|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Effect (descriptions) | | Risk Difference | Frailty Assessment | Sample Size | CKD Severity | Reference |
| Biological | |  | |  |  |  |  |  |
|  | Cardiovascular | Hypertension\* | | RR 1.6 (1.26-2.04) | Fried Phenotypes | 205 | CKD stage 5D (hemodialysis) | (Yadla, John, &Mummadi, 2017)\* |
| Peripheral vascular disease\* | | RR 1.58 (1.34-1.8) | Fried Phenotypes | 205 | CKD stage 5D (hemodialysis) | (Yadla et al., 2017)\* |
| Left ventricular dysfunction\* | | RR 1.18 (1.03-1.36) | Fried Phenotypes | 205 | CKD stage 5D (hemodialysis) | (Yadla et al., 2017)\* |
| Endothelial dysfunction | | r= -0.367 (p= 0.004) | Fried Phenotypes | 61 | CKD stages 3-5 | (Mansur, 2012) |
| 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 | (Kirsten LJohansen, Chertow, Jin, &Kutner, 2007) |
|  | Cerebrovascular | Cerebrovascular Accident | | RR 1.34 (1.19-1.5) | Fried Phenotypes | 205 | CKD stage 5D (hemodialysis) | (Yadla et al., 2017)\* |
|  | Pulmonary | COPD | | OR 1.68 (1.16-2.45) | Fried Phenotypes | 10256 | CKD stages 1-5 | (Wilhelm-Leen, Hall, M, &Chertow, 2009) |
|  | Immunological | Inflammatory | |  |  |  |  |  |
|  | IL-6\* | Worse frailty | Fried Phenotypes | 762 | CKD stage 5D (hemodialysis) | (K LJohansen et al., 2017)\* |
|  | CRP | After adjustment, OR 1.76 (1.28-2.41) to 1.50 (1.07-2.09) | Fried Phenotypes | 5888 | Chronic kidney insufficiency, serum creatinine ≥1.3mg/dL | (Shlipak et al., 2004) |
|  | Fibrinogen |
|  | Endocrinologic/ Metabolic | Diabetes | | Frailty scores +0.7 points per year | Fried Phenotypes | 762 | CKD stage 5D (hemodialysis) | (K LJohansen et al., 2017)\* |
| OR 1.68 (1.16-2.45) | Fried Phenotypes | 10256 | CKD stages 1-5 | (Wilhelm-Leen et al., 2009) |
| Obesity (IMC ≥ 30 kg/m2) | | OR 6.63 (1.16-36.77) | Fried Phenotypes | 61 | CKD stages 3-5 | (Mansur, 2012) |
| Higher parathyroid hormones (PTH) | | r= 0.30 (p= 0.01) | Fried Phenotypes | 61 | CKD stages 3-5 | (Mansur, 2012) |
|  | Body Composition | Higher fat mass | | r= 0.25 (p= 0.04) | Fried Phenotypes | 61 | CKD stages 3-5 | (Mansur, 2012) |
|  | Cancer | Cancer | | OR 1.89 (1.19-2.99) | Fried Phenotypes | 10256 | CKD stages 1-5 | (Wilhelm-Leen et al., 2009) |
|  | Arthritis | Arthritis | | OR 3.34 (2.08-5.38) | Fried Phenotypes | 10256 | CKD stages 1-5 | (Wilhelm-Leen et al., 2009) |
|  | Laboratory Data | eGFR (mL/min/1.72m^2) | |  |  |  |  |  |
|  | eGFRcys <30 | Frailty prevalence 2.8 | Fried Phenotypes | 336 | CKD stages 1-4 | (Roshanravan et al., 2012)\* |
| eGFRcys 30-44 | Frailty prevalence 2.1 |
| eGFRcys >60 | Referent |
| Serum Albumin Concentrations (g/dL) | | Frailty scores  -1.1 points per g/dL | Fried Phenotypes | 762 | CKD stage 5D (hemodialysis) | (K LJohansen et al., 2017)\* |
| Serum Creatinine <4 mg/dL\* | | RR 1.46 (1.22-1.71) | Fried Phenotypes | 205 | CKD stage 5D (hemodialysis) | (Yadla et al., 2017)\* |
| Testosterone, per 50% lower free testosterone\* | |  | Fried Phenotypes | 440 | CKD stage 5D (hemodialysis), men | (Chiang et al., 2018)\* |
|  | 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) | Fried Phenotypes | 5888 | Chronic kidney insufficiency, serum creatinine ≥1.3mg/dL | (Shlipak et al., 2004) |
| LDL, HDL | |
| Lifestyle | | Smoking\* | | RR 1.18 (1.04-1.34) | Fried Phenotypes | 205 | CKD stage 5D (hemodialysis) | (Yadla et al., 2017)\* |
| Ethnicity | | Hispanic\* | | Frailty scores +0.6 points per year | Fried Phenotypes | 762 | CKD stage 5D (hemodialysis) | (K LJohansen et al., 2017)\* |

Bibliography

Chiang, J. M., Kaysen, G. A., Segal, M., Chertow, G. M., Delgado, C., &Johansen, K. L. (2018). Low testosterone is associated with frailty, muscle wasting and physical dysfunction among men receiving hemodialysis: a longitudinal analysis. *Nephrology Dialysis Transplantation*. doi:10.1093/ndt/gfy252

Johansen, K. L., Chertow, G. M., Jin, C., &Kutner, N. G. (2007). Significance of frailty among dialysis patients. *Journal of the American Society of Nephrology*, *18*, 2960–2967.

Johansen, K. L., Dalrymple, L. S., Delgado, C., Chertow, G. M., Segal, M. R., Chiang, J., …Kaysen, G. A. (2017). Factors Associated with Frailty and Its Trajectory among Patients on Hemodialysis. *Clin J Am Soc Nephrol*, *12*, 1100–1108.

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

Roshanravan, B., Khatri, M., Robinson-Cohen, C., Levin, G., Patel, K.V, deBoer, I. H., …Kestenbaum, B. (2012). A prospective study of frailty in nephrology-referred patients with CKD. *Am J Kidney Dis*, *60*, 912–921.

Shlipak, M. G., Stehman-Breen, C., Fried, L. F., Song, X., Siscovick, D., Fried, L. P., …Newman, A. B. (2004). The Presence of Frailty in Elderly Persons with Chronic Renal Insufficiency. *American Journal of Kidney Diseases*, *43*, 861–867.

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

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