needs replication and testing using Fried criteria, particularly its subcomponents as well as physician using either a Likert or CFS should be done in other large home dialysis programs. If our findings are independently validated, risk factors such as muscle strength and weight loss should be targeted as potentially modifiable through exercise and nutrition programs. From a clinical perspective, physicians should consider incorporating frailty screen as part of the Home dialysis assessments, and offer early assisted support to frail patients as they are likely to benefit from such supports to lower risk of technique failure and mortality. From a policy perspective, identifying the number of frail patients in the home dialysis program may help policy makers provide resources for exercise clinics, nutrition support and assisted home dialysis.

Strengths of this study include its prospective nature, the use of multiple frailty measures and evaluating their association with important clinical outcomes of technique failure and death. The most notable limitation, however, is that the study evaluated prevalent patients on home dialysis which introduces a survivor bias. Furthermore, the study only looked at those in a single center. Ideally, a larger multi-center study of incident patients would be done in the future. As well, although we identified risk factors that are associated with mortality and technique failure, such as weakness and weight loss, it remains to be seen if modification of these factors is associated with improved outcomes.

Conclusions

Objective and subjective measures of frailty were associated with near to greater than a two-fold increase in risk of technique failure or death, independent of age, sex, and the comorbidity index described above. Frailty testing is easy to do and most components can be assessed at the bedside. External validation followed by clinical implementation of the frailty assessment as part of the home dialysis evaluation should be considered as the next steps.

Table 1: Baseline characteristics of the study cohort by Modified Fried Frailty status

Variable	Not Frail	Frail	P-Value
N	78	31	
Modality			
Peritoneal Dialysis	24	9	
Home Hemodialysis	54	22	
Demographics			
Age (years)	51 (43, 64)	64 (51, 73)	<0.001
Race (% Caucasian)	60.3%	74.2%	0.191
Sex (% female)	33.3%	32.3%	0.178
Systolic BP (mmHg)	127 (114, 146)	127 (113, 149)	0.77
Diastolic BP (mmHg)	81.5 (69, 91)	75 (68, 81)	<0.001
Weight (kg)	76.7 (64.6, 89)	80.9 (63.7, 96)	0.058
Labs			
Hemoglobin (g/L)	110 (100, 118)	106 (95, 118)	0.002
HbA1c (%)	5.9 (5.4, 7.9)	7.66 (6.3, 8.64)	<0.001
eGFR (mL/min/1.73m^2)	7 (5, 9)	7 (6, 9)	0.22
Creatinine (μmol/L)	689 (556, 939)	625 (531, 783)	0.002
Serum Albumin (g/L)	34 (31, 37)	31 (26, 33)	<0.001
Serum Phosphorus (mmol/L)	1.65 (1.31, 2.01)	1.61 (1.28, 1.9)	0.35
Comorbidities (%)			
Previous MI	10.3%	9.7%	0.27
Diabetes (Type I or II)	33.3%	71.0%	<0.001
Peripheral Vascular Disease	14.1%	22.6%	0.122
Cirrhosis	1.2%	0.0%	0.72
Gastrointestinal Disease	16.7%	12.9%	0.21
COPD	3.9%	3.2%	0.42
Hypertension	78.2%	90.3%	0.078
Dyslipidemia	51.3%	41.9%	0.115
Pulmonary Hypertension	5.1%	0.0%	0.26
Arthritis	29.5%	41.9%	0.082
Congestive Heart Failure	10.3%	6.5%	0.26
Depression	9.0%	19.4%	0.083
Visual/Hearing Impairment	33.3%	61.3%	0.005
Neurologic Disease	6.4%	25.8%	0.007
Malignancy	11.5%	19.4%	0.132

Table 2: Agreement between frailty assessment tools

Frailty Scale	Prevalence %	Agreement (Cohen's Kappa)			
		Modified Fried	SPPB	Physician Impression	Nurse Impression
Modified Fried	27.7%		0.55	0.46	0.38
SPPB	42.2%	0.55		0.36	0.39
Physician Impression	25.7%	0.46	0.36		0.63
Nurse Impression	18.3%	0.38	0.39	0.63	

Table 3: Cox proportional hazards models for the outcomes of technique failure and mortality

	Outcome								
	Technique Failure			Death			Composite		
Frailty Model	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Fried	1.93	0.99-3.75	0.053	3.51	1.85-6.66	<0.001	2.41	1.42-4.11	0.001
Adjusted Fried	2.50	1.18-5.29	0.017	2.49	1.24-4.96	0.010	2.46	1.36-4.45	0.003
SPPB	1.09	0.57-2.06	0.81	3.59	1.81-7.13	<0.001	1.83	1.1-3.07	0.020
Adjusted SPPB	1.26	0.57-2.77	0.57	2.36	1.04-5.33	0.04	1.87	0.99-3.53	0.054
Physician Impression	2.01	1.04-3.88	0.036	3.84	2.03-7.28	<0.001	2.50	1.48-4.2	<0.001
Adjusted Physician Impression	2.46	1.15-5.25	0.020	2.88	1.4-5.93	0.004	2.53	1.39-4.6	0.002
Nurse Impression	1.33	0.58-3.03	0.51	3.83	1.97-7.42	<0.001	2.50	1.41-4.42	0.002
Adjusted Nurse Impression	1.47	0.62-3.48	0.39	2.59	1.25-5.36	0.011	2.42	1.31-4.47	0.005

Table 4: Cox proportional hazards models of Modified Fried components and study outcomes

	Outcome								
	Technique Failure			Death			Composite		
Fried Component	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Slowness	0.96	0.45-2.01	0.91	2.76	1.44-5.28	0.002	1.64	0.96-2.82	0.072
Adjusted Slowness	0.96	0.43-2.17	0.93	1.85	0.92-3.74	0.08	1.49	0.82-2.69	0.189
Weakness	1.67	0.89-3.14	0.109	3.72	1.84-7.52	<0.001	2.18	1.3-3.66	0.003
Adjusted Weakness	2.19	1.1-4.35	0.025	2.99	1.46-6.12	0.003	2.33	1.35-4.05	0.003
Exhaustion	1.03	0.54-1.96	0.94	1.63	0.86-3.09	0.13	1.32	0.79-2.2	0.30
Adjusted Exhaustion	0.98	0.51-1.91	0.96	1.33	0.7-2.53	0.39	1.24	0.73-2.1	0.43
Low Activity	1.50	0.77-2.9	0.23	2.21	1.09-4.47	0.028	1.42	0.84-2.42	0.194
Adjusted Low Activity	1.68	0.84-3.34	0.140	1.85	0.9-3.79	0.093	1.38	0.8-2.37	0.25
Weight Loss	2.64	1.21-5.78	0.016	1.39	0.65-2.94	0.39	2.15	1.14-4.05	0.018
Adjusted Weight Loss	3.72	1.53-9.04	0.004	1.27	0.56-2.89	0.57	2.53	1.22-5.23	0.013

References

1. United States Renal Data System. 2016 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016. The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in now way should be seen as an official policy or interpretation of the U.S. government.
2. Merkus MP, Jager KJ, Dekker FW, Boeschoten EW, Stevens P, Krediet RT. Quality of life in patients on chronic dialysis: Self-assessment 3 months after the start of treatment. American Journal of Kidney Diseases 1997;29:584-92.
3. Lee CP, Chertow GM, Zenios SA. An Empiric Estimate of the Value of Life: Updating the Renal Dialysis Cost-Effectiveness Standard. Value in Health 2009;12:80-7.
4. Weinhandl ED, Liu J, Gilbertson DT, Arneson TJ, Collins AJ. Survival in Daily Home Hemodialysis and Matched Thrice-Weekly In-Center Hemodialysis Patients. Journal of the American Society of Nephrology 2012;23:895-904.
5. Fenton SSA, Schaubel DE, Desmeules M, et al. Hemodialysis versus peritoneal dialysis: A comparison of adjusted mortality rates. American Journal of Kidney Diseases 1997;30:334-42.
6. Lee H, Manns B, Taub K, et al. Cost analysis of ongoing care of patients with end-stage renal disease: The impact of dialysis modality and dialysis access. American Journal of Kidney Diseases 2002;40:611-22.
7. Oreopoulos DG, Thodis E, Passadakis P, Vargemezis V. Home dialysis as a first option: a new paradigm. International urology and nephrology 2009;41:595.
8. Kolesnyk I, Dekker FW, Boeschoten EW, Krediet RT. TIME-DEPENDENT REASONS FOR PERITONEAL DIALYSIS TECHNIQUE FAILURE AND MORTALITY. Peritoneal Dialysis International 2010;30:170-7.
9. Seshasai RK, Mitra N, Chaknos CM, et al. Factors Associated With Discontinuation of Home Hemodialysis. Am J Kidney Dis 2016;67:629-37.
10. Jager KJ, Merkus MP, Dekker FW, et al. Mortality and technique failure in patients starting chronic peritoneal dialysis: Results of the Netherlands Cooperative Study on the Adequacy of Dialysis. Kidney International 1999;55:1476-85.
11. Woodrow G, Turney JH, Brownjohn AM. Technique failure in peritoneal dialysis and its impact on patient survival. Peritoneal Dialysis International 1997;17:360-4.
12. Fried LP, Tangen CM, Walston J, et al. Frailty in Older AdultsEvidence for a Phenotype. The Journals of Gerontology: Series A 2001;56:M146-M57.
13. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care. The Journals of Gerontology: Series A 2004;59:M255-M63.
14. Guralnik JM, Simonsick EM, Ferrucci L, et al. A Short Physical Performance Battery Assessing Lower Extremity Function: Association With Self-Reported Disability and Prediction of Mortality and Nursing Home Admission. Journal of Gerontology 1994;49:M85-M94.
15. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ : Canadian Medical Association Journal 2005;173:489-95.

16. Roshanravan B, Khatri M, Robinson-Cohen C, et al. A Prospective Study of Frailty in Nephrology-Referred Patients With CKD. American Journal of Kidney Diseases 2012;60:912-21.
17. Wilhelm-Leen ER, Hall YN, Tamura MK, Chertow GM. Frailty and Chronic Kidney Disease: The Third National Health and Nutrition Evaluation Survey. The American Journal of Medicine 2009;122:664-71.e2.
18. Walker SR, Brar R, Eng F, et al. Frailty and physical function in chronic kidney disease: the CanFIT study. Canadian Journal of Kidney Health and Disease 2015;2:32.
19. Johansen KL, Chertow GM, Jin C, Kutner NG. Significance of Frailty among Dialysis Patients. Journal of the American Society of Nephrology 2007;18:2960-7.
20. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. Journal of Clinical Epidemiology 1992;45:613-9.
21. Hude Q, Vijaya S, Patricia H, et al. Coding Algorithms for Defining Comorbidities in ICD-9-CM and ICD-10 Administrative Data. Medical Care 2005;43:1130-9.
22. Washburn RA, Smith KW, Jette AM, Janney CA. The physical activity scale for the elderly (PASE): Development and evaluation. Journal of Clinical Epidemiology 1993;46:153-62.
23. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. Applied psychological measurement 1977;1:385-401.
24. Alfaadhel TA, Soroka SD, Kiberd BA, Landry D, Moorhouse P, Tennankore KK. Frailty and Mortality in Dialysis: Evaluation of a Clinical Frailty Scale. Clinical Journal of the American Society of Nephrology 2015.
25. McAdams-DeMarco MA, Law A, Salter ML, et al. Frailty as a Novel Predictor of Mortality and Hospitalization in Hemodialysis Patients of All Ages. Journal of the American Geriatrics Society 2013;61:896-901.
26. Salter ML, Gupta N, Massie AB, et al. Perceived frailty and measured frailty among adults undergoing hemodialysis: a cross-sectional analysis. BMC Geriatrics 2015;15:52.