

Adverse Health Effects of Frailty in CKD Patients

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Cause

	Effect (descriptions)	Risk Difference	CKD severity	Frailty Assessment	Sample Size	Reference
Biological						
Cardiovascular	Hypertension*	RR 1.6 (1.26-2.04)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	1
	Peripheral vascular disease*	RR 1.58 (1.34-1.8)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	1
	Left ventricular dysfunction*	RR 1.18 (1.03-1.36)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	1
	Endothelial dysfunction	r= -0.367 (p= 0.004)	CKD stages 3-5	Fried Phenotypes	61	2
		OR 3.86 (1.00-14.88)				
	Permanent vascular access (fistula or graft)	HR 0.71 (0.51-0.98)	CKD stage 5D (maintenance hemodialysis)	Fried Phenotypes	2275	3
Cerebrovascular	Cerebrovascular Accident	RR 1.34 (1.19-1.5)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	1
Pulmonary	COPD	OR 1.68 (1.16-2.45)	CKD stages 1-5	Fried Phenotypes	10256	4
Immunological	Inflammatory					
	IL-6*	Worse frailty	CKD stage 5D (hemodialysis)	Fried Phenotypes	762	5
	CRP	After adjustment, OR	Chronic kidney	Fried	5888	6

		Fibrinogen	1.76 (1.28-2.41) to 1.50 (1.07-2.09)	insufficiency, serum creatinine ≥ 1.3 mg/dL	Phenotypes		
Endocrinologic/ Metabolic	Diabetes		Frailty scores +0.7 points per year	CKD stage 5D (hemodialysis)	Fried Phenotypes	762	⁵
			OR 1.68 (1.16-2.45)	CKD stages 1-5	Fried Phenotypes	10256	⁴
		Obesity (IMC ≥ 30 kg/m ²)	OR 6.63 (1.16-36.77)	CKD stages 3-5	Fried Phenotypes	61	²
		Higher parathyroid hormones (PTH)	r= 0.30 (p= 0.01)	CKD stages 3-5	Fried Phenotypes	61	²
Body Composition	Higher fat mass		r= 0.25 (p= 0.04)	CKD stages 3-5	Fried Phenotypes	61	²
Cancer	Cancer		OR 1.89 (1.19-2.99)	CKD stages 1-5	Fried Phenotypes	10256	⁴
Arthritis	Arthritis		OR 3.34 (2.08-5.38)	CKD stages 1-5	Fried Phenotypes	10256	⁴
Laboratory Data	eGFR (mL/min/1.72m ²)						
	eGFRcys <30		Frailty prevalence 2.8	CKD stages 1-4	Fried Phenotypes	336	⁷
	eGFRcys 30-44		Frailty prevalence 2.1				
	eGFRcys >60		Referent				

		Serum Albumin Concentrations (g/dL)	Frailty scores -1.1 points per g/dL	CKD stage 5D (hemodialysis)	Fried Phenotypes	762	⁵
		Serum Creatinine <4 mg/dL*	RR 1.46 (1.22-1.71)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	¹
		Testosterone, per 50% lower free testosterone*		CKD stage 5D (hemodialysis), men	Fried Phenotypes	440	⁸
		being frail	OR 1.40 (1.05-1.53)				
		becoming frail over 12 months	OR 1.40 (1.07-1.73)				
		Hemoglobin	Adjusted, OR 1.76 (1.28-2.41) to 1.50 (1.07-2.09)	Chronic kidney insufficiency, serum creatinine ≥1.3mg/dL	Fried Phenotypes	5888	⁶
		LDL, HDL					
Lifestyle		Smoking*	RR 1.18 (1.04-1.34)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	¹
Ethnicity		Hispanic*	Frailty scores +0.6 points per year	CKD stage 5D (hemodialysis)	Fried Phenotypes	762	⁵

Prevalence

	Effect (descriptions)	Prevalence	CKD Severity	Frailty Assessment	Sample Size	Reference
Biological						
Cardiovascular	Heart Failure	30% vs 12%	CKD stages 1-4	Fried Phenotypes	336	⁷
	Angina	34% vs. 22%	CKD stages 1-4	Fried Phenotypes	336	⁷
Cerebrovascular	Cerebrovascular Disease Prevalence (%)	26.4 vs. 12.0	ESRD	Fried Phenotypes	324	⁹
Neurological	Brain Wave	F vs. NF	ESRD, under chronic dialysis	Simple FRAIL scale (SFS)	46	¹⁰
	Global DAR	283 ± 679 vs. 2971 ± 4859				
	DARs (left frontal)	135 ± 250 vs. 3073 ± 4702				
	DAR (left TO)	197 ± 318 vs. 3708 ± 6398				
	DAR (central)	55 ± 96 vs. 1773 ± 3262				
	DAR (right TO)	187 ± 261 vs. 4400 ± 7763				
	Global DTABR	191 ± 469 vs. 1781 ± 2793				

			DTABR (left frontal)	86 ± 158 vs. 1680 ± 2388				
			DTABR (left TO)	130 ± 210 vs. 1884 ± 2828				
			DTABR (central)	39 ± 65 vs. 1132 ± 1957				
			DTABR (right TO)	126 ± 178 vs. 2960 ± 5271				
	Cognitive	Mini-Mental State Examination (MMSE)			Elderly, ≥65y/o	Edmonton Frail Scale (EFS)	137	11
			Spearman's correlation coefficient of EFS scores with gross MMSE scores	-0.607 (p<0.01)				
		Executive Function		F vs. NF at cohort entry				
			Trail Making Tests A (TMTA) scores	+12.08	ESRD	Fried Phenotypes	324	9
			Trail Making Tests B (TMTB) scores	+33.15	ESRD	Fried Phenotypes	324	9
	Microbiota	Gut Microbiota Composition		F vs. NF	Stage 3b-4, eGFR 15-45ml/min	Fried Phenotype score	64 (and 15 control subjects)	12
			Malnutrition-Inflammation-Score (MIS)	7.6 vs. 3.9				
			Abundance of unclassified	Directly proportional to				

			Mogibacteriaceae and Oscillospira	MIS				
			Abundance of Akkermansia, Ruminococcus, and Eubacterium	Inversely proportional to MIS				
			Bacterial Abundance of some genera (Mogibacteriaceae, Coriobacteriaceae, Eggerthella, Erwinia, Coprobacillus, Anaerotruncus, etc)	↑				
	Immunological	Inflammatory						
			CRP (ln CRP) (mg/dL)	1.12 vs 0.28	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	119	13
			IL6 (ln IL6) (mg/dL)	2.45 vs. 1.58				
		Mycophenolate mofetil (MMF) dose reduction (MDR)		F vs. NF	CKD stage 5T	Fried Phenotypes	525	14
			1 year since KT (%)	44 vs 40				
			2 years since KT (%)	54 vs. 45				
			3 years since KT (%)	67 vs. 51				
		Viral infection		F vs. NF				
			HCV (n=37)	36 vs. 1	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	1

Functional Status	Disability		F vs. NF				
		At least one disability in activities of daily Living (ADLs)	15% vs. 5%	CKD stages 1-4	Fried Phenotypes	336	7
		At least one disability in instrumental activities of daily living (IADLs)	60% vs. 28%				
		At least one disability in mobility tasks	40% vs. 18%				
		Less ADL-independent	55% vs. 91%	≥ 65 yo, predialysis, eGFR < 20 mL/min	Groningen frailty indicator (GFI)	65	15
	Ability to perform basic activities of daily living		33.33% vs 76.4%	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	16
	Ability to perform transfers		38.8% vs. 84.7%				
Endocrinologic/ Metabolic	Diabetes		F vs. NF				
		Prevalence	64% vs. 49%	CKD stages 1-4	Fried Phenotypes	336	7
	Obesity		F vs. NF				
		Prevalence	64% vs. 50%	CKD stages 1-4	Fried Phenotypes	336	7
		Prevalence	51.8% vs. 23.9%	ESRD	Fried Phenotypes	324	9

		BMI based on dry weight	31.5 vs. 27.6				
Body Composition	Appendicular						
		Appendicular skeletal muscle mass index (ASMI)	6.8 vs. 7.7	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	¹⁷
		Higher appendicular fat percentage (for left, right lower and left, right upper extremities, respectively)	SFS scores				
		Left lower extremity	$\beta = 0.34$; $t = 2.32$; $p = 0.03$	ESRD	Simple FRAIL scale	44	¹⁸
		Right lower extremity	$\beta = 0.3$; $t = 2.05$; $p = 0.048$				
		Left upper extremity	$\beta = 0.37$; $t = 2.66$; $p = 0.01$				
		Right upper extremity	$\beta = 0.43$; $t = 3.09$; $p < 0.01$				
		Higher appendicular fat percentage (for left, right lower and left, right upper extremities, respectively)	Frail/Prefrail vs. Nonfrail				
		Left lower extremity	$\beta = 0.33$; $t =$	ESRD	self- report	44	¹⁸

			2.31; p = 0.03		instrument		
		Right lower extremity	$\beta = 0.32$; t = 2.28; p = 0.03		evaluating five dimensions of		
		Right upper extremity	$\beta = 0.33$; t = 2.35; p = 0.03		frailty (fatigue, resistance, ambulation, illnesses, and weight loss)		
	Lower lean mass						
			F/PF vs. NF				
		Whole body (kg)	34.7 vs. 43.1	ESRD	Simple FRAIL scale	44	18
		Cephalic area (g)	3059 vs. 3288				
		Trunk area (kg)	17.4 vs. 22.1				
		Right upper limb (g)	1831 vs. 2493				
		Left upper limb (g)	1869 vs. 2515				
		Right lower limb (g)	4920 vs. 6114				
		Left lower limb (g)	4650 vs. 6349				
			F vs. NF				
		lean body mass (i.e. sarcopenia) (in frail vs. nonfrail)	57.1% vs .14.7%	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	17
	BMI		22.53 vs. 26.16	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	16

Laboratory Data	eGFR (mL/min/1.72m ²)		18 vs. 50	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	17
		eGFRcys <30	Frailty prevalence 2.8	CKD stages 1-4	Fried Phenotypes	336	7*
		eGFRcys 30-44	Frailty prevalence 2.1				
		eGFRcys >60	Referent				
	Prealbumin (PRAB) (mg/dL)		28.9 vs. 38.3	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	17
	Serum albumin (g/L)		Pearson correlation coefficient r = -0.263 (p = 0.025)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	19
			38 vs. 41	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	17
			2.92 vs. 3.48	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	119	13
			3.61 vs. 3.85	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	16
			Frail with depression vs. Frail without depression vs. Nonfrail	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	20

		Calcium (mmol/L)	2.24 vs. 2.36	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	17
		Creatinine (umol/L)	299 vs. 115				
		Hemoglobin (g/dL)	Pearson correlation coefficient $r = -0.336$ ($p = 0.004$)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	19
			6.49 vs. 8.07 ($p = 0.037$)				
			10.35 vs. 10.97	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	16
		25-hydroxy vitamin D (ng/mL)	Pearson correlation coefficient $r = -0.363$ ($p = 0.002$)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	19
			11.58 vs. 17.09 ($p = 0.005$)				
	Miscellaneous	Dialysis clearance rate	↑	ESRD, under chronic dialysis	Simple FRAIL scale (SFS)	46	10
	Psychological						
	Mood	Mood Change	Negative change	CKD stage 5D (hemodialysis)	Edmonton Frail Scale (EFS)	N/A	21
	Mental Health						

	Anxiety	Hospital Anxiety and Depression Scale (HADS)	<u>Women</u> : ↑ in global, psychological, social frailty <u>Men</u> : ↑ in Physical frailty	ESRD, under online-haemodiafiltration (OL-HDF)	N/A	97	²²
	Depression	Hospital Anxiety and Depression Scale (HADS)	<u>Men</u> ↑ in global, psychological, physical frailty	ESRD, under online-haemodiafiltration (OL-HDF)	N/A	97	²²
		Incidence (%) (Self-reported Major Depression Inventory)	83 vs. 6	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	¹⁷
	Mental Function	Post-KT delirium	9.0% vs. 3.9%	CKD stage 5T	Fried Phenotypes	893	²³
	Sociological						
	Isolation						
	Interaction	Interaction with family	Good				²⁴
	Physical activity	Minnesota Leisure Time Activity (LTA)	95 vs. 735 (p<0.001)	CKD stage 5D (hemodialysis)	Fried Phenotypes	68	²⁵
		Low Physical Activity Questionnaire (LoPAQ)	280 vs. 798 (p=0.003)				
		Sitting (hours/day)	6.5 vs. 5 (p=0.04)				
	Nutritional Status	Overall subjective global assessment	5.04 vs. 5.41	CKD stage 5D	In-house	178	²⁰

	(SGA) (weight loss, anorexia, subcutaneous fat, muscle mass) (Frail with depression vs. Frail without depression vs. Nonfrail)		vs. 5.75 (p < 0.0001)	(peritoneal dialysis)	Chinese questionnaire		
			Spearman's rank correlation coefficient r = - 0.44, p < 0.0001	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	26
	Malnutrition inflammation score (MIS) (frail with depression vs. frail without depression vs. nonfrail)		9.48 vs. 7.13 vs. 5.12 (p < 0.0001)	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	20
			Spearman's rank correlation coefficient r = 0.40, p < 0.0001	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	26
Quality of Life	HRQoL						
		SF-36					
		Scores in physical functioning, blood pressure, role physical, and physical component summary	↓	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	17

		domains					
	Kidney Disease Quality of Life (KDQoL)		F vs. NF				
		Physical health	33.7 vs. 40.7	ESRD CKD stage 5D (conventional hemodialysis)	Fried Phenotypes	151	27
		Kidney disease effects	51.6 vs. 66.8				
Independence	Functional Independence Measure (FIM)			Elderly, ≥65y/o	Edmonton Frail Scale (EFS)	137	11
	Spearman's correlation coefficient	Frailty diagnosis with global FIM	-0.703 (p<0.001)				
		Frailty diagnosis with motor FIM	-0.714 (p<0.001)				
		Frailty diagnosis with cognitive FIM	-0.575 (p<0.001)				
		EFS scores with gross FIM	-0.53 (p<0.01)				
Health-care utilization	Hospitalization		90% vs. 53% (p = 0.04)	≥ 65 yo, predialysis, eGFR < 20 mL/min	Groningen frailty indicator (GFI)	65	15
		Cumulative number of inpatient health-care visits	↑	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	17
		Cumulative number of emergency health-care visits					
		Cumulative number of total health-care visits					

		Admissions/year	0.77727 vs. 0.2838	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	¹⁶
Composite	Number of complications (complications identified at data collection: High Pressure Cramping, Anemia, Weight loss Pain, Weakness, Weight gain Constipation, Heart Arrhythmia, Headache, Itch, Recurrent infections, Arterial hypertension)		Spearman's correlation 0.666 (p=0.000 in table) (p<0.05 in text)	Elderly (≥ 60 yo), with diagnosis of CKD	Edmonton Frail Scale	35	²⁸
	Higher number of comorbid conditions		6 vs. 4 (p = 0.03)				
	Charlson's comorbidity score		Spearman's rank correlation coefficient r = 0.40 (p < 0.0001)	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	²⁶

Complications

	Effect (descriptions)	Risk Difference	CKD Severity	Frailty Assessment	Sample Size	Reference
Biological						
Cardiovascular	Cerebrovascular Accident	OR 1.55 (1.05-2.99)	CKD stage 5D (hemodialysis)	Fried Phenotypes	2275	³
	QRS duration					
	Edmonton frailty scale	β coefficient = -0.29, t = -2.03 (p = 0.048)	CKD stage 5D (chronic hemodialysis)	Edmonton frailty scale	41	²⁹
	Simple FRAIL scale	β coefficient = -0.27, t = -1.84 (p = 0.05)		Simple FRAIL scale		
	Vascular Access failure	HR 2.63 (1.03-6.71)	ESRD (CKD stage 5D)	Self-reported simple FRAIL scale	51	³⁰
Renal Function Decline	Risk for death or dialysis therapy	2.5 (1.4-4.4)-fold greater	CKD stages 1-4	Fried Phenotypes	336	⁷
Immunological	Mycophenolate mofetil (MMF) dose reduction (MDR)	HR 1.29 (1.01-1.66)	CKD stage 5T	Fried Phenotypes	525	¹⁴
Cognitive	Modified Mini-Mental State (3MS)	-2.37 to -2.80 (1 year) (p=0.03)	ESRD	Fried Phenotypes	324	⁹
	Declined, 1-4 years post-KT (points/week)	Slope = -0.04 vs. 0.005	CKD stage 5T	Fried physical frailty phenotypes (PFP)	665	³¹

		At 4 year post-KT (points)	-5.5 (87.4 vs. 92.9)				
Functional status	Disability		F vs. Prefrail vs. NF				
		Need for activities of daily livings (ADL) assistance	OR 11.32 (5.49-23.32) vs. 1.93 (1.01-3.68) vs. 1.00	CKD stage 5D (hemodialysis)	Fried Phenotypes	742	³²
Diabetes	Diabetes		OR 1.35 (1.10-1.65)	CKD stage 5D	Fried Phenotypes	2275	³
Body composition	Bones						
		Bone Mineral Density (BMD)	One year follow-up, with frailty	ESRD CKD stage 5D (chronic hemodialysis)	Simple FRAIL Scale (SFS)	43	³³
		L1	$\beta = -0.4$, $t = -2.18$, $p=0.04$				
		L4	$\beta = -0.39$, $t = -2.1$, $p=0.046$				
		Femur Neck (FN)	$\beta = -0.5$, $t = -2.96$, $p<0.01$				
			$\beta = -4$, $t = -3.17$, $p = 0.004$				
		Total	$\beta = -0.53$, $t = -3.27$, $p < 0.01$	ESRD CKD stage 5D	Simple FRAIL Scale (SFS)	43	³³

					(chronic hemodialysis)			
		Areas	One year follow-up, with frailty	ESRD CKD stage 5D (chronic hemodialysis)	Simple FRAIL Scale (SFS)	43	33	
		Average L-spine areas	$\beta = -0.48$, t = -2.84, p < 0.01					
		Changes of average L-spine areas	$\beta = -0.5$, t = -3.02, p<0.01					
		Z-score	One year follow-up, with frailty					
		Percentage change of L1 Z-score	$\beta = -0.45$, t = -2.11, p=0.049					
		Vertebral Compression Fracture (VCF)	OR 1.8 (p = 0.01)	ESRD CKD stage 5D (chronic hemodialysis)	Simple FRAIL Scale (SFS)	43	34	
		Quantitative ultrasound (QUS) parameters of calcaneus						
		Speed of sound (SOS)	Standardized β (range, p value)	CKD stage 5D (maintenance hemodialysis)	Fried Phenotypes	214	35	
		Female (Five frailty criteria)	Negative (-0.253 to -0.439, p \leq 0.034)					

			Male (All criteria significant except weight loss)	Negative (-0.277 to -0.402, $p \leq$ 0.003)				
			Broadband ultrasound attenuation (BUA)	Standardized β (range, p value)				
			Female (All criteria significant except weakness and weight loss)	Negative (-0.209 to -0.354, $p \leq$ 0.045)				
			Male (All criteria significant except weight loss)	Negative (-0.171 to -0.371, $p \leq$ 0.045)				
			Stiffness index	Standardized β (range, p value)				
			Female (All criteria significant except weight loss)	Negative (-0.271 to -0.461, $p \leq$ 0.018)				
			Male (Five frailty criteria)	Negative (-0.183 to -0.461, $p \leq$ 0.048)				
			Muscles					
			Quadriceps muscle area (magnitude of association	Multivariable coefficient -30.3		Performance-based frailty (PbF)	80	36

		with PbF vs. 10 years of age)	cm ² (p = 0.02) vs. -6.6 cm ² (p = 0.0001)				
Laboratory data	Serum Albumin Concentrations (g/dL)						
		<3.2 vs. ≥3.9	OR 1.89 (1.30-2.59)		Fried Phenotypes	2275	³
		Hypoalbuminemia	Negative association (p = 0.01)	CKD stage 5D (maintenance hemodialysis) (ESRD)	Simple Frail Scale	46	³⁷
Psychological							
	Delirium	Post-KT delirium	OR 2.05 (1.02-4.13)	CKD stage 5T	Fried Phenotypes	893	²³
	Distress	Distress Thermometer	β = 0.35, t = 3.0 (95% CL = 0.12-0.58) (p = 0.003)	CKD stage 5D (hemodialysis)	Canadian frailty score	382	³⁸
Quality of Life	HRQoL						
		Fair/Poor HRQOL at follow-up (median 9.4 mo)	aOR 2.79 (1.32-5.90)	ESRD CKD stage 5T	Fried Phenotypes	233	³⁹
		Worsening HRQOL at follow-up (median 9.4 mo)	aRR 2.91 (1.08-7.80)				
		SF-36					
		Hierarchical regression	29% (p<0.001)	CKD stage 2-4	Fried Phenotypes	168	⁴⁰

		R ² change (effects of frailty on HRQoL) in Physical Component Summary (PCS)					
		Hierarchical regression R ² change (effects of frailty on HRQoL) in Mental Component Summary (MCS)	21.3% (p<0.001)				
		Physical components	Simple linear regression coefficient = -1.12 (-1.47 to -0.76) (p < 0.001)	CKD stages 3-5 (predialysis treatment)	Fried Phenotypes	61	41
		Mental components	Simple linear regression coefficient = -0.75 (-1.40 to -.016)				
		SF-12					
		MCS	Effect estimate 0.94 (0.91-0.97) (p<0.01)	CKD stage 5D (peritoneal dialysis, n=129; hemodialysis,	The Canadian Study of Health and Aging Clinical Frailty Scale (CFS)	251	42
		PCS	Effect estimate				

			0.88 (0.84-0.91) (p<0.01)	n=122)			
			KDQOL-SF scores within 3 months post-KT	F vs. NF			
			At KT	↓	CKD stage 5T	Fried Phenotypes	443 ⁴³
			Physical HRQoL	-6.31 points (95% CI -8.16 to -4.46)			
			Kidney disease-specific HRQoL	-6.53 points (95% CI -9.17 to -3.89)			
			Post-KT	Greater improvement			
			Physical HRQoL	1.35 points/month (0.65 to 2.05) vs. 0.34 points/month (-0.17 to 0.85)			
			Kidney disease-specific HRQoL	3.75 points/month (2.89 to 4.60) vs. 2.41 points/month			

					(1.78 to 3.04)				
				Constituent domains	Greater improvement				
				General health	4.93 points/month (3.51 to 6.35) vs. 2.87 points/month (1.82 to 3.92)				
				Effects of ESRD on daily living	7.10 points/month (5.68 to 8.51) vs. 4.01 points/month (2.99 to 5.03)				
				Cognitive function	2.88 points/month (1.80 to 3.96) vs. 1.28 points/month (0.50 to 2.07)				
				Social interaction	1.18 points/month (-0.06 to 2.43) vs. -				

					0.57 points/month (- 1.47 to 0.33)				
				Illness Intrusiveness Rating Scale	Effect estimate 1.14 (1.09-1.20)	CKD stage 5D (peritoneal dialysis, n=129; hemodialysis, n=122)	The Canadian Study of Health and Aging Clinical Frailty Scale (CFS)	251	42
				Barthel Index	Effect estimate 0.89 (0.86-.093)				
				Symptom score	Effect estimate 1.23 (1.13-1.34)				
				Hospital Anxiety and Depression Scale	Effect estimate 1.21 (1.11-1.31)				
				Falls	HR 2.1 (1.21- 3.92)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	1
					OR 2.39 (1.22- 4.71)	CKD stage 5D (maintenance hemodialysis)	Fried frailty index	762	44
				Higher numbers of falls	HR 3.09 (1.38- 6.90)	CKD stage 5D (hemodialysis)		95	45
				Time to first fall or fracture requiring medical attention	HR 1.60 (1.16- 2.20)	CKD stage 5D (maintenance hemodialysis)	Modified Fried Phenotypes by Bao Y ⁴⁶ .	1646	47
Graft Loss				Death-censored graft loss					

		F vs. NF (in patients with depressive symptoms)	aHR 6.20 (1.67, 22.95) vs. 3.16 (0.90, 11.04)	CKD stage 5T	Fried Phenotypes	773	⁴⁸
Health-care utilization	Hospitalization/Death		HR 1.56 (1.36-1.79)	CKD stage 5D	Fried Phenotypes	2275	³
	Hospitalization		HR 2.06 (1.18-3.58)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	¹
			aHR 1.80 (1.4-2.3)	CKD stage 5D (maintenance hemodialysis & peritoneal dialysis)	Adopted	1658	⁴⁹
			Relative risk = 1.43 (1.00-2.03)	CKD stage 5D (hemodialysis)	Fried Phenotypes	146	⁵⁰
		Number of hospitalizations for all causes	beta = 0.29 (p < 0.0001)	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	²⁶
		Number of hospitalizations related to cardiovascular events	beta = 0.37 (p < 0.0001)				
		Non-vascular access-related hospitalizations	aHR 1.98 (1.41-1.87) (內文應該寫錯，無勘誤)	CKD stage 5D	Fried Phenotypes	2275	³
	Time to first hospitalization		HR 1.26 (1.09-1.45)	CKD stage 5D (maintenance dialysis)	Earlier modification of Fried Phenotypes by Johansen et al ³ , but	1576	⁴⁶

				without weight loss.		
	Early Hospital Readmission (EHR)	aRR 1.61 (1.81-2.19) (p=0.002)	CKD stage 5T	Fried Phenotypes	383	51
	Duration of hospitalization					
	Hospital stay (days per year of follow up) (frail with depression vs. frail without depression vs. nonfrail)	26.62 (IQR 10.65-61.18) vs. 14.05 (IQR 3.57-37.27) vs. 8.04 (IQR 0.91-19.42) (p<0.0001)	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	20
	Total length of hospital stay	beta = 0.34 (p < 0.0001)	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	26
	Longer Length of Stay (LOS)					
	with delayed graft function (DGF), LOS	Relative Risk 1.15 (1.03-1.29)	CKD stage 5T	Fried Phenotypes	589	52
	With DGF, LOS ≥2 weeks	OR 1.57 (1.06-2.33)				
	≥2 weeks		CKD stage 5 to 5T	Fried Phenotypes	569	53
	Change in 3 categories (more frail)	OR 2.02 (1.20-3.40)				
	Change in frailty scores (more frail)	OR 1.92 (1.13-3.25)				
	With depressive symptoms (aRR difference between F	aRR 1.88 (1.70-2.08) vs. 1.38	CKD stage 5T	Fried Phenotypes	773	48

		and NF)	(1.27-1.52)				
		CES-D score (10-point increase) (aRR increase between F and NF)	aRR 1.23 (1.16-1.31) vs. 1.17 (1.08-1.27)				
Mortality	Mortality		2.17 fold	CKD stage 5T	Fried Phenotypes	537	⁵⁴
			HR 1.57 (1.25-1.97)	CKD stage 5D (maintenance dialysis)	Earlier modification of Fried Phenotypes by Johansen et al ³ , but without weight loss.	1576	⁴⁶
			HR 2.24 (1.60-3.15)	CKD stage 5D	Fried Phenotypes	2275	³
			HR 1.22 (1.04-1.43)	CKD stage 5D (incident chronic dialysis)	CFS	390	⁵⁵
			HR 4.28 (1.22-14.98)	Predialysis (eGFR ≤ 25 mL)	PRISMA questionnaire & Timed up and Go test	104	⁵⁶
			aHR 9.83 (1.80-53.7)	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	119	¹³
			HR 2.60 (1.04-6.49)	CKD stage 5D (hemodialysis)	Fried Phenotypes	146	⁵⁰
			HR 2.37 (1.11-5.02)	CKD stage 5D (maintenance hemodialysis & peritoneal dialysis)	Adopted	1658	⁴⁹

		20.45% vs. 12.36% (p<0.005)	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	16
	Performance-based frailty	HR 2.16 (1.41-3.29)	CKD stage 5D (hemodialysis)	Fried Phenotypes & a definition that substitutes self-reported measures available on the Medical Outcomes Study 36-Item Short Form (SF-36) for the physical performance and exhaustion criteria.	771	57
	Self-reported function-based frailty	HR 1.93 (1.24-3.00)				
	Patients who met both performance- and self-reported function-based frailty	HR 2.46 (1.51-4.01)				
	F vs. NF (in patients with depressive symptoms)	aHR 2.62 (1.03, 6.70) vs. 1.92 (0.68, 5.38)	CKD stage 5T	Fried Phenotypes	773	48
	At 24-month follow up, frail with depression vs. frail without depression vs. nonfrail	62.5% vs. 71.4% vs 86.6% (p=0.001)	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	20
	Prediction ability of comorbidities in F vs. NF	HR 0.75 (0.44-1.29) vs. 1.66 (1.17-2.35)	CKD stage 5T (KT candidates, on waitlist)	Fried Phenotypes	2086	58
	Out of 10 deceased within 1 year of initiation (percentage of F vs. NF)	30% vs. 9%	≥ 65 yo, predialysis, eGFR < 20 mL/min	Groningen frailty indicator (GFI)	65	15
	Risk for death or dialysis	2.5 (1.4-4.4)-fold	CKD stages 1-4	Fried Phenotypes	336	7

	therapy	greater				
	All-cause mortality					
	Adjusted	HR 1.66 (1.03-2.67)	CKD stage 5D (incident chronic dialysis)	Fried Phenotypes	370	59
	Among BMI ≥ 30 kg/m ²	HR 3.77 (1.10-12.92)				
	Above median Waist-Hip Ratio (WHR)	HR 2.38 (1.17-4.82)				
	Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) patients' mortality	HR 2.43 (1.48-3.99)	CKD stage 5D to 5T (RRT [hemodialysis, peritoneal dialysis, transplantation])	Inability to walk without help	425	60
	Mortality of patients with monoclonal gammopathy and ESRD caused by myeloma cast nephropathy (MCN), immunoglobulin light chain amyloidosis (ALA), or light-chain deposition disease (LCDD)	HR, 1.93 (1.58-2.36)	CKD stage 5D to 5T (RRT [hemodialysis, peritoneal dialysis, transplantation])	Inability to walk without help	1462	61
	Post-KT mortality					
	Change in 3 categories (more frail)	HR 2.27 (1.11-4.65)	CKD stage 5 to 5T	Fried Phenotypes	569	53
	Change in frailty scores	HR 2.36 (1.12-				

	(more frail)	4.99)				
Composite	Composite outcomes of all-cause death or cardiovascular hospitalization	HR 23.58 (1.61-346.03)	CKD stage 5D ESRD	Multidimensional frailty score based on comprehensive geriatric assessment (CGA) protocol	46	⁶²
	30-day postoperative (KT) complications according to Comprehensive Complication Index (CCI)	β =13.31, 95% CI 5.72-20.89 (p = 0.0007)	CKD stage 5T	Groningen Frailty Indicator	150	⁶³

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