

## Sarcopenia, chronic kidney disease and the risk of mortality and end stage renal disease: findings from 428,331 individuals in the UK Biobank

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### Introduction

Sarcopenia describes a degenerative and generalised skeletal muscle disorder involving the loss of muscle mass and function. In studies of the general population, sarcopenia is associated with adverse outcomes including falls, frailty, and mortality. However it remains an under-recognised yet important clinical problem in an ever-increasing ageing and multimorbid renal population. Whilst sarcopenia has been widely studied in end-stage renal disease (ESRD) patients, there is limited evidence of its prevalence and effects in those not requiring renal replacement therapy (RRT), particularly in large cohort studies and using the latest sarcopenia definitions. Using the UK Biobank, we aimed to identify the prevalence of sarcopenia in individuals with CKD and its association with mortality and risk of ESRD.

### Methods

428,331 participants were categorised into a CKD (defined as eGFR <60ml/min/1.73m<sup>2</sup> not requiring dialysis) and a non-CKD comparative group (no evidence of CKD). Sarcopenia was diagnosed using the EWGSOP2 criteria: 'probable sarcopenia' (low handgrip strength (HGS) <27 and 16kg, males and females respectively); 'confirmed sarcopenia' (low HGS plus low muscle mass, appendicular lean mass <7.0 and 5.5 kg/m<sup>2</sup> by bioelectrical impedance); and 'severe sarcopenia' (low HGS and muscle mass plus slow gait speed). Patients requiring existing RRT were excluded. Patients were followed up until death or until they reached incident ESRD, defined as the need for RRT. All-cause mortality was extracted from national death records. Patients were followed up for a median of 9.0 years and data analysed using Cox modelling.

### Results

CKD (non-dialysis) was identified in n=8,768 individuals (mean age 62.7 (±5.9) years, 44% male, eGFR 52.5 (±7.7) ml/min/1.73m<sup>2</sup>) compared to n=419,563 in the non-CKD comparative group (mean age 56.1 (±8.1) years, 47% male). Probable sarcopenia was identified in 10% of individuals with CKD compared to 5% in those without CKD (P<0.001). Confirmed sarcopenia was observed in 0.3% of those with CKD (vs. 0.2% in the non-CKD group, P<0.001). 0.2% of CKD patients satisfied all three criteria (severe sarcopenia) compared to 0.03% in those without CKD (P<0.001).

In CKD, regardless of criteria, sarcopenia was associated with a significant increased risk of mortality: probable sarcopenia, hazard ratio (HR) 2.1 (95%CI 2.0 to 2.2), P<0.001; confirmed sarcopenia, HR 4.1 (95%CI 2.1 to 8.0), P<0.001; severe sarcopenia, HR 5.1 (95%CI 2.1 to 12.3), P<0.001. 53 patients reached ESRD. Patients with probable sarcopenia were two-fold more likely to reach ESRD (hazard ratio (HR) 2.3 (95%CI 1.7 to 3.1), P<0.001)

### Conclusions

In the largest cohort of its kind, probable sarcopenia was present in 10% of individuals with CKD. The risk of sarcopenia was significantly higher in those with CKD than those without. Regardless of criteria, CKD patients with sarcopenia were ~2-5 times more likely to die than those without sarcopenia. Patients with probable sarcopenia were twice more likely to require RRT. Our results show that sarcopenia is an

important predictor of mortality and ESRD in early non-dialysis CKD. Measuring markers of sarcopenia as standard practice may identify those most at risk of future adverse events and in need of appropriate interventions to mitigate its negative effects.