Adverse Health Effects of Frailty in CKD Patients

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Cause

	Effect (descriptions)	Risk Difference	CKD severity	Frailty Assessment	Sample Size	Reference
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	[2]
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) OR 3.86 (1.00-14.88)	CKD stages 3-5	Fried Phenotypes	61	[3]
Vascular access	Use of a permanent vascular access (fistula or graft)	HR 0.71 (0.51-0.98)	CKD stage 5D (hemodialysis)	Fried Phenotypes	2275	[4]
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	[5]
Inflammatory	IL-6	Worse frailty	CKD stage 5D	Fried	762	[2]

			(hemodialysis)	Phenotypes		
	CRP	After adjustment, OR 1.76 (1.28-2.41) to 1.50 (1.07-2.09)	Chronic kidney insufficiency, serum creatinine ≥ 1.3 mg/dL	Fried Phenotypes	5888	[6]
	Fibrinogen					
Endocrinologic/ Metabolic	Diabetes	Frailty scores +0.7 points per year	CKD stage 5D (hemodialysis)	Fried Phenotypes	762	[2]
		OR 1.68 (1.16-2.45)	CKD stages 1-5	Fried Phenotypes	10256	[5]
	Obesity (IMC ≥ 30 kg/m^2)	OR 6.63 (1.16-36.77)	CKD stages 3-5	Fried Phenotypes	61	[3]
	Higher parathyroid hormones (PTH)	r= 0.30 (p= 0.01)	CKD stages 3-5	Fried Phenotypes	61	[3]
Body Composition	Higher fat mass	r= 0.25 (p= 0.04)	CKD stages 3-5	Fried Phenotypes	61	[3]
Cancer	Cancer	OR 1.89 (1.19-2.99)	CKD stages 1-5	Fried Phenotypes	10256	[5]
Arthritis	Arthritis	OR 3.34 (2.08-5.38)	CKD stages 1-5	Fried Phenotypes	10256	[5]
Laboratory Data	eGFR (mL/min/1.72m^2) reference: > 60					
	eGFRcys < 30	Frailty prevalence 2.8	CKD stages 1-4	Fried Phenotypes	336	[7]
	eGFRcys 30-44	Frailty prevalence 2.1				

Serum Albumin Concentrations (g/dL)	Frailty scores -1.1 points per g/dL	CKD stage 5D (hemodialysis)	Fried Phenotypes	762	[2]
Serum Creatinine <4 mg/dL*	RR 1.46 (1.22-1.71)	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	[1]
Testosterone, every 50% lower free form		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)				
25-hydroxy vitamin D (ng/mL)	Pearson correlation coefficient r = -0.363 (p = 0.002)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	[9]
	11.58 vs. 17.09 (p = 0.005)				
Hemoglobin	Pearson correlation coefficient r = -0.336 (p = 0.004)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	[9]
	6.49 g/dL vs. 8.07 g/dL (p = 0.037)				
	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	Adjusted, OR 1.76 (1.28-2.41) to 1.50	Chronic kidney insufficiency, serum	Fried Phenotypes	5888	[6]

	(1.07-2.09)	creatinine ≥1.3mg/dL

Non-adjusted differences in comorbidity and system-based influences

		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 (%)	26.4 vs. 12.0	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[10]
	Vascular Access	Catheter vs. Native/Prosthetic FAVI (%)	61.6% vs. 27.78/11.11%	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	[11]
	Endocrinologic/ Metabolic	Diabetes (%)	F vs. NF				
			64% vs. 49%	CKD stages 1-4	Fried Phenotypes	336	[7]
		Obesity (%)	F vs. NF				
			64% vs. 50%	CKD stages 1-4	Fried Phenotypes	336	[7]
			51.8% vs. 23.9%	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[10]
		BMI based on dry weight	31.5 vs. 27.6	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[10]
		BMI	22.53 vs. 26.16	CKD stage 5D	Fried	320	[11]

				(hemodialysis)	Phenotypes		
Cognitive	Executive Function		F vs. NF				
		Trail Making Tests A (TMTA) scores	+12.08	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[10]
		Trail Making Tests B (TMTB) scores	+33.15	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[10]
Immunological	Inflammatory						
		CRP (ln CRP) (mg/dL)	1.12 vs 0.28	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	119	[12]
		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	[13]
		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) (capitals)	36 vs. 1	CKD stage 5D (hemodialysis)	Fried Phenotypes	205	[1]
Body Composition	Lower lean mass						
		Lean body mass (in frail vs. nonfrail) (%)	57.1% vs .14.7%	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
Laboratory Data	Prealbumin (PRAB) (mg/dL)		28.9 vs. 38.3	CKD stage 1-5	Edmonton Frail Scale	41	[12]

					(EFS)		
		Serum albumin (mg/L)	Pearson correlation coefficient r = -0.263 (p = 0.025)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	[9]
			38 vs. 41	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
			29.2 vs. 34.8	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	119	[12]
			36.1 vs. 38.5	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	[11]
		Frail with depression vs. Frail without depression vs. Nonfrail	32.9 vs. 34.9 vs. 35.8 (p=0.025)	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	[15]
		Calcium (mmol/L)	2.24 vs. 2.36	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
		Hemoglobin (g/dL)	10.35 vs. 10.97	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	[11]
	Miscellaneous	Dialysis clearance rate (Kt/V and urea	↑	CKD stage 5D	FRAIL scale	46	[16]

		reduction ratio)			(chronic dialysis)			
	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 (EFS)	35	[17]
		Higher number of comorbid conditions		6 vs. 4 (p = 0.03)	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
		Charlson's comorbidity score		Spearman's rank correlation coefficient r = 0.40 (p < 0.0001)	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	[18]
Functional Status		Disability		F vs. NF				
			≥1 disability in activities of daily Living (ADLs)	15% vs. 5%	CKD stages 1-4	Fried Phenotypes	336	[7]
			≥1 disability in instrumental activities of daily living (IADLs)	60% vs. 28%				

			≥1 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	[19]
		Ability to perform basic activities of daily living		33.33% vs 76.4%	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	[11]
		Ability to perform transfers		38.8% vs. 84.7%				
Microbiota								
	Gut microbiota	Malnutrition-Inflammation-Score (MIS)		7.6 vs. 3.9	Stage 3b-4, eGFR 15-45ml/min	Fried Phenotype score	64 (and 15 control subjects)	[20]
			Abundance of unclassified Mogibacteriaceae and Oscillospira	Directly proportional to MIS				
			Abundance of Akkermansia, Ruminococcus, and Eubacterium	Inversely proportional to MIS				
		Bacterial Abundance of some genera (Mogibacteriacee, Coriobacteriacee, Eggerthella, Erwinia, Coprobacillus, Anaerotruncus, etc)		↑				
Neurological								

	EEG	Brain Wave		F vs. NF	ESRD, under chronic dialysis	FRAIL scale	46	[16]
			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				
Psychological								
	Mood	Mood Change		Negative change	CKD stage 5D (hemodialysis)	Edmonton Frail Scale	N/A	[21]

					(EFS)		
Mental Health							
	Anxiety	Hospital Anxiety and Depression Scale (HADS)	Women:↑in global, psychological, social frailty Men:↑in Physical frailty	ESRD, under online-haemodiafiltration (OL-HDF)	N/A	97	[22]
	Depression	Hospital Anxiety and Depression Scale (HADS)	Men↑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	[14]
Mental Function		Post-KT delirium	9.0% vs. 3.9%	CKD stage 5T	Fried Phenotypes	893	[23]
Sociological							
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 (SGA) (weight loss, anorexia, subcutaneous fat, muscle mass) (Frail with depression vs. Frail without depression vs. Nonfrail)	5.04 vs. 5.41 vs. 5.75 ($p < 0.0001$)	CKD stage 5D (peritoneal dialysis)	In-house Chinese questionnaire	178	[15]
		Spearman's rank correlation coefficient $r = -0.44$, $p < 0.0001$	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	[18]
	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	[15]
		Spearman's rank correlation coefficient $r = 0.40$, $p < 0.0001$	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	[18]
Quality of Life	HRQoL					
	SF-36					
	Scores in physical functioning, blood pressure, role physical,	↓	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]

		and physical component summary 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	[26]
		Kidney disease effects	51.6 vs. 66.8				
Independence	Functional Independence Measure (FIM)			Elderly, ≥65y/o	Edmonton Frail Scale (EFS)	137	[27]
	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	[19]
		Cumulative number of inpatient health-care visits	↑	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
		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	[11]

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	[4]
	QRS duration	β coefficient = −0.29, t = −2.03 (p = 0.048)	CKD stage 5D (chronic hemodialysis)	Edmonton frailty scale (EFS)	41	[28]
		β coefficient = −0.27, t = −1.84 (p = 0.05)		FRAIL scale		
	Vascular Access failure	HR 2.63 (1.03-6.71)	ESRD (CKD stage 5D)	Self-reported FRAIL scale	51	[29]
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	[13]
Cognitive	Modified Mini-Mental State (3MS)	-2.37 to -2.80 (1 year) (p=0.03)	ESRD	Fried Phenotypes	324	[10]
	Declined, 1-4 years post-KT (points/week)	Slope = -0.04 vs. 0.005	CKD stage 5T	Fried physical frailty phenotypes (PFP)	665	[30]
	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	[31]
Diabetes	Diabetes	OR 1.35 (1.10-1.65)	CKD stage 5D	Fried Phenotypes	2275	[4]
Body composition	Lower lean mass	F/PF vs. NF				
	Whole body (kg)	34.7 vs. 43.1	CKD stage 5D (hemodialysis)	Self- report instrument evaluating five dimensions of frailty (fatigue, resistance, ambulation, illnesses, and weight loss)	44	[32]
	Cephalic/trunk (g)	3059 vs. 3288 (cephalic); 17.4 vs. 22.1 (trunk)				
	Right/Left upper limb (g)	1831 vs. 2493 (right); 1869 vs. 2515 (left)				
	Right/Left lower limb (g)	4920 vs. 6114 (right); 4650 vs. 6349 (left)				
	Bones					

Bone Mineral Density (BMD)	One year follow-up, with frailty	ESRD CKD stage 5D (chronic hemodialysis)	FRAIL Scale	43	[33]
L1	ß = −0.4, t =−2.18, p=0.04				
L4	ß =−0.39, t =−2.1, p=0.046				
Femur Neck (FN)	ß =−0.5, t= −2.96, p<0.01				
	β = −4, t = −3.17, p = 0.004				
Total	ß = −0.53, t = −3.27, p < 0.01	ESRD CKD stage 5D (chronic hemodialysis)	FRAIL Scale	43	[33]
Areas	One year follow-up, with frailty	ESRD CKD stage 5D (chronic hemodialysis)	FRAIL Scale	43	[33]
Average L-spine areas	ß = −0.48, t =−2.84, p < 0.01				
Changes of average L-spine areas	ß = −0.5, t =−3.02, p<0.01				
Z-score	One year follow-up, with frailty				

	Percentage change of L1 Z-score	ß = −0.45, t =−2.11, p=0.049				
	Vertebral Compression Fracture (VCF)	OR 1.8 (p = 0.01)	ESRD CKD stage 5D (chronic hemodialysis)	FRAIL Scale	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 ≤ 0.034)				
	Male (All criteria significant except weight loss)	Negative (-0.277 to -0.402, p ≤ 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 ≤ 0.045)				

	Male (All criteria significant except weight loss)	Negative (-0.171 to -0.371, p ≤ 0.045)			
	Stiffness index	Standardized β (range, p value)			
	Female (All criteria significant except weight loss)	Negative (-0.271 to -0.461, p ≤ 0.018)			
	Male (Five frailty criteria)	Negative (-0.183 to -0.461, p ≤ 0.048)			
Muscles					
Quadriceps muscle area (magnitude of association with PbF vs. 10 years of age)	Multivariable coefficient -30.3 cm^2 (p = 0.02) vs. -6.6 cm^2 (p = 0.0001)	CKD stage 5D (hemodialysis)	Performance-based frailty (PbF)	80	[36]
Appendicular skeletal muscle mass index (ASMI)	Unadjusted 6.8 vs. 7.7; adjusted p < 0.05	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
Fat					

	Appendicular fat percentage	FRAIL scale				
	Left/Right lower extremity	t = 2.32; p = 0.03 (left); t = 2.05; p = 0.048 (right)	CKD stage 5D (hemodialysis)	FRAIL scale	44	[32]
	Left/Right upper extremity	t = 2.66; p = 0.01 (left); t = 3.09; p = <0.01 (right)				
	Appendicular fat percentage	Frail/Prefrail vs. Nonfrail				
	Left/Right lower extremity	t = 2.31; p = 0.03 (left); t = 2.28; p = 0.03 (right)	CKD stage 5D (hemodialysis)	Self- report instrument evaluating five dimensions of frailty (fatigue, resistance, ambulation, illnesses, and weight loss)	44	[32]
	Right upper extremity	t = 2.35; p = 0.03				
	Sarcopenia	aOR 12.2 (2.27-65.5)	CKD stage 5D (peritoneal dialysis)	Clinical Frailty Scale (CFS)	11912	[12]
Laboratory data	Serum Albumin Concentrations (g/dL)					
	<3.2 vs. ≥3.9	OR 1.89 (1.30-2.59)	CKD stage 5D	Fried Phenotypes	2275	[4]
	Hypoalbuminemia	Negative association (p =	CKD stage 5D (maintenance	Frail Scale	46	[37]

		0.01)	hemodialysis) (ESRD)			
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 R^2 change (effects of frailty on HRQoL) in Physical Component Summary (PCS)	29% (p<0.001)	CKD stage 2-4	Fried Phenotypes	168	[40]
	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, n=122)	The Canadian Study of Health and Aging Clinical Frailty Scale (CFS)	251	[42]
PCS	Effect estimate 0.88 (0.84-0.91) ($p<0.01$)				
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-	−6.53 points				

specific HRQoL	(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	[4]
	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 &	Adopted	1658	[49]

		peritoneal dialysis)			
	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	[18]
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	[4]
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 [4], but without weight loss.	1576	[46]
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	[15]

	Total length of hospital stay	beta = 0.34 (p < 0.0001)	CKD stage 5D (peritoneal dialysis)	Chinese questionnaire	193	[18]
	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 and NF)	aRR 1.88 (1.70-2.08) vs. 1.38 (1.27-1.52)	CKD stage 5T	Fried Phenotypes	773	[48]
	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 [4], but without weight loss.	1576	[46]
		HR 2.24 (1.60-	CKD stage 5D	Fried Phenotypes	2275	[4]

		3.15)			
		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)	CFS	119	[12]
		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	[11]
	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	771	[57]
	Self-reported function-based frailty	HR 1.93 (1.24-3.00)				
	Patients who met both performance- and self-reported function-based	HR 2.46 (1.51-4.01)				

frailty			exhaustion criteria.		
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	[15]
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	[19]
Risk for death or dialysis therapy	2.5 (1.4-4.4)-fold greater	CKD stages 1-4	Fried Phenotypes	336	[7]
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	HR 2.43 (1.48-	CKD stage 5D to 5T	Inability to walk without	425	[60]

	antibody (ANCA)-associated vasculitides (AAV) patients' mortality	3.99)	(RRT [hemodialysis, peritoneal dialysis, transplantation])	help		
	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 (more frail)	HR 2.36 (1.12-4.99)				
Composite	Composite outcomes of all-cause death or cardiovascular hospitalization	HR 23.58 (1.61-346.03)	CKD stage 5D (hemodialysis)	Multidimensional frailty score based on comprehensive geriatric assessment (CGA) protocol	46	[62]
	30-day postoperative (KT) complications according to Comprehensive Complication	β=13.31, 95% CI 5.72-20.89 (p = 0.0007)	CKD stage 5T	Groningen Frailty Indicator	150	[63]

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