Adverse Health Effects of Frailty in CKD Patients

[Cause 2](#_Toc3044269)

[Prevalence 5](#_Toc3044270)

[Complications 17](#_Toc3044271)

[Bibliography 32](#_Toc3044272)

Cause

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Effect (descriptions) | | Risk Difference | CKD severity | Frailty Assessment | Sample Size | Reference |
| Biological | |  | |  |  |  |  |  |
|  | Cardiovascular | Hypertension\* | | RR 1.6 (1.26-2.04) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | [1](#Yadla) |
| Peripheral vascular disease\* | | RR 1.58 (1.34-1.8) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | [1](#Yadla) |
| Left ventricular dysfunction\* | | RR 1.18 (1.03-1.36) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | [1](#Yadla) |
| Endothelial dysfunction | | r= -0.367 (p= 0.004) | CKD stages 3-5 | Fried Phenotypes | 61 | 2 |
| OR 3.86 (1.00-14.88) |
| Permanent vascular access (fistula or graft) | | HR 0.71 (0.51-0.98) | CKD stage 5D (maintenance hemodiaysis) | Fried Phenotypes | 2275 | 3 |
|  | Cerebrovascular | Cerebrovascular Accident | | RR 1.34 (1.19-1.5) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | [1](#Yadla) |
|  | Pulmonary | COPD | | OR 1.68 (1.16-2.45) | CKD stages 1-5 | Fried Phenotypes | 10256 | 4 |
|  | Immunological | Inflammatory | |  |  |  |  |  |
|  | IL-6\* | Worse frailty | CKD stage 5D (hemodialysis) | Fried Phenotypes | 762 | 5 |
|  | CRP | After adjustment, OR 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 |
|  | Fibrinogen |
|  | Endocrinologic/ Metabolic | Diabetes | | Frailty scores +0.7 points per year | CKD stage 5D (hemodialysis) | Fried Phenotypes | 762 | 5 |
| OR 1.68 (1.16-2.45) | CKD stages 1-5 | Fried Phenotypes | 10256 | 4 |
| Obesity (IMC ≥ 30 kg/m2) | | OR 6.63 (1.16-36.77) | CKD stages 3-5 | Fried Phenotypes | 61 | 2 |
| Higher parathyroid hormones (PTH) | | r= 0.30 (p= 0.01) | CKD stages 3-5 | Fried Phenotypes | 61 | 2 |
|  | Body Composition | Higher fat mass | | r= 0.25 (p= 0.04) | CKD stages 3-5 | Fried Phenotypes | 61 | 2 |
|  | Cancer | Cancer | | OR 1.89 (1.19-2.99) | CKD stages 1-5 | Fried Phenotypes | 10256 | 4 |
|  | Arthritis | Arthritis | | OR 3.34 (2.08-5.38) | CKD stages 1-5 | Fried Phenotypes | 10256 | 4 |
|  | Laboratory Data | eGFR (mL/min/1.72m^2) | |  |  |  |  |  |
|  | eGFRcys <30 | Frailty prevalence 2.8 | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
| eGFRcys 30-44 | Frailty prevalence 2.1 |
| eGFRcys >60 | Referent |
| Serum Albumin Concentrations (g/dL) | | Frailty scores  -1.1 points per g/dL | CKD stage 5D (hemodialysis) | Fried Phenotypes | 762 | 5 |
| Serum Creatinine <4 mg/dL\* | | RR 1.46 (1.22-1.71) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | 1 |
| Testosterone, per 50% lower free testosterone\* | |  | CKD stage 5D (hemodialysis), men | Fried Phenotypes | 440 | 8 |
|  | being frail | OR 1.40 (1.05-1.53) |
|  | becoming frail over 12 months | OR 1.40 (1.07-1.73) |
| Hemoglobin | | Adjusted, OR 1.76 (1.28-2.41) to 1.50 (1.07-2.09) | Chronic kidney insufficiency, serum creatinine ≥1.3mg/dL | Fried Phenotypes | 5888 | 6 |
| LDL, HDL | |
| Lifestyle | | Smoking\* | | RR 1.18 (1.04-1.34) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | 1 |
| Ethnicity | | Hispanic\* | | Frailty scores +0.6 points per year | CKD stage 5D (hemodialysis) | Fried Phenotypes | 762 | 5 |

Prevalence

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | Effect (descriptions) | | | | Prevalence | CKD Severity | Frailty Assessment | Sample Size | Reference |
| Biological | | |  | | | |  |  |  |  |  |
|  | Cardiovascular | | Heart Failure | | | | 30% vs 12% | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
| Angina | | | | 34% vs. 22% | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
|  | Cerebrovascular | | Cerebrovascular Disease Prevalence (%) | | | | 26.4 vs. 12.0 | ESRD | Fried Phenotypes | 324 | 9 |
|  | Neurological | | Brain Wave | | | | F vs. NF | ESRD, under chronic dialysis | Simple FRAIL scale (SFS) | 46 | 10 |
|  | Global DAR | | | 283 ± 679 vs. 2971 ± 4859 |
|  | DARs (left frontal) | | | 135 ± 250 vs. 3073 ± 4702 |
|  | DAR (left TO) | | | 197 ± 318 vs. 3708 ± 6398 |
|  | DAR (central) | | | 55 ± 96 vs. 1773 ± 3262 |
|  | DAR (right TO) | | | 187 ± 261 vs. 4400 ± 7763 |
|  | Global DTABR | | | 191 ± 469 vs. 1781 ± 2793 |
|  | DTABR (left frontal) | | | 86 ± 158 vs. 1680 ± 2388 |
|  | DTABR (left TO) | | | 130 ± 210 vs. 1884 ± 2828 |
|  | DTABR (central) | | | 39 ± 65 vs. 1132 ± 1957 |
|  | DTABR (right TO) | | | 126 ± 178 vs. 2960 ± 5271 |
|  | Cognitive | | Mini-Mental State Examination (MMSE) | | | |  | Elderly, ≥65y/o | Edmonton Frail Scale (EFS) | 137 | 11 |
|  | Spearman’s correlation coefficient of EFS scores with gross MMSE scores | | | -0.607 (p<0.01) |
| Executive Function | | | | F vs. NF at cohort entry |  |  |  |  |
|  | Trail Making Tests A (TMTA) scores | | | +12.08 | ESRD | Fried Phenotypes | 324 | 9 |
|  | Trail Making Tests B (TMTB) scores | | | +33.15 | ESRD | Fried Phenotypes | 324 | 9 |
|  | Microbiota | | Gut Microbiota Composition | | | | F vs. NF | Stage 3b-4, eGFR 15-45ml/min | Fried Phenotype score | 64 (and 15 control subjects) | 12 |
|  | Malnutrition-Inflammation-Score (MIS) | | | 7.6 vs. 3.9 |
|  |  | | Abundance of unclassified 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) | | | ↑ |
| Immunological | | Inflammatory | | | |  |  |  |  |  |
|  | | CRP (ln CRP) (mg/dL) | | 1.12 vs 0.28 | CKD stage 5D (peritoneal dialysis) | Clinical Frailty Scale (CFS) | 119 | 13 |
|  | | IL6 (ln IL6) (mg/dL) | | 2.45 vs. 1.58 |
| Mycophenolate mofetil (MMF) dose reduction (MDR) | | | | F vs. NF | CKD stage 5T | Fried Phenotypes | 525 | 14 |
|  | 1 year since KT (%) | | | 44 vs 40 |
|  | 2 years since KT (%) | | | 54 vs. 45 |
|  | 3 years since KT (%) | | | 67 vs. 51 |
| Viral infection | | | | F vs. NF |  |  |  |  |
|  | HCV (n=37) | | | 36 vs. 1 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | 1 |
|  | Functional Status | | Disability | | | | F vs. NF |  |  |  |  |
|  | At least one disability in activities of daily Living (ADLs) | | | 15% vs. 5% | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
|  | At least one disability in instrumental activities of daily living (IADLs) | | | 60% vs. 28% |
|  | At least one disability in mobility tasks | | | 40% vs. 18% |
|  | Less ADL-independent | | | 55% vs. 91% | ≥ 65 yo, predialysis, eGFR < 20 mL/min | Groningen frailty indicator (GFI) | 65 | 15 |
| Ability to perform basic activities of daily living | | | | 33.33% vs 76.4% | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | 16 |
| Ability to perform transfers | | | | 38.8% vs. 84.7% |
|  | Endocrinologic/ Metabolic | | Diabetes | | | | F vs. NF |  |  |  |  |
|  | Prevalence | | | 64% vs. 49% | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
| Obesity | | | | F vs. NF |  |  |  |  |
|  | Prevalence | | | 64% vs. 50% | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
|  | Prevalence | | | 51.8% vs. 23.9% | ESRD | Fried Phenotypes | 324 | 9 |
|  | BMI based on dry weight | | | 31.5 vs. 27.6 |
| Body Composition | | Appendicular | | | |  |  |  |  |  |
|  | Appendicular skeletal muscle mass index (ASMI) | | | 6.8 vs. 7.7 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
|  | Higher appendicular fat percentage (for left, right lower and left, right upper extremities, respectively) | | | SFS scores |  |  |  |  |
|  |  | | Left lower extremity | β = 0.34; t = 2.32; p = 0.03 | ESRD | Simple FRAIL scale | 44 | 18 |
|  |  | | Right lower extremity | β = 0.3; t = 2.05; p = 0.048 |
|  |  | | Left upper extremity | β = 0.37; t = 2.66; p = 0.01 |
|  |  | | Right upper extremity | β = 0.43; t = 3.09; p = <0.01 |
|  | Higher appendicular fat percentage (for left, right lower and left, right upper extremities, respectively) | | | Frail/Prefrail vs. Nonfrail |  |  |  |  |
|  |  | | Left lower extremity | β = 0.33; t = 2.31; p = 0.03 | ESRD | self- report instrument evaluating five dimensions of frailty (fatigue, resistance, ambulation, illnesses, and weight loss) | 44 | 18 |
|  |  | | Right lower extremity | β = 0.32; t = 2.28; p = 0.03 |
|  |  | | Right upper extremity | β = 0.33; t = 2.35; p = 0.03 |
| Lower lean mass | | | |  |  |  |  |  |
|  | | | | F/PF vs. NF |  |  |  |  |
|  | Whole body (kg) | | | 34.7 vs. 43.1 | ESRD | Simple FRAIL scale | 44 | 18 |
|  | Cephalic area (g) | | | 3059 vs. 3288 |
|  | Trunk area (kg) | | | 17.4 vs. 22.1 |
|  | Right upper limb (g) | | | 1831 vs. 2493 |
|  | Left upper limb (g) | | | 1869 vs. 2515 |
|  | Right lower limb (g) | | | 4920 vs. 6114 |
|  | Left lower limb (g) | | | 4650 vs. 6349 |
|  | | | | F vs. NF |  |  |  |  |
|  | lean body mass (i.e. sarcopenia) (in frail vs. nonfrail) | | | 57.1% vs .14.7% | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
| BMI | | | | 22.53 vs. 26.16 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | 16 |
|  | Laboratory Data | | eGFR (mL/min/1.72m^2) | | | | 18 vs. 50 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
|  | eGFRcys <30 | | | Frailty prevalence 2.8 | CKD stages 1-4 | Fried Phenotypes | 336 | 7\* |
| eGFRcys 30-44 | | | Frailty prevalence 2.1 |
| eGFRcys >60 | | | Referent |
| Prealbumin (PRAB) (mg/dL) | | | | 28.9 vs. 38.3 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
| Serum albumin (g/L) | | | | Pearson correlation coefficient r = -0.263 (p = 0.025) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 74 | 19 |
| 38 vs. 41 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
| 2.92 vs. 3.48 | CKD stage 5D (peritoneal dialysis) | Clinical Frailty Scale (CFS) | 119 | 13 |
| 3.61 vs. 3.85 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | 16 |
|  | Frail with depression vs. Frail without depression vs. Nonfrail | | | 32.9 vs. 34.9 vs. 35.8 (p=0.025) | CKD stage 5D (peritoneal dialysis) | In-house Chinese questionnaire | 178 | 20 |
| Calcium (mmol/L) | | | | 2.24 vs. 2.36 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
| Creatinine (umol/L) | | | | 299 vs. 115 |
| Hemoglobin (g/dL) | | | | Pearson correlation coefficient r = -0.336 (p = 0.004) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 74 | 19 |
| 6.49 vs. 8.07 (p = 0.037) |
| 10.35 vs. 10.97 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | 16 |
| 25-hydroxy vitamin D (ng/mL) | | | | Pearson correlation coefficient r = -0.363 (p = 0.002) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 74 | 19 |
| 11.58 vs. 17.09 (p = 0.005) |
|  | Miscellaneous | | Dialysis clearance rate | | | | ↑ | ESRD, under chronic dialysis | Simple FRAIL scale (SFS) | 46 | 10 |
| Psychological | | |  | | | |  |  |  |  |  |
|  | Mood | | Mood Change | | | | Negative change | CKD stage 5D (hemodialysis) | Edmonton Frail Scale (EFS) | N/A | 21 |
|  | Mental Health | |  | | | |  |  |  |  |  |
|  |  | Anxiety | Hospital Anxiety and Depression Scale (HADS) | | | | 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 | 17 |
|  | Mental Function | | Post-KT delirium | | | | 9.0% vs. 3.9% | CKD stage 5T | Fried Phenotypes | 893 | 23 |
| Sociological | | |  | | | |  |  |  |  |  |
|  | Isolation | |  | | | |  |  |  |  |  |
|  | Interaction | | Interaction with family | | | | Good |  |  |  | 24 |
| Physical activity | | | Minnesota Leisure Time Activity (LTA) | | | | 95 vs. 735 (p<0.001) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 68 | 25 |
| Low Physical Activity Questionnaire (LoPAQ) | | | | 280 vs. 798 (p=0.003) |
| Sitting (hours/day) | | | | 6.5 vs. 5 (p=0.04) |
| Nutritional Status | | | Overall subjective global assessment (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 | 20 |
| Spearman’s rank correlation coefficient r = -0.44, p < 0.0001 | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | 26 |
| Malnutrition inflammation score (MIS) (frail with depression vs. frail without depression vs. nonfrail) | | | | 9.48 vs. 7.13 vs. 5.12 (p < 0.0001) | CKD stage 5D (peritoneal dialysis) | In-house Chinese questionnaire | 178 | 20 |
| Spearman’s rank correlation coefficient r = 0.40, p < 0.0001 | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | 26 |
| Quality of Life | | | HRQoL | | | |  |  |  |  |  |
|  | SF-36 | | |  |  |  |  |  |
|  |  | | Scores in physical functioning, blood pressure, role physical, and physical component summary domains | ↓ | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
| Kidney Disease Quality of Life (KDQoL) | | | | F vs. NF |  |  |  |  |
|  | Physical health | | | 33.7 vs. 40.7 | ESRD CKD stage 5D (conventional hemodialysis) | Fried Phenotypes | 151 | 27 |
|  | Kidney disease effects | | | 51.6 vs. 66.8 |
| Independence | | | Functional Independence Measure (FIM) | | | |  | Elderly, ≥65y/o | Edmonton Frail Scale (EFS) | 137 | 11 |
| Spearman’s correlation coefficient | Frailty diagnosis with global FIM | | | -0.703 (p<0.001) |
| Frailty diagnosis with motor FIM | | | -0.714 (p<0.001) |
| Frailty diagnosis with cognitive FIM | | | -0.575 (p<0.001) |
| EFS scores with gross FIM | | | -0.53 (p<0.01) |
| Health-care utilization | | | Hospitalization | | | | 90% vs. 53% (p = 0.04) | ≥ 65 yo, predialysis, eGFR < 20 mL/min | Groningen frailty indicator (GFI) | 65 | 15 |
|  | Cumulative number of inpatient health-care visits | | | ↑ | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 17 |
|  | Cumulative number of emergency health-care visits | | |
|  | Cumulative number of total health-care visits | | |
|  | Admissions/year | | | 0.77727 vs. 0.2838 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | 16 |
| Composite | | | Number of complications (complications identified at data collection: High Pressure Cramping, Anemia, Weight loss Pain, Weakness, Weight gain Constipation, Heart Arrhythmia, Headache, Itch, Recurrent infections, Arterial hypertension) | | | | Spearman’s correlation 0.666 (p=0.000 in table) (p<0.05 in text) | Elderly (≥ 60 yo), with diagnosis of CKD | Edmonton Frail Scale | 35 | 28 |
| Higher number of comorbid conditions | | | | 6 vs. 4 (p = 0.03) |  |  |  |  |
| Charlson’s comorbidity score | | | | Spearman’s rank correlation coefficient r = 0.40 (p < 0.0001) | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | 26 |

Complications

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Effect (descriptions) | | | | | Risk Difference | CKD Severity | Frailty Assessment | Sample Size | Reference |
| Biological | |  | | | | |  |  |  |  |  |
|  | Cardiovascular | Cerebrovascular Accident | | | | | OR 1.55 (1.05-2.99) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 2275 | 3 |
| QRS duration | | | | |  |  |  |  |  |
|  | Edmonton frailty scale | | | | β coefficient = −0.29, t = −2.03 (p = 0.048) | CKD stage 5D (chronic hemodialysis) | Edmonton frailty scale | 41 | 29 |
|  | Simple FRAIL scale | | | | β coefficient = −0.27, t = −1.84 (p = 0.05) | Simple FRAIL scale |
| Vascular Access failure | | | | | HR 2.63 (1.03-6.71) | ESRD  (CKD stage 5D) | Self-reported simple FRAIL scale | 51 | 30 |
|  | Renal Function Decline | Risk for death or dialysis therapy | | | | | 2.5 (1.4-4.4)-fold greater | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
|  | Immunological | Mycophenolate mofetil (MMF) dose reduction (MDR) | | | | | HR 1.29 (1.01-1.66) | CKD stage 5T | Fried Phenotypes | 525 | 14 |
|  | Cognitive | Modified Mini-Mental State (3MS) | | | | | -2.37 to -2.80 (1 year) (p=0.03) | ESRD | Fried Phenotypes | 324 | 9 |
|  | Declined, 1-4 years post-KT (points/week) | | | | Slope = -0.04 vs. 0.005 | CKD stage 5T | Fried physical frailty phenotypes (PFP) | 665 | 31 |
|  | At 4 year post-KT (points) | | | | -5.5 (87.4 vs. 92.9) |
|  | Functional status | Disability | | | | | F vs. Prefrail vs. NF |  |  |  |  |
|  | Need for activities of daily livings (ADL) assistance | | | | OR 11.32 (5.49-23.32) vs. 1.93 (1.01-3.68) vs. 1.00 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 742 | 32 |
|  | Diabetes | Diabetes | | | | | OR 1.35 (1.10-1.65) | CKD stage 5D | Fried Phenotypes | 2275 | 3 |
|  | Body composition | Bones | | | | |  |  |  |  |  |
|  | Bone Mineral Density (BMD) | | | | One year follow-up, with frailty | ESRD  CKD stage 5D (chronic hemodialysis) | Simple FRAIL Scale (SFS) | 43 | 33 |
|  |  | L1 | | | 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) | Simple FRAIL Scale (SFS) | 43 | 33 |
|  | Areas | | | | One year follow-up, with frailty | ESRD  CKD stage 5D (chronic hemodialysis) | Simple FRAIL Scale (SFS) | 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) | Simple FRAIL Scale (SFS) | 43 | 34 |
|  | Quantitative ultrasound (QUS) parameters of calcaneus | | | |  |  |  |  |  |
|  |  | Speed of sound (SOS) | | | Standardized β (range, p value) | CKD stage 5D (maintenance hemodialysis) | Fried Phenotypes | 214 | 35 |
|  |  |  | Female  (Five frailty criteria) | | Negative (-0.253 to -0.439, p ≤ 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 cm2 (p = 0.02) vs. -6.6 cm2 (p = 0.0001) |  | Performance-based frailty (PbF) | 80 | 36 |
|  | Laboratory data | Serum Albumin Concentrations (g/dL) | | | | |  |  |  |  |  |
|  | <3.2 vs. ≥3.9 | | | | OR 1.89 (1.30-2.59) |  | Fried Phenotypes | 2275 | 3 |
|  | Hypoalbuminemia | | | | Negative association (p = 0.01) | CKD stage 5D (maintenance hemodialysis) (ESRD) | Simple Frail Scale | 46 | 37 |
| Psychological | |  | | | | |  |  |  |  |  |
|  | Delirium | Post-KT delirium | | | | | OR 2.05 (1.02-4.13) | CKD stage 5T | Fried Phenotypes | 893 | 23 |
|  | Distress | Distress Thermometer | | | | | β = 0.35, *t* = 3.0 (95% CL = 0.12-0.58) (p = 0.003) | CKD stage 5D (hemodialysis) | Canadian frailty score | 382 | 38 |
| Quality of Life | | HRQoL | | | | |  |  |  |  |  |
|  | Fair/Poor HRQOL at follow-up (median 9.4 mo) | | | | aOR 2.79 (1.32-5.90) | ESRD  CKD stage 5T | Fried Phenotypes | 233 | 39 |
|  | Worsening HRQOL at follow-up (median 9.4 mo) | | | | aRR 2.91 (1.08-7.80) |
|  | SF-36 | | | |  |  |  |  |  |
|  |  | Hierarchical regression 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-specific HRQoL | | −6.53 points (95% CI -9.17 to -3.89) |
|  | Post-KT | | | Greater improvement |
|  |  |  | Physical HRQoL | | 1.35 points/month (0.65 to 2.05) vs. 0.34 points/month (-0.17 to 0.85) |
|  |  |  | Kidney disease-specific HRQoL | | 3.75 points/month (2.89 to 4.60) vs. 2.41 points/month (1.78 to 3.04) |
|  |  |  | Constituent domains | | Greater improvement |
|  |  |  |  | General health | 4.93 points/month (3.51 to 6.35) vs. 2.87 points/month (1.82 to 3.92) |
|  |  |  |  | Effects of ESRD on daily living | 7.10 points/month (5.68 to 8.51) vs. 4.01 points/month (2.99 to 5.03) |
|  |  |  |  | Cognitive function | 2.88 points/month (1.80 to 3.96) vs. 1.28 points/month (0.50 to 2.07) |
|  |  |  |  | Social interaction | 1.18 points/month (-0.06 to 2.43) vs. -0.57 points/month (-1.47 to 0.33) |
|  | Illness Intrusiveness Rating Scale | | | | Effect estimate 1.14 (1.09-1.20) | CKD stage 5D  (peritoneal dialysis, n=129; hemodialysis, n=122) | The Canadian Study of Health and Aging Clinical Frailty Scale (CFS) | 251 | 42 |
|  | Barthel Index | | | | Effect estimate 0.89 (0.86-.093) |
|  | Symptom score | | | | Effect estimate 1.23 (1.13-1.34) |
|  | Hospital Anxiety and Depression Scale | | | | Effect estimate 1.21 (1.11-1.31) |
| Falls | | | | | HR 2.1 (1.21-3.92) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | 1 |
| OR 2.39 (1.22-4.71) | CKD stage 5D (maintenance hemodialysis) | Fried frailty index | 762 | 44 |
|  | Higher numbers of falls | | | | HR 3.09 (1.38-6.90) | CKD stage 5D (hemodialysis) |  | 95 | 45 |
|  | Time to first fall or fracture requiring medical attention | | | | HR 1.60 (1.16-2.20) | CKD stage 5D (maintenance hemodialysis) | Modified Fried Phenotypes by Bao Y 46. | 1646 | 47 |
| Graft Loss | | Death-censored graft loss | | | | |  |  |  |  |  |
|  | F vs. NF (in patients with depressive symptoms) | | | | aHR 6.20 (1.67, 22.95) vs. 3.16 (0.90, 11.04) | CKD stage 5T | Fried Phenotypes | 773 | 48 |
| Health-care utilization | | Hospitalization/Death | | | | | HR 1.56 (1.36-1.79) | CKD stage 5D | Fried Phenotypes | 2275 | 3 |
| Hospitalization | | | | | HR 2.06 (1.18-3.58) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | 1 |
| aHR 1.80 (1.4-2.3) | CKD stage 5D (maintenance hemodialysis & peritoneal dialysis) | Adopted | 1658 | 49 |
| Relative risk = 1.43 (1.00-2.03) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 146 | 50 |
|  | Number of hospitalizations for all causes | | | | beta = 0.29 (p < 0.0001) | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | 26 |
|  | Number of hospitalizations related to cardiovascular events | | | | beta = 0.37 (p < 0.0001) |
|  | Non-vascular access-related hospitalizations | | | | aHR 1.98 (1.41-1.87) (內文應該寫錯，無勘誤) | CKD stage 5D | Fried Phenotypes | 2275 | 3 |
| Time to first hospitalization | | | | | HR 1.26 (1.09-1.45) | CKD stage 5D (maintenance dialysis) | Earlier modification of Fried Phenotypes by Johansen et al 3, but 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 | 20 |
|  | Total length of hospital stay | | | | beta = 0.34 (p < 0.0001) | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | 26 |
| Longer Length of Stay (LOS) | | | | |  |  |  |  |  |
|  | with delayed graft function (DGF), LOS | | | | Relative Risk 1.15 (1.03-1.29) | CKD stage 5T | Fried Phenotypes | 589 | 52 |
|  | With DGF, LOS ≥2 weeks | | | | OR 1.57 (1.06-2.33) |
|  | ≥2 weeks | | | |  | CKD stage 5 to 5T | Fried Phenotypes | 569 | 53 |
|  |  | Change in 3 categories (more frail) | | | OR 2.02 (1.20-3.40) |
|  |  | Change in frailty scores (more frail) | | | OR 1.92 (1.13-3.25) |
|  | With depressive symptoms (aRR difference between F 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 3, but without weight loss. | 1576 | 46 |
| HR 2.24 (1.60-3.15) | CKD stage 5D | Fried Phenotypes | 2275 | 3 |
| HR 1.22 (1.04-1.43) | CKD stage 5D (incident chronic dialysis) | CFS | 390 | 55 |
| HR 4.28 (1.22-14.98) | Predialysis (eGFR ≤ 25 mL) | PRISMA questionnaire & Timed up and Go test | 104 | 56 |
| aHR 9.83 (1.80-53.7) | CKD stage 5D (peritoneal dialysis) | Clinical Frailty Scale (CFS) | 119 | 13 |
| HR 2.60 (1.04-6.49) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 146 | 50 |
| HR 2.37 (1.11-5.02) | CKD stage 5D (maintenance hemodialysis & peritoneal dialysis) | Adopted | 1658 | 49 |
| 20.45% vs. 12.36% (p<0.005) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | 16 |
|  | Performance-based frailty | | | | HR 2.16 (1.41-3.29) | CKD stage 5D (hemodialysis) | Fried Phenotypes & a definition that substitutes self-reported measures available on the Medical Outcomes Study 36-Item Short Form (SF-36) for the physical performance and exhaustion criteria. | 771 | 57 |
|  | Self-reported function-based frailty | | | | HR 1.93 (1.24-3.00) |
|  | Patients who met both performance- and self-reported function-based frailty | | | | HR 2.46 (1.51-4.01) |
|  | F vs. NF (in patients with depressive symptoms) | | | | aHR 2.62 (1.03, 6.70) vs. 1.92 (0.68, 5.38) | CKD stage 5T | Fried Phenotypes | 773 | 48 |
|  | At 24-month follow up, frail with depression vs. frail without depression vs. nonfrail | | | | 62.5% vs. 71.4% vs 86.6% (p=0.001) | CKD stage 5D (peritoneal dialysis) | In-house Chinese questionnaire | 178 | 20 |
|  | Prediction ability of comorbidities in F vs. NF | | | | HR 0.75 (0.44-1.29) vs. 1.66 (1.17-2.35) | CKD stage 5T (KT candidates, on waitlist) | Fried Phenotypes | 2086 | 58 |
|  | Out of 10 deceased within 1 year of initiation (percentage of F vs. NF) | | | | 30% vs. 9% | ≥ 65 yo, predialysis, eGFR < 20 mL/min | Groningen frailty indicator (GFI) | 65 | 15 |
| Risk for death or dialysis 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/m2 | | | | 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 (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  ESRD | Multidimensional frailty score based on comprehensive geriatric assessment (CGA) protocol | 46 | 62 |
| 30-day postoperative (KT) complications according to Comprehensive Complication Index (CCI) | | | | | β=13.31, 95% CI 5.72-20.89 (p = 0.0007) | CKD stage 5T | Groningen Frailty Indicator | 150 | 63 |

Bibliography

1. Yadla, M., John, J. &Mummadi, M. A study of clinical assessment of frailty in patients on maintenance hemodialysis supported by cashless government scheme. *Saudi J. Kidney Dis. Transplant.* (2017). doi:10.4103/1319-2442.198102

2. Mansur, H. N. Fragilidade na doença renal crônica: prevalência e fatores associados. (2012).

3. Johansen, K. L., Chertow, G. M., Jin, C. &Kutner, N. G. Significance of frailty among dialysis patients. *J. Am. Soc. Nephrol.* **18**, 2960–2967 (2007).

4. Wilhelm-Leen, E. R., Hall, Y. N., M, K. T. &Chertow, G. M. Frailty and chronic kidney disease: the Third National Health and Nutrition Evaluation Survey. *Am J Med* **122**, 664–71 e2 (2009).

5. Johansen, K. L. *et al.* Factors Associated with Frailty and Its Trajectory among Patients on Hemodialysis. *Clin J Am Soc Nephrol* **12**, 1100–1108 (2017).

6. Shlipak, M. G. *et al.* The Presence of Frailty in Elderly Persons with Chronic Renal Insufficiency. *Am. J. Kidney Dis.* **43**, 861–867 (2004).

7. Roshanravan, B. *et al.* A prospective study of frailty in nephrology-referred patients with CKD. *Am J Kidney Dis* **60**, 912–921 (2012).

8. Chiang, J. M. *et al.* Low testosterone is associated with frailty, muscle wasting and physical dysfunction among men receiving hemodialysis: a longitudinal analysis. *Nephrol. Dial. Transplant.* (2018). doi:10.1093/ndt/gfy252

9. McAdams-Demarco, M. A. *et al.* Frailty and cognitive function in incident hemodialysis patients. *Clin. J. Am. Soc. Nephrol.* **10**, 2181–2189 (2015).

10. Chao, C.-T., Lai, H.-J., Tsai, H.-B., Yang, S.-Y. &Huang, J.-W. Frail phenotype is associated with distinct quantitative electroencephalographic findings among end-stage renal disease patients: an observational study. *BMC Geriatr.* **17**, 277 (2017).

11. Fabrício-Wehbe, S. C. C. *et al.* Cross-cultural adaptation and validity of the ‘Edmonton Frail Scale - EFS’ in a Brazilian elderly sample. *Rev. Lat. Am. Enfermagem* **17**, 1043–1049 (2009).

12. Margiotta, E. *et al.* SuO004GUT MICROBIOTA COMPOSITION AND FRAILTY IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE. *Nephrol. Dial. Transplant.* **33**, i618–i618 (2018).

13. Kamijo, Y., Kanda, E., Ishibashi, Y. &Yoshida, M. Sarcopenia and Frailty in PD: Impact on Mortality, Malnutrition, and Inflammation. *Perit. Dial. Int.* **38**, 447–454 (2018).

14. McAdams-Demarco, M. A. *et al.* Frailty, mycophenolate reduction, and graft loss in kidney transplant recipients. *Transplantation* **99**, 805–810 (2015).

15. Meulendijks, F. G. *et al.* Groningen frailty indicator in older patients with end-stage renal disease. *Ren. Fail.* **37**, 1419–1424 (2015).

16. Bancu, I. *et al.* Frail Patient in Hemodialysis: A New Challenge in Nephrology-Incidence in Our Area, Barcelones Nord and Maresme. *J. Aging Res.* **2017**, 7624139 (2017).

17. Adame Perez, S. I., Senior, P. A., Field, C. J., Jindal, K. &Mager, D. R. Frailty, Health-Related Quality of Life, Cognition, Depression, Vitamin D and Health-Care Utilization in an Ambulatory Adult Population with Type 1 or Type 2 Diabetes Mellitus and Chronic Kidney Disease: A Cross-Sectional Analysis. *Can. J. Diabetes* (2018). doi:10.1016/j.jcjd.2018.06.001

18. Chao, C.-T., Chan, D.-C. &Huang, J.-W. Frail Phenotype Might Be Associated With Higher Appendicular but Not Truncal Fat Among End-Stage Renal Disease Patients. *Journal of pain and symptom management* **53**, e1–e4 (2017).

19. Demircioglu, D. The Association of Vitamin D Levels and the Frailty Phenotype Among Non-geriatric Dialysis Patients: A Cross-sectional Study. *Clinics* (2018). doi:10.6061/clinics/2018/e116

20. Szeto, C.-C. *et al.* Depression and Physical Frailty Have Additive Effect on the Nutritional Status and Clinical Outcome of Chinese Peritoneal Dialysis. *Kidney Blood Press. Res.* **43**, 914–923 (2018).

21. DeSouza Orlandi, F. &Gesualdo, G. D. Assessment of the frailty level of elderly people with chronic kidney disease undergoing hemodialysis. *ACTA Paul. Enferm.* **27**, 29–34 (2014).

22. Sales, C. *et al.* SP651ANXIETY AND DEPRESSION IN END STAGE RENAL DISEASE PATIENTS AND ITS ASSOCIATION WITH CLINICAL AND LABORATORIAL DATA. *Nephrol. Dial. Transplant.* **32**, iii355-iii355 (2017).

23. Haugen, C. E. *et al.* Incidence, Risk Factors, and Sequelae of Post-kidney Transplant Delirium. *J. Am. Soc. Nephrol.* **29**, 1752–1759 (2018).

24. Moffatt, H., Moorhouse, P., Mallery, L., Landry, D. &Tennankore, K. Using the Frailty Assessment for Care Planning Tool (FACT) to screen elderly chronic kidney disease patients for frailty: the nurse experience. *Clin. Interv. Aging* **13**, 843 (2018).

25. Johansen, K. L., Painter, P., Delgado, C. &Doyle, J. Characterization of physical activity and sitting time among patients on hemodialysis using a new physical activity instrument. *J. Ren. Nutr.* **25**, 25–30 (2015).

26. Ng, J. K.-C. *et al.* Frailty in Chinese Peritoneal Dialysis Patients: Prevalence and Prognostic Significance. *Kidney Blood Press. Res.* **41**, 736–745 (2016).

27. Noori, N., Sharma Parpia, A., Lakhani, R., Janes, S. &Goldstein, M. B. Frailty and the Quality of Life in Hemodialysis Patients: The Importance of Waist Circumference. *J. Ren. Nutr.* **28**, 101–109 (2018).

28. deSousa Meira, A. *et al.* Frailty in elderly patients with chronic kidney disease under conservative treatment. *Rev. da Rede Enferm. do Nord.* **17**, 386–392 (2016).

29. Chao, C.-T. &Huang, J.-W. Frailty severity is significantly associated with electrocardiographic QRS duration in chronic dialysis patients. *PeerJ* **3**, e1354 (2015).

30. Chao, C.-T., Chiang, C.-K., Huang, J.-W. &Hung, K.-Y. Self-reported frailty among end-stage renal disease patients: A potential predictor of dialysis access outcomes. *Nephrology (Carlton, Vic.)* **22**, 333–334 (2017).

31. Chu, N. M. *et al.* Frailty and Changes in Cognitive Function after Kidney Transplantation. *J. Am. Soc. Nephrol.* **30**, 336–345 (2019).

32. Kutner, N. G., Zhang, R., Allman, R. M. &Bowling, C. B. Correlates of ADL difficulty in a large hemodialysis cohort. *Hemodial Int* **18**, 70–77 (2014).

33. Chao, C.-T., Huang, J.-W. &Chan, D.-C. Frail phenotype might herald bone health worsening among end-stage renal disease patients. *PeerJ* **5**, e3542 (2017).

34. Chao, C.-T., Chiang, C.-K., Huang, J.-W. &Chan, D.-C. Effect of Frail Phenotype on Bone Mass and Vertebral Compression Fracture in Individuals Undergoing Dialysis. *Journal of the American Geriatrics Society* **64**, e19-21 (2016).

35. Yoneki, K. *et al.* Association between frailty and bone loss in patients undergoing maintenance hemodialysis. *J. Bone Miner. Metab.* (2018). doi:10.1007/s00774-017-0898-4

36. Delgado, C., Doyle, J. W. &Johansen, K. L. Association of frailty with body composition among patients on hemodialysis. *J. Ren. Nutr.* **23**, 356–362 (2013).

37. Chao, C.-T. *et al.* Simple self-report FRAIL scale might be more closely associated with dialysis complications than other frailty screening instruments in rural chronic dialysis patients. *Nephrology (Carlton).* **20**, 321–328 (2015).

38. Camilleri, S., Chong, S., Tangvoraphonkchai, K., Yoowannakul, S. &Davenport, A. Effect of Self-Reported Distress Thermometer Score on the Maximal Handgrip and Pinch Strength Measurements in Hemodialysis Patients. *Nutr. Clin. Pract.* **32**, 682–686 (2017).

39. McAdams-DeMarco, M. A. *et al.* Frailty and Health-Related Quality of Life in End Stage Renal Disease Patients of All Ages. *J. frailty aging* **5**, 174–179 (2016).

40. Lee, S. J., Son, H. &Shin, S. K. Influence of frailty on health-related quality of life in pre-dialysis patients with chronic kidney disease in Korea: a cross-sectional study. *Health Qual. Life Outcomes* **13**, 70 (2015).

41. Mansur, H. N., Colugnati, F. A., Grincenkov, F. R. &Bastos, M. G. Frailty and quality of life: a cross-sectional study of Brazilian patients with pre-dialysis chronic kidney disease. *Heal. Qual Life Outcomes* **12**, 27 (2014).

42. Iyasere, O. U. *et al.* Quality of Life and Physical Function in Older Patients on Dialysis: A Comparison of Assisted Peritoneal Dialysis with Hemodialysis. *Clin. J. Am. Soc. Nephrol.* **11**, 423–430 (2016).

43. McAdams-DeMarco, M. A. *et al.* Frailty and Postkidney Transplant Health-Related Quality of Life. *Transplantation* **102**, 291–299 (2018).

44. Kutner, N. G., Zhang, R., Huang, Y. &Wasse, H. Falls among hemodialysis patients: potential opportunities for prevention? (2014). doi:10.1093/ckj/sfu034

45. McAdams-DeMarco, M. A. *et al.* Frailty and falls among adult patients undergoing chronic hemodialysis: a prospective cohort study. *BMC Nephrol* **14**, 224 (2013).

46. Bao, Y., Dalrymple, L., Chertow, G. M., Kaysen, G. A. &Johansen, K. L. Frailty, dialysis initiation, and mortality in end-stage renal disease. *Arch Intern Med* **172**, 1071–1077 (2012).

47. Delgado, C. *et al.* Association of Self-Reported Frailty with Falls and Fractures among Patients New to Dialysis. *Am. J. Nephrol.* **42**, 134–140 (2015).

48. Konel, J. M. *et al.* Depressive symptoms, frailty, and adverse outcomes among kidney transplant recipients. *Clin. Transplant.* **32**, e13391 (2018).

49. Lee, S.-Y. *et al.* The prevalence, association, and clinical outcomes of frailty in maintenance dialysis patients. *J. Ren. Nutr.* **27**, 106–112 (2017).

50. McAdams-DeMarco, M. A. *et al.* Frailty as a novel predictor of mortality and hospitalization in individuals of all ages undergoing hemodialysis. *J Am Geriatr Soc* **61**, 896–901 (2013).

51. McAdams-DeMarco, M. A. *et al.* Frailty and Early Hospital Readmission After Kidney Transplantation. *Am. J. Transplant.* **13**, 2091–2095 (2013).

52. McAdams-DeMarco, M. A. *et al.* Frailty, Length of Stay, and Mortality in Kidney Transplant Recipients: A National Registry and Prospective Cohort Study. *Ann. Surg.* **266**, 1084–1090 (2017).

53. Chu, N. M. *et al.* Dynamic Frailty Before Kidney Transplantation-Time of Measurement Matters. *Transplantation* (2019). doi:10.1097/TP.0000000000002563

54. McAdams-DeMarco, M. A. *et al.* Frailty and mortality in kidney transplant recipients. *Am. J. Transplant* **15**, 149–154 (2015).

55. Alfaadhel, T. A. *et al.* Frailty and mortality in dialysis: evaluation of a clinical frailty scale. *Clin. J. Am. Soc. Nephrol.* **10**, 832–840 (2015).

56. Ali, H., Abdelaziz, T., Abdelaal, F. &Baharani, J. Assessment of prevalence and clinical outcome of frailty in an elderly predialysis cohort using simple tools. *Saudi J. Kidney Dis. Transpl.* **29**, 63–70 (2018).

57. Johansen, K. L. *et al.* Association of Performance-Based and Self-Reported Function-Based Definitions of Frailty with Mortality among Patients Receiving Hemodialysis. *Clin. J. Am. Soc. Nephrol.* **11**, 626–632 (2016).

58. Pérez Fernández, M. *et al.* Comorbidity, Frailty, and Waitlist Mortality among Kidney Transplant Candidates of All Ages. *Am. J. Nephrol.* **49**, 103–110 (2019).

59. Fitzpatrick, J. *et al.* Frailty, body composition and the risk of mortality in incident hemodialysis patients: the Predictors of Arrhythmic and Cardiovascular Risk in End Stage Renal Disease study. *Nephrol. Dial. Transplant* **34**, 346–354 (2019).

60. Romeu, M. *et al.* Survival of patients with ANCA-associated vasculitis on chronic dialysis: data from the French REIN registry from 2002 to 2011. *QJM* **107**, 545–555 (2014).

61. Decourt, A. *et al.* Trends in Survival and Renal Recovery in Patients with Multiple Myeloma or Light-Chain Amyloidosis on Chronic Dialysis. *Clin. J. Am. Soc. Nephrol.* **11**, 431–441 (2016).

62. Lee, S. W. *et al.* Is Frailty a Modifiable Risk Factor of Future Adverse Outcomes in Elderly Patients with Incident End-Stage Renal Disease? *J. Korean Med. Sci.* **32**, 1800–1806 (2017).

63. Schopmeyer, L. *et al.* Frailty has a significant influence on postoperative complications after kidney transplantation-a prospective study on short-term outcomes. *Transpl. Int.* **32**, 66–74 (2019).