## FRAILTY in dialysis patients Relevance and pitfalls

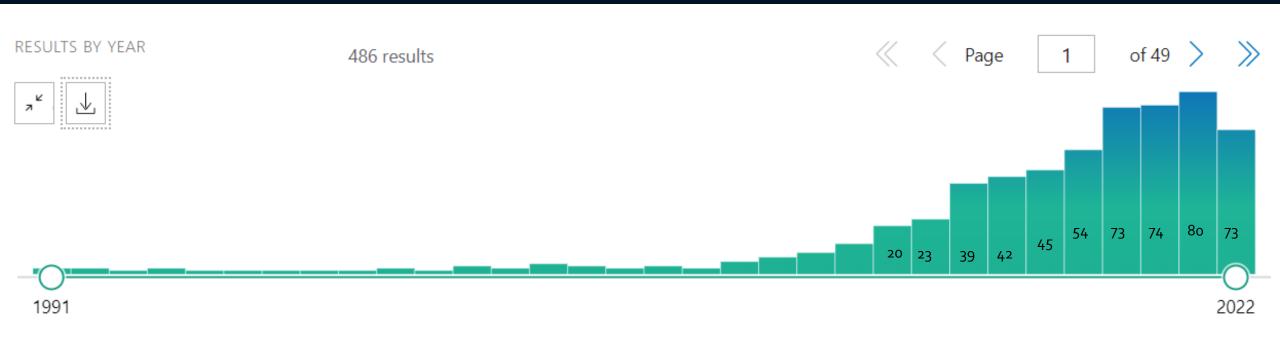


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Category	Disclosure Information
Employer	Nothing to disclose.
Ownership Interest	Nothing to disclose.
Consultancy	IDS; Nephrolytix; Alentis Therapeutics; ARK Bioscience;
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Speakers Bureau	Nothing to disclose.
Other Interests or Relationships	Nothing to disclose.



#### Chronic Kidney Disease

• Role of the kidney:

Metabolite waste excretion (drug excretion)

Control of solutes (ions), acid/base balance and fluids

Blood pressure control

Endocrine function



#### End stage renal disease (ESRD)

- Hypertension
- Accumulation of uremic toxins ("uremia")
- Accumulation of fluids (edema, pulmonary congestion)
- Hyperkaliemia and acidosis
- Anemia, hypocalcemia, vitamin D deficit, hyperparathyroidism (renal osteodystrophy)

#### Renal Replacement therapy

- Hemodialysis
- Peritoneal dialysis
- Renal transplantation

#### Renal Replacement therapy

- Hemodialysis: chronic inflammation, oxidative stress
- Peritoneal dialysis
- Renal transplantation



Sweden Norway

UK, Wales Spain, Cantabria

Austria

France Spain, Galicia

Romania

All countries

Spain, Aragon

Spain, Castile-La Mancha

Spain, Basque country

Spain, Castile and León

Spain, Valencian region

Spain, Canary Islands

Belgium, Dutch-speaking

Belgium, French-speaking

Spain, Extremadura

Spain, Andalusia

Spain, Navarre

Spain, Murcia

Spain, Asturias

Spain, Community of Madrid

the Netherlands UK, England

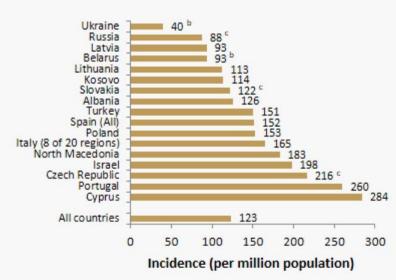
# Unadjusted incidence renal registries providing individual patient data | Spain, La Rioja | Spain, La Rioja | Switzerland | UK, Scotland | UK, Northern Ireland | 108 | 108 | 108 | 108 | 108 | 109 | 104 | 109 | 108 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 | 109 |

## Incident patients accepted for RRT in 2019 at day 1

by country

#### Unadjusted incidence

renal registries providing aggregated data



a patients younger than 20 years of age are not included; b patients younger than 18 years of age are not included; ada includes patients receiving dialysis only

189 a

191

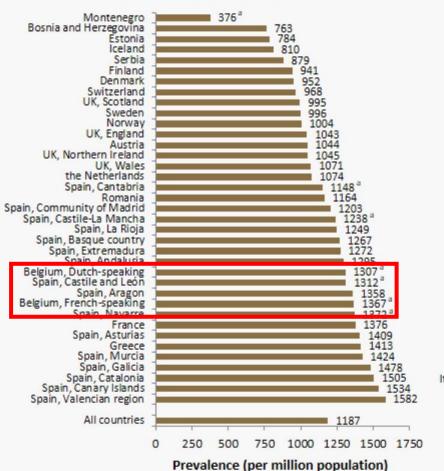
150

Incidence (per million population)



#### Unadjusted prevalence

renal registries providing individual patient data

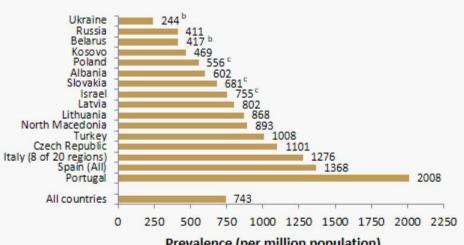


#### **Prevalent patients** on RRT in 2019

by country

#### Unadjusted prevalence

renal registries providing aggregated data



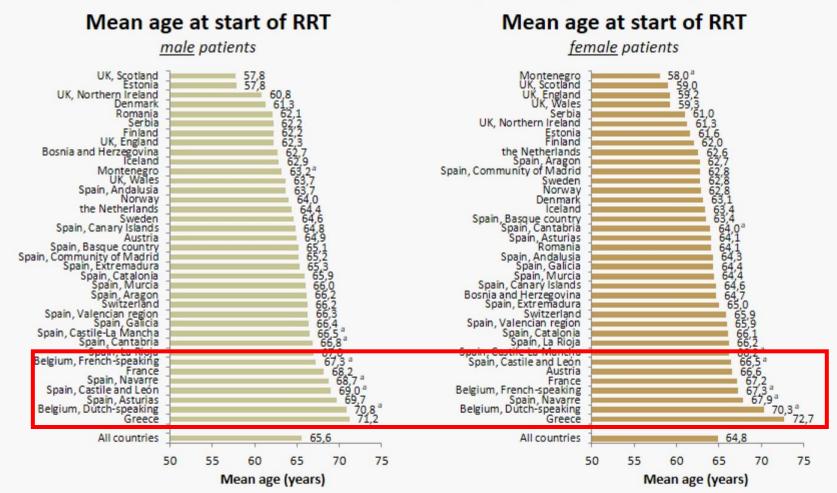
Prevalence (per million population)

a patients younger than 20 years of age are not included; b patients younger than 18 years of age are not included; data includes patients receiving dialysis only



## Incident patients accepted for RRT in 2019, at day 1

registries providing individual patient data only

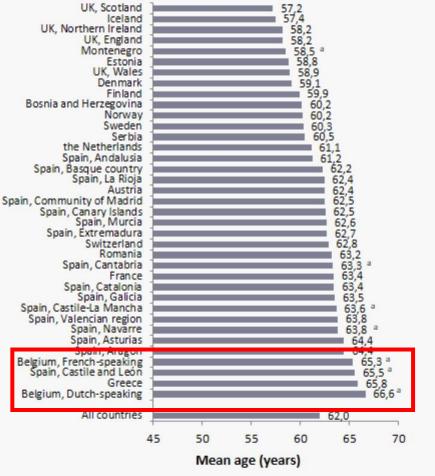


<sup>&</sup>lt;sup>a</sup> patients younger than 20 years of age are not included;



#### Mean age on 31 December 2019

renal registries providing individual patient data

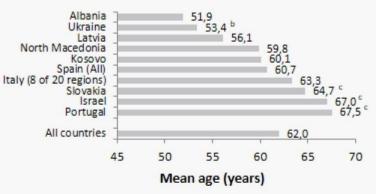


## Prevalent patients on RRT in 2019

mean age

#### Mean age on 31 December 2019

renal registries providing aggregated data

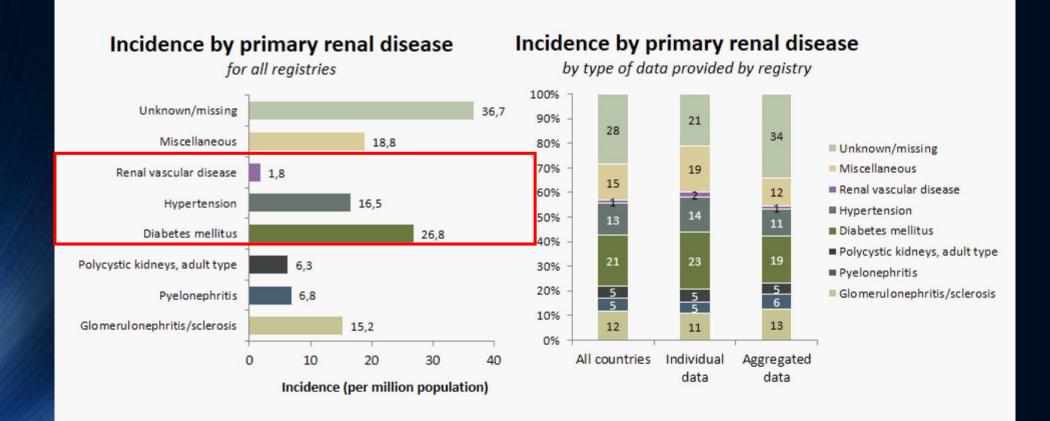


a patients younger than 20 years of age are not included; b patients younger than 18 years of age are not included; ada includes patients receiving dialysis only



## Incident patients accepted for RRT in 2019, at day 1

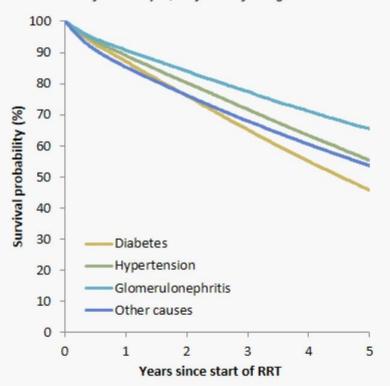
by primary renal disease





#### Adjusted patient survival by primary renal disease Incident RRT patients

#### from day 1, adjusted for age and sex



## Survival probability cohort 2010-2014

by primary renal disease

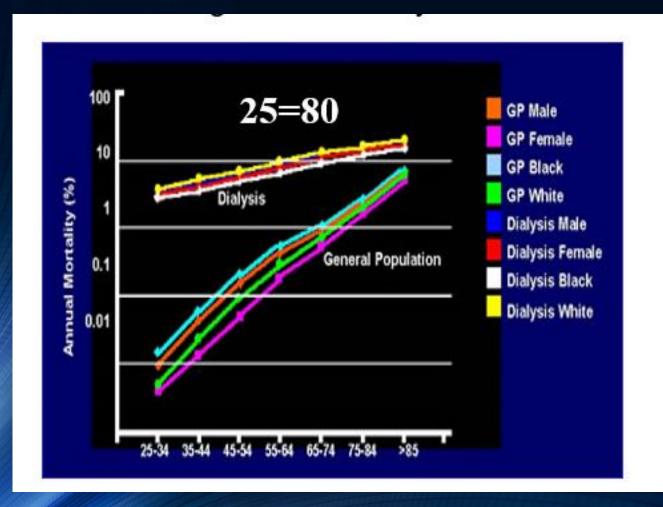


Unadjusted 5-year survival: 42,3% for dialysis 86,6% if graft from deceased donors 94,4% if graft from living kidney donors

Survival probabilities were adjusted for fixed values for age (67 years), sex (63% men), and the primary renal disease distribution (24% diabetes mellitus, 19% hypertension / renal vascular disease, 11% glomerulonephritis and 46% other primary renal diseases).

Cox regression model was used to calculate survival probabilities.

#### Cardiovascular mortality



Foley RN. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis 1998 Nov;32(5 Suppl 3):S112-S119.

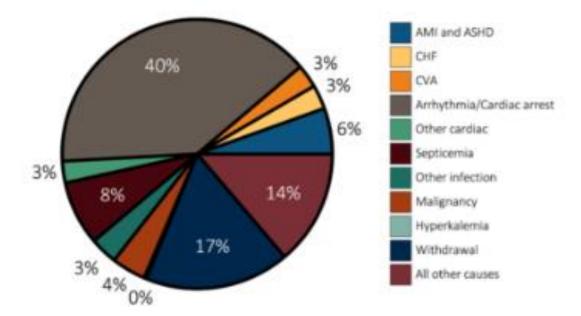


Figure 2. Causes of Death in ESRD Patients (USRDS 2017)

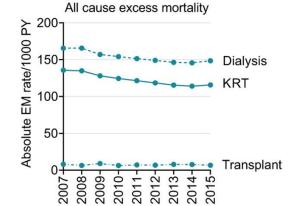
#### Data from the ERA-EDTA Registry were examined for trends in excess mortality in European adults on kidney replacement therapy.

Does improvement in KRT survival only reflect better survival in the general population?

- ► Excess mortality (EM): mortality in KRT patients minus expected mortality in the matched general population
- ▶ Data from 280,075 incident adult KRT patients from 12 European countries



Cause of death	Relative EM risk per 5 year (95%CI)				
Cause of death	Dialysis	Transplant			
All-cause	0.86 (0.85 - 0.86)	1.16 (1.07 - 1.26)			
Atheromatous CVD	0.72 (0.70 - 0.74)	1.29 (0.97 - 1.73)			
Non-atheromatous CVD	0.90 (0.88 - 0.92)	1.00 (0.80 - 1.23)			
Infections	0.90 (0.87 - 0.92)	0.99 (0.86 - 1.14)			
Malignancies	0.95 (0.90 - 1.00)	2.51 (1.35-4.68)			



#### **CONCLUSION:**

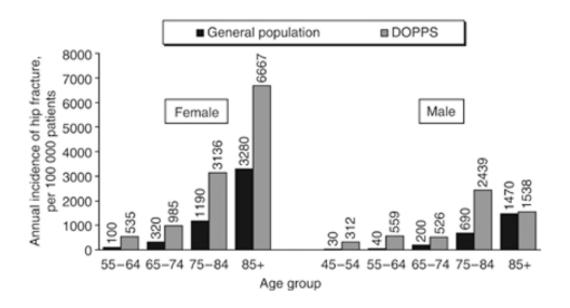
Survival on dialysis has improved more than in the general population, especially for atheromatous CVD. In transplant recipients, the EM risk increased, still the EM rate was low.



Boenink, 2020

FFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

#### Comorbidities



Kidney Int. 2014 January; 85(1): 166-173. doi:10.1038/ki.2013.279.

#### High rates of death and hospitalization follow bone fracture among hemodialysis patients

Francesca Tentori, MD<sup>1,2</sup>, Keith McCullough, MS<sup>1</sup>, Ryan D. Kilpatrick, PhD<sup>3</sup>, Brian D. Bradbury, DSc<sup>3,4</sup>, Bruce M. Robinson, MD<sup>1,5</sup>, Peter G. Kerr, MD<sup>6</sup>, and Ronald L. Pisoni, PhD<sup>1</sup>

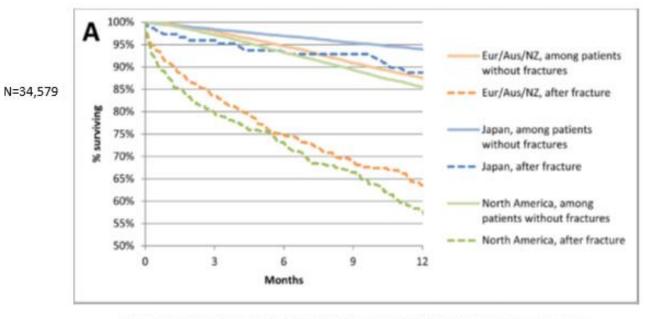


Figure 5A & 5B. Time to death and hospitalization among DOPPS participants who experienced and those who did not experience a fracture requiring hospitalization, by DOPPS region Panel A: Unadjusted survival (time to death) by DOPPS region.

Jadoul M, Kidney Int ,2006, p1358

#### So, hemodialysis patients

- They are old
- Accumulation of uremic toxins, chronic inflammation, acidosis
- Anorexia and difficulties in diet => protein energy wasting syndrome
- They have (a lot of) comorbidities (diabetes, vascular diseases, bone disease)
- Mortality is high

• A high prevalence of frailty would not be a big surprise!

#### Definition of Frailty

« Frailty is a <u>biologic</u> syndrome of <u>decreased</u> <u>reserve</u> and <u>resistance</u> to stressors, resulting from <u>cumulative</u> declines across multiple physiologic systems, and causing <u>vulnerability</u> to adverse outcomes »

#### FRAILTY according to FRIED, >65 y

#### **5 CRITERIA**

Scoring

0 criteria: robust

1-2 criteria: pre-frailty

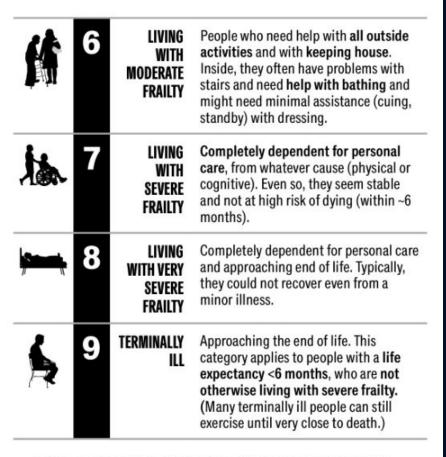
≥ 3 criteria: frailty

Easy and inexpensive Objective and subjective Functional tests

Criteria	Threshold
Shrinking: Unintentional weight loss (self reported)	4.5 kg or 5% in the past year
Weakness: Hand Grip Strength  Men  BMI ≤ 24  BMI 24.1-26  BMI 26.1-28  BMI > 28  Women  BMI ≤ 23  BMI ≥ 3.1-26  BMI 26.1-29	≤ 29 kg ≤ 30 kg ≤ 30 kg ≤ 32 kg ≤ 17 kg ≤ 17.3 kg ≤ 18 kg
Poor endurance and energy: Self reported exhaustion	two statements are read.  (a) I felt that everything I did was an effort  (b) I could not get going.  Then "How often in the last week did you feel this way?" rarely or none of the time=o, some or a little of the time (1−2 days)=1, moderate amount of the time (3−4 days),=2, most of the time=3.  Subjects answering "2" or "3" to either of these questions are categorized as frail
Slowness: Walking speed on 4,5 m  Men  Height ≤ 173 cm  Height > 173 cm  Women  Height ≤ 159 cm  Height > 159 cm	≥ 7 seconds ≥ 6 seconds ≥ 7 seconds ≥ 6 seconds
Level of activity (kcal/week) (Minnesota Leisure Time Activity questionnaire) Men Women	< 383 Kcal/week < 270 Kcal/week

#### **CLINICAL FRAILTY SCALE**

*	1	VERY FIT	People who are robust, active, energetic and motivated. They tend to exercise regularly and are among the fittest for their age.
•	2	FIT	People who have <b>no active disease symptoms</b> but are less fit than category 1. Often, they exercise or are very <b>active occasionally</b> , e.g., seasonally.
Ť	3	MANAGING Well	People whose medical problems are well controlled, even if occasionally symptomatic, but often are not regularly active beyond routine walking.
•	4	LIVING WITH Very Mild Frailty	Previously "vulnerable," this category marks early transition from complete independence. While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up" and/or being tired during the day.
	5	LIVING WITH MILD Frailty	People who often have more evident slowing, and need help with high order instrumental activities of daily living (finances, transportation, heavy housework). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, medications and begins to restrict light housework.



#### SCORING FRAILTY IN PEOPLE WITH DEMENTIA

The degree of frailty generally corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In moderate dementia, recent memory is very impaired, even though they seemingly can remember their past life events well.

They can do personal care with prompting.

In severe dementia, they cannot do personal care without help.

In very severe dementia they are often bedfast. Many are virtually mute.



Clinical Frailty Scale ©2005-2020 Rockwood, Version 2.0 (EN). All rights reserved. For permission: www.geriatricmedicineresearch.ca Rockwood K et al. A global clinical measure of fitness

and frailty in elderly people. CMAJ 2005;173:489-495.

#### FRAILTY IN DIALYSIS PATIENTS

CLINICAL EPIDEMIOLOGY

www.jasn.org

#### Significance of Frailty among Dialysis Patients

Kirsten L. Johansen,\*<sup>†‡</sup> Glenn M. Chertow,<sup>†‡</sup> Chengshi Jin,<sup>‡</sup> and Nancy G. Kutner<sup>§</sup>

\*Nephrology Section, San Francisco VA Medical Center, †Division of Nephrology, University of California, San Francisco, and †Department of Epidemiology and Biostatistics, University of California, San Francisco, California; and §Department of Rehabilitation Medicine, Emory University, Atlanta, Georgia

J Am Soc Nephrol 18: 2960-2967, 2007.

Dialysis Morbidity and Mortality Study (DMMS) Wave 2, 1996-1997: n=2275 Incident dialysis representative of US dialysis population PD over-represented One-year follow-up (death and hospitalization)

Table 1. Baseline characteristics by availability of frailty criteria

Variable	Complete Data $(n = 2275)$
Age (yr; mean ± SD)	58.2 ± 15.5
Gender (% male)	53.4
Race (%)	
white	65.4
black	26.5
Asian	2.3
other	5.8
Serum albumin (mg/dl; mean ± SD) <sup>b</sup>	$3.5 \pm 0.6$
BMI (kg/m²; mean ± SD)	$25.8 \pm 5.8$
Peritoneal dialysis (%)	48.1
Comorbidity (%)	
diabetes	47.6
CAD	31.4
cerebrovascular disease	8.7
peripheral vascular disease	15.3
cancer	8.4
Current smoker (%)	13.9
Married (%)	56.4
Employed (%)	13.8
High school graduate (%)	69.8
Medicaid (%)	26.8
<sup>a</sup> BMI body mass index: CAD coronary artery disease	

<sup>&</sup>lt;sup>a</sup>BMI, body mass index; CAD, coronary artery disease.

Table 2. Proportion of patients overall and by age meeting individual and collective criteria for frailty

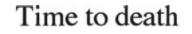
Patients	n	Frail
Overall	2275	67.7
Age (yr)		
<40	306	44.4
40 to 50	352	61.1
50 to 60	440	66.4
60 to 70	570	74.2
70 to 80	475	78.1
>80	132	78.8

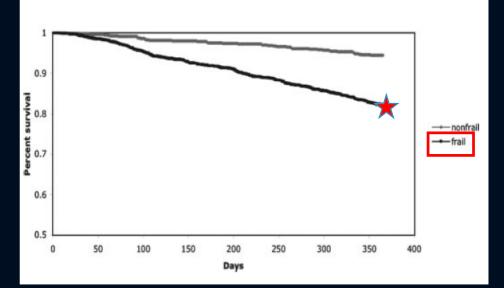
<sup>&</sup>lt;sup>b</sup>To convert mg/dl to g/L, multiply by 10.

Table 3	<b>3.</b> Pr	edictors	of	frailty <sup>a</sup>
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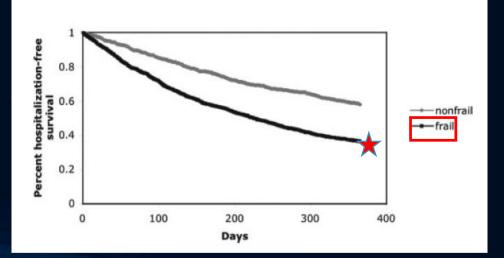
Variable	OR	95% CI
Age	1.02	1.01 to 1.03
Female gender	1.55	1.27 to 1.88
Race		
white	1.0 (referent)	
black	0.90	0.72 to 1.13
Asian	0.56	0.30 to 1.05
other	1.01	0.26 to 3.92
BMI (kg/m²)		
<19	1.41	0.93 to 2.13
19 to <25	1.0 (referent)	
25 to <30	0.98	0.78 to 1.22
≥30	1.00	0.77 to 1.30
Serum albumin concentration (g/dl)		
<3.2	1.89	1.43 to 2.49
3.2 to <3.5	1.32	1.00 to 1.76
3.5 to <3.9	1.06	0.84 to 1.35
≥3.9	1.0 (referent)	
Dialysis modality (PD)	0.80	0.65 to 0.97
Comorbidity		
diabetes	1.35	1.10 to 1.65
CAD	1.17	0.92 to 1.48
PAOD	1.19	0.88 to 1.60
CVA	1.55	1.05 to 2.29
cancer	1.39	0.95 to 2.04

<sup>&</sup>lt;sup>a</sup>CVA, cerebrovascular accident; PAOD, peripheral arterial occlusive disease; PD, peritoneal dialysis.





#### Time to death or first hospitalization



**Table 4.** Multivariable analysis of the association of frailty with 1-yr mortality

with 1-yi filortailty	
Variable	HR (95% CI)
Frailty	2.24 (1.60 to 3.15)
Age	1.03 (1.02 to 1.04)
Female gender	1.09 (0.86 to 1.38)
Race	
white	1.0 (referent)
black	1.01 (0.75 to 1.36)
Asian	0.91 (0.40 to 2.06)
other	0.84 (0.12 to 6.02)
Hispanic	1.20 (0.82 to 1.78)
BMI (kg/m²)	
<19	1.11 (0.78 to 1.58)
19 to <25	1.0 (referent)
25 to <30	0.62 (0.46 to 0.82)
≥30	0.57 (0.40 to 0.81)
Serum albumin concentration (g/dl) <sup>a</sup>	
<3.2	1.83 (1.30 to 2.59)
3.2 to <3.5	1.09 (0.74 to 1.59)
3.5 to <3.9	1.04 (0.73 to 1.49)
≥	1.0 (referent)
Dialysis modality (PD)	1.03 (0.81 to 1.31)
Comorbidity	
diabetes	1.10 (0.86 to 1.41)
CAD	1.36 (1.07 to 1.73)
peripheral vascular disease	1.55 (1.19 to 2.00)
CVA	1.13 (0.81 to 1.56)
cancer	1.26 (0.90 to 1.76)
Employment status	0.47 (0.25 to 0.87)
Marital status	0.86 (0.68 to 1.09)
Smoking	1.25 (0.88 to 1.77)
<sup>a</sup> To convert mg/dl to g/L, multiply by 10.	

Components of Frailty	CHS N=5888, >65 years	WHI Woods et al	USRDS DMMS Wave 2	
Slowness/ weakness	Slowness: Slowest quintile on a 15-ft walk test, stratified by gender and height Weakness: Weakest quintile in grip strength measured by handheld dynamometer, stratified by gender and BMI quartiles	Rand-36 PF <75. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf Lifting or carrying groceries Climbing several flights of stairs Climbing one flight of stairs Bending, kneeling, or stooping Walking more than a mile Walking several blocks Walking one block Bathing or dressing yourself	=2points	Re Co Qı
Poor endurance/ exhaustion	Based on two questions from the CES-D Depression Scale: a. I felt that everything I did was an effort. b. I could not get going. How often in the last week did you feel this way? 0 = rarely or none of the time (<1 d) 1 = some or a little of the time (1 to 2 d) 2 = a moderate amount of the time (3 to 4 d) 3 = most of the time. Individuals answering 2 or 3 to either of these questions were categorized as meeting the exhaustion criterion.	Rand-36 Vitality <55 How much of the time during the last 30 d Did you feel wom out? Did you feel tired?  Did you have a lot of energy? Did you feel full of pep?	Rand-36 Vitality <55	
Physical inactivity	Based on the short version of the Minnesota Leisure Time Activity questionnaire. The lowest quintile of activity stratified by gender was considered inactive.	Detailed physical activity questionnaire assessing frequency and duration of walking and mild, moderate, and strenuous activities. Kcal of weekly energy expenditure was calculated, and those in the lowest quartile were scored positive for inactivity.	How often do you exercise (do physical activity during your leisure time)? Daily or almost daily 4 to 5 times a week 2 to 3 times a week About once a week Less than once a week Almost never or never Individuals answering "almost never or never" were classified as inactive.	
Unintentional weight loss	"In the last year, have you lost more than 10 pounds unintentionally (i.e., not due to dieting or exercise)?" Individuals who responded "yes" met the weight loss criterion.	No measure was available at baseline. At follow-up, measured weight loss or subject-reported weight loss was used.	Undemourished or cachectic (malnourished), as assessed by data abstractor	

Retrospective analysis Cohort relatively young Questionnaires (QoL, SF36)="self-reported" frailty



Hemodialysis International 2013; 17:41-49

#### A closer look at frailty in ESRD: Getting the measure right

Patricia PAINTER, 1 Michael KUSKOWSKI2

<sup>1</sup>Department of Physical Therapy, University of Utah, Salt Lake City, Utah, USA; <sup>2</sup> Geriatric Research Education and Clinical Center (GRECC), Minneapolis VA Medical Center, Minneapolis, Minnesota, USA

#### N=188 prevalent home dialysis

Frailty measured: 33,7%

Frailty self-reported: 78,2%

Salter et al. BMC Geriatrics (2015) 15:52 DOI 10.1186/s12877-015-0051-y



#### **RESEARCH ARTICLE**

**Open Access** 

Perceived frailty and measured frailty among adults undergoing hemodialysis: a cross-sectional analysis

Megan L Salter<sup>1,2,3\*†</sup>, Natasha Gupta<sup>3†</sup>, Allan B Massie<sup>1,3</sup>, Mara A McAdams-DeMarco<sup>1,3</sup>, Andrew H Law<sup>1,3</sup>, Reside Lorie Jacob<sup>5</sup>, Luis F Gimenez<sup>6</sup>, Bernard G Jaar<sup>1,4,6,7</sup>, Jeremy D Walston<sup>2,8,9</sup> and Dorry L Segev<sup>1,3\*</sup>

#### N=146 prevalent hemodialysis

Very poor concordance between measured frailty, self-reported frailty ( $\kappa = 0.07$ ) and frailty estimated by nurses ( $\kappa = 0.27$ ) or nephrologists ( $\kappa = 0.24$ ) (especially in the elderly)

**AJKD** 

Am J Kidney Dis. 2014 Oct;64(4):600-7.

**Original Investigation** 

Comparison of Self-report—Based and Physical Performance—Based Frailty Definitions Among Patients Receiving Maintenance Hemodialysis

Kirsten L. Johansen, MD, <sup>1,2,3,4</sup> Lorien S. Dalrymple, MD, MPH, <sup>1,5</sup> Cynthia Delgado, MD, <sup>1,2,3</sup> George A. Kaysen, MD, PhD, <sup>1,5</sup> John Kornak, PhD, <sup>1,4</sup> Barbara Grimes, PhD, <sup>1,4</sup> and Glenn M. Chertow, MD, MPH<sup>1,6</sup>

**ACTIVE/ADIPOSE study** 

N=731 prevalent hemodialysis

Frailty measured: 29%

Frailty self-reported: 53%

Only 3% of frail when measured are not self-reported frail

ORIGINAL RESEARCH

J Ren Nutr. 2013 Sep;23(5):356-62.

### Association of Frailty With Body Composition Among Patients on Hemodialysis

Cynthia Delgado, MD, Julie W. Doyle, MS, and Kirsten L. Johansen, MD

N=80 prevalent hemodialysis

Frailty measured: 59%

Frailty self-reported: 63%

Frail by both: 55%



Contents lists available at ScienceDirect

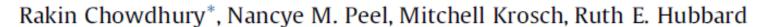
#### Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger



Review

Frailty and chronic kidney disease: A systematic review



Centre for Research in Geriatric Medicine, The University of Queensland, Brisbane, Queensland, Australia



Table 2 Dialysis Patients.

Study	Study Characteristics	Study Population	Primary Outcome	Study Design	EAI	Prailty Assessment	Prevalence of frailty
Bao et al. (2012)	N= 1576 2female = 45 Mean	Comprehensive Dialys is Study HD% = 89.3	Frailty prevalence dialysis cohort. GFR at dialysis initiation and its relationship with frailty	Secondary analysis of an established	1.62	Modified Pried	73%
McAdams- DeMarco et al. (2013a)	age= 59.6 years N= 146 3female = 47 Mean age= 61 years (+/- 13.6)	USA Single haemodialysis centre HDX = 100 USA	Prevalence of frailty and outcome assessment	cohort Primary prospective study	1,67	Ried	41.8%
Delgado et al. (2013)	N=80 %female = 37 Mean age= 55 years (+/- 13)	Nandrolone and Exercise Study HD% = 100 USA	A comparison of function based frailty assessment and performance based tests. Body composition and frailty status.	Secondary analysis of an established cohort	1,19	Modified Pried: Performance based and Function Based Criteria	59% (performance based)
Painter and Kuskowski (2013)	N= 188 % Temale = 56 Mean age = 54.4 (+/- 16) years	Renal Exercise Demonstration Study HD% = 100 USA	Analysis of two methods of applying the Fried phenotype for frailty: questionnaire based physical function vs measurement	Secondary analysis of an established cohort	1,81	Fried	24% (measured physical function)
Johansen et al. (2007)	N= 2275 % Temale = 47 Mean age= 58 years (+/- 16)	Dialys is Morbidity/ Mortality Study HD%=519 USA	Investigation of the prevalence and predictors of frailty amongst dialysis patients and correlation with adverse health outcomes. Prospective cohort study	Secondary analysis of an established cohort	1.71	Modified Ried	68%
Kutner et al. (2014)	N= 742 3female = 40.6 Mean age= 57 years (+/- 14.1)	ACTIVE/ADIPOSE Study HD% = 100 USA	Frailty and its association with ADI. difficulties	Secondary analysis of an established cohort	1.71	Pried	14%
McAdams- DeMarco et al. (2013b)	N= 95 3female = 46	Single dialysis centre HD% = 100 USA	Association of frailty with risk of falls in patients with ESKD	Primary prospective study	1.71	Pried	46.3%
Orlandi and Gesualdo (2014)	N=60 %female = 30 Mean age= 71 years (+/- 6.9)	Single dialysis centre HD% = 100 Brazil	Assessment of frailty in elderly patients undergoing dialysis	Primary prospective study	1.10	Edmonton Prailty scale	38%
Salter, Gupta, & Massie (2015)	N= 146 3female = 46.6 Mean age= 61 years	Single dialysis centre HD% = 100 USA	Comparison between measured frailty and clinician perceived fraility	Primary prospective study	1.71	Fried	41.7%
Chao, Hsu, & Chang (2015)	N= 46 % female = 53 Mean age = 67.3 (+/- 11.9) years	Single dialysis centre HD% = 100 Taiwan	Exploring frailty in a rural dialysis centre in Taipei and comparison between different self-reported measures of Brailty.	Primary prospective study	1,52	FRAIL scale amongst others.	19,6%
Alfaadhel et al. (2015)		Single dialysis centre HDx = 100 USA	Assessed whether the dinicians perception of frailty correlated with outcomes in a population of patients on dialysis.	Primary prospective study	1,81	Clinical frailty scale	26%
lyasere, Brown, & Johansson (2016)	N= 251 %female = 40.7 Median age = 76 (70-81 years IQR)	HD%=48,6	Comparison of frailty and quality of life between patients on haemodi alysis with those on peritoneal dialysis. Cross sectional analysis	Primary prospective study	1.57	Clinical frailty scale	47.4% (overall
McAdams- DeMarco, Tan, & Salter (2015)	N= 324 Xfemale = 43.5 Mean age= 54.8 years (+/- 13.3)	Predictors of arrhythmic and cardiovas cular risk in ESKD Study. HDX = 100 USA	Investigated the relationship between frailty and cognition both at base line and at one year of follow up. Prospective cohort study		1.76	Pried	34%
Diost, Kalf, Vogtlander, & van Munster (2016)	N= 95 %female = 43 Mean age= 65.2 years (+/- 12)	Single dialysis centre HDX = 44 Netherlands	Comparison between prevalence of frailty assessed using the frailty index versus the Fried Frailty Phenotype. Cross sectional analysis	Primary prospective Study	1,76	Fried and Frailty Index	36,8% (measured using H)

### N=14 14 to 73%



Check for updates



#### CLINICAL STUDY

**3** OPEN ACCESS

#### Frailty in hemodialysis and prediction of poor short-term outcome: mortality, hospitalization and visits to hospital emergency services

Cesar Garcia-Canton<sup>a,b</sup>, Ana Rodenas<sup>a</sup>, Celia Lopez-Aperador<sup>b</sup>, Yaiza Rivero<sup>a</sup>, Gloria Anton<sup>c</sup>, Tania Monzon<sup>c</sup>, Noa Diaz<sup>a</sup>, Nicanor Vega<sup>d</sup>, Juan F. Loro<sup>b</sup>, Angelo Santana<sup>e</sup> and Noemi Esparza<sup>a</sup>

<sup>a</sup>Department of Nephrology, Insular University Hospital of Gran Canaria, Gran Canaria, Spain; <sup>b</sup>Faculty of Health Sciences, University of Las Palmas de Gran Canaria, Gran Canaria, Spain; <sup>c</sup>Avericum Dialysis Center, Gran Canaria, Spain; <sup>d</sup>Department of Nephrology, University Hospital of Gran Canaria Dr Negrin, Las Palmas, Spain; <sup>e</sup>Faculty of Mathematics, University of Las Palmas de Gran Canaria, Gran Canaria, Spain

- Spain
- N=277, prevalent dialysis patients, median age 65 years





**CLINICAL STUDY** 

**3** OPEN ACCESS

Frailty in hemodialysis and prediction of poor short-term outcome: al emergency services

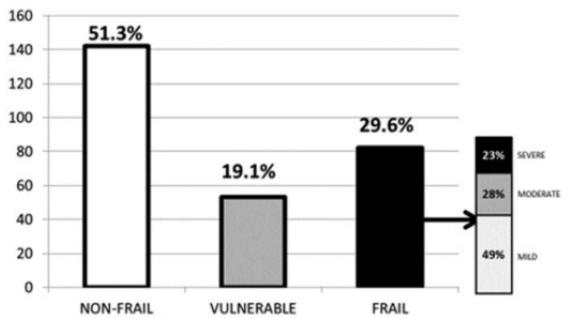


Figure 1. Prevalence of frailty among our hemodialysis population according to the Edmonton Frail Scale (EFS)

#### Questionnaire

Treatment (Gy/Fr, Chemotherapy): Previous radiotherapy/chemotherapy

Demographics: Patient chart no: Yaiza Rivero<sup>a</sup> Noemi Espa

Canaria, Spain;

ran Canaria, Spa

Marital status:

Single / Married / long term partnership / Widowed / Divorced or separated

Cancer diagnosis:

Stage:

Check for updates

Self employed Employed full-time Care for grandchildren regularly

2 POINTS

#### **Edmonton Frail Scale**

lathematics, Uni FRAILTY DOMAIN Please imagine that this pre-Cognition drawn circle is a clock. I would (clock test) like you to place the numbers in the correct positions then place the hands to indicate a time of 'ten after eleven'.

In the past year, how many times have you been admitted to a hospital? General health status >2 In general, how would you describe your health? With how many of the following 5-8 Functional activities do you require help? (Meal preparation, shopping. independence transportation, telephone, housekeeping, laundry, nousekeeping, laundry, managing money, taking medications) When you need help, can you count on someone who is willing Always Sometimes Never Social support count on someone who is willing and able to meet your needs?
Do you use five or more different prescription medications on a regular basis?
At times, do you forget to take your prescription medications?
Have you recently lost weight such that your clothing has become lower? Medication use Yes Yes become looser?

Do you often feel sad or depressed? Mood Do you have a problem with Continence losing control of urine when you Functional 11-20 sec chair with your back and arms resting. Then, when I say 'GO', please stand up and walk at a safe and comfortable pace to the Patient unwilling Requires mark on the floor (approx. 3m away), return to the chair and sit TOTAL







#### **CLINICAL STUDY**

**3** OPEN ACCESS



Frailty in hemodialysis and prediction of poor short-term outcome: al emergency services

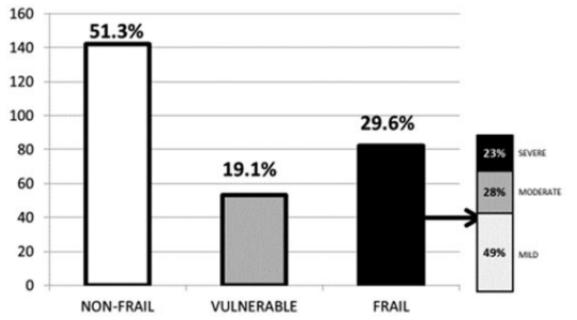
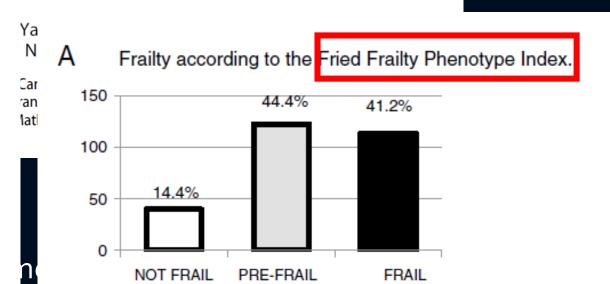


Figure 1. Prevalence of frailty among our hemodialysis population according to the Edmonton Frail Scale (EFS)







Clinical Kidney Journal, 2022, vol. 15, no. 1, 145–152

doi: 10.1093/ckj/sfab137 Advance Access Publication Date: 16 July 2021 Original Article

#### ORIGINAL ARTICLE

## Correlations, agreement and utility of frailty instruments in prevalent haemodialysis patients: baseline cohort data from the FITNESS study

Benjamin M. Anderson • <sup>1,2</sup>, Muhammad Qasim<sup>1,3</sup>, Gonzalo Correa<sup>4</sup>, Felicity Evison<sup>5</sup>, Suzy Gallier<sup>5,6</sup>, Charles J. Ferro • <sup>1,7</sup>, Thomas A. Jackson • <sup>2,8</sup> and Adnan Sharif • <sup>1,3</sup>

- 485 hemodialysis patients in UK, median age 63 years
- Frailty phenotype, Frailty index, Edmonton Clinical Frailty, Clinical Frailty Score

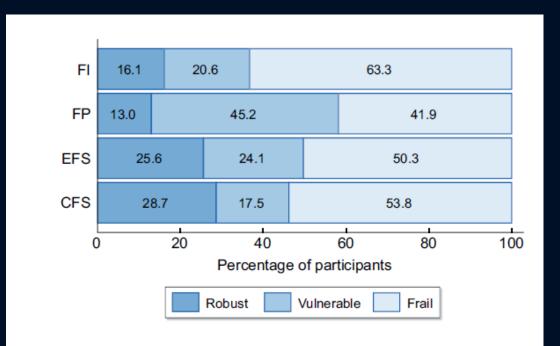


FIGURE 2: Percentage of participants classified as robust, vulnerable or frail by different frailty instruments: FI, FP, EFS and CFS.

The intraclass correlation coefficient across the scores was 0.628 (95% CI 0.585–0.669) = Weak agreement

#### Prevalence of frailty in CHU Liège n = 108 (unpublished data)

n=108	Hommes : n=71	Femmes : n=37	56%
% de Fragiles	38/71 (53%)	23/37 (62%)	
Fragiles à 3 critères / 5	20%	16%	
Fragiles à 4 critères / 5	23%	35%	
Fragiles à 5 critères / 5	11%	11%	
Fragiles de moins de 50 ans	5/31 (		
Fragiles de plus de 50 ans	58/77		
Fragiles de plus de 60 ans	51/64		
Fragiles de plus de 70 ans	29/34		

**Tableau 3 :** Prévalence de patients fragiles, ventilation sur la base du genre, de l'âge et du score obtenu selon les critères de Fried.

66% of men

Age: 64 [28] y

BMI: 24 [7] kg/m<sup>2</sup>

## Even considering the "true" Fried criteria, the methodology is important







Clinical Kidney Journal, 2018, vol. 11, no. 4, 555-558

doi: 10.1093/ckj/sfx139 Advance Access Publication Date: 19 December 2017 Original Article

ORIGINAL ARTICLE

Hand grip strength measurement in haemodialysis patients: before or after the session?

Pierre Delanaye<sup>1,\*</sup>, Kevin Quinonez<sup>1,\*</sup>, Fanny Buckinx<sup>2</sup>, Jean-Marie Krzesinski<sup>1</sup> and Olivier Bruyère<sup>2</sup>

<sup>1</sup>Department of Nephrology, Dialysis, Hypertension, University of Liège (ULg CHU), Liège, Belgium and <sup>2</sup>Department of Public Health, Epidemiology and Health Economics, University of Liège (ULg CHU), Liège, Belgium

- 101 prevalent hemodialysis patients, 64% men, median age (66 years)
- HGS measured before and after dialysis session
- Measurements repeated three times with an interval of 5 s between measurements and the higher value used for analysis

Table 2. HGS results in the global population and according to gender

	Median (P25; P75) HGS (kg) before dialysis	Median (P25; P75) HGS (kg) after dialysis	P-values (before and after dialysis) (Wilcoxon test)	Percentage decrease in HGS
All $(n = 101)$	28 (20–38.5)	,	<0.0001	41
Men $(n = 65)$	34 (24–40.5)		<0.0001	42
Women $(n = 36)$	20 (14–26)		<0.0001	39

HGS results are significantly lower in women. All results after dialysis were significantly lower than results before dialysis. P25 and P75 for 25th and 75th percentiles, respectively.

Table 3. Absolute and relative differences between HGS according to gender and baseline HGS (low versus normal)

	Absolute median (P25; P75) difference of HGS before and after dialysis	Relative median (P25; P75) difference of HGS before and after dialysis (%)	P-values (before and after dialysis) (Wilcoxon test)
All $(n = 101)$ Men $(n = 65)$ Women $(n = 36)$ Low baseline results $(n = 41)$	-4 (0; -6) -4 (0; -6) -2 (1; -4) -2 (0; -4)	-11 (0; -20) -9 (0; -17) -14 (-3; -23) -14 (0; -22)	<0.0001 <0.0001 <0.0001 <0.0001
Normal baseline results (n = 60)	-4 (0; -6)	-10 (0; -17)	<0.0001

P25 and P75 for 25th and 75th percentiles, respectively.

# Frailty as a risk factor (independent of age) for mortality, hospitalisation, falls is confirmed

# Frailty, Dialysis Initiation, and Mortality in End-Stage Renal Disease

Yeran Bao, MD; Lorien Dalrymple, MD, MPH; Glenn M. Chertow, MD, MPH; George A. Kaysen, MD, PhD; Kirsten L. Johansen, MD

Arch Intern Med. 2012;172(14):1071-1077.

Clin J Am Soc Nephrol 10: 2181-2189, 2015.

Amanda Vinson (D), Kenneth West (, Arsh Jain 3,

# Frailty and Cognitive Function in Incident Hemodialysis Patients

Mara A. McAdams-DeMarco,\*† Jingwen Tan,\* Megan L. Salter,\*† Alden Gross,\* Lucy A. Meoni,†§ Bernard G. Jaar,\*<sup>§</sup> Wen-Hong Linda Kao,\*\* Rulan S. Parekh,<sup>§</sup>¶\*\* Dorry L. Segev,\*† and Stephen M. Sozio§

Frailty as a Novel Predictor of Mortality and Hospitalization in Individuals of All Ages Undergoing Hemodialysis

Mara A. McAdams-DeMarco, PhD,\*† Andrew Law, ScM,\*† Megan L. Salter, PhD,\*† Brian Boyarsky, BA,\* Luis Gimenez, MD,<sup>‡§¶</sup> Bernard G. Jaar, MD, MPH,<sup>†‡§¶</sup> Jeremy D. Walston, MD,\*\* and Dorry L. Segev, PhD, MD\*†

J Am Geriatr Soc 61:896–901, 2013.

#### The Prevalence, Association, and Clinical Outcomes of Frailty in Maintenance Dialysis Patients

So-Young Lee, MD, PhD,\* Dong Ho Yang, MD, PhD,\* Eunah Hwang, MD, PhD,†
Seock Hui Kang, MD, PhD,‡ Sun-Hee Park, MD, PhD,§ Tae Woo Kim, MD, PhD,¶
Duk Hyun Lee, MD, PhD,\*\* Kisoo Park, MD, PhD,†† and Jun Chul Kim, MD, PhD,‡‡

Journal of Renal Nutrition, Vol 27, No 2 (March), 2017: pp 106-112

McAdams-DeMarco et al. BMC Nephrology 2013, 14224
http://www.biomedcentral.com/1471-2369/14/224

RESEARCH ARTICLE

Open Access

Frailty and falls among adult nationts undergoing

Frailty and falls among adult patients undergoing chronic hemodialysis: a prospective cohort study

Mara A McAdams-DeMarco<sup>1,2</sup>, Sunitha Suresh<sup>3</sup>, Andrew Law<sup>1,2</sup>, Megan L Salter<sup>1,2</sup>, Luis F Gimenez<sup>4,5,6</sup>, Bernard G Jaar<sup>2,4,5,6</sup>, Jeremy D Walston<sup>7</sup> and Dorry L Segev<sup>1,2,8\*</sup>

Canadian Society of Rephrology Canadian Society of Rephrology



Clinical Interventions in Aging

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ORIGINAL RESEARCH

Frailty in Older Patients Undergoing Hemodialysis

and Its Association with All-Cause Mortality:

A Prospective Cohort Study

Yidan Guo<sup>1</sup>, Ru Tian<sup>1</sup>, Pengpeng Ye<sup>2</sup>, Yang Luo ® 1

Frailty and Mortality in Dialysis: Evaluation of a Clinical Frailty Scale

Talal A. Alfaadhel,\* Steven D. Soroka,\* Bryce A. Kiberd,\* David Landry,\* Paige Moorhouse,† and Karthik K. Tennankore\*

Clin J Am Soc Nephrol 10: 832-840, 2015.

Nephrol Dial Transplant (2016) 31: 2041–2048 doi: 10.1093/ndt/gfw074 Advance Access publication 21 April 2016

Factors influencing withdrawal from dialysis: a national registry study

# Comparison of the association between six different frailty scales and clinical events in patients on hemodialysis

Background



Frailty is highly prevalent in patients who require hemodialysis (HD) therapy and is associated with an increased risk of adverse health outcomes. Few studies have compared the relationship between various frailty scales and prognosis in patients undergoing HD therapy.

Methods	Two hemodialysis clinics in Japan (n = 315) 68 y
Frailty scales:	Combined assessment (objective + questionnaire)
Ö	Objective assessment  Questionnaire-based assessment
6	Medical staff impression assessment
Outcomes:	Hospitalization + Fracture

Results		Prevalence	Outcomes (incidence rate ratio)
<b>⇔</b> • <b>©</b>	Fried Frailty Phenotype Study of Osteoporotic Fractures Inde	24.1% 14.6%	1.62 (1.49-1.76) 1.42 (1.10-1.83)
Ö	Short Physical Performance Battery	29.2%	1.79 (1.11 – 2.88)
	Frail Screening Index FRAIL scale K between 0,24-0,58	33.7% 27.6%	1.38 (0.60–3.18) 1.30 (0.88–1.92)
6	Clinical Frailty Scale	17.8%	1.65 (1.04–2.61)

Conclusion

Objective assessments and medical staff impression assessment may be useful prognostic predictors for patients on HD. Questionnaire-based assessment should be carefully considered when used as a measurement of frailty.



# Comparison of the association between six different frailty scales and clinical events in patients on hemodialysis

Background



Frailty is highly prevalent in patients who require hemodialysis (HD) therapy and is associated with an increased risk of adverse health outcomes. Few studies have compared the relationship between various frailty scales and prognosis in patients undergoing HD therapy.

# Two hemodialysis clinics in Japan (n = 315) 68 y Frailty scales: Combined assessment (objective + questionnaire) Objective assessment Questionnaire-based assessment Medical staff impression assessment Outcomes:

Hospitalization

Results		Prevalence	Outcomes (incidence rate ratio)
M (E)	Fried Frailty Phenotype	24.1%	1.62 (1.49-1.76)
₩+1	Study of Osteoporotic Fractures Index	14.6%	1.42 (1.10–1.83)
Ö	Short Physical Performance Battery	29.2%	1.79 (1.11 – 2.88)
(E)X	Frail Screening Index	33.7%	1.38 (0.60-3.18)
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6	Clinical Frailty Scale	17.8%	1.65 (1.04–2.61)

Conclusion

Objective assessments and medical staff impression assessment may be useful prognostic predictors for patients on HD. Questionnaire-based assessment should be carefully considered when used as a measurement of frailty.





- In the definition (FRIED)
- Objective measurements (strict adherence to FRIED criteria) are probably better than self-reported
- Standardization of the measurement



# What about guidelines?





**National Kidney Foundation** 

## KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN CKD: 2020 UPDATE

T. Alp Ikizler, Jerrilynn D. Burrowes, Laura D. Byham-Gray, Katrina L. Campbell, Juan-Jesus Carrero, Winnie Chan, Denis Fouque, Allon N. Friedman, Sana Ghaddar, D. Jordi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple, Daniel Teta, Angela Yee-Moon Wang, and Lilian Cuppari

Nephrol Dial Transplant (2016) 31: ii1-ii66 doi: 10.1093/ndt/gfw356



#### Clinical Practice Guideline

Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR <45 mL/min/1.73 m<sup>2</sup>)

Ken Farrington, Adrian Covic, Fillipo Aucella, Naomi Clyne, Leen de Vos, Andrew Findlay, Denis Fouque, Tomasz Grodzicki, Osasuyi Iyasere, Kitty J. Jager, Hanneke Joosten, Juan Florencio Macias, Andrew Mooney, Dorothea Nitsch, Marijke Stryckers, Maarten Taal, James Tattersall, Dieneke Van Asselt, Nele Van den Noortgate, Ionut Nistor and Wim Van Biesen for the ERBP guideline development group

Q4a: What is the best alternative method to assess functional decline in older and/or frail patients with advanced CKD

- 4a.1 We recommend a simple score be used on a regular basis to assess functional status in older patients with CKD stage 3b–5d) with the intention to identify those who would benefit from a more in-depth geriatric assessment and rehabilitation (1C).
- 4a.2 We recommend most simple scores, including self-report scales and field tests ([sit-to-stand (STS), gait speed or 6-min walk test] have comparable and sufficient discriminating power to identify patients with decreased functional status (1C).

#### 1.3 Statement on Handgrip Strength

1.3.1 In adults with <u>CKD 1-5D</u>, we suggest that handgrip strength may be used as an indicator of protein-energy status and functional status when baseline data (prior measures) are available for comparison (2B).

## PERSPECTIVES

- Standardization of the definition (and of the measurements)
- Role of biomarkers to detect frailty?

## Myostatin and Insulin-Like Growth Factor 1 Are Biomarkers of Muscle Strength, Muscle Mass, and Mortality in Patients on Hemodialysis



Pierre Delanaye, MD, PhD,\*<sup>1</sup> Stanislas Bataille, MD,†'‡'§'<sup>1</sup> Kevin Quinonez, MD,\* Fanny Buckinx, PhD,¶ Xavier Warling, MD, PhD,\*\* Jean-Marie Krzesinski, MD, PhD,\* Hans Pottel, PhD,†† Stéphane Burtey, MD, PhD,†'§ Olivier Bruyère, PhD,¶ and Etienne Cavalier, EuSpLM, PhD‡‡

Journal of Renal Nutrition, Vol 29, No 6 (November), 2019: pp 511-520

- Two hospitals in Liège (n=123), one in Marseille (n=81)
- HGS
- Muscle by bioimpedance (Marseille)
- One-year mortality

 Table 1. Demographics and Biochemistry Description of Cohorts

Variables	Whole (n = 204)	Liège1 (n = 67)	Liège2 (n = 56)	Marseille (n = 81)	P Value
Age	71 [58; 81]	65 [46; 77]	70 [58; 77]	77 [69; 85]*	<.0001
Gender (% of men)	60	64	55	60	NS
Residual renal function (>200 mL/day) (%)	69	49	88†	72*	<.0001
Dialysis vintage (months)	29.5 [15.0; 54.5]	24 [14.0; 51.5]	33.5 [18.0; 56.0]	32.0 [13.8; 70.0]	NS
Height (cm)	166 ± 10	168 ± 11	166 ± 10	165 ± 9	NS
Dry weight (kg)	71 ± 16	71 ± 17	73 ± 17	69 ± 15	NS
Dialysis time per session (hour)	$4.0 \pm 0.4$	$3.9 \pm 0.3$	$3.8 \pm 0.4$	$4.2 \pm 0.5^*$	<.0001
Hemodiafiltration (%)	50	69	100†	0*	<.000
Diabetes (%)	42	42	41	42	NS
Bicarbonates (mmol/L)	$23.5 \pm 3.8$	$21.3 \pm 2.8$	22.7 ± 2.8+	26.0 ± 3.7*	<.000
Hemoglobin (g/dL)	10.9 ± 1.2	$10.7 \pm 1.2$	11.4 ± 1.1*	10.7 ± 1.3	.003
Calcium (mmol/L)	$2.20 \pm 0.18$	$2.22 \pm 0.18$	$2.18 \pm 0.19$	2.19 ± 0.18	NS
Phosphorus (mmol/L)	1.56 [1.25; 1.92]	1.75 [1.35; 2.06]	1.46 [1.19; 1.92]	1.50 [1.2; 1.7]+	.016
PTH (multiples of the upper normal limit values)	4.9 [2.6; 8.4]	4.8 [2.6; 7.8]	7.8 [5.6; 11.2]*	3.2 [1.8; 5.8]	<.000
25OH-vitamin D (ng/mL)	30 [21; 39]	38 [27; 45]	21 [13; 31]*	31 [23; 38]	<.000
CRP (mg/L)	6 [2; 15]	7 [2; 15]	5 [2; 10]	8 [3; 23]	.048
Creatinine (mg/dL)	$7.51 \pm 2.61$	$8.02 \pm 2.82$	$7.74 \pm 2.56$	$6.92 \pm 2.37 \pm$	.028
Albumin (g/L)	38 [35; 40]	40 [38; 42]*	36 [34; 39]	38 [34; 39]	<.000
Prealbumin (g/L)	0.28 [0.22; 0.33]	0.30 [0.24; 0.35]	0.28 [0.25; 0.32]	0.26 [0.20; 0.33]+	.006
Handgrip strength	20 [14; 29]	26 [20; 36]*	21 [16; 29]	17 [12; 24]	<.000
Handgrip strength (men)	25 [19; 34]	32 [22; 40]	26 [20; 31]	20 [14; 26]	<.000
Handgrip strength (women)	16 [11; 20]	20 [18; 24]	16 [10; 20]	12 [9; 14]	<.000
Decreased handgrip strength (%)	67	42	66†	88*	<.000
Myostatin (pg/mL)	2573 [1662; 3703]	3008 [1978; 4295]	3357 [2184; 4892]	1755* [1163; 2670]	<.000
IGF-1 (μg/L)	118 [84; 172]	152 [88; 208]	123 [90; 168]	104 [76; 152]†	.002

CRP, C-reactive protein; IGF-1, insulin-like growth factor 1; NS, not significant; PTH, parathyroid hormone.

<sup>\*</sup>If P < .05 in comparison with the two other cohorts.

<sup>†</sup>If P < .05 in comparison with Liège 1.

 $<sup>\</sup>pm$ If P < .05 in comparison with Liège2.

**Table 2.** Pearson Correlations Between Biomarkers and Handgrip Strength in the Exploratory Liège1 Cohort (n = 67)

Biomarkers	Correlation (r) (95% CI)	P Values
Activin A	-0.09 (-0.33 to 0.16)	NS
Follistatin	0.007 (-0.23 to 0.25)	NS
PIIINP	0.0008 (-0.23 to 0.25)	NS
IGF-1	0.44 (0.22 to 0.61)	.0002
Myostatin	0.50 (0.30 to 0.66)	<.0001

CI, confidence interval; IGF-1, insulin-like growth factor 1; NS, not significant; PIINP, procollagen III N-terminal peptide.

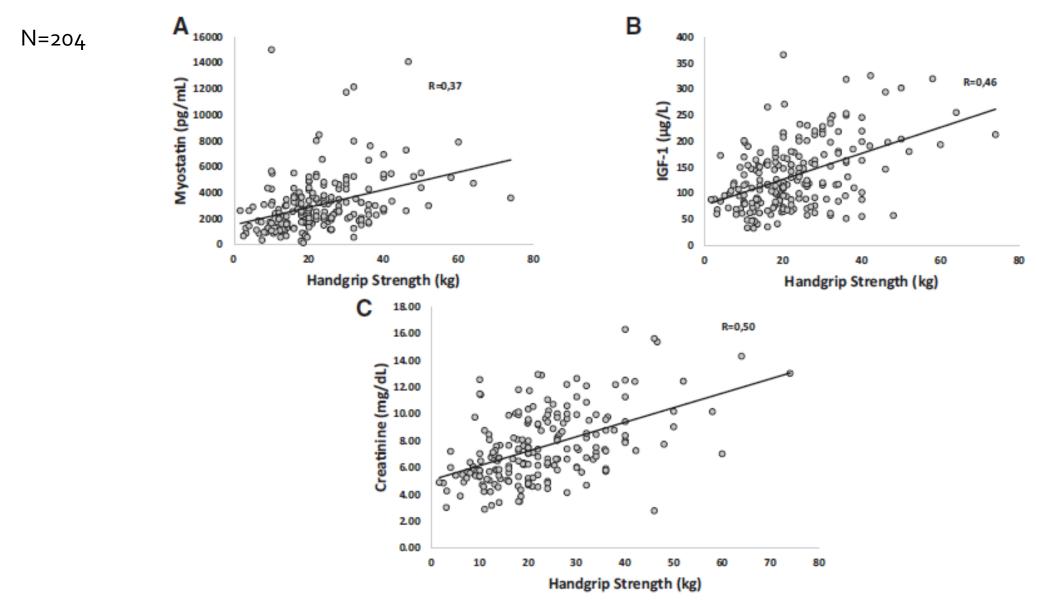


Figure 1. Coefficient of correlation between handgrip strength and myostatin (A), IGF-1 (B), and serum creatinine (C). IGF-1, insulin-like growth factor 1.

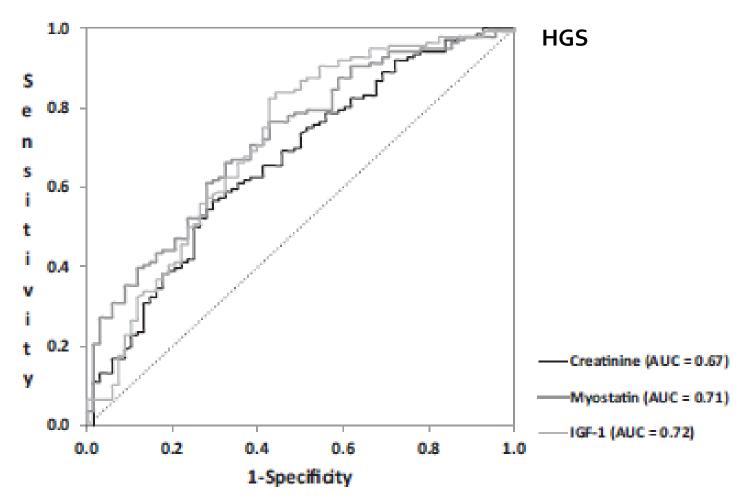


Figure 2. ROC curves for myostatin, IGF-1, and serum creatinine to detect a decreased HGS. AUC, area under the curve; HGS, handgrip strength; IGF-1, insulin-like growth factor 1; ROC, receiver operating characteristic.

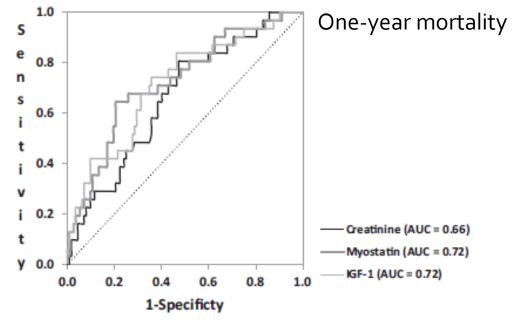


Figure 3. ROC curves for myostatin, IGF-1, and serum creatinine to predict mortality at 1 year (unadjusted). AUC, area under the curve; IGF-1, insulin-like growth factor 1; ROC, receiver operating characteristic.

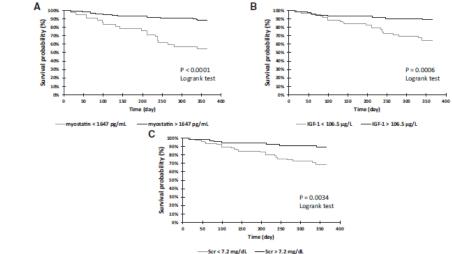


Figure 4. Survival curves within 1 year for myostatin (A), IGF-1 (B), and serum creatinine (C) (unadjusted). IGF-1, insulin-like growth factor 1.

**Table 5.** Association Between Plasmatic Concentrations of Myostatin and IGF-1 and One-Year Survival: Cox Proportional Hazards Models (n = 143)

	Univariate Analy	ysis
Included variables	HR [95% CI]	P Value
Univariate model		
Age	1.041 [1.012-1.071]*	.0052
Gender	_	NS
Albumin	1.09 [1.02-1.16]*	.0069
Prealbumin+	2.72 [1.84-4.03]*	<.0001
CRP	1.006 [1.002-1.011]*	.0033
Hemodiafiltration	4.61 [1.40-15.2]*	.0119
Serum creatinine*	1.27 [1.07-1.52]	.0073
Myostatin±	1.81 [1.26-2.58]*	.012
IGF-1§	1.15 [1.06-1.25]*	.0008
Multivariable models		
Model 1		
Age	-	NS
Gender	-	NS
Myostatin	1.49 [1.03-2.15]	.0356
IGF-1	1.11 [1.01-1.21]	.025
Model 2		
Age	-	NS
Gender	-	NS
Albumin	-	NS
CRP	-	NS
Hemodiafiltration	-	NS
Serum creatinine	-	NS
Myostatin	1.49 [1.03-2.15]	.0356
IGF-1	1.11 [1.01-1.21]	.0250
Model 3		
Age	-	NS
Gender	-	NS
Albumin	-	NS
Prealbumin†	2.72 [1.84-4.03]	<.0001
CRP		NS
Hemodiafiltration	-	NS
Serum creatinine	-	NS
Myostatin	-	NS
IGF-1	-	NS

CI, confidence interval; CRP, C-reactive protein; HR, Hazard Ratio; IGF-1, insulin-like growth factor 1; NS, not significant.

<sup>\*</sup>HR for a serum creatinine decrease of 1 mg/dL.

<sup>†</sup>HR for a prealburnin decrease of 0.1 g/L.

<sup>‡</sup>HR for a myostatin decrease of 1000 pg/mL.

<sup>§</sup>HR for a IGF-1 decrease of 10 μg/L.

### Conclusions: TO DO LIST and PERSPECTIVES

- The prevalence of frailty in hemodialysis patients is very high
- Standardization of the definition (and of the measurements)
- Role of biomarkers to detect frailty?
- Role of frailty in the decision to start dialysis?
- Role of frailty in the assessment of eligibility for renal transplantation?
- To be interventional

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#### Framework to reduce frailty in hemodialysis patients

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Special Article

#### Frailty Consensus: A Call to Action

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- Exercise (resistance and aerobic)
- Caloric and protein support
- Vitamin D
- Reduction of polypharmacy









# CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN CHRONIC KIDNEY DISEASE: 2019 UPDATE

## Intradialytic exercises

Blood Purification **Review – Advances in CKD 2022** 

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## **Exercise in Dialysis: Ready for Prime Time?**

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- Many small studies with moderate benefits (but no hard endpoints)...but most patients were probably not frail
- Three RCTs (6- till 12-months of intervention) ...but disappointing results...
- One RCT (6-months) showed benefits on left ventricular mass (MRI)
- Remains underused (less than 10% of dialysis centers propose this activity), need for kinesiologists and physiotherapists (nephrologists do not feel comfortable with prescription although majority of them think it is useful)...and so, funding...
- Dialysis is source of fatigue in itself, risk of cramps, hypotension
- High % of drop-out









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