Adverse Health Effects of Frailty in CKD Patients

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Cause

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Effect (descriptions) | | Risk Difference | CKD severity | Frailty Assessment | Sample Size | Reference |
| Lifestyle | | Smoking\* | | RR 1.18 (1.04-1.34) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | 1 |
| Ethnicity | | Hispanic\* | | Frailty scores +0.6 points per year | CKD stage 5D (hemodialysis) | Fried Phenotypes | 762 | 2 |
| Biological | |  | |  |  |  |  |  |
|  | Cardiovascular | Hypertension\* | | RR 1.6 (1.26-2.04) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | [1](#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 | 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](#Yadla) |
|  | 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 | | After adjustment, OR 1.76 (1.28-2.41) to 1.50 (1.07-2.09) | Chronic kidney insufficiency, serum creatinine ≥ 1.3 mg/dL | Fried Phenotypes | 5888 | 6 |
| Fibrinogen | |
|  | Endocrinologic/ Metabolic | Diabetes | | Frailty scores +0.7 points per year | CKD stage 5D (hemodialysis) | Fried Phenotypes | 762 | 2 |
| OR 1.68 (1.16-2.45) | CKD stages 1-5 | Fried Phenotypes | 10256 | 5 |
| Obesity (IMC ≥ 30 kg/m2) | | OR 6.63 (1.16-36.77) | CKD stages 3-5 | Fried Phenotypes | 61 | 3 |
| Higher parathyroid hormones (PTH) | | r= 0.30 (p= 0.01) | CKD stages 3-5 | Fried Phenotypes | 61 | 3 |
|  | Body Composition | Higher fat mass | | r= 0.25 (p= 0.04) | CKD stages 3-5 | Fried Phenotypes | 61 | 3 |
|  | Cancer | Cancer | | OR 1.89 (1.19-2.99) | CKD stages 1-5 | Fried Phenotypes | 10256 | 5 |
|  | Arthritis | Arthritis | | OR 3.34 (2.08-5.38) | CKD stages 1-5 | Fried Phenotypes | 10256 | 5 |
|  | Laboratory Data | eGFR (mL/min/1.72m^2) reference: > 60 | |  |  |  |  |  |
|  | eGFRcys < 30 | Frailty prevalence 2.8 | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
| eGFRcys 30-44 | Frailty prevalence 2.1 |
| Serum Albumin Concentrations (g/dL) | | Frailty scores  -1.1 points per g/dL | CKD stage 5D (hemodialysis) | Fried Phenotypes | 762 | 2 |
| Serum Creatinine <4 mg/dL\* | | RR 1.46 (1.22-1.71) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | 1 |
| Testosterone, every 50% lower free form | |  | CKD stage 5D (hemodialysis), men | Fried Phenotypes | 440 | 8 |
|  | being frail | OR 1.40 (1.05-1.53) |
|  | becoming frail over 12 months | OR 1.40 (1.07-1.73) |
| 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 (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 |  |  |  |  |
|  | 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 (ASMI) | | | 6.8 vs. 7.7 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | 14 |
|  | 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 dialysis) | Clinical Frailty Scale (CFS) | 119 | 12 |
| 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 | 19 |
| 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 | 20 |
| Functional Status | | | | Disability | | | | F vs. NF |  |  |  |  |
|  | | | ≥1 disability in activities of daily Living (ADLs) | 15% vs. 5% | CKD stages 1-4 | Fried Phenotypes | 336 | 7 |
|  | | | ≥1 disability in instrumental activities of daily living (IADLs) | 60% vs. 28% |
|  | | | ≥1 disability in mobility tasks | 40% vs. 18% |
|  | | | Less ADL-independent | 55% vs. 91% | ≥ 65 yo, predialysis, eGFR < 20 mL/min | Groningen frailty indicator (GFI) | 65 | 21 |
| 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) | 22 |
|  | | | 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 | 23 |
|  | 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 | 24 |
|  |  | | Depression | Hospital Anxiety and Depression Scale (HADS) | | | | Men↑in global, psychological, physical frailty | ESRD, under online-haemodiafiltration (OL-HDF) | N/A | 97 | 24 |
| 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 | 25 |
| Sociological | | | |  | | | |  |  |  |  |  |
|  | Interaction | | | Interaction with family | | | | Good |  |  |  | 26 |
| Physical activity | | | | Minnesota Leisure Time Activity (LTA) | | | | 95 vs. 735 (p<0.001) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 68 | 27 |
| 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 | 20 |
| 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 | 20 |
| 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 | 14 |
| 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 | 28 |
|  | 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 | 21 |
|  | 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 hemodialysis) | FRAIL Scale | 43 | 33 |
|  | Areas | | | | One year follow-up, with frailty | ESRD  CKD stage 5D (chronic hemodialysis) | FRAIL Scale | 43 | 33 |
|  |  | Average L-spine areas | | | ß = −0.48, t =−2.84, p < 0.01 |
|  |  | Changes of average L-spine areas | | | ß = −0.5, t =−3.02, p<0.01 |
|  | Z-score | | | | One year follow-up, with frailty |
|  |  | Percentage change of L1 Z-score | | | ß = −0.45, t =−2.11, p=0.049 |
|  | Vertebral Compression Fracture (VCF) | | | | OR 1.8 (p = 0.01) | ESRD  CKD stage 5D (chronic hemodialysis) | FRAIL Scale | 43 | 34 |
|  | Quantitative ultrasound (QUS) parameters of calcaneus | | | |  |  |  |  |  |
|  |  | Speed of sound (SOS) | | | Standardized β (range, p value) | CKD stage 5D (maintenance hemodialysis) | Fried Phenotypes | 214 | 35 |
|  |  |  | Female  (Five frailty criteria) | | Negative (-0.253 to -0.439, p ≤ 0.034) |
|  |  |  | Male  (All criteria significant except weight loss) | | Negative (-0.277 to -0.402, p ≤ 0.003) |
|  |  | Broadband ultrasound attenuation (BUA) | | | Standardized β (range, p value) |
|  |  |  | Female  (All criteria significant except weakness and weight loss) | | Negative (-0.209 to -0.354, p ≤ 0.045) |
|  |  |  | Male  (All criteria significant except weight loss) | | Negative (-0.171 to -0.371, p ≤ 0.045) |
|  |  | Stiffness index | | | Standardized β (range, p value) |
|  |  |  | Female  (All criteria significant except weight loss) | | Negative (-0.271 to -0.461, p ≤ 0.018) |
|  |  |  | Male  (Five frailty criteria) | | Negative (-0.183 to -0.461, p ≤ 0.048) |
| Muscles | | | | |  |  |  |  |  |
|  | Quadriceps muscle area (magnitude of association with PbF vs. 10 years of age) | | | | Multivariable coefficient -30.3 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) | 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 | 25 |
|  | 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 | 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 | 20 |
|  | Number of hospitalizations related to cardiovascular events | | | | beta = 0.37 (p < 0.0001) |
|  | Non-vascular access-related hospitalizations | | | | aHR 1.98 (1.41-1.87) (內文應該寫錯，無勘誤) | CKD stage 5D | Fried Phenotypes | 2275 | 4 |
| Time to first hospitalization | | | | | HR 1.26 (1.09-1.45) | CKD stage 5D (maintenance dialysis) | Earlier modification of Fried Phenotypes by Johansen et al 4, but without weight loss. | 1576 | 46 |
| Early Hospital Readmission (EHR) | | | | | aRR 1.61 (1.81-2.19) (p=0.002) | CKD stage 5T | Fried Phenotypes | 383 | 51 |
| Duration of hospitalization | | | | |  |  |  |  |  |
|  | Hospital stay (days per year of follow up) (frail with depression vs. frail without depression vs. nonfrail) | | | | 26.62 (IQR 10.65-61.18) vs. 14.05 (IQR 3.57-37.27) vs. 8.04 (IQR 0.91-19.42) (p<0.0001) | CKD stage 5D (peritoneal dialysis) | In-house Chinese questionnaire | 178 | 17 |
|  | Total length of hospital stay | | | | beta = 0.34 (p < 0.0001) | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | 20 |
| Longer Length of Stay (LOS) | | | | |  |  |  |  |  |
|  | with delayed graft function (DGF), LOS | | | | Relative Risk 1.15 (1.03-1.29) | CKD stage 5T | Fried Phenotypes | 589 | 52 |
|  | With DGF, LOS ≥2 weeks | | | | OR 1.57 (1.06-2.33) |
|  | ≥2 weeks | | | |  | CKD stage 5 to 5T | Fried Phenotypes | 569 | 53 |
|  |  | Change in 3 categories (more frail) | | | OR 2.02 (1.20-3.40) |
|  |  | Change in frailty scores (more frail) | | | OR 1.92 (1.13-3.25) |
|  | With depressive symptoms (aRR difference between F and NF) | | | | aRR 1.88 (1.70-2.08) vs. 1.38  (1.27-1.52) | CKD stage 5T | Fried Phenotypes | 773 | 48 |
|  | CES-D score (10-point increase) (aRR increase between F and NF) | | | | aRR 1.23 (1.16-1.31) vs. 1.17 (1.08-1.27) |
| Mortality | | Mortality | | | | | 2.17 fold | CKD stage 5T | Fried Phenotypes | 537 | 54 |
| HR 1.57 (1.25-1.97) | CKD stage 5D (maintenance dialysis) | Earlier modification of Fried Phenotypes by Johansen et al 4, but without weight loss. | 1576 | 46 |
| HR 2.24 (1.60-3.15) | 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 | 21 |
| 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 (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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