Adverse Health Effects of Frailty in CKD Patients

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)	CKD stages 3-5	Fried Phenotypes	61	[3]
			OR 3.86 (1.00-14.88)				
	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 (hemodialysis)	Fried Phenotypes	762	[2]
		CRP Fibrinogen	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]
	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	336	[7]

			eGFRcys 30-44	Frailty prevalence 2.1		Phenotypes		
		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)				
		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						

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	[9]
	Endocrinologic/ Metabolic	Diabetes (%)					
			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	[9]
		BMI based on dry weight	31.5 vs. 27.6	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[9]
		BMI	22.53 vs. 26.16	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	[10]
	Cognitive	Mini-Mental State Examination		Elderly, ≥65y/o	Edmonton Frail	137	[11]

		(MMSE)				Scale (EFS)		
			Spearman's correlation coefficient of EFS scores with gross MMSE scores	-0.607 (p<0.01)				
		Executive Function		F vs. NF				
			Trail Making Tests A (TMTA) scores	+12.08	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[9]
			Trail Making Tests B (TMTB) scores	+33.15	CKD stage 5D (hemodialysis)	Fried Phenotypes	324	[9]
	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	Appendicular						
			Appendicular skeletal muscle mass index	6.8 vs. 7.7	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]

			(ASMI)					
			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	[15]
			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	[15]
			Right upper extremity	t = 2.35; p = 0.03				
		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	[15]
			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)				
			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 (EFS)	41	[14]
		Serum albumin (g/L)		Pearson correlation coefficient r = -0.263 (p = 0.025)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	[16]
				38 vs. 41	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
				29.2 vs. 34.8	CKD stage 5D (peritoneal	Clinical Frailty Scale (CFS)	119	[12]

				dialysis)			
			36.1 vs. 38.5	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	[10]
		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	[17]
		Calcium (mmol/L)	2.24 vs. 2.36	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]
		Hemoglobin (g/dL)	Pearson correlation coefficient r = -0.336 (p = 0.004)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	[16]
			6.49 vs. 8.07 (p = 0.037)				
			10.35 vs. 10.97	CKD stage 5D (hemodialysis)	Fried Phenotypes	320	[10]
		25-hydroxy vitamin D (ng/mL)	Pearson correlation coefficient r = -0.363 (p = 0.002)	CKD stage 5D (hemodialysis)	Fried Phenotypes	74	[16]
			11.58 vs. 17.09				

			(p = 0.005)				
	Miscellaneous	Dialysis clearance rate (Kt/V and urea reduction ratio)	↑	CKD stage 5D (chronic dialysis)	FRAIL scale	46	[18]
	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	[28]
		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	[26]
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	60% vs. 28%				

			activities of daily living (IADLs)					
			≥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	[10]
		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	[18]
		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 (EFS)	N/A	[21]
	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	[17]
		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	[17]
		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	↓	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	[14]

		physical, 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	[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	[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	[10]

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	[29]
			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	[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	[13]
	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	[4]
	Body composition	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	FRAIL Scale	43	[33]

						hemodialysis)			
			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			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)	CKD stage 5D	Fried Phenotypes	2275	[4]
	Hypoalbuminemia	Negative association (p = 0.01)	CKD stage 5D (maintenance hemodialysis) (ESRD)	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	[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 & 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	[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	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	[17]
	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 [4], but without weight loss.	1576	[46]
		HR 2.24 (1.60-3.15)	CKD stage 5D	Fried Phenotypes	2275	[4]
		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	[10]
	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	[17]
	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	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 (hemodialysis)	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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