Epidemiology and mechanism of Frailty in dialysis patients

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Trust, Moral, Universal, Hand in Hand

Outlines

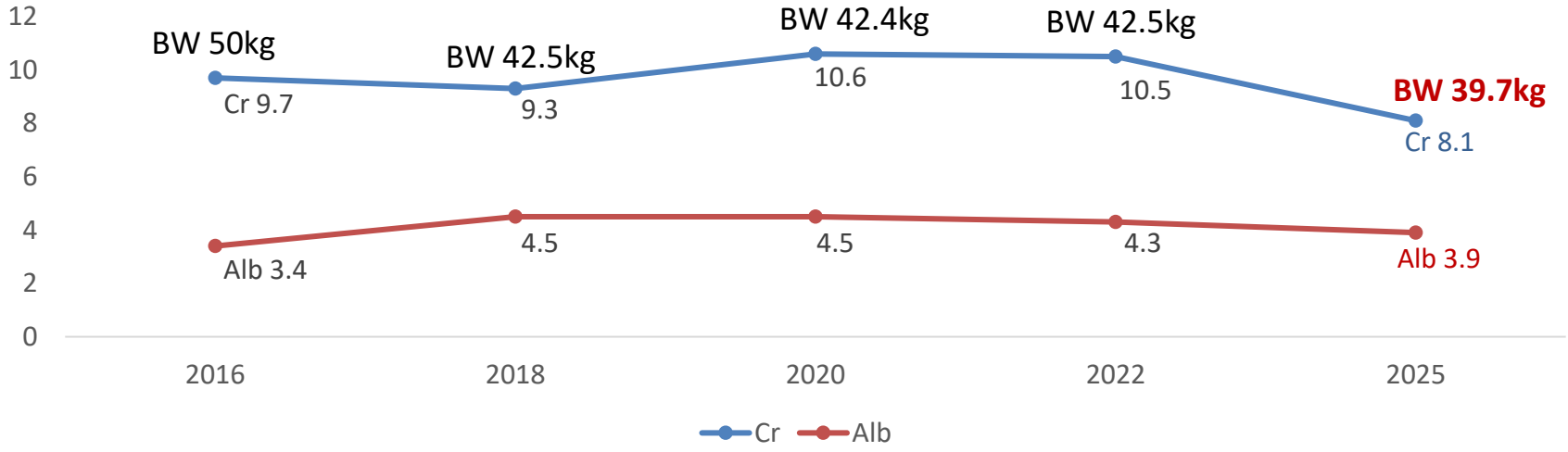
- Case study
- Frailty and epidemiology
- Pathophysiology of frailty
- Characteristics of frailty in dialysis patients
- Conclusions

Case study

TMUH

- A 74-year-old woman without systemic disease, developed **AKI** (RPGN, biopsy: ANCA GN s/p plasma exchange and immunosuppressives), progressed to **ESRD** s/p regular HD thrice a week since **8 yrs ago**
- BH 150cm, BW 39.7kg, **BMI 17.6**
- Hb 10.9, **Alb 4.0**, Ca 9.0 P 2.6
- Med: sacubitril/valsartan 100mg qd, folic acid 1# qd, vit B complex 1# qd, CaCO3 1# tid with meal, rosuvastatin 10mg qd, calcitriol 0.5ug tiw, famotidine 1# bid, darbepoetin alfa 20ug QW

Cont.


12
10
8
6
4
2
0
BW 50kg
Cr 9.7
BW 42.5kg
9.3
BW 42.4kg
10.6
BW 42.5kg
10.5
BW 39.7kg
Cr 8.1
Alb 3.4
4.5
4.5
4.3
Alb 3.9
2016
2018
2020
2022
2025
Cr
Alb


R
Portable


RA


R


R1

Cont.

- She reported less energy, and walk fewer distances as compared to before in recent 3 months

- Q1. Is she frail? How to evaluate it?
- Q2. What is the impact of frailty in dialysis patients?

Q1. WHAT IS FRAILTY AND THE EPIDEMIOLOGY OF FRAILTY IN KIDNEY DISEASE?

Introduction

TMUH

- What is frailty?
  - Frailty is characterized by a decline in both physiological state and cognitive state →a combination of symptoms, including weight loss, exhaustion, low physical activity, weakness, and slow walking speed
  - Not a single organ system or disease, but rather a multisystem syndrome
- It leads to **poor quality of life**, and higher risk of hospitalization, infection, cardiovascular events, dialysis-associated complications, and death

Kidney Int. 2024; 106(1): 35-49

Diagnosis

- Currently, **no universal definition of frailty** has been established
- Comprehensive geriatric assessment
  - Physical
  - Functional
  - Cognitive
  - Psychosocial

Common used diagnostic tools

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Clinical frailty scale (CFS)

Grade 4-5: mildly frail
(May need someone help)

Grade 6: moderately frail
(need someone help)

Grade 7-9: severely frail
(completely dependent)

Common used diagnostic tools

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Frailty Phenotype

Unintended Weight Loss	Exhaustion	Weakness	Slowness	Low Physical Activity
4.5 kg or more than 5% of body weight within a year	Self-Report (2 questions from the CES-D)	Jamar Handgrip dynamometer	Gait speed in meters/second (over 4 meters)	Short version of Minnesota Leisure Time Activity-Kcal/Kg
				

Robust: 0 criteria; Pre-Frail: 1-2 criteria; Frail: 3 or more criterion

Fried LP et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56:** M146–56.

J Gerontol A Biol Sci Med Sci. 2001; 56(3): M146-56

CGA (Comprehensive geriatric assessment)

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Problem	Assessment Tool	Result	Abnormal Value
Mental state			
1. Delirium	CAM	None	
2. Cognitive	MMSE	22	<24
3. Depression	GDS-5	0	≥2

Problem	Assessment Tool	Result	Abnormal Value
Functional status			
1. Frailty	CFS	5	≥5
2. Activities of daily living	ADL Score	9	<95
	IADL Score	5	<5
3. Mobility and gait	SARC-F	7	≥4
	Calf Circumference	25 cm	M<34, F<33
	Handgrip	24	M<28kg, F<18kg
	TUG	15 sec	>12 sec
4. Falls	Morse Fall Scale	60	>45
5. Nutrition	MNA-SF	7	<11
	Oral Problems	Yes	
	Swallowing difficulty	No	
6. Skin Risk	Pressure sore (Braden)	19	≤16
7. Vision impairment		No	
8. Hearing impairment		No	

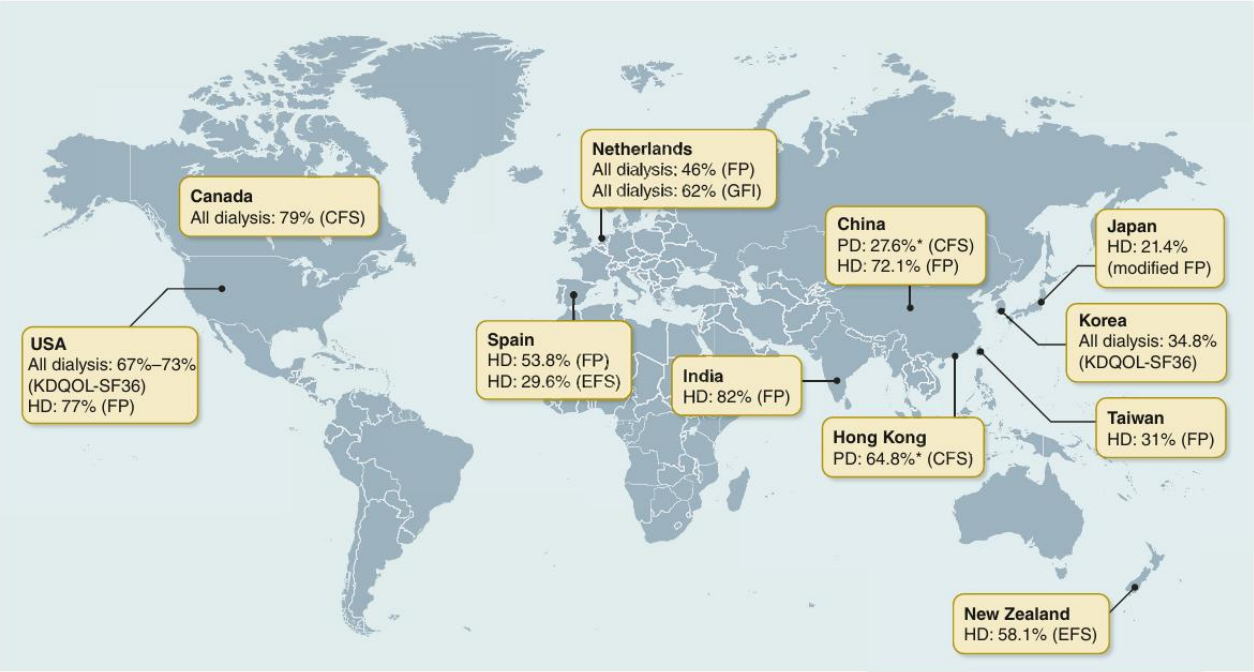
CGA (Comprehensive geriatric assessment)

TMUH

Problem	Assessment Tool	Result	Abnormal Value
Subjective problem			
1. Exhaustion (>3 days / wk)		Yes	
2. Memory Decline	Self-report	Yes	
3. BW loss (>5% in recent 1 yr)		No	
4. Poor appetite		No	

Case discussion with multi-disciplinary team

Prevalence of Frailty



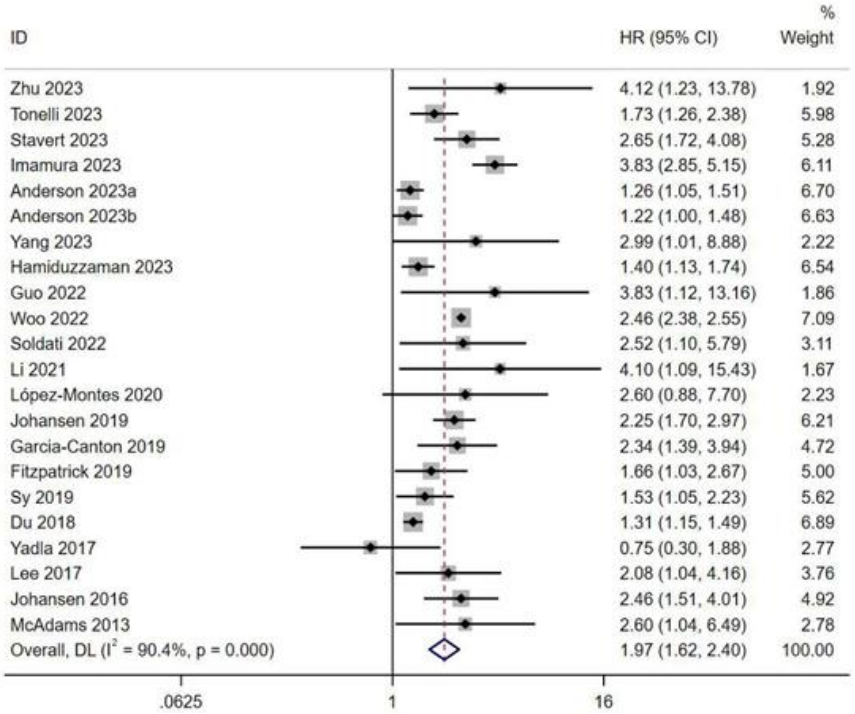
HD: 30-80%

PD: 14-69%

CKD: 12-40%

Kidney Int. 2024; 106(1): 35-49

Frailty with poor outcomes

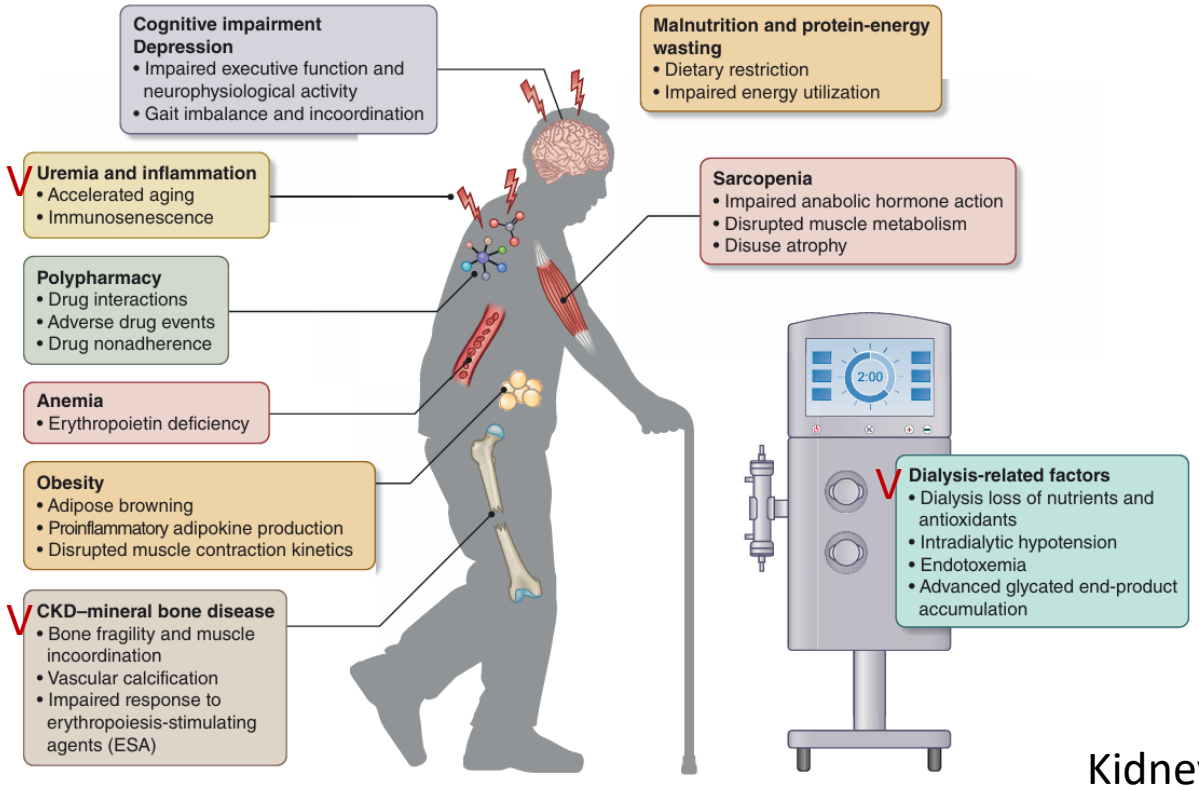


Risk of mortality in patients undergoing HD between **frail and non-frail** patients

Ren Fail. 2024; 46(2): 2367716

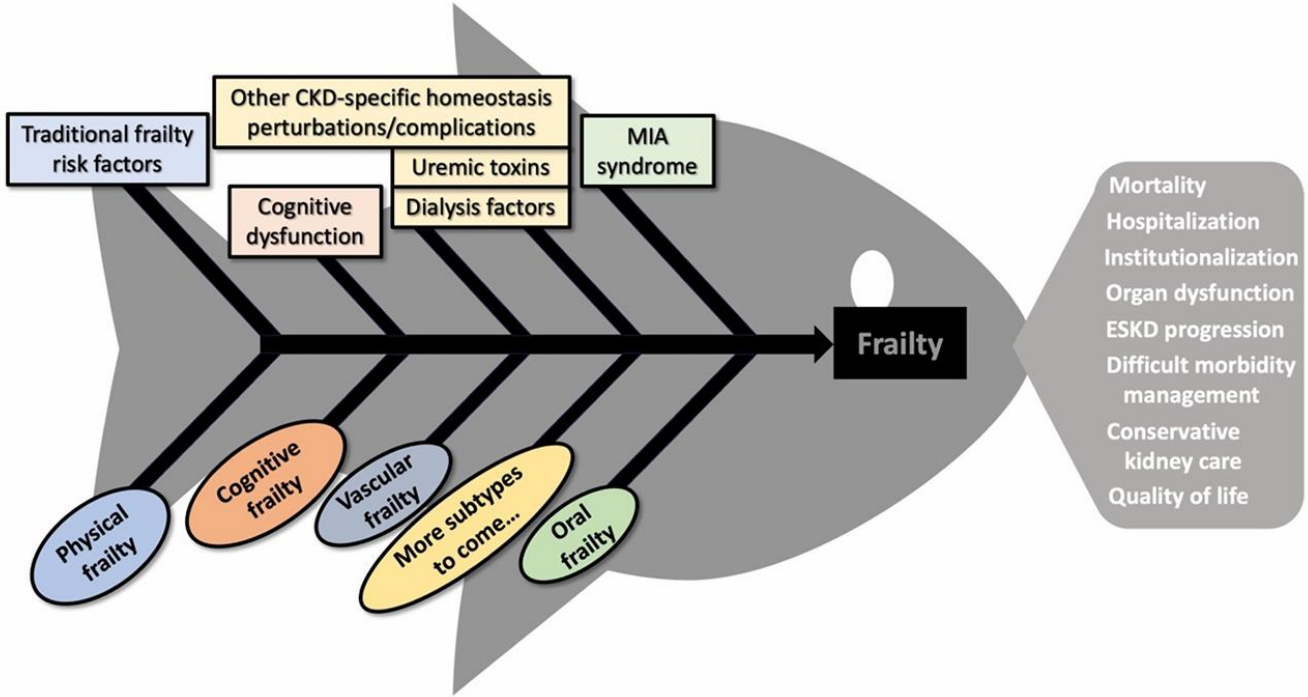
Q2. WHAT IS THE PATHOPHYSIOLOGY OF FRAILTY IN KIDNEY DISEASE PATIENTS?

Contributor to frailty in patients on dialysis



Kidney Int. 2024; 106(1): 35-49

Risk factors and Frailty



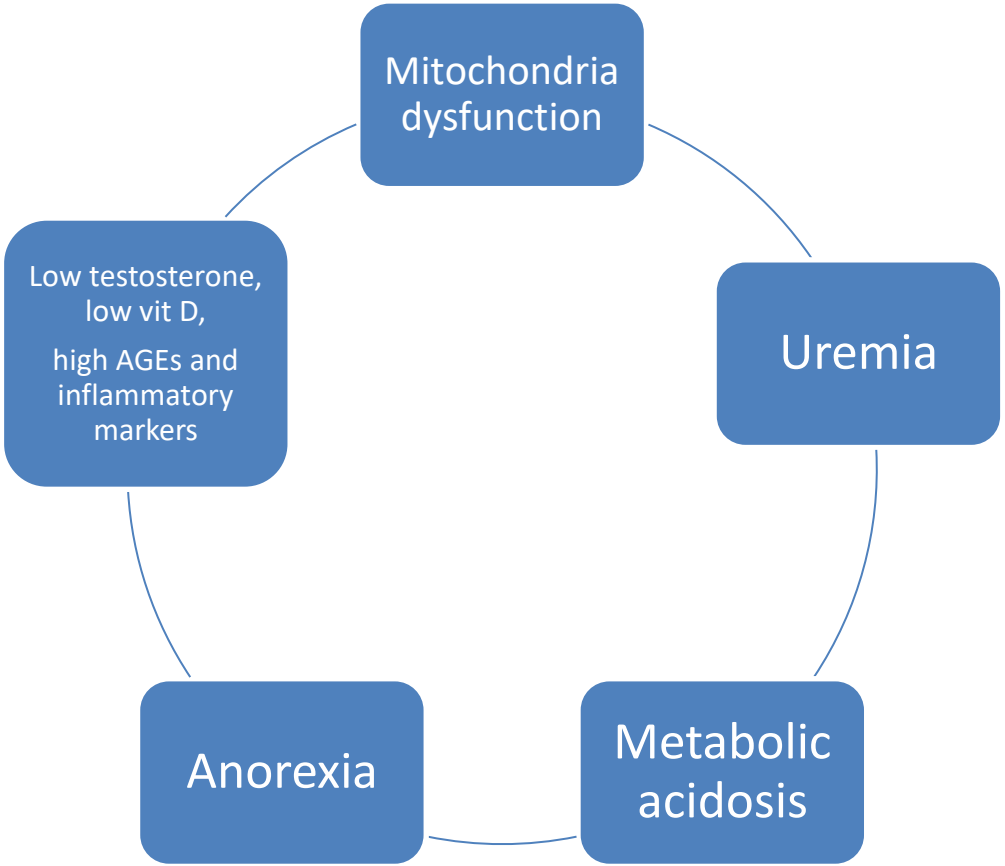
Kidney Res Clin Pract. 2025 Jan 21

Pathogenesis

- Accumulation of senescent cells into multiple tissues and proinflammatory signaling→ "**inflammageing**"
- Aging
- Inflammation
- Oxidative stress
- Malnutrition
- Protein-energy wasting (PEW)
- Dysregulation of renin-angiotensin activity
- CKD-specific factors (ex. uremia, mineral bone disease, and dialysis treatment)

Kidney Int Rep 2024; 9: 791-806

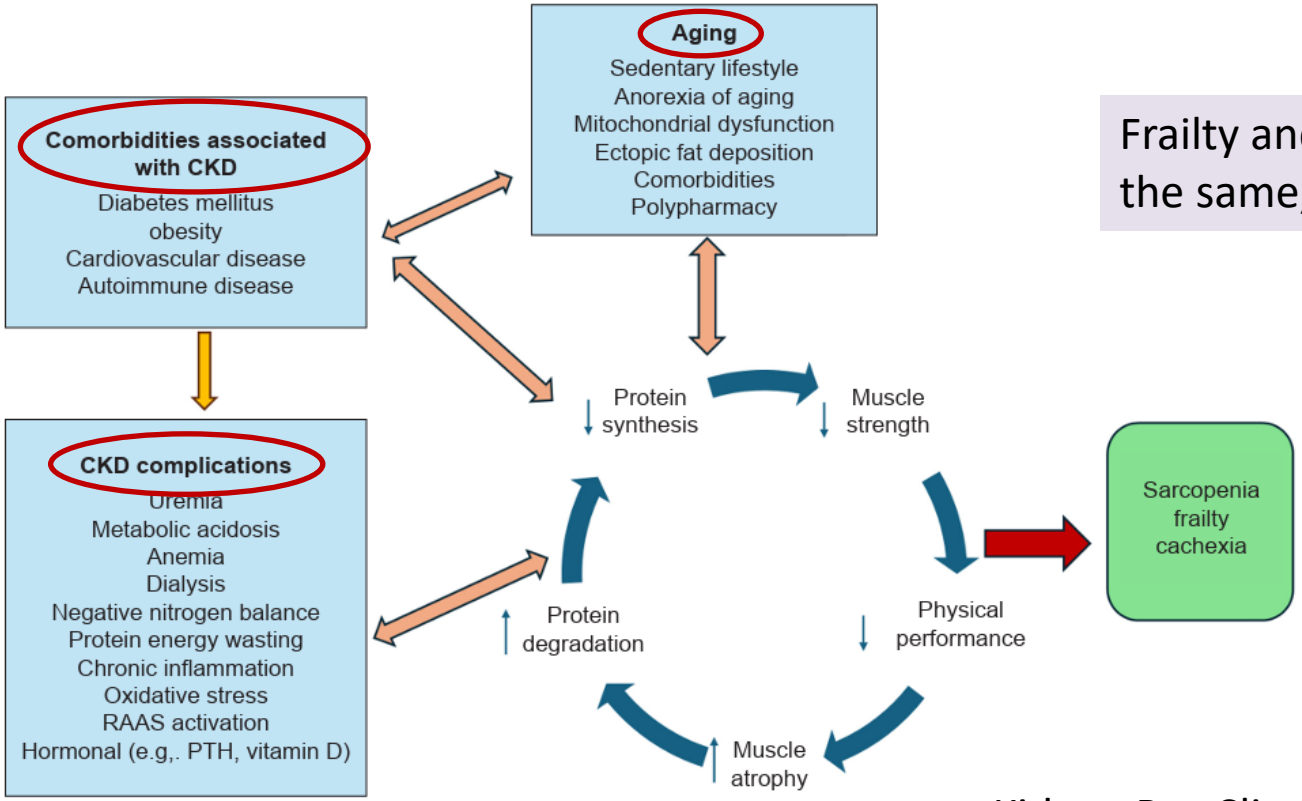
Mechanisms of Frailty



Poor skeletal muscle strength, low muscle mass, poor muscle performance
→ **Sarcopenia**

High burden of **senescent** cell, high **inflammatory** cytokines/chemokines
→ **Frailty**

Mechanisms of Frailty

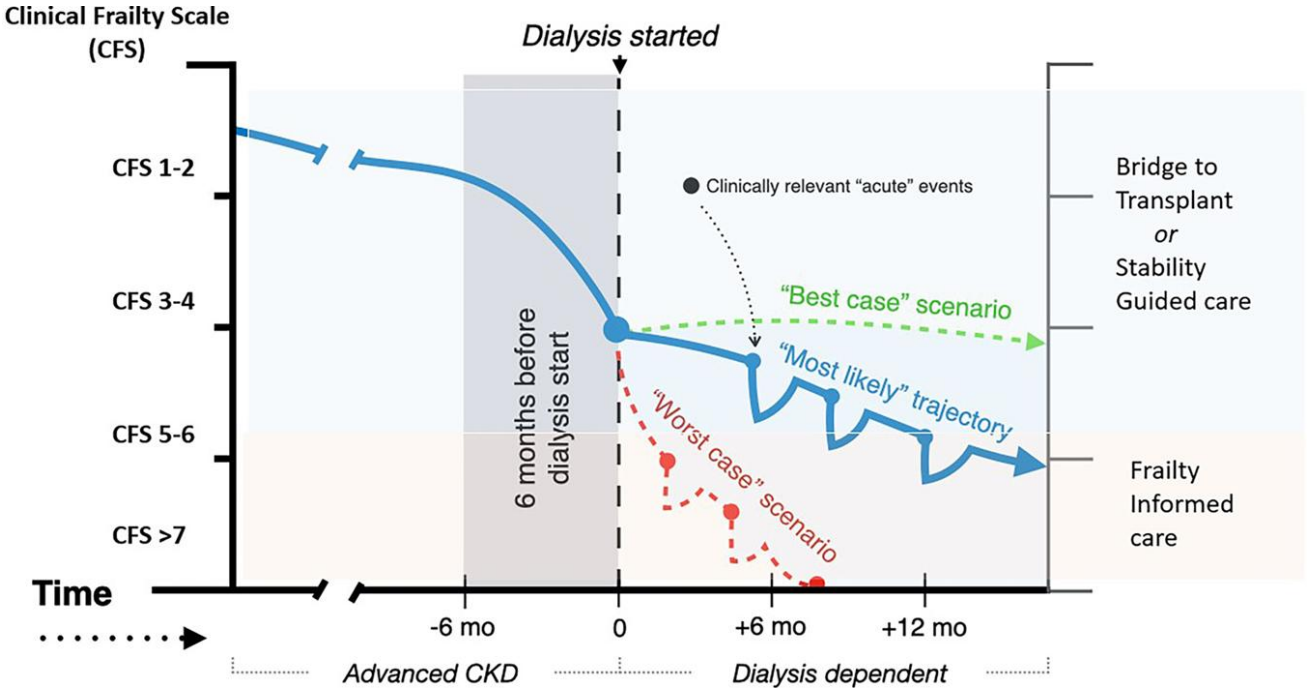


Frailty and sarcopenia not the same, but often coexist

Kidney Res Clin Pract. 2025 Jan 21

Q3. WHAT IS THE CHARACTERISTICS OF FRAILTY IN KIDNEY DISEASE PATIENTS?

CKD health trajectory



Perit Dial Int. 2025; 45(2): 70-73

Functional decline in CKD

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Table 3. Multivariable Logistic Regressions of Any (N = 5592), Balance (N = 5591), and Falling (N = 5590) Problems in the Past Year

	Self-report a Dizziness, Balance and/or Fall Problem			Self-report a Balance Problem			Self-report a Falling Problem		
Variable	Odds Ratio	95% CI	*P*-Value	Odds Ratio	95% CI	*P*-Value	Odds Ratio	95% CI	*P*-Value
CKD stage									
Normal/controls	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Stage 3A/3B	1.54	1.29, 1.83	**<.001**	1.44	1.18, 1.75	**<.001**	1.39	1.07, 1.83	**.02**
Stage 4/5	2.07	1.26, 3.40	**.004**	1.71	1.01, 2.90	**.05**	1.29	0.63, 2.62	.49

Increased balance, falling issues, and slower gait found in patients with **increased CKD severity and lower 25(OH)D status**

J Ren Nutr. 2019; 29(6): 490-497

Characteristics of Frailty in dialysis

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- Positive association with frailty
  - Age
  - Comorbidities
  - Ca (>10.0), P (<3.5 and >6.0), iPTH (<60)
  - Beta-2-microglobulin
- Negative association with frailty
  - **Albumin**
  - **Creatinine index (dialysis-based markers of muscle mass)**

Am J Kidney Dis. 2024; 84(5): 601-612

Functional status in incident HD

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Table 4. Association of Functional Status with Early Mortality After the Start of Hemodialysis.

Outcomes	Levels of Functional Disability		
	Mild/None	*Moderate*	*Severe*
Death within 3 months			
Number of events / Number of patients	65/3,192	239/2,935	343/1,537
Proportion, %	2.04	8.14	22.3
Risk ratio of death (95% confidence interval) †			
Univariate analysis	Reference	4.00 (1.11 to 1.60)	11.0 (8.41 to 14.3)
Case-mix adjusted	Reference	3.41 (2.59 to 4.50)	8.39 (6.42 to 11.0)
Multivariate adjusted	Reference	2.38 (1.80 to 3.10)	3.93 (2.96 to 5.22)

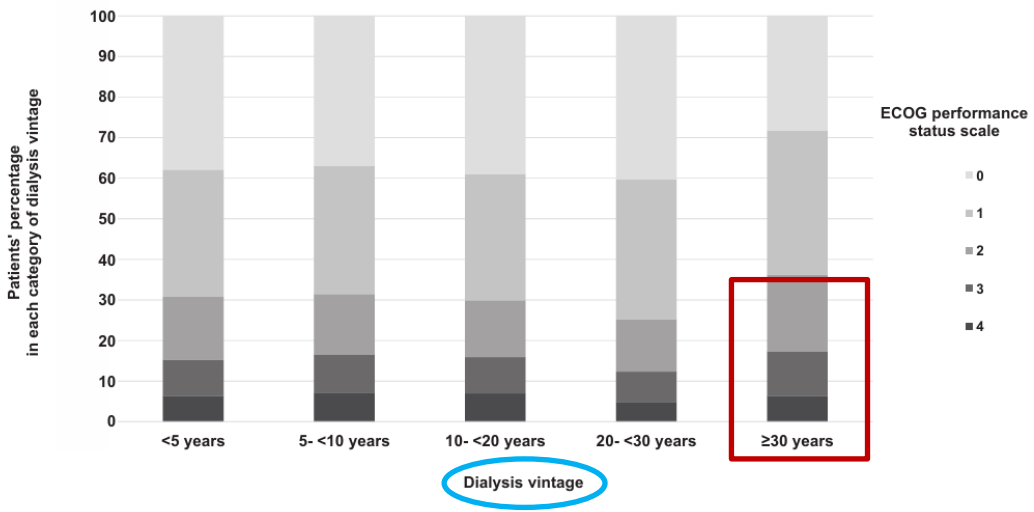
Increased risk of mortality if ADLs moderately to severely impaired

Available data do not suggest improvement in frailty upon initiation of dialysis; rather, the trajectory appears **higher levels of dependence in ADLs after dialysis initiation**

Semin Dial. 2013; 26(6): 690-6
PLoS One. 2016; 11(6): e0156951

Dialysis vintage

N = 227,136

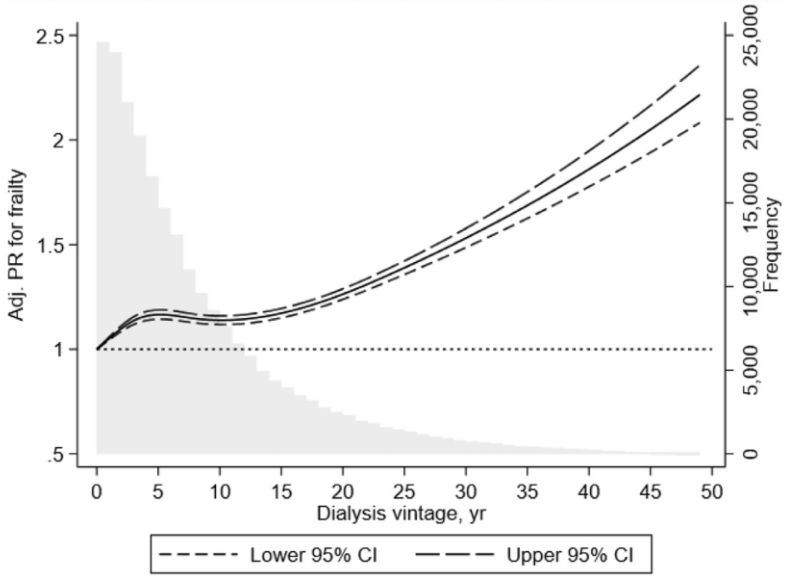


- Japan, ESKD patients aged >50 yrs who received dialysis in 2018
- **Frailty: defined as ≥ 2** on the Eastern Cooperative Oncology Group Performance Status (ECOG PS)
- **Bedridden status: defined as grade 4** on the ECOG PS scale

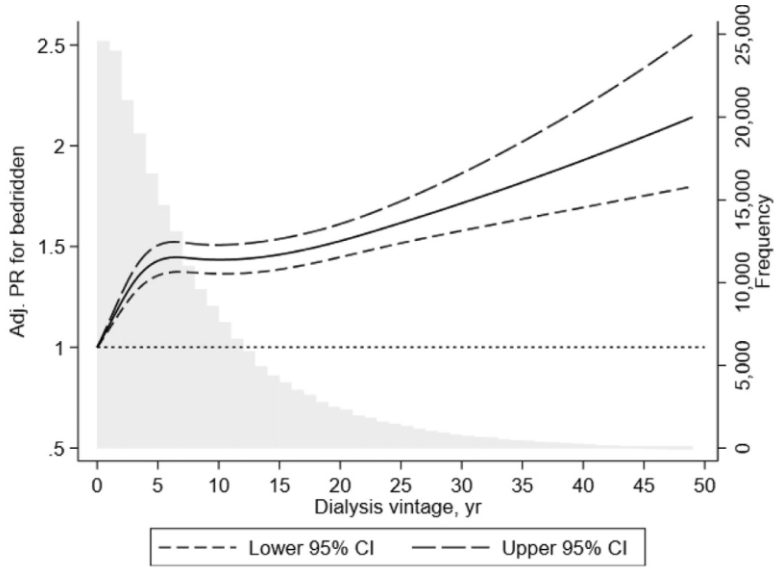
Long-term dialysis therapy, particularly **> 30 yrs**, associated with deterioration of physical function and frailty

Am J Kidney Dis. 2024; 84(5): 601-612

Dialysis vintage



Dialysis vintage vs **Frailty**



Dialysis vintage vs **Bed-ridden**

Am J Kidney Dis. 2024; 84(5): 601-612

Functional decline in incident dialysis

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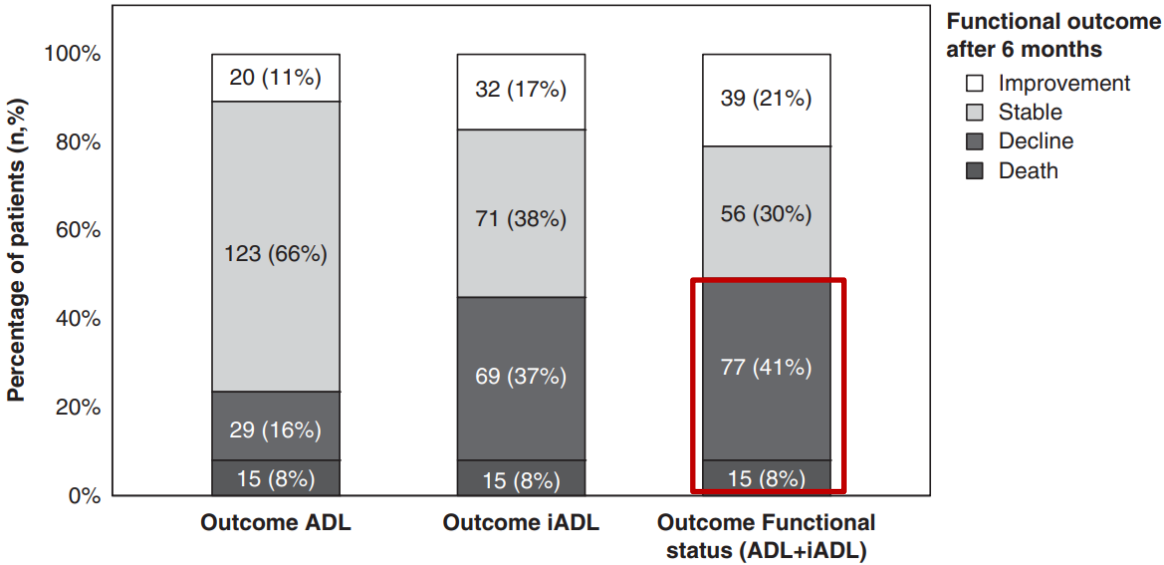
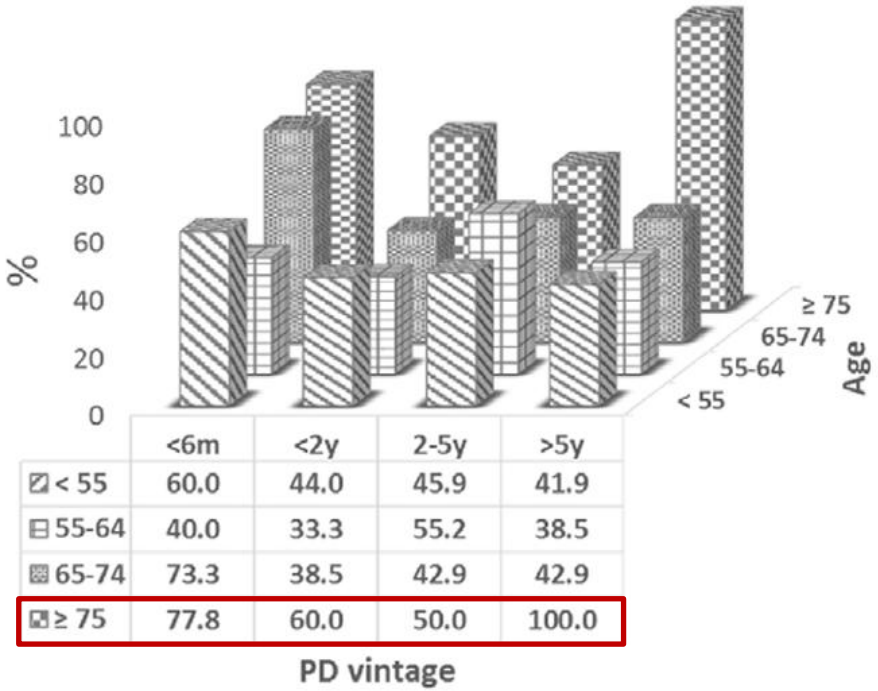
- ESKD, ≥65 years (N = 196), geriatric assessment
- Functional decline within **the first 6 months** after initiating dialysis is highly prevalent



Clin J Am Soc Nephrol. 2019; 14(7): 1039-47

PD patients



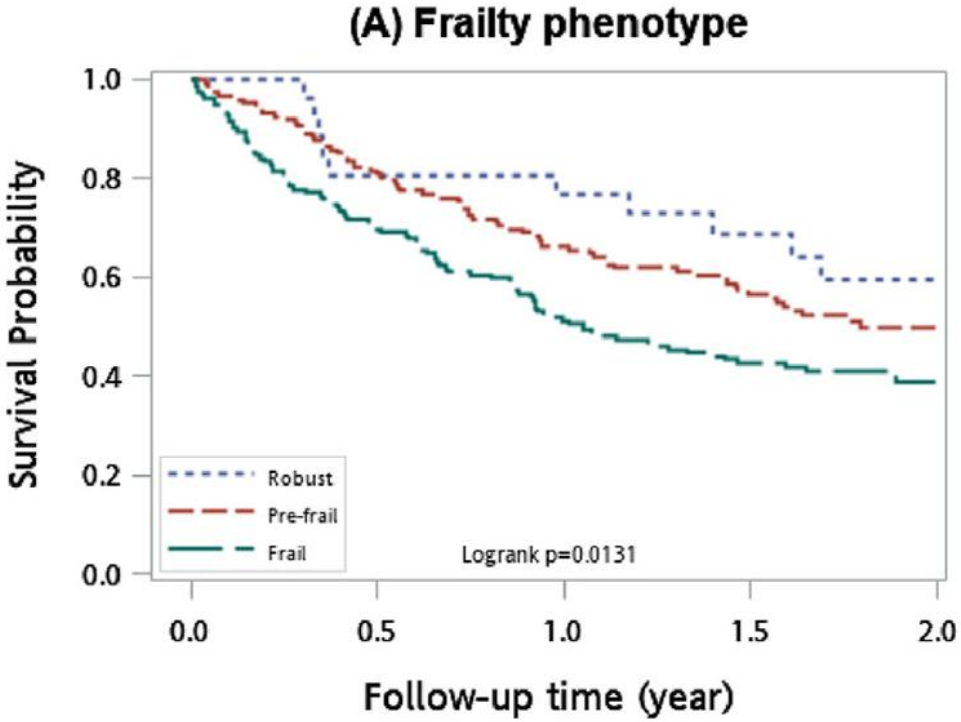
	<6m	<2y	2-5y	>5y
< 55	60.0	44.0	45.9	41.9
55-64	40.0	33.3	55.2	38.5
65-74	73.3	38.5	42.9	42.9
≥ 75	77.8	60.0	50.0	100.0

PD vintage

- NTUH, prospective, PD patients (N = 337), **Frailty phenotype**
- Predictors for frailty
  - **Old age**
  - **Diabetes mellitus**
  - **Gout**
  - **Sleep disorder**

J Formos Med Assoc. 2024; 123(2): 248-256

PD patients



Frail patients presented the worse outcomes (overall survival)

J Formos Med Assoc. 2024; 123(2): 248-256

CONCLUSIONS

Conclusions

- Frailty is highly prevalent in dialysis patients, and it is a combination of symptoms, associated with poor outcomes
- Aging, comorbidities and CKD/dialysis complications are contributors to frailty in kidney disease patients
- Accumulation of senescent cells and inflammageing are the central roles of frailty development
- Clinical frailty scale and Frailty phenotype are commonly used diagnostic tools
- Frailty phenotype included weight loss, exhaustion, weakness, slowness, and low physical activity
- Functional decline/prone to frailty is seen as aging, CKD progression, initiation of dialysis, and increased dialysis vintage

Xin Yi Campus

Shuang Ho Campus

Thank you for your attention!

TMU Hospital

Shuang Ho Hospital

Wan Fang Hospital

Hsin Kuo Min Hospital

Taipei Neuroscience Institute

Taipei Cancer Center