|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | 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 | (Johansen, Chertow, Jin, &Kutner, 2007) |
| QRS duration | | | | |  |  |  |  |  |
|  | Edmonton frailty scale | | | | β coefficient = −0.29, t = −2.03 (p = 0.048) | CKD stage 5D (chronic hemodialysis) | Edmonton frailty scale | 41 | (Chao &Huang, 2015) |
|  | 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 | (Chao, Chiang, Huang, &Hung, 2017) |
|  | Renal Function Decline | Risk for death or dialysis therapy | | | | | 2.5 (1.4-4.4)-fold greater | CKD stages 1-4 | Fried Phenotypes | 336 | (Roshanravan et al., 2012) |
|  | Immunological | Mycophenolate mofetil (MMF) dose reduction (MDR) | | | | | HR 1.29 (1.01-1.66) | CKD stage 5T | Fried Phenotypes | 525 | (McAdams-Demarco, Law, et al., 2015) |
|  | Cognitive | Modified Mini-Mental State (3MS) | | | | | -2.37 to -2.80 (1 year) (p=0.03) | ESRD | Fried Phenotypes | 324 | (McAdams-Demarco, Tan, et al., 2015) |
|  | Declined, 1-4 years post-KT (points/week) | | | | Slope = -0.04 vs. 0.005 | CKD stage 5T | Fried physical frailty phenotypes (PFP) | 665 | (Chu, Gross, et al., 2019) |
|  | 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 | (N GKutner, Zhang, Allman, &Bowling, 2014) |
|  | Diabetes | Diabetes | | | | | OR 1.35 (1.10-1.65) | CKD stage 5D | Fried Phenotypes | 2275 | (Johansen et al., 2007) |
|  | Body composition | Bones | | | | |  |  |  |  |  |
|  | Bone Mineral Density (BMD) | | | | One year follow-up, with frailty | ESRD  CKD stage 5D (chronic hemodialysis) | Simple FRAIL Scale (SFS) | 43 | (Chao, Huang, &Chan, 2017) |
|  |  | 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 | (Chao, Huang, et al., 2017) |
|  | Areas | | | | One year follow-up, with frailty | ESRD  CKD stage 5D (chronic hemodialysis) | Simple FRAIL Scale (SFS) | 43 | (Chao, Huang, et al., 2017) |
|  |  | 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 | (Chao, Chiang, Huang, &Chan, 2016) |
|  | Quantitative ultrasound (QUS) parameters of calcaneus | | | |  |  |  |  |  |
|  |  | Speed of sound (SOS) | | | Standardized β (range, p value) | CKD stage 5D (maintenance hemodialysis) | Fried Phenotypes | 214 | (Yoneki et al., 2018) |
|  |  |  | 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 | (Delgado, Doyle, &Johansen, 2013) |
|  | Laboratory data | Serum Albumin Concentrations (g/dL) | | | | |  |  |  |  |  |
|  | <3.2 vs. ≥3.9 | | | | OR 1.89 (1.30-2.59) |  | Fried Phenotypes | 2275 | (Johansen et al., 2007) |
|  | Hypoalbuminemia | | | | Negative association (p = 0.01) | CKD stage 5D (maintenance hemodialysis) (ESRD) | Simple Frail Scale | 46 | (Chao et al., 2015) |
| Psychological | |  | | | | |  |  |  |  |  |
|  | Delirium | Post-KT delirium | | | | | OR 2.05 (1.02-4.13) | CKD stage 5T | Fried Phenotypes | 893 | (Haugen et al., 2018) |
|  | 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 | (Camilleri, Chong, Tangvoraphonkchai, Yoowannakul, &Davenport, 2017) |
| 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 | (M AMcAdams-DeMarco et al., 2016) |
|  | 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 | (S. J.Lee, Son, &Shin, 2015) |
|  |  | 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 | (Mansur, Colugnati, Grincenkov, &Bastos, 2014) |
|  |  | 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 | (Iyasere et al., 2016) |
|  |  | 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 | (Mara AMcAdams-DeMarco et al., 2018) |
|  |  | 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 | (Iyasere et al., 2016) |
|  | 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 | (Yadla, John, &Mummadi, 2017) |
| OR 2.39 (1.22-4.71) | CKD stage 5D (maintenance hemodialysis) | Fried frailty index | 762 | (Nancy GKutner, Zhang, Huang, &Wasse, 2014) |
|  | Higher numbers of falls | | | | HR 3.09 (1.38-6.90) | CKD stage 5D (hemodialysis) |  | 95 | (M AMcAdams-DeMarco, Suresh, et al., 2013) |
|  | 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 (Bao, Dalrymple, Chertow, Kaysen, &Johansen, 2012). | 1646 | (Delgado et al., 2015) |
| 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 | (Konel et al., 2018) |
| Health-care utilization | | Hospitalization/Death | | | | | HR 1.56 (1.36-1.79) | CKD stage 5D | Fried Phenotypes | 2275 | (Johansen et al., 2007) |
| Hospitalization | | | | | HR 2.06 (1.18-3.58) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 205 | (Yadla et al., 2017) |
| aHR 1.80 (1.4-2.3) | CKD stage 5D (maintenance hemodialysis & peritoneal dialysis) | Adopted | 1658 | (S.-Y.Lee et al., 2017) |
| Relative risk = 1.43 (1.00-2.03) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 146 | (M AMcAdams-DeMarco, Law, et al., 2013) |
|  | Number of hospitalizations for all causes | | | | beta = 0.29 (p < 0.0001) | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | (Ng et al., 2016) |
|  | 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 | (Johansen et al., 2007) |
| 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 (Johansen et al., 2007), but without weight loss. | 1576 | (Bao et al., 2012) |
| Early Hospital Readmission (EHR) | | | | | aRR 1.61 (1.81-2.19) (p=0.002) | CKD stage 5T | Fried Phenotypes | 383 | (M. A.McAdams-DeMarco et al., 2013) |
| 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 | (Szeto et al., 2018) |
|  | Total length of hospital stay | | | | beta = 0.34 (p < 0.0001) | CKD stage 5D (peritoneal dialysis) | Chinese questionnaire | 193 | (Ng et al., 2016) |
| 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 | (Mara AMcAdams-DeMarco et al., 2017) |
|  | With DGF, LOS ≥2 weeks | | | | OR 1.57 (1.06-2.33) |
|  | ≥2 weeks | | | |  | CKD stage 5 to 5T | Fried Phenotypes | 569 | (Chu, Deng, et al., 2019) |
|  |  | 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 | (Konel et al., 2018) |
|  | 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 | (M AMcAdams-DeMarco et al., 2015) |
| HR 1.57 (1.25-1.97) | CKD stage 5D (maintenance dialysis) | Earlier modification of Fried Phenotypes by Johansen et al (Johansen et al., 2007), but without weight loss. | 1576 | (Bao et al., 2012) |
| HR 2.24 (1.60-3.15) | CKD stage 5D | Fried Phenotypes | 2275 | (Johansen et al., 2007) |
| HR 1.22 (1.04-1.43) | CKD stage 5D (incident chronic dialysis) | CFS | 390 | (Alfaadhel et al., 2015) |
| HR 4.28 (1.22-14.98) | Predialysis (eGFR ≤ 25 mL) | PRISMA questionnaire & Timed up and Go test | 104 | (Ali, Abdelaziz, Abdelaal, &Baharani, 2018) |
| aHR 9.83 (1.80-53.7) | CKD stage 5D (peritoneal dialysis) | Clinical Frailty Scale (CFS) | 119 | (Kamijo, Kanda, Ishibashi, &Yoshida, 2018) |
| HR 2.60 (1.04-6.49) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 146 | (M AMcAdams-DeMarco, Law, et al., 2013) |
| HR 2.37 (1.11-5.02) | CKD stage 5D (maintenance hemodialysis & peritoneal dialysis) | Adopted | 1658 | (S.-Y.Lee et al., 2017) |
| 20.45% vs. 12.36% (p<0.005) | CKD stage 5D (hemodialysis) | Fried Phenotypes | 320 | (Bancu et al., 2017) |
|  | 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 | (Johansen et al., 2016) |
|  | 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 | (Konel et al., 2018) |
|  | 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 | (Szeto et al., 2018) |
|  | 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 | (Pérez Fernández et al., 2019) |
|  | 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 | (Meulendijks et al., 2015) |
| Risk for death or dialysis therapy | | | | | 2.5 (1.4-4.4)-fold greater | CKD stages 1-4 | Fried Phenotypes | 336 | (Roshanravan et al., 2012) |
| All-cause mortality | | | | |  |  |  |  |  |
|  | Adjusted | | | | HR 1.66 (1.03-2.67) | CKD stage 5D (incident chronic dialysis) | Fried Phenotypes | 370 | (Fitzpatrick et al., 2019) |
|  | 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 | (Romeu et al., 2014) |
| 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 | (Decourt et al., 2016) |
| Post-KT mortality | | | | |  |  |  |  |  |
|  | Change in 3 categories (more frail) | | | | HR 2.27 (1.11-4.65) | CKD stage 5 to 5T | Fried Phenotypes | 569 | (Chu, Deng, et al., 2019) |
|  | 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 | (S. W.Lee et al., 2017) |
| 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 | (Schopmeyer et al., 2019) |

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