Provider Perception of Frailty Is Associated with Dialysis Decision Making in Patients with Advanced CKD

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www.cjasn.org Vol 16 April, 2021

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Frailty is common in CKD patients

- Older patients with CKD often have a considerable comorbid burden
- Also have high rates of functional decline[1]
- Prevalence of frailty in CKD is also substantial
  - Reported prevalence as high as 73% in older dialysis patients [3]
  - Increased levels of frailty are associated with lower levels of kidney function[2]
  - Frailty is also associated with faster rates of eGFR decline[4]

1. Hall R et al. Breaking the cycle of functional decline in older dialysis patients. Semin Dial. 31(5):462-467, 2018.
2. Bao Y et al. Frailty, Dialysis Initiation, and Mortality in End-Stage Renal Disease. Arch Intern Med. 172(14):1071-7, 2012
3. Chowdhury R et al. Frailty and chronic kidney disease: A systematic review. Arch Gerontol Geriatr. 68:135-42,2017.
4. Guerville et al. Estimated glomerular filtration rate decline and incident frailty in older adults. CJASN 14:1597-1604, 2019

What is frailty?

- Multi-dimensional construct conceptionalised as the sum of alterations in physiologic systems that leads to increased vulnerability to adverse health outcomes[1]
- Frailty is a process theorized to be in part attributable to chronic inflammation[2]
  - Some studies in frail CKD patients have shown raised levels of pro inflammatory cytokines[3]

1. Fried LP et al. Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 59: 255–263, 2004
2. Delgado C. Frailty and CKD Chicken or the egg? CJASN 14:1554-1556, 2019
3. Shlipak et al. Elevations of inflammatory and procoagulant biomarkers in elderly people with renal insufficiency. Circulation, 107(1)87-92, 2003

There are many methods used to assess frailty

- There is a lack of consensus about how frailty should be measured
- Many different tools are used to assess frailty
  - Objective measures of physical performance
  - Questionnaires used to describe a frailty phenotype
  - Sum of objective deficits and laboratory tests used to determine a continuous frailty index[3]
  - Simple subjective measures such as an “eyeball” test of frailty[4]

1. Fried LP et al. Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 59: 255–263, 2004
2. Delgado C. Frailty and CKD Chicken or the egg? CJASN 14:1554-1556, 2019
3. Fried LP et al. Frailty in older adults: Evidence for a phenotype. JGerontol Abiol Sci Med Sci 56: M146–M156, 2001
4. Rockwood K et a. A global clinical measure of fitness and frailty in elderly people. CMAJ 173: 489–495, 2005

There is variability in the tools used to assess frailty in CKD

- A systematic review of 32 studies that reported frailty in CKD patients identified 20 different frailty instruments[1]
  - Majority used Fried criteria (72%) however variations in interpretation of the five characteristics
- Lack of a common language limits the generalisability and comparability of findings

1. Chowdhury R et al. Frailty and chronic kidney disease: A systematic review. Arch Gerontol Geriatr. 2017;68:135-42.

Frailty is associated with poor outcomes

- In the general population, most measures of frailty are associated with poor clinical outcomes[1]
- Studies in CKD patients show that frailty negatively affects survival[2] and hospitalisations[3]
- Frailty also impacts on both mental and physical quality of life[4]
- Few studies have examined the effect of frailty on the clinical trajectory of patient with advanced CKD
  - Impact of frailty on ESKD treatment decision making

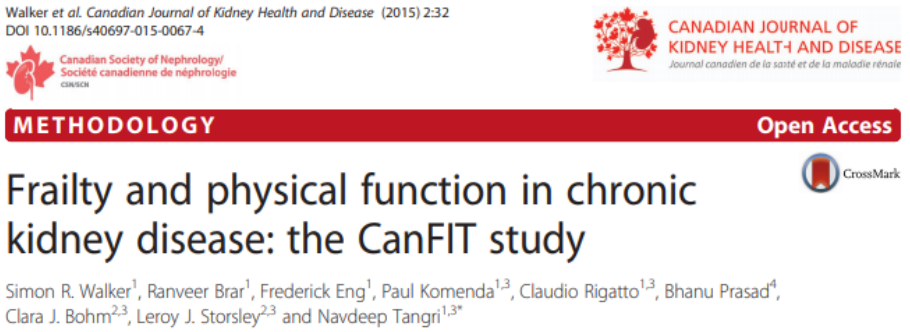
1. Fried LP et al. Frailty in older adults: Evidence for a phenotype. JGerontol Abiol Sci Med Sci 56: M146–M156, 2001
2.Pugh J et al. Frailty and comorbidity are independent predictors of outcome in patients referred for pre-dialysis education. Clin Kidney J 9: 324–329, 2016
3. Chowdhury R et al. Frailty and chronic kidney disease: A systematic review. Arch Gerontol Geriatr. 68:135-42, 2017.
4. Lee SJ et al. Influence of frailty on health-related quality of life in pre-dialysis patients with chronic kidney disease in Korea: a cross-sectional study. Health and Quality of life outcomes, 13:70-77, 2015.

Study design

- Prospective cohort study of patients with advanced CKD

- Measured frailty, physical function, comorbidities and clinical outcomes
- Examined the agreement between objective and subjective frailty measures and physical function
- Assessed the association between frailty, physical function and future dialysis decisions and mortality

CanFIT


Walker et al. Canadian Journal of Kidney Health and Disease (2015) 2:32
DOI 10.1186/s40697-015-0067-4
Canadian Society of Nephrology/ Société canadienne de néphrologie
CANADIAN JOURNAL OF KIDNEY HEALTH AND DISEASE
Journal canadien de la santé et de la maladie rénale
METHODOLOGY
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Frailty and physical function in chronic kidney disease: the CanFIT study

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- Canadian Frailty Observation and Interventions Trial
- Multi-centre prospective observational cohort study
- Aimed to recruit 600 pts
  - Annual follow up until death, opt out, loss to fu, study completion
- Patients followed for outcomes of mortality, morbidity and hospitalisation
- Patients excluded if unable to provide informed consent, unable to speak English, blind, history of dementia, or previous dialysis treatment

Data collection

- Comorbid conditions
  - At baseline by self report and medical record review
  - Comorbidity count constructed using commonly used indices
    - MI, CVA, DM, PVD, cirrhosis, GI disease, COPD, CCF, HT, PAH, arthritis, weight loss, depression, anxiety/panic attacks, asthma, visual and hearing impairments, malignancy, severe psychologic stress or acute medical issue
- Frailty assessment tools
  - Fried criteria used for objective assessment
  - Subjective physician and nurse ratings collected

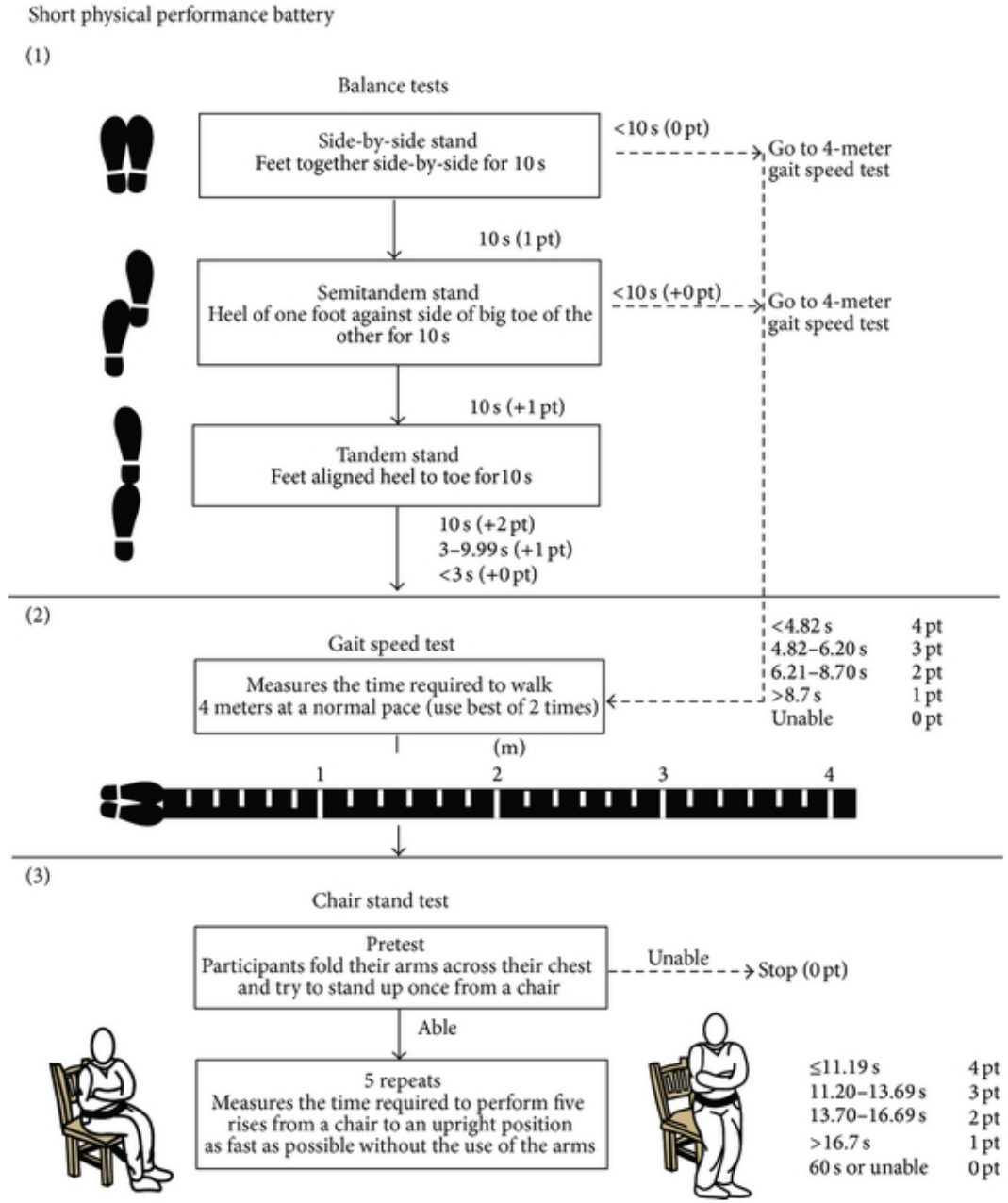
Fried criteria

Table 1. **Frailty phenotype model and Fried's criteria**

Frailty criteria	Indicators*
Shrinking**	Baseline >10lb of unintentional weight loss over the past year
Exhaustion	Self-reported exhaustion
Weakness	Maximal grip strength in kg using a hydraulic handheld dynamometer; lowest 20% stratified by gender and BMI quartiles
Slowness	Time in seconds to walk 15 feet at usual pace; slowest 20% stratified by gender and standing height
Low physical activity	Weighted score of kilocalories expended per week in physical activities that 'you have done in the past two weeks' ● Males <383kcal/week ● Females <270kcal/week
Frailty = presence of three or more of the five criteria	

BMI = Body mass index; * Measurements used in the Cardiovascular Health Study; ** Loss of muscle mass or weight loss.

Source: Adapted from Fried et al (2001).


Short physical performance battery
(1)
Balance tests
Side-by-side stand
Feet together side-by-side for 10 s
<10 s (0 pt)
Go to 4-meter gait speed test
10 s (1 pt)
Semitandem stand
Heel of one foot against side of big toe of the other for 10 s
<10 s (+0 pt)
Go to 4-meter gait speed test
10 s (+1 pt)
Tandem stand
Feet aligned heel to toe for10 s
10 s (+2 pt)
3–9.99 s (+1 pt)
<3 s (+0 pt)
(2)
Gait speed test
Measures the time required to walk 4 meters at a normal pace (use best of 2 times)
<4.82 s 4 pt
4.82–6.20 s 3 pt
6.21–8.70 s 2 pt
>8.7 s 1 pt
Unable 0 pt
(m)
1
2
3
4
(3)
Chair stand test
Pretest
Participants fold their arms across their chest and try to stand up once from a chair
Unable
Stop (0 pt)
Able
5 repeats
Measures the time required to perform five rises from a chair to an upright position as fast as possible without the use of the arms
≤11.19 s 4 pt
11.20–13.69 s 3 pt
13.70–16.69 s 2 pt
>16.7 s 1 pt
60 s or unable 0 pt

Outcomes

- Primary
  - Agreement between objective and subjective frailty measures and physical function
- Secondary
  - Association between above measures with choice of dialysis modality (in-centre HD versus home therapies (HD or PD) at dialysis initiation
  - Mortality
- Assessed at Jan 31, 2020

Statistical analysis

- Agreement between different frailty tools and physical function calculated using Cohen *k*
- Associations between frailty, physical function and secondary outcomes evaluated with logistic regression models and cox proportional hazards models
- Patients followed until Jan 31, 2020 or until outcome
- Each component of the Fried frailty criteria and physical function also evaluated separately as a predictor of the outcomes in unadjusted and adjusted models

Study flow diagram

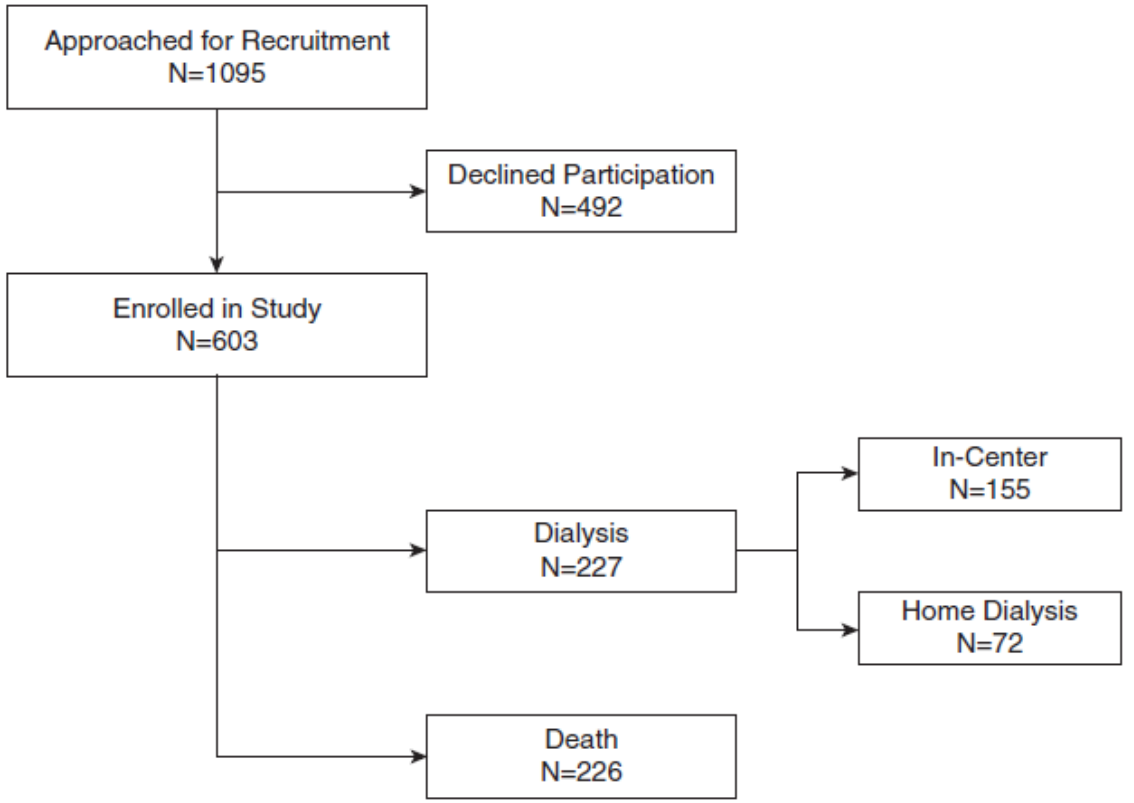


Figure 1. | Study flow diagram.

Table 1. Baseline characteristics by Fried frailty criteria of participants in the Canadian Frailty Observation and Interventions Trial

Variable	Not Frail	Frail
N	399	204
Demographics		
Age[a]	66 (54–73)	73 (65–82)
Sex (% women)[b]	144 (36)	103 (51)
Race (% White)[b]	326 (82)	163 (80)
Clinical measurements[a]		
Systolic BP, mm Hg	136 (124–149)	138 (123–153)
Diastolic BP, mm Hg	75 (67–83)	70 (63–80)
Weight, kg	86 (72–101)	81 (70–92)
Creatinine, mg/dl	3.05 (2.25–4.01)	3.06 (2.26–3.96)
eGFR, ml/min per 1.73 m^2	19 (13–25)	18 (13–24)
Hemoglobin, g/dl	11.6 (10.7–12.7)	11.1 (10.1–12.2)
Serum albumin, g/dl	3.6 (3.3–3.9)	3.5 (3.2–3.8)
Serum phosphate, mg/dl	4.1 (3.5–4.7)	4.3 (3.7–4.9)
Urine ACR, mg/g[c]	51 (7–173)	71 (9–237)
HbA1c, %[c]	6.2 (5.6–7.5)	6.3 (5.7–7.6)
Comorbidities[b]		
Previous MI (%)	80 (20)	43 (22)
Diabetes, type 1 or 2 (%)	209 (52)	135 (66)
Peripheral vascular disease (%)	31 (8)	44 (22)
Gastrointestinal disease (%)	71 (18)	47 (24)
Malignancy (%)	81 (20)	41 (20)
COPD (%)	22 (6)	24 (12)
Hypertension (%)	336 (84)	187 (92)
Arthritis (%)	138 (35)	108 (53)
Congestive heart failure (%)	32 (8)	35 (17)
Depression (%)	59 (15)	42 (21)
Visual/hearing impairment (%)	196 (49)	138 (68)
Neurologic disease (%)	36 (9)	53 (26)
Comorbidity index[a]	3 (2–4)	4 (3–5)
CKD stage at enrollment[b] **(% stage 5)**		
CKD stage	115 (28.8)	63 (30.9)
Median kidney failure risk,[c] **%**		
5-yr risk	21	21

ACR, albumin-to-creatinine ratio; HbA1c, hemoglobin A1c; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease.
[a]Continuous variables are reported as medians and interquartile ranges. Mann–Whitney *U* test was used to compare continuous variables.
[b]Categorical variables are reported as percentages and compared using chi-squared tests.
[c]Variables are reported in complete cases (urine ACR missing =27%, HbA1c missing =35%).

Prevalence of frailty depended on the assessment tool used

Table 2. Agreement between frailty and physical function assessments

Assessment Tool	Prevalence, %	Agreement, κ			
		Fried	Short Physical Performance Battery	Physician Impression	Nurse Impression
Fried	34		0.43	0.33	0.31
Short Physical Performance Battery	55	0.43		0.29	0.32
Physician impression	44	0.33	0.29		0.45
Nurse impression	36	0.31	0.32	0.45	

Table 3. Associations of frailty and physical function measures with dialysis choice and all-cause mortality

Model[a]	Death, $n=226$			Dialysis Choice: In Center = 155; Home = 72)[c]		
	N (%)	Unadjusted Hazard Ratio (95% Confidence Interval)	Adjusted[b] Hazard Ratio (95% Confidence Interval)	N (%)	Unadjusted Odds Ratio (95% Confidence Interval)	Adjusted[b] Odds Ratio (95% Confidence Interval)
Fried criteria						
Present	117 (52)	2.79 (2.14 to 3.64)	1.96 (1.47 to 2.61)	58 (37)	1.85 (0.97 to 3.49)	1.55 (0.77 to 3.13)
Not present	109 (48)	1 (reference)	1 (reference)	97 (63)	1 (reference)	1 (reference)
Physician impression						
Present	115 (51)	2.32 (1.78 to 3.04)	1.48 (1.11 to 1.98)	61 (39)	3.72 (1.79 to 7.72)	3.41 (1.56 to 7.44)
Not present	111 (49)	1 (reference)	1 (reference)	94 (61)	1 (reference)	1 (reference)
Nurse impression						
Present	104 (46)	2.27 (1.64 to 3.16)	1.52 (1.09 to 2.11)	71 (46)	4.05 (1.96 to 8.33)	3.87 (1.76 to 8.51)
Not present	122 (54)	1 (reference)	1 (reference)	84 (54)	1 (reference)	1 (reference)
Short Physical Performance Battery						
Present	165 (73)	2.87 (2.14 to 3.86)	1.96 (1.42 to 2.70)	85 (55)	2.12 (1.19 to 3.76)	1.86 (0.99 to 3.53)
Not present	61 (27)	1 (reference)	1 (reference)	70 (45)	1 (reference)	1 (reference)

[a]All exposures in models were categorical.
[b]Models adjusted for age, sex, and comorbidity count.
[c]Analysis was performed in participants who initiated dialysis for kidney failure. Odds ratio refers to odds of choosing in-center dialysis.

Supplemental Table 4: Associations of Fried components with dialysis choice and all-cause mortality

	Death (N=226)			Dialysis choice (In-Center = 155, Home = 72)[c,d]		
Fried Component[a]	N (%)	Unadjusted HR (95% CI)	Adjusted[b] HR (95% CI)	N (%)	Unadjusted OR (95% CI)	Adjusted[b] OR (95% CI)
Slowness						
Present	114 (50)	2.94 (2.26-3.82)	1.99 (1.49-2.65)	48 (31)	1.86 (0.95-3.65)	1.48 (0.70-3.15)
Not present	112 (50)	1 (reference)	1 (reference)	107 (69)	1 (reference)	1 (reference)
Weakness						
Present	145 (64)	2.32 (1.77-3.05)	1.61 (1.20-2.18)	76 (49)	1.81 (1.01-3.22)	1.52 (0.82-2.83)
Not present	81 (36)	1 (reference)	1 (reference)	79 (51)	1 (reference)	1 (reference)
Exhaustion						
Present	96 (42)	1.33 (1.02-1.74)	1.42 (1.08-1.85)	72 (46)	1.45 (0.82-2.56)	1.39 (0.77-2.50)
Not present	130 (58)	1 (reference)	1 (reference)	83 (54)	1 (reference)	1 (reference)
Low Physical Activity						
Present	155 (69)	1.57 (1.18-2.07)	1.22 (0.91-1.62)	108 (70)	2.31 (1.29-4.11)	2.15 (1.19-3.86)
Not present	71 (31)	1 (reference)	1 (reference)	47 (30)	1 (reference)	1 (reference)
Weight Loss						
Present	41 (18)	1.40 (0.98-2.01)	1.33 (0.91-1.93)	27 (17)	1.59 (0.68-3.68)	1.52 (0.82-2.83)
Not present	185 (82)	1 (reference)	1 (reference)	128 (83)	1 (reference)	1 (reference)

Abbreviations: HR, Hazard Ratio; OR, Odds Ratio; CI, Confidence Interval
[a]All exposures in models were categorical
[b]Models adjusted for age, sex, and comorbidity count.
[c]Analysis was performed in participants who initiated dialysis for kidney failure.
[d]OR refers to odds of choosing in-center dialysis

Supplemental Table 5: Association of Short Physical Performance Battery components with dialysis choice and all-cause mortality

	Death (226)	Dialysis Choice (In-Center = 155, Home = 72)[c,d]
Model[a]		
	HR (95% CI)	**OR (95% CI)**
Chair Stand Unadjusted	3.61 (2.35-5.57)	2.85 (1.55-5.27)
Chair Stand Adjusted*	2.52 (1.61-3.94)	2.61 (1.35-5.09)
Gait Unadjusted	2.79 (2.15-3.62)	2.09 (1.08-4.03)
Gait Adjusted*	1.82 (1.36-2.43)	1.71 (0.82-3.59)
Balance Unadjusted	2.47 (1.89-3.23)	1.47 (0.81-2.68)
Balance Adjusted*	1.85 (1.39-2.46)	1.31 (0.69-2.48)

Abbreviations: HR, Hazard Ratio; OR, Odds Ratio; CI, Confidence Interval

[a]All exposures were modelled as continuous variables with a range of 0-4 according to SPPB cut-offs(21).

[b]Models adjusted for age, sex, and comorbidity count.

[c]Analysis was performed in participants who initiated dialysis for kidney failure.

[d]OR refers to odds of choosing facility based dialysis

Discussion

- Prevalence of frailty in this cohort of advanced CKD patients varied widely depending on the frailty assessment used

- Different frailty and physical function tools did not identify the same individuals as being frail or having poor physical function

- Subjective measures of frailty were more strongly associated with treatment decisions
- Whereas objective frailty and poor physical function were more associated with mortality

- These findings emphasise that although frailty and poor physical function are common in CKD patients, the choice of the tool is important in determining prognostic value in the advanced CKD population

- This is the largest study to examine agreement between subjective and objective measures of frailty in CKD patients and it found little agreement
  - Another study by Salter et al did cross sectional analysis of agreement btw physician/nurses/patient perceived frailty and also reported poor agreement (K=0.24-0.27)[1]

1. Salter ML et al. Perceived frailty and measured frailty among adults undergoing hemodialysis: A cross-sectional analysis. BMC Geriatr 15: 52, 2015

- This study reported on the novel relationship between frailty and dialysis modality
- This study showed that physicians/nurses were more likely to recommend in centre HD to patients perceived as frail versus those diagnosed as frail using Fried or SPPB based criteria
- Discordance is concerning as provider perception had poor agreement with objective measures of frailty/physical function and was not as strongly associated with mortality
- Suggests that clinical opinion alone may be an insensitive guide for dialysis modality choice

- Suggests that objective measures of frailty should be included when giving advice on treatment
- In the UK, an electronic frailty index (eFI) is generated for every community-dweller aged over 75 years using data from their GP Health Checks[1]
  - This is now mandated in the UK National Institute of Clinical Excellence (NICE) Clinical Practice Guidelines[2]
  - Used to target individuals for intervention
  - Health resource planning

1. Clegg A et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. Age and Ageing. 2016;45(3):353-60.
2. Excellence NIfHaC. Multimorbidity: clinical assessment and management. 2016.

- Measures of lower limb extremity physical function (eg.chair stand test) had strong association with death and modality selection and have the potential to be performed bedside
- Future studies should examine this concept and whether incorporation of an objective frailty measure and/or physical function test should be incorporated into a dialysis decision support tool

Strengths and limitations

- Strengths
  - Study design: prospective, multicentre and collection of broad baseline variables in addition to frailty and physical function measures
  - Advanced CKD (mean eGFR 20) population
  - Longitudinal desing
- Limitations
  - Single baseline frailty measurement and examined association to downstream events
  - No data on choice of supportive non dialysis care so unable to assess its impact on modality and mortality
  - No assessment of social factors such as caregiver support, education level, SE status

Relation between different frailty measures and physical function and their association with dialysis modality choice (home based vs facility based) and all-cause mortality in patients with advanced CKD

CJASN
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PROSPECTIVE

Canadian Frailty Observation and Interventions Trial (CanFIT)

Advanced CKD

Demographics
Comorbidities
Laboratory results

Frailty Assessment Tools
Objective
Subjective
Physical Function

n = 603

Frailty Assessment Tool	Prevalence of Frailty	Outcomes
Fried Frailty Criteria *Objective*	**34%**	**2-fold** higher risk of all-cause mortality
Short Physical Performance Battery *Physical function*	**55%**	
Physician Impression *Subjective*	**44%**	**3 to 4x** more likely to choose facility based dialysis
Nurse Impression *Subjective*	**36%**	

1455 days — **227** Kidney Failure Dialysis — **226** died

Conclusion Objective measures (Frailty and SPPB) were more strongly associated with mortality, and subjective measures of frailty were more strongly associated with dialysis modality choice.

Ranveer S. Brar, Reid H. Whitlock, Paul V.J Komenda, et al. ***Provider Perception of Frailty Is Associated with Dialysis Decision Making in Patients with Advanced CKD***. CJASN doi: 10.2215/CJN.12480720. **Visual Abstract by Edgar Lerma, MD, FASN**