# Body composition and weakness of hand grip strength and pinch strength in patients with chronic kidney disease from different ethnic backgrounds


## Abstract

### Background

Chronic kidney disease (CKD) patients commonly report muscle weakness and fatigue. Losing muscle mass increases mortality, so we wished to determine the main factors associated with loss of muscle mass and weakness.

### Methods

Anthropometric measurements were made in CKD patients attending a specialised clinic, along with hand grip strength (HGS), pinch strength (PS) and body composition (muscle mass and fat mass) using segmental bioimpedance assessment.

### Results

We reviewed the results of 161 CKD patients; 105 male (65.2%), mean age 70.3±15 years, body mass index (BMI) 28.8±6.7 kg/m$^2$. In multivariable models both HGS and PS were independently negatively associated with age (standardised β (St β -0.35 (95% confidence limits (CL) -0.32 to -0.14) and St β -0.38 (-0.65 to -0.02), p<0.001 respectively, and positively with appendicular muscle in the arm tested (St β 0.34 (2.5-6.3) and St β 0.24 (0.17-0.98), p<0.001 and p=0.006, respectively. In addition, HGS was associated with male gender (St β 0.19 (0.7-7.5), p=0.019), and negatively with % body fat (St β -0.22 (-0.36 to -0.07), p=0.003). There were 47(29.2%) Asian patients who had lower total skeletal muscle mass/height ratio and appendicular muscle

mass/BMI ratio compared to other ethnicities (9.6±1.8 vs 10.5±1.6 kg/$m^2$; p<0.01 and 0.73±0.23 vs 0.83±0.33 $m^2$, p<0.01).

Conclusions.

In CKD patients, we found that muscle weakness measured by HGS and PS was associated with increasing age and loss of appendicular muscle mass. HGS was also weaker with increasing fat mass and female gender, whereas PS was weaker in patients of Asian ethnicity.

## Introduction

Chronic kidney disease (CKD), as defined by a condition which impairs kidney function, affects more than three million United Kingdom (UK) citizens. CKD patients frequently report symptoms of muscle weakness, fatigue and muscle wasting leading to reduced quality of life, increased morbidity and mortality risk .[1-3] CKD patients may be potentially at greater risk of sarcopenia compared to other patient groups due to the retention of uraemic toxins, anaemia, CKD-bone mineral disease (CKD-BMD), vitamin D deficiency, metabolic acidosis, inflammation with increased catabolism, mitochondrial dysfunction coupled with dietary restrictions, and reduced physical activity .[1,4]

Clinical practice has changed over the last two decades with the availability of erythropoietin stimulating agents to treat anaemia, vitamin D analogues to aid the management of CKD-BMD, and bicarbonate supplementation to correct metabolic acidosis. As such we wished to review

which factors in today's clinical practice were associated with muscle weakness.

## Materials and Methods

CKD patients attending a specialist university hospital clinic were reviewed by a single dietician. Physical activity and muscle strength were assessed by using the Sarc-F questionnaire .[5] At the same visit anthropometric measurements of height, weight, and triceps skin fold thickness (TSF), mid upper arm circumference (MUAC), mid arm muscle circumference (MAMC) using a non-stretch tape measure and the Harpenden skinfold calliper (HSB-BI, Baty International Ltd, West Sussex, UK) and corrected mid-upper arm muscle area (CMUAMA) calculated ,[6] along with hand grip strength (HGS) (Kern MAP 80K1, Kern & Sohn GmbH Co., Balingen, Germany) and pinch strength (PS) (Jamar digital plus, Lafayette Instrument, Lafayette, USA) , and body composition using bioimpedance, as part of the standard dietetic clinical assessment.[7-8] The highest value of three HGS and PS measurements were recorded.

Bioimpedance assessment measurements were made following a standardised protocol with an 8 electrode multi-frequency segmental bioimpedance device (MFBIA) (InBody 720, Seoul, South Korea) , which was regularly serviced and calibrated, and previously validated against dual-energy x-ray absorptiometry .[9-10] Patients with implantable cardiac devices, amputations, infected foot ulcers and those with limb atrophy were excluded.

Patient laboratory data, medications, and Stoke-Davies co-morbidity were obtained from hospital computer records.[11] Sarcopenia was defined

using the 2019 European Working Group on Sarcopenia in Older People (EWGSOP) and 2020 Asian Working Group (AWG) for Sarcopenia algorithms .[2,12]

## Statistical analysis

Data was checked for normality, and data expressed as mean ± standard deviation, or median (interquartile range), with comparisons made using standard statistical tests (t test, Mann Whitney U test, ANOVA and Kruskal Wallis, Chi square), with adjustments for small numbers and appropriate post-hoc testing (Tukey and Games-Howell). Univariate analysis was by Spearman correlation, and a multivariable regression analysis was performed using a step backward approach, using all variables with a $p<0.1$ correlation, with variables excluded if not statistically significant, unless they improved the model fit. Models were checked for collinearity and variable inflation factor. Analyses were conducted with standard analytical tools (Prism 8.4. Graph Pad, San Diego and IBM SPSS version 25, IBM Armonk, New York, USA).

## Ethics

Our retrospective audit of clinical practice complied with the UK National Health Service (NHS) health research authority guidelines for clinical audit and service development with all patient data anonymised (https://www.hra.nhs.uk), and approved and registered with the University Hospital.

## Results

Contemporaneous data was available for 161 patients (table 1). The majority of patients were male, and almost 50% were diabetic. Underlying renal disease was thought to be due to diabetes 32.3%, ischaemia or hypertension in 29.8%, interstitial renal diseases 18.6%, unclassified 12.4% and glomerular diseases 6.8%. The majority were of white ethnicity, followed by Asian, all but one South-Asian and then Black, 3 patients were ofanother ethnicity. The median Sarc-F score was 2, with around 33% of patients having an increased Sarc-F score of 4 or more. Asian patients had lower strength, both HGS and PS, when compared to all other ethnicities (Figure 1), and also had lower total skeletal muscle mass (SMM) and lower SMM adjusted for height compared to other ethnicities (Figure 2). Appendicular muscle mass (APM) and APM adjusted for body mass index were lower in Asians compared to other ethnicities (20.8±7.7 vs 22.5±5.3 kg, $p<0.05$; and 0.73±0.23 vs 0.83±0.33 $m^2$, $p<0.05$), as Asians had greater percentage of body fat (36.6±11.2 vs 31.6±10.5%, $p<0.05$).

Using the current EWGSOP and AWGS algorithms defining sarcopenia, then 10% of the African patients fulfilled all criteria, compared to no patients from the other ethnic groups.

On univariate regression HGS and PS were positively associated with muscle mass in the dominant arm, skeletal muscle mass, appendicular muscle mass, male gender, haemoglobin, serum albumin and creatinine and

negatively associated with age, albumin, Sarc-F score, body fat (Table 2). Neither were associated with eGFR (r=-0.03, p=0.19 and r=0.00, p=0.98 respectively).

In a multivariable regression model HGS was independently associated with muscle mass in the dominant arm and male gender and negatively with age and % body fat (Table 3). PS was again independently associated with muscle mass in the dominant arm, but also Asian ethnicity, and negatively associated with age.

## Discussion

Whereas the body has fat reserves that can be mobilised, there is no equivalent protein store. As such skeletal muscle, which accounts for around 50% of total body protein, is the major physiological reserve, and if proteins or amino acids are required, then skeletal muscle is broken down .1 As individuals age after their mid-30s, then muscle mass tends to be lost. The term sarcopenia was first introduced to differentiate this normal physiological loss of muscle from an accelerated or pathological loss of muscle mass [13] Using the Sarc-F screening questionnaire around 1/3 of our patients had significantly high enough scores to warrant further investigation for sarcopenia . [2,5,12] There have been debates about the relevance of measuring muscle mass in patients with muscle weakness, as infiltration of muscle with fat could potentially maintain muscle bulk . [14] However, although we found on univariate analysis that there was a negative association between both HGS and PS with measures of body fat, the strongest positive associations with HGS and PS in our patients were with both total body skeletal muscle mass,

muscle mass in the dominant arm and total appendicular muscle mass. Compared to earlier studies which used single or multiple frequency bioimpedance devices measuring whole body muscle mass, we were able to measure segmental muscle mass in the arms and legs . [15-17] However, we did not find an association between assessments of muscle mass in the arm based on standard anthropometric methods.

Whereas appendicular muscle mass was relatively well maintained, with very few of our patients having sarcopenia according to current clinical guideline definitions, [2,3,12,18], muscle strength was reduced, particularly in our male patients across ethnic groups, when compared to studies reporting on age equivalent healthy patients.[19-21] Loss of muscle strength with loss of muscle mass may be due to increased catabolism, associated with inflammation and metabolic acidosis .[1,22] However, we found no relationship between HGS or PS and serum C reactive protein or bicarbonate, although there was an association with serum albumin. Previous reports have commented on a lower serum albumin in patients with CKD , [4] whether this reflects educed nutritional status ,[23] or is more a marker of inflammation remains debated .[24]

In addition to muscle weakness patients with CKD typically report fatigue. Muscle fatigue could be exacerbated by uraemic solutes, anaemia or vitamin D deficiency.[14,22] In our study we observed no effect of serum urea, creatinine, estimated renal glomerular filtration rate, stage of CKD, vitamin D levels, or prescription of vitamin D3, or parathyroid hormone on HGS or PS.

Patients with CKD have been reported to have reduced active energy expenditure ,[25] and exercise programmes have been reported to increase

muscle strength ,[26-27] reduce fatigue and improve quality of life .[28] The Sarc-F questionnaire provides some information about physical fitness and there was a univariate association between muscle strength and lower Sarc-F scores, whereas there was no such association with co-morbidity scores.

We noted that patients from an Asian background had lower muscle mass compared to white and black patients and had a lower appendicular muscle mass compared to other ethnicities.[12,29] This supports previous reports in kidney dialysis patients and has been recognised by guideline committees which have proposed different parameters for defining sarcopenia in Asian patients compared to European .[2,12,18] Not only is muscle mass lost with age, but there is often an increase in truncal fat as people age, and this has led to the concept of sarcopenic obesity ,[14] and our Asian patients had a higher appendicular muscle mass to body mass index ratio compared to other ethnicities.

We report on a cohort of CKD patients attending a specialist CKD clinic designed to prepare patients for dialysis, pre-emptive transplantation or conservative care. As such, our patients were receiving treatment for anaemia, metabolic acidosis, CKD-bone mineral disease and cardiovascular risk factors, including blood pressure and fluid management. Unlike previous studies which reported only a weak statistical association between muscle mass and HGS in CKD patients,[30] suggesting a divergence between muscle mass and function, by using segmental bioimpedance we demonstrated a very much stronger association between measurements of limb muscle mass and muscle strength.

Although CKD patients have many potential causes as to why they may be at greater risk of muscle weakness and fatigue ranging from anaemia, to metabolic causes including loss of renal function with retention of uraemic toxins, acidosis, vitamin D deficiency, hyperparathyroidism, inflammation with increased catabolism, to reduced physical activity, we found that loss of muscle strength as assessed by HGS was independently associated with increasing age and body fat, female gender and loss of muscle in the arm. Similarly, weak PS was associated with increasing age and loss of muscle mass in the arm, but also Asian ethnicity. As such, in the modern era, by treating anaemia with erythropoietin stimulating agents, correcting metabolic acidosis and treating vitamin D deficiency, the main causes of muscle weakness in CKD patients are age, and the associates of age, loss of appendicular muscle and gain in body fat.

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Figure 1. Hand grip strength (HGS) and pinch gauge strength (PS) in Asian patients and other ethnicities. *p<0.05, ** p<0.01 vs other ethnicities. Date expressed as median, interquartile and 95% confidence limits

Figure 2. Skeletal muscle mass (SMM) and SMM indexed for height (SMMI) in Asian patients and other ethnicities. *p<0.05, ** p<0.01 vs other ethnicities. Date expressed as median, interquartile and 95% confidence limits