

* Risk factors or causes of frailty among CKD patients.

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

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

		eGFRcys <30	Frailty prevalence 2.8	Fried Phenotypes	336	CKD stages 1-4	6*
		eGFRcys 30-44	Frailty prevalence 2.1				
		eGFRcys >60	Referent				
		Serum Albumin Concentrations (g/dL)	Frailty scores -1.1 points per g/dL	Fried Phenotypes	762	CKD stage 5D (hemodialysis)	4*
		Serum Creatinine <4 mg/dL*	RR 1.46 (1.22-1.71)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1*
		Testosterone, per 50% lower free testosterone*		Fried Phenotypes	440	CKD stage 5D (hemodialysis), men	7*
		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)	Fried Phenotypes	5888	Chronic kidney insufficiency, serum creatinine ≥1.3mg/dL	5
		LDL, HDL					
Lifestyle		Smoking*	RR 1.18 (1.04-	Fried	205	CKD stage 5D	1*

		1.34)	Phenotypes		(hemodialysis)	
Ethnicity	Hispanic*	Frailty scores +0.6 points per year	Fried Phenotypes	762	CKD stage 5D (hemodialysis)	⁴ *

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	Effect (descriptions)	Prevalence	CKD Severity	Frailty Assessment	Sample Size	Reference
Biological						
Cardiovascular	Heart Failure	30% vs 12%	CKD stages 1-4	Fried Phenotypes	336	³
	Angina	34% vs. 22%	CKD stages 1-4	Fried Phenotypes	336	³
Cerebrovascular	Cerebrovascular Disease Prevalence (%)	26.4 vs. 12.0	ESRD	Fried Phenotypes	324	⁵
Neurological	Brain Wave	F vs. NF	ESRD, under chronic dialysis	Simple FRAIL scale (SFS)	46	⁶
	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		Elderly, ≥65y/o	Edmonton	137	⁷

		(MMSE)				Frail Scale (EFS)		
			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	⁵
			Trail Making Tests B (TMTB) scores	+33.15	ESRD	Fried Phenotypes	324	⁵
	Microbiota	Gut Microbiota Composition			Stage 3b-4, eGFR 15-45ml/min	Fried Phenotype score	64 (and 15 control subjects)	¹⁰
			Malnutrition-Inflammation-Score (MIS)	7.6 vs. 3.9				
			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 (Mogibacteriaceae,	↑				

		Coriobacteriacee, Eggerthella, Erwinia, Coprobacillus, Anaerotruncus, etc)					
Immunological	Mycophenolate mofetil (MMF) dose reduction (MDR)		F vs. NF	CKD stage 5T	Fried Phenotypes	525	9
		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	CKD stages 1-4	Fried Phenotypes	336	3
		At least one disability in activities of daily Living (ADLs)	15% vs. 5%				
		At least one disability in instrumental activities of daily living (IADLs)	60% vs. 28%				
		At least one disability in mobility tasks	40% vs. 18%				
Endocrinologic/	Diabetes		F vs. NF				

	Metabolic		Prevalence	64% vs. 49%	CKD stages 1-4	Fried Phenotypes	336	³
			Obesity	F vs. NF				
			Prevalence	64% vs. 50%	CKD stages 1-4	Fried Phenotypes	336	³
			Prevalence	51.8% vs. 23.9%	ESRD	Fried Phenotypes	324	⁵
			BMI based on dry weight	31.5 vs. 27.6				
	Body Composition		Appendicular skeletal muscle mass index (ASMI)	6.8 vs. 7.7	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	¹¹
			Low lean body mass (i.e. sarcopenia) (in frail vs. nonfrail)	57.1% vs .14.7%				
	Laboratory Data		eGFR (mL/min/1.72m ²)	18 vs. 50	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	¹¹
			eGFRcys <30	Frailty prevalence 2.8	CKD stages 1-4	Fried Phenotypes	336	^{3*}
			eGFRcys 30-44	Frailty prevalence 2.1				
			eGFRcys >60	Referent				
			Albumin (g/L)	38 vs. 41	CKD stage 1-5	Edmonton	41	¹¹

		Calcium (mmol/L)	2.24 vs. 2.36		Frail Scale (EFS)		
		Creatinine (umol/L)	299 vs. 115				
	Miscellaneous	Dialysis clearance rate	↑	ESRD, under chronic dialysis	Simple FRAIL scale (SFS)	46	⁶
	Psychological						
	Mood	Mood Change	Negative change	CKD stage 5D (hemodialysis)	Edmonton Frail Scale (EFS)	N/A	¹³
	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	¹⁴
	Depression	Hospital Anxiety and Depression Scale (HADS)	<u>Men</u> ↑ in global, psychological, physical frailty	ESRD, under online-haemodiafiltration (OL-HDF)	N/A	97	¹⁴
		Incidence (%) (Self-reported Major Depression Inventory)	83 vs. 6	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	¹¹
	Mental Function	Post-KT delirium	9.0% vs. 3.9%	CKD stage 5T	Fried	893	¹⁵

					Phenotypes		
Sociological							
Isolation							
Interaction		Interaction with family	Good				16
Quality of Life	HRQoL						
	SF-36						
		Scores in physical functioning, blood pressure, role physical, and physical component summary domains	↓	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	11
	Falls (times)		115 vs. 12	CKD stage 5D (hemodialysis)	Fried Frailty Phenotypes	205	1
Independence	Functional Independence Measure (FIM)			Elderly, ≥65y/o	Edmonton Frail Scale (EFS)	137	7
	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						
		Cumulative number of inpatient health-care visits	↑	CKD stage 1-5	Edmonton Frail Scale (EFS)	41	11
		Cumulative number of emergency health-care visits					
		Cumulative number of total health-care visits					
		>3 times (n=141)	127 vs. 14	CKD stage 5D (hemodialysis)	Fried Frailty Phenotypes	205	1
		1-2 times (n=64)	40 vs. 24				

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	Effect (descriptions)	Risk Difference	Frailty Assessment	Sample Size	CKD Severity	Reference
Biological						
Cardiovascular	Cerebrovascular Accident	OR 1.55 (1.05-2.99)	Fried Phenotypes	2275	CKD stage 5D (hemodialysis)	⁴
	Permanent Vascular Access (fistula or graft)	HR 0.71 (0.51-0.98)	Fried Phenotypes	2275	CKD stage 5D (hemodialysis)	⁴
Renal Function Decline	Risk for death or dialysis therapy	2.5 (1.4-4.4)-fold greater	Fried Phenotypes	336	CKD stages 1-4	³
Immunological	Mycophenolate mofetil (MMF) dose reduction (MDR)	HR 1.29 (1.01-1.66)	Fried Phenotypes	525	CKD stage 5T	⁹
Cognitive	Modified Mini-Mental State (3MS)	-2.37 to -2.80 (1 year)	Fried Phenotypes	324	ESRD	⁵
Diabetes	Diabetes	OR 1.35 (1.10-1.65)	Fried Phenotypes	2275	CKD stage 5D	⁴
Laboratory data	Serum Albumin Concentrations (g/dL)		Fried Phenotypes	2275	CKD stage 5D	⁴
	<3.2 vs. ≥3.9	OR 1.89 (1.30-2.59)				
Psychological						
Delirium	Post-KT delirium	OR 2.05 (1.02-	Fried	893	CKD stage 5T	¹⁵

			4.13)	Phenotypes			
Quality of Life	HRQoL						
	SF-36						
		Hierarchical regression R ² change (effects of frailty on HRQoL) in Physical Component Summary (PCS)	29% (p<0.001)	Fried Phenotypes	168	CKD stage 2-4	17
		Hierarchical regression R ² change (effects of frailty on HRQoL) in Mental Component Summary (MCS)	21.3% (p<0.001)				
		KDQOL-SF scores in physical and kidney disease-specific HRQoL		Fried Phenotypes	443	CKD stage 5T	18
		At KT	↓				
		Post-KT	Greater increase				
Health-care utilization	Falls		HR 2.1 (1.21-3.92)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1
	Hospitalization/Death		HR 1.56 (1.36-1.79)	Fried Phenotypes	2275	CKD stage 5D	4
	Hospitalization		HR 2.06 (1.18-3.58)	Fried Phenotypes	205	CKD stage 5D (hemodialysis)	1

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