Cause of Frailty

Item	Description	References
Positive Narration		
Model: CKD→lower energy intake→sarcopenia→physical frailty Lower entergy intake: 1/3 of patients with ESRD present anorexia; uremic milieu and inflammation→loss of appetite; Sarcopenia: physical inactivity→reduced lean body mass→sarcopenia; metabolic acidosis→sarcopenia		**Nixon, A. C., Bampouras, T. M., Pendleton, N., Woywodt, A., Mitra, S., & Dhaygude, A. (2017). Frailty and chronic kidney disease: current evidence and continuing uncertainties. Clinical kidney journal, 11(2), 236-245.**
Sarcopenia	Influences each other.	**Johansen, K. L., Delgado, C., Bao, Y., & Tamura, M. K. (2013, November). Frailty and dialysis initiation. In Seminars in dialysis (Vol. 26, No. 6, pp. 690-696).**
Acidosis (inducing 1.sarcopenia [caspase-3 and the ubiquitin proteasome system, inhibits intracellular signalling of insulin and IGF-1 and increases adrenal glucocorticoid production] and 2. pain + itch [ASIC3 and TDAG8])	(We further adjusted for comorbid conditions that we had hypothesized to be related to frailty (diabetes, arthritis, cancer, chronic liver disease, and chronic lung disease) but not caused by chronic kidney disease.)	**Wilhelm-Leen, E. R., Hall, Y. N., Tamura, M. K., & Chertow, G. M. (2009). Frailty and chronic kidney disease: the third national health and nutrition evaluation survey. The American journal of medicine, 122(7), 664-671.**
	(In subsequent analyses, we also adjusted for factors that often complicate chronic kidney disease to potentially explain any association identified between chronic kidney disease and frailty. These factors included sarcopenia (estimated using bioelectrical impedance analysis parameters), anemia (hemoglobin concentration), acidosis (serum bicarbonate concentration), inflammation (C-reactive protein concentration), vitamin D deficiency, and overt cardiovascular disease, as described above.)	
	Acidosis is the key contributor of sarcopenia and frailty.	**Nixon, A. C., Bampouras, T. M., Pendleton, N., Woywodt, A., Mitra, S., & Dhaygude, A. (2017). Frailty and chronic kidney disease: current evidence and continuing uncertainties. Clinical kidney journal, 11(2), 236-245.**
Dialysis clearance rate ***p.s. dialysis clearance rate = Kt/V + urea reduction ratio***	Dialysis clearance rates measured the same time as frailty: moderately to severely frail patients have higher dialysis clearance rates.	**(1)**Chao, C.-T., Lai, H.-J., Tsai, H.-B., Yang, S.-Y., &Huang, J.-W. (2017). Frail phenotype is associated with distinct quantitative electroencephalographic findings among end-stage renal disease patients: an observational study. BMC Geriatrics, 17(1), 277.
Diabetes mellitus, hypertension (HTN), cerebrovascular accident (CVA), left ventricular dysfunction (LVD), peripheral vascular disease (PVD), smoking, hepatitis C, inadequate dialysis, intradialytic hypotension (IDH), interdialytic weight gain, low serum creatinine <4 mg/dL, and anemia (Hb <10 g/dL)	On univariate analysis, statistically significantly different between frail and nonfrail groups.	**Yadla, M., John, J. P., & Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. Saudi Journal of Kidney Diseases and Transplantation, 28(1), 15.**
HTN, PVD, CVA, anemia, smoking, and IDH	On multivariate analysis, statistically signigicantly different between frail and nonfrail groups	**Yadla, M., John, J. P., & Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. Saudi Journal of Kidney Diseases and Transplantation, 28(1), 15.**
HTN, CVA, LVD, PVD, smoking, IDH, Kt/V (dialysis adequacy), serum creatinine, and hemoglobin	RR=1.1-1.5 between frail and nonfrail groups	**Yadla, M., John, J. P., & Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. Saudi Journal of Kidney Diseases and Transplantation, 28(1), 15.**
Uraemia	Uremia (malnutrition, anemia, metabolic acidosis, fluid overload) → Frailty (weight loss, exhaustion, weakness, low physical activity)	**Johansen, K. L., Delgado, C., Bao, Y., &Tamura, M. K. (2013). Frailty and dialysis initiation. In Seminars in dialysis (Vol. 26, pp. 690–696). Wiley Online Library.**
Testosterone	OR, per 50% lower free testosterone (95% CI): Being frail: 1.40 (1.12–1.69); Becoming frail over 12 months: 1.40 (1.07–1.73)	**Chiang, J. M., Kaysen, G. A., Segal, M., Chertow, G. M., Delgado, C., & Johansen, K. L. (2018). Low testosterone is associated with frailty, muscle wasting and physical dysfunction among men receiving hemodialysis: a longitudinal analysis. Nephrology Dialysis Transplantation.**
Inflammatory state	The inflammatory state is also associated with an increase in resting energy expenditure that may contribute to the imbalance of muscle protein homeostasis and, in turn, the frailty syndrome [18, 19].	**Nixon, A. C., Bampouras, T. M., Pendleton, N., Woywodt, A., Mitra, S., & Dhaygude, A. (2017). Frailty and chronic kidney disease: current evidence and continuing uncertainties. Clinical kidney journal, 11(2), 236-245.**
Viral infection - HCV	**Frailty vs. Nonfrail in patients with serological infections due to hepatitis C (number of patients)**	**Yadla, M., John, J. P., & Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. Saudi Journal of Kidney Diseases and Transplantation, 28(1), 15.**
	36 vs. 1 (P = 0.004)	
Negative narration		
The relationship between frailty and chronic kidney disease cannot be fully explained by the increased prevalence of sarcopenia, anemia, acidosis, inflammation, and overt cardiovascular disease among persons with chronic kidney disease		**Wilhelm-Leen, E. R., Hall, Y. N., Tamura, M. K., & Chertow, G. M. (2009). Frailty and chronic kidney disease: the third national health and nutrition evaluation survey. The American journal of medicine, 122(7), 664-671.**

Adverse Psyhological Effects of Frailty Among CKD Patients				
Related adverse health effects	Method	References Conditions Data	p-value	Sample Group
Mood	The Edmonton Frail Scale	**Orlandi & Gesualdo, 2014**		N/A
		The Edmonton Frail Scale itself evaluates nine domains, with mood being one of		
Good interaction with family	Interview	**Moffatt, Moorhouse, Mallery, Landry, & Tennankore, 2018**		
		Interview only		
Cognitive impairments	Review	**Kittiskulnam, P. et al. (2016). Consequences of CKD on Functioning. Seminars in Nephrology, 36(4), 305–318.**		
		There's no adverse health effects of frailty other than mortality and morbidities		
	Grouping: Nonfrail, intermediate frail, and frail. Fried frailty phenotype.	**McAdams-Demarco, M. A., Tan, J., Salter, M. L., Gross, A., Meoni, L. A., Jaar, B. G., … Sozio, S. M. (2015). Frailty and cognitive function in incident hemodialysis patients. Clinical Journal of the American Society of Nephrology, 10(12), 2181–2189.**		A longitudinal cohort study (Predictors of Arrhythmic and Cardiovascular Risk in ESRD [PACE] trial; R01DK072367) with 324 adults enrolled (November 2008 to July 2012), 95% of which were enrolled within the first month of hemodialysis. Patients location: 27 free-standing dialysis centers in Baltimore, Maryland, and six surrounding counties. Eligible criteria: ≥ 18 years at enrollment and the ability to speak English.
	Cognitive function: Global cognitive function: Modified Mini-Mental State (3MS); Speed/Attention: Trail Making Tests A and B (TMTA and TMTB)*.	**Nonfrail vs. Intermediate Frail vs. Frail**		
	Cognitive impairment was defined as a score <80 for the 3MS, a time 1.5 SD above the mean (from this cohort) for the TMTA/TMTB.	At cohort entry: 3MS (points): Reference vs. -1.29 (-3.05 to 0.48) vs. -2.37 (-4.21 to -0.53); TMTA (seconds): Reference vs. 6.12 (−0.94 to 13.18) vs. 12.08 (4.73 to 19.43); TMTB (seconds): Reference vs. 19.87 (−2.34 to 42.08) vs. 33.15 (9.88 to 56.42)	At cohort entry: 3MS: 0.01; TMTA: <0.001; TMTB: 0.01	
	*The TMTA and TMTB are time tests that measure executive function. Both of these tests assess scanning, speed of processing, attention and concentration, and psychomotor speed, and the TMTB further assesses cognitive shifting and complex sequencing function. The tests measure the time required to connect a series of sequentially numbered (TMTA) and numbered/lettered (TMTB) circles.	At 1-year follow-up: 3MS (points): Reference vs. −1.74 (−4.16 to 0.69) vs. −2.80 (−5.37 to −0.24)	At 1-year follow-up: 3MS: 0.03	
Functional independence		**Fabrício-Wehbe, Suzele Cristina Coelho, Schiaveto, Fábio Veiga, Vendrusculo, Thaís Ramos Pereira, Haas, Vanderlei José, Dantas, Rosana Aparecida Spadoti, & Rodrigues, Rosalina Aparecida Partezani. (2009). Adaptação cultural e validade da Edmonton Frail Scale - EFS em uma amostra de idosos brasileiros. Revista Latino-Americana de Enfermagem, 17(6), 1043-1049.**		A subsample of 137 elderly people was selected from 515 elderly using simple random sampling (SRS).
	Frailty grouping: Edmonton Frail Scale (EFS).	**Spearman's correlation coefficient of frailty diagnosis with global, motor, and cognitive FIM**		
	Functional independence: Functional Independence Measure (FIM).	Spearman's correlation coefficient: -0.703 (moderate), -0.714 (moderate), -0.575 (weak)	All correlations: <0.01	
	Cognitive assessment: Mini-Mental State Examination (MMSE).	**Spearman's correlation coefficient of frailty scores (EFS) with gross functional dependence (FIM) and the gross MMSE score**		
		Spearman's correlation coefficient: -0.53 and -0.607 (weak)	<0.01	
		Spearman's correlation coefficient between functional independence on the EFS and FIM scores		
		Spearman's correlation coefficient: -0.5	<0.01	
Depression	descriptive cross-sectional study	**SI, A. P., Senior, P. A., Field, C. J., Jindal, K., & Mager, D. R. (2018). Frailty, Health Related Quality of Life, Cognition, Depression, Vitamin D and Health Care Utilization in an Ambulatory Adult Population with Type 1 and Type 2 Diabetes Mellitus and Chronic Kidney Disease: a cross sectional analysis. Canadian Journal of Diabetes.**		41 ambulatory adults (41 through 83 years of age) with type 1 (n=3) or type 2 (n=38) diabetes mellitus and CKD (stages 1 through V). Exclusion criteria: Thoses who were on dialysis (estimated glomerular filtration rate <10 mL/min/1.73 m^2) and had body weights >136 kg, and coinciding comorbidities known to influence vitD metabolism were excluded.
		Frail vs. Nonfrail		
	Depression: the validated, self-reported Major Depression Inventory (scores ≥20 are considered abnormal)		Depression: 0.0002	
HRQOL	Narrative	**Soni, R. K., Weisbord, S. D., & Unruh, M. L. (2010). Health-related quality of life outcomes in chronic kidney disease. Current opinion in nephrology and hypertension, 19(2), 153.**		
		Narrative only		
		Kanauchi, M., Kubo, A., Kanauchi, K., & Saito, Y. (2008). Frailty, health-related quality of life and mental well-being in older adults with cardiometabolic risk factors. International journal of clinical practice, 62(9), 1447-1451.		
		Nonfrail vs. Frail		
			≤ 0.001	
	descriptive cross-sectional study	**SI, A. P., Senior, P. A., Field, C. J., Jindal, K., & Mager, D. R. (2018). Frailty, Health Related Quality of Life, Cognition, Depression, Vitamin D and Health Care Utilization in an Ambulatory Adult Population with Type 1 and Type 2 Diabetes Mellitus and Chronic Kidney Disease: a cross sectional analysis. Canadian Journal of Diabetes.**		41 ambulatory adults (41 through 83 years of age) with type 1 (n=3) or type 2 (n=38) diabetes mellitus and CKD (stages 1 through V). Exclusion criteria: Thoses who were on dialysis (estimated glomerular filtration rate <10 mL/min/1.73 m^2) and had body weights >136 kg, and coinciding comorbidities known to influence vitD metabolism were excluded.
		Frail vs. Nonfrail		
	HRQoL: the validated self-reported SF-36		SF-36 scores (adjusted for differences in CKD stage): physical functioning: 0.004 blood pressure: 0.001 role physical: 0.003 physical component summary: 0.002	
	PREPROCESSING **Frailty:** Fried phenotypes **Grouping:** nonfrail and frail (intermediate frail and frail combined) **HRQOL:** KDQOL-SF (generic core [Short Form-36 (SF-36)] and 11 multi-item kidney disease-specific scales), scores linearly converted to 0 to 100 scales. **ANALYSIS METHOD** **Relationship between frailty and physical, mental, and kidney disease-specific HRQOL at KT:** Multivariable linear regression **Within-individual changes in HRQOL scores among frail and nonfrail recipients:** paired t test **HRQOL between frail and nonfrail:** Student t	**McAdams-DeMarco, M. A., Olorundare, I. O., Ying, H., Warsame, F., Haugen, C. E.,**		443 KT recipients at Johns Hopkins Hospital (n = 370), Baltimore, Maryland (May 2014 to May 2017) and the University of Michigan (N = 73), Ann Arbor, Michigan (March 2015 to June 2016).
		Frail vs. Nonfrail (At Kidney Transplant)		
			Worse physical HRQOL: <0.001	
			Worse kidney disease-specific HRQOL: 0.001	
			Similar mental HRQOL: 0.43	
		Frail vs. Nonfrail (Post-Kidney Transplant)		
			Greater rates of improvement in:	
		Physical HRQOL: 1.35 points/month (95% CI, 0.65-2.05) vs. 0.34 points/month (95% CI, −0.17-0.85)	(1) physical HRQOL: 0.02	
		Kidney Disease-specific HRQOL: 3.75 points/month (95% CI, 2.89-4.60) vs. 2.41 points/month (95% CI, 1.78-3.04)	(2) kidney disease-specific HRQOL: 0.01	
		Mental HRQOL: 0.54 points/month (95% CI, −0.17-1.25) vs. 0.46 points/month (95% CI, −0.06-0.98)	No difference in mental HRQOL: 0.85	
	HRQOL: includes **PCS** (Physical Component Summary, calculated based on physical functioning, role limitations due to physical problems, body pain, and general health perception) and **MCS** (Mental Component Summary, calculated base on role limitations due to emotional problems, social func- tioning, mental health, and vitality).	**Lee, S. J., Son, H., & Shin, S. K. (2015). Influence of frailty on health-related quality of life in pre-dialysis patients with chronic kidney disease in Korea: A cross-sectional study. Health and Quality of Life Outcomes, 13(1).**		Conducted at an outpatient CKD clinic in a general hospital in Korea from March to September 2014.
		Model 2 (hierarchical regression, frailty included) vs. Model 1 (frailty excluded)		
		R^2 change = 29%	Lower PCS: <0.001	
		R^2 change = 21.3%	Lower MCS: <0.001	

Adverse Physiological Effects of Frailty Among CKD Patients					
Related adverse health effect	Method	References Conditions Data	p-value	Sample Group	comment
CHF: Limiting implementation and tolerability of conventional		**Murad, K., & Kitzman, D. W. (2012). Frailty and multiple comorbidities in the elderly**		N/A	
	No data support	**Frailty and multiple comorbidities often limit implementation and tolerability of**			
Heart failure	Prevalent diseases: defined based on participant responses to the SKS questionnaire, medication use, laboratory findings, and hospitalizations that occurred after initial SKS enrollment, but prior to frailty assessment. Frailty: Fried Phenotypes	**Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K. V., De Boer, I. H., ... & Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. American Journal of Kidney Diseases, 60(6), 912-921.**		Seattle Kidney Study (SKS) 336 non-dialysis-dependent patients with stages 1-4 CKD with eGFR <90 mL/min/1.73 m^2 or evidence of microalbuminuria enrolled in the Seattle Kidney Study, a clinic-based cohort study. Finding compared with community-dwelling older adults in the Cardiovascular Health Study.	
		Nonfrail vs. Frail			
		Heart Failure Prevalence (%):12 vs. 30			
Angina	Prevalent diseases: defined based on participant responses to the SKS questionnaire, medication use, laboratory findings, and hospitalizations that occurred after initial SKS enrollment, but prior to frailty assessment. Frailty: Fried Phenotypes	**Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K. V., De Boer, I. H., ... & Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. American Journal of Kidney Diseases, 60(6), 912-921.**		Seattle Kidney Study (SKS) 336 non-dialysis-dependent patients with stages 1-4 CKD with eGFR <90 mL/min/1.73 m^2 or evidence of microalbuminuria enrolled in the Seattle Kidney Study, a clinic-based cohort study. Finding compared with community-dwelling older adults in the Cardiovascular Health Study.	
		Nonfrail vs. Frail			
		Angina Prevalence(%): 22 vs. 34			
Brain wave	Frailty: simple FRAIL scale (SFS), Fatigue, Resistance, Ambulation, Illness, and Loss of body weight (leading to the acronym "FRAIL")	**Chao, C.-T., Lai, H.-J., Tsai, H.-B., Yang, S.-Y., &Huang, J.-W. (2017). Frail phenotype is associated with distinct quantitative electroencephalographic findings among end-stage renal disease patients: an observational study. BMC Geriatrics, 17(1), 277.**		Patients with ESRD under chronic dialysis with catastrophic illness certificates were prospectively enrolled from National Taiwan University Hospital Jinshan branch	
	Brain wave: electroencephalography, a total of 21 silver/silver chloride cup electrodes were placed on the scalp, as per International 10-20 system.	**moderate to severe frailty v. none to mild frailty**		Exclusion criteria: refusal to participate and pregnancy	
	Continuous variables were expressed as mean ± standard deviation and compared between groups using a Student's t-test or one-way analysis of variance (ANOVA)	DAR (global): 283 ± 679 vs. 2971 ± 4859	DAR (gloibal): 0.02		
	Spectral analysis with brain EEG mapping for the different frequency bands was also done to evaluate anatomical clustering.	DARs (left frontal): 135 ± 250 vs. 3073 ± 4702	DARs (left frontal): 0.01		
		left TO: 197 ± 318 vs. 3708 ± 6398,	Left TO: 0.01		
		Central: 55 ± 96 vs. 1773 ± 3262,	Central: 0.03		
		right TO: 187 ± 261 vs. 4400 ± 7763,	Right TO: 0.02		
		global DTABR: 191 ± 469 vs. 1781 ±	Global DTABR: 0.02		
		DTABRs (left frontal): 86 ± 158 vs.	DTABR (left frontal): <0.01		
		left TO: 130 ± 210 vs. 1884 ± 2828	Left TO: 0.01		
		Central: 39 ± 65 vs. 1132 ± 1957	Central: 0.02		
		right TO DTABR: 126 ± 178 vs. 2960 ±	Right TO DTABR: 0.03		
			Overall: 0.02		
Diabetes	Prevalent diseases: defined based on participant responses to the SKS questionnaire, medication use, laboratory findings, and hospitalizations that occurred after initial SKS enrollment, but prior to frailty assessment. Frailty: Fried Phenotypes	**Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K. V., De Boer, I. H., ... & Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. American Journal of Kidney Diseases, 60(6), 912-921.**		Seattle Kidney Study (SKS) 336 non-dialysis-dependent patients with stages 1-4 CKD with eGFR <90 mL/min/1.73 m^2 or evidence of microalbuminuria enrolled in the Seattle Kidney Study, a clinic-based cohort study. Finding compared with community-dwelling older adults in the Cardiovascular Health Study.	
		Nonfrial vs. Frail			
		Diabetes Prevalence (%): 49 vs. 64			
Obese	Prevalent diseases: defined based on participant responses to the SKS questionnaire, medication use, laboratory findings, and hospitalizations that occurred after initial SKS enrollment, but prior to frailty assessment. Frailty: Fried Phenotypes	**Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K. V., De Boer, I. H., ... & Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. American Journal of Kidney Diseases, 60(6), 912-921.**		Seattle Kidney Study (SKS) 336 non-dialysis-dependent patients with stages 1-4 CKD with eGFR <90 mL/min/1.73 m^2 or evidence of microalbuminuria enrolled in the Seattle Kidney Study, a clinic-based cohort study. Finding compared with community-dwelling older adults in the Cardiovascular Health Study.	
		Nonfrail vs. Frail			
		Obese (% in all nutritional status): 50 vs. 64			
		McAdams-DeMarco, M. A., Tan, J., Salter, M. L., Gross, A., Meoni, L. A., Jaar, B. G., ... & Sozio, S. M. (2015). Frailty and cognitive function in incident hemodialysis patients. Clinical Journal of the American Society of Nephrology, 10(12), 2181-2189.		A longitudinal cohort study (Predictors of Arrhythmic and Cardiovascular Risk in ESRD [PACE] trial; R01DK072367) with 324 adults enrolled (November 2008 to July 2012), 95% of which were enrolled within the first month of hemodialysis. Patients location: 27 free-standing dialysis centers in Baltimore, Maryland, and six surrounding counties.	
		Nonfrail vs. Intermediate Frail vs. Frail (at baseline)			
	Body mass index (BMI): self-reportd height and dry weight.	Dry weight body mass index (kg/m^2): 27.6 vs. 29.7 vs. 31.5	Dry weight body mass index (kg/m^2): 0.004	Eligible criteria: ≥ 18 years at enrollment and the ability to speak English.	
		Obese (%): 23.9 vs. 41.8 vs. 51.8	Obese: <0.001		
Disability ADL (activities of daily living) IADL (instrumental activities of daily living) Falls	assessed by asking about difficulties with 15 tasks of daily life, including ADLs, instrumental ADLs (IADLs), and mobility tasks.	**Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K. V., De Boer, I. H., ... & Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. American Journal of Kidney Diseases, 60(6), 912-921.**		Seattle Kidney Study (SKS) 336 non-dialysis-dependent patients with stages 1-4 CKD with eGFR <90 mL/min/1.73 m^2 or evidence of microalbuminuria enrolled in the Seattle Kidney Study, a clinic-based cohort study. Finding compared with community-dwelling older adults in the Cardiovascular Health Study.	
		Nonfrail vs. Frail			
		ADL (%):5 vs. 15	ADL: 0.009		
		IADL (%):28 vs. 60	IADL: <0.001		
		Mobility Disability (%):18 vs. 40	Mobility Disability: 0.001		
Cerebrovascular disease	**Participant-reported medical history, augmented with data from US Centers for Medicare and Medicaid Services Form-2728 and from chart abstraction**: other comorbidities including cardiovascular diseases, congestive heart failure, rheumatoid arthritis, cancer, diabetes, hypertension, or chronic obstructive lung diseases. Unknown for cerebrovascular disease, not mentioned specifically.	**McAdams-DeMarco, M. A., Tan, J., Salter, M. L., Gross, A., Meoni, L. A., Jaar, B. G., ... & Sozio, S. M. (2015). Frailty and cognitive function in incident hemodialysis patients. Clinical Journal of the American Society of Nephrology, 10(12), 2181-2189.**		A longitudinal cohort study (Predictors of Arrhythmic and Cardiovascular Risk in ESRD [PACE] trial; R01DK072367) with 324 adults enrolled (November 2008 to July 2012), 95% of which were enrolled within the first month of hemodialysis. Patients location: 27 free-standing dialysis centers in Baltimore, Maryland, and six surrounding counties.	Although previous studies of adults with CKD have found that lower kidney function is associated with worse cognitive function (36,37), we have identified a high-risk subgroup of patients with ESRD: namely, those who are frail who have more profound cognitive loss.
		Nonfrail vs. Intermediate frail vs. Frail		Eligible criteria: ≥ 18 years at enrollment and the ability to speak English.	
		Cerebrovascular disease(%): 12.0 vs. 22.1 vs. 26.4	Cerebrovascular disease: 0.03		
Mycophenolate mofetil (MMF) dose reduction (MDR)	**Frailty identification:** Fried frailty phenotypes, ≥2 components **Grouping**: Frail (frail and intermediate frail are both referred to as frail empirically) and nonfrail **Definition of MDR**: a reduction in MMF immunosuppression to <2000 mg/day for Mycophenolate mofetil (Cellcept) and <1440 mg/day for mycophenolic acid (Myfortic).	McAdams-DeMarco, M. A., Law, A., Tan, J., Delp, C., King, E. A., Orandi, B., ... &		Single-center study, 525 KT patients. Prevalence of: frailty (at KT): 19.5% intermediate frailty (at KT): 33.2%	
		Nonfrail vs. Frail			
		MDR over time % (95% CI): **1 year since KT: 40 (34-47) vs. 44 (39-51)** **2 years since KT: 45 (39-52) vs. 54 (48-61)** **3 years since KT: 51 (44-58) vs. 67 (59-75)**	Cumulative incidence of MDR: Log Rank P=0.02		
		Hazard ratio of MDR: 1.29 (95% CI, 1.01-1.66)	Hazard ratio of MDR: 0.04		
Laboratory data	descriptive cross-sectional study	**Si, A. P., Senior, P. A., Field, C. J., Jindal, K., & Mager, D. R. (2018). Frailty, Health Related Quality of Life, Cognition, Depression, Vitamin D and Health Care Utilization in an Ambulatory Adult Population with Type 1 and Type 2 Diabetes Mellitus and Chronic Kidney Disease: a cross sectional analysis. Canadian Journal of Diabetes.**		41 ambulatory adults (41 through 83 years of age) with type 1 (n=3) or type 2 (n=38) diabetes mellitus and CKD (stages 1 through V).	
		Frail vs. Nonfrail		Exclusion criteria: Those on dialysis (estimated glomerular filtration rate <10 mL/min/1.73 m^2) and had body weights >136 kg. Coinciding comorbidities known to influence vitD metabolism were excluded.	
	Laboratory data: routine clinical blood work	Laboratory data: eGFR (mL/min/1.72 m2): 18±9 vs. 50± 29; Albumin (g/L): 38±2.7 vs. 41±2.8; Creatinine (umol/L): 299 (160–408) vs. 115 (82–227); Calcium (mmol/L): 2.24±0.18 2.36± 0.13	Laboratory data: eGFR: 0.007; Albumin: 0.04; Creatinine: <0.05; Calcium: 0.05		
	Frailty: Fried frailty criteria (>3 frail, <3 nonfrail) Primary outcome: prevalence of frailty among the studied population Secondary outcome: frailty as a marker of falls, hospitalizations, and deaths or not	**Yadla, M., John, J. P., & Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. Saudi Journal of Kidney Diseases and Transplantation, 28(1), 15.**		205 prospective patients out of a total of 221 patients undergoing maintenance hemodialysis in Saudi center for organ transplantation were studied for the predictors of frailty.	
		Frail vs. Nonfrail (causal relationship doubt)			
		HTN, CVA, LVD, PVD, smoking, IDH, serum creatinine, and hemoglobin: RR: 1.1-1.5	Significant		
	eGFRcys and eGFRcr: categorized using a priori–accepted categories of ≥60, 45-59, 30-44, and <30 mL/min/1.73 m^2.	**Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K. V., De Boer, I. H., ... & Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. American Journal of Kidney Diseases, 60(6), 912-921.**		Seattle Kidney Study (SKS) 336 non-dialysis-dependent patients with stages 1-4 CKD with eGFR <90 mL/min/1.73 m^2 or evidence of microalbuminuria enrolled in the Seattle Kidney Study, a clinic-based cohort study. Finding compared with community-dwelling older adults in the Cardiovascular Health Study.	
		Nonfrail vs. Frail			
		After adjustment including diabetes, eGFRcys categories of <30 and 30-44 mL/min/1.73 m^2 were associated with a 2.8- (95% CI, 1.3-6.3) and 2.1 (95% CI, 1.0-4.7)-fold greater prevalence of frailty compared with GFRcys >60 mL/min/1.73 m^2.			
Body composition		**Si, A. P., Senior, P. A., Field, C. J., Jindal, K., & Mager, D. R. (2018). Frailty, Health Related Quality of Life, Cognition, Depression, Vitamin D and Health Care Utilization in an Ambulatory Adult Population with Type 1 and Type 2 Diabetes Mellitus and Chronic Kidney Disease: a cross sectional analysis. Canadian Journal of Diabetes.**		41 ambulatory adults (41 through 83 years of age) with type 1 (n=3) or type 2 (n=38) diabetes mellitus and CKD (stages 1 through V).	
		Frail vs. Nonfrail			

Other Adverse Health Effects of Frailty Among CKD Patients				
Related adverse health effects	**Method**	**References**		**Sample Group**
		Conditions		
		Data	**p-value**	
Nosocomial infections			~~Heuberger, 2013 : RR = 2.1, 1.1–3.8, p < 0.001 (in frail, further increase with cancer)~~	
Health-care utilization	descriptive cross-sectional	**SI, A. P., Senior, P. A., Field, C. J., Jindal, K., & Mager, D. R. (2018). Frailty, Health Related Quality of Life, Cognition, Depression, Vitamin D and Health Care Utilization in an Ambulatory Adult Population with Type 1 and Type 2 Diabetes Mellitus and Chronic Kidney Disease: a cross sectional analysis. Canadian Journal of Diabetes.**		"41 ambulatory adults (41 through 83 years of age) with type 1 (n=3) or type 2 (n=38) diabetes mellitus and CKD (stages 1 through V). Exclusion criteria: Thoses who were on dialysis (estimated glomerular filtration rate <10 mL/min/1.73 m^2) and had body weights >136 kg, and coinciding comorbidities known to influence vitD metabolism were excluded. "
		Frail vs. Nonfrail		
	Cumulative individual health-care events (numbers and types) between 2012 and 2017: A chart review conducted using electronic medical records		Health-care utilization : Higher cumulative number of inpatient (p<0.001), emergency (p=0.002) and total (p=0.001) health-care visits	
	Frailty: Fried frailty criteria (>3 frail, <3 nonfrail) Primary outcome: prevalence of frailty among the studied population Secondary outcome: frailty as a marker of falls, hospitalizations, and deaths or not	**Yadla, M., John, J. P., & Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. Saudi Journal of Kidney Diseases and Transplantation, 28(1), 15.**		205 prospective patients out of a total of 221 patients undergoing maintenance hemodialysis in Saudi center for organ transplantation were studied for the predictors of frailty.
		Frail vs. Nonfrail		
		Hospitalizations: >3 (141): 127 vs. 14 1-2 (64): 40 vs. 24 HR for hospitalizations: 2.06 (95% CI, 1.18-3.58)	Hospitalizations: <0.01	
Dialysis therapy	At baseline, participants are without dialysis	**Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K. V., De Boer, I. H., ... & Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. American Journal of Kidney Diseases, 60(6), 912-921.**		Seattle Kidney Study (SKS) 336 non-dialysis-dependent patients with stages 1-4 CKD with eGFR <90 mL/min/1.73 m^2 or evidence of microalbuminuria enrolled in the Seattle Kidney Study, a clinic-based cohort study. Finding compared with community-dwelling older adults in the Cardiovascular Health Study.
	Associations of frailty components with time dialysis therapy: A Cox proportional hazards model with robust standard variance estimation (adjusted for potential confounding variables)	**Frail vs. Nonfrail**		
		After adjustment, the frailty phenotype was associated with an estimated 2.5 (95% CI, 1.4-4.4)-fold greater risk of dialysis therapy.		
Falls	Frailty: Fried frailty criteria (>3 frail, <3 nonfrail) Primary outcome: prevalence of frailty among the studied population Secondary outcome: frailty as a marker of falls, hospitalizations, and deaths or not	**Yadla, M., John, J. P., & Mummadi, M. (2017). A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. Saudi Journal of Kidney Diseases and Transplantation, 28(1), 15.**		205 prospective patients out of a total of 221 patients undergoing maintenance hemodialysis in Saudi center for organ transplantation were studied for the predictors of frailty.
		Frail vs. Nonfrail		
		Falls: 115 vs. 12 HR for falls: 2.1 (95% CI, 1.21-3.92)	Falls: <0.001	

雙重變項	Patients with MBD had poorer HRQoL with respect to burden of kidney disease, WS, PF and general health [(β (SE): -7.9 (3.88), p = 0.042; -9.5 (3.99), p = 0.018; -3.0 (1.22) p = 0.014; -3.6 (1.48), p = 0.015, respectively].	
Hemodialysis 大約等同於 CKD	Although previous studies of adults with CKD have found that lower kidney function is associated with worse cognitive function (36,37), we have identified a high-risk subgroup of patients with ESRD: namely, those who are frail who have more profound cognitive loss.	McAdams-DeMarco, M. A., Tan, J., Salter, M. L., Gross, A., Meoni, L. A., Jaar, B. G., ... & Sozio, S. M. (2015). Frailty and cognitive function in incident hemodialysis patients. Clinical Journal of the American Society of Nephrology, 10(12), 2181-2189.
Corroboration	Although that result is included here for the sake of simple verification and corroboration, the most appropriate validation analysis in this case is the known-groups strategy, as presented earlier, since the assessment of the MMSE diagnosis depends on the elderly patients' education level.	Fabrício-Wehbe, Suzele Cristina Coelho, Schiaveto, Fábio Veiga, Vendrusculo, Thaís Ramos Pereira, Haas, Vanderlei José, Dantas, Rosana Aparecida Spadoti, & Rodrigues, Rosalina Aparecida Partezani. (2009). Adaptação cultural e validade da Edmonton Frail Scale - EFS em uma amostra de idosos brasileiros. Revista Latino-Americana de Enfermagem, 17(6), 1043-1049.