|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | Effect (descriptions) | | | | Prevalence | CKD Severity | Frailty Assessment | Sample Size | Reference |
| Biological | | |  | | | |  |  |  |  |  |
|  | Cardiovascular | | Heart Failure | | | | 30% vs 12% | CKD stages 1-4 | Fried Phenotypes | 336 | (Roshanravan et al., 2012) |
| Angina | | | | 34% vs. 22% | CKD stages 1-4 | Fried Phenotypes | 336 | (Roshanravan et al., 2012) |
|  | Cerebrovascular | | Cerebrovascular Disease Prevalence (%) | | | | 26.4 vs. 12.0 | ESRD | Fried Phenotypes | 324 | (McAdams-Demarco, Tan, et al., 2015) |
|  | Neurological | | Brain Wave | | | | F vs. NF | ESRD, under chronic dialysis | Simple FRAIL scale (SFS) | 46 | (Chao, Lai, Tsai, Yang, &Huang, 2017) |
|  | 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 | (Fabrício-Wehbe et al., 2009) |
|  | 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 | (McAdams-Demarco, Tan, et al., 2015) |
|  | Trail Making Tests B (TMTB) scores | | | +33.15 | ESRD | Fried Phenotypes | 324 | (McAdams-Demarco, Tan, et al., 2015) |
|  | Microbiota | | Gut Microbiota Composition | | | | F vs. NF | Stage 3b-4, eGFR 15-45ml/min | Fried Phenotype score | 64 (and 15 control subjects) | (Margiotta et al., 2018) |
|  | 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 | (Kamijo, Kanda, Ishibashi, &Yoshida, 2018) |
|  | | 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 | (McAdams-Demarco, Law, et al., 2015) |
|  | 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 | (Yadla, John, &Mummadi, 2017) |
|  | 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 | (Roshanravan et al., 2012) |
|  | 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 | (Meulendijks et al., 2015) |
| Ability to perform basic activities of daily living | | | | 33.33% vs 76.4% | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | (Bancu et al., 2017) |
| 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 | (Roshanravan et al., 2012) |
| Obesity | | | | F vs. NF |  |  |  |  |
|  | Prevalence | | | 64% vs. 50% | CKD stages 1-4 | Fried Phenotypes | 336 | (Roshanravan et al., 2012) |
|  | Prevalence | | | 51.8% vs. 23.9% | ESRD | Fried Phenotypes | 324 | (McAdams-Demarco, Tan, et al., 2015) |
|  | 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 | (Adame Perez, Senior, Field, Jindal, &Mager, 2018) |
|  | 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 | (Chao, Chan, &Huang, 2017) |
|  |  | | 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 | (Chao, Chan, et al., 2017) |
|  |  | | 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 | (Chao, Chan, et al., 2017) |
|  | 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 | (Adame Perez et al., 2018) |
| BMI | | | | 22.53 vs. 26.16 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | (Bancu et al., 2017) |
|  | Laboratory Data | | eGFR (mL/min/1.72m^2) | | | | 18 vs. 50 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | (Adame Perez et al., 2018) |
|  | eGFRcys <30 | | | Frailty prevalence 2.8 | CKD stages 1-4 | Fried Phenotypes | 336 | (Roshanravan et al., 2012)\* |
| 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 | (Adame Perez et al., 2018) |
| Serum albumin (g/L) | | | | Pearson correlation coefficient r = -0.263 (p = 0.025) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 74 | (Demircioglu, 2018) |
| 38 vs. 41 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | (Adame Perez et al., 2018) |
| 2.92 vs. 3.48 | CKD stage 5D (peritoneal dialysis) | Clinical Frailty Scale (CFS) | 119 | (Kamijo et al., 2018) |
| 3.61 vs. 3.85 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | (Bancu et al., 2017) |
|  | 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 | (Szeto et al., 2018) |
| Calcium (mmol/L) | | | | 2.24 vs. 2.36 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | (Adame Perez et al., 2018) |
| 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 | (Demircioglu, 2018) |
| 6.49 vs. 8.07 (p = 0.037) |
| 10.35 vs. 10.97 | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | (Bancu et al., 2017) |
| 25-hydroxy vitamin D (ng/mL) | | | | Pearson correlation coefficient r = -0.363 (p = 0.002) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 74 | (Demircioglu, 2018) |
| 11.58 vs. 17.09 (p = 0.005) |
|  | Miscellaneous | | Dialysis clearance rate | | | | ↑ | ESRD, under chronic dialysis | Simple FRAIL scale (SFS) | 46 | (Chao, Lai, et al., 2017) |
| Psychological | | |  | | | |  |  |  |  |  |
|  | Mood | | Mood Change | | | | Negative change | CKD stage 5D (hemodialysis) | Edmonton Frail Scale (EFS) | N/A | (DeSouza Orlandi &Gesualdo, 2014) |
|  | 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 | (Sales et al., 2017) |
|  |  | Depression | Hospital Anxiety and Depression Scale (HADS) | | | | Men↑in global, psychological, physical frailty | ESRD, under online-haemodiafiltration (OL-HDF) | N/A | 97 | (Sales et al., 2017) |
| Incidence (%) (Self-reported Major Depression Inventory) | | | | 83 vs. 6 | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | (Adame Perez et al., 2018) |
|  | Mental Function | | Post-KT delirium | | | | 9.0% vs. 3.9% | CKD stage 5T | Fried Phenotypes | 893 | (Haugen et al., 2018) |
| Sociological | | |  | | | |  |  |  |  |  |
|  | Isolation | |  | | | |  |  |  |  |  |
|  | Interaction | | Interaction with family | | | | Good |  |  |  | (Moffatt, Moorhouse, Mallery, Landry, &Tennankore, 2018) |
| Physical activity | | | Minnesota Leisure Time Activity (LTA) | | | | 95 vs. 735 (p<0.001) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 68 | (Johansen, Painter, Delgado, &Doyle, 2015) |
| 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 | (Szeto et al., 2018) |
| Spearman’s rank correlation coefficient r = -0.44, p < 0.0001 | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | (Ng et al., 2016) |
| 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 | (Szeto et al., 2018) |
| Spearman’s rank correlation coefficient r = 0.40, p < 0.0001 | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | (Ng et al., 2016) |
| 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 | (Adame Perez et al., 2018) |
| 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 | (Noori, Sharma Parpia, Lakhani, Janes, &Goldstein, 2018) |
|  | Kidney disease effects | | | 51.6 vs. 66.8 |
| Independence | | | Functional Independence Measure (FIM) | | | |  | Elderly, ≥65y/o | Edmonton Frail Scale (EFS) | 137 | (Fabrício-Wehbe et al., 2009) |
| 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 | (Meulendijks et al., 2015) |
|  | Cumulative number of inpatient health-care visits | | | ↑ | CKD stage 1-5 | Edmonton Frail Scale (EFS) | 41 | (Adame Perez et al., 2018) |
|  | 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 | (Bancu et al., 2017) |
| 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 | (deSousa Meira et al., 2016) |
| 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 | (Ng et al., 2016) |

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