Screening tests for sarcopenia in patients with chronic kidney disease

Abstract (250 words)

Background

Patients with chronic kidney disease (CKD) are at increased risk of muscle wasting. Screening tools for sarcopenia, including the Sarc-F questionnaire are now advocated for clinical practice. We wished to compare using the Sarc-F tool with standard measurements of hand grip (HGS) strength and appendicular muscle mass index (APMI).

Methods

We retrospectively reviewed Sarc-F questionnaires completed by patients with CKD, along with contemporaneous measurements of HGS and bioimpedance measured APMI .

Results

146 patients; 94 male (64.4%), mean age 70.5±15 years, body mass index 28.7±6.3 kg/m^2 were screened, and 46 screened positive for sarcopenia, with a lower median HGS (19.3(14.2-24.7) vs 25.6 (19.7-32) kg) and greater body fat (38.3±11.5 vs 30.6±11.5%), both p<0.001,, with more non-white ethnicity (63 vs 44%), p<0.05, but there were no other differences. Step-wise adding HGS, and then APMI cut offs, the prevalence of sarcopenia fell from 31.5% to 20.7-24.7% and 2.8-4.8% respectively, with 45.5-62.8% having reduced HGS strength and 11.0-28.1% reduced APMI, depending on which guidelines were applied. Using the most recent European, and ethnicity adjusted cut-off values then there were no statistical differences in the prevalence of sarcopenia with or without the Sarc-F screening tool.

Conclusions.

By starting with the Sarc-F screening tool, a number of our patients with CKD would then have been excluded from subsequent investigation for sarcopenia. However, overall screening with the Sarc-F tool did not lead to a significant difference in the prevalence of sarcopenia, when using current and ethnicity adjusted guidelines, compared to combining HGS and APMI alone.

Introduction

Sarcopenia is a recognised clinical condition that is associated with an increased risk of falls and fractures, respiratory and cardiac disease, loss of cognitive function, lower quality of life and increased mortality [1].

Patients with chronic kidney disease (CKD) are at increased risk of sarcopenia due to a variety of metabolic factors, including anaemia, vitamin D deficiency, insulin resistance, increased catabolism and oxidative stress, coupled with dietary restrictions, urinary protein losses, and reduced physical activity [2,3].

To be able to intervene and treat sarcopenia, screening tools are required to detect sarcopenia. The European Working Group on Sarcopenia in Older People (EWGSOP) suggested using a step-wise approach to define and diagnose sarcopenia, based on an initial screening questionnaire, the Sarc-F [4], followed by assessment of muscle strength and then measurement of skeletal muscle mass [1].

As we serve a multi-ethnic population, we wished to determine the prevalence of sarcopenia in our patients,with CKD using the EWGSOP

approach, but also comparing their guideline cut offs to those advocated by other national and international guideline committees.

Materials and Methods

Patients with CKD attending a specialist UK university hospital clinic were reviewed by a single dietician and completed the Sarc-F questionnaire [4] between May and August 2018. At the same visit hand grip strength (HGS) was measured by the handgrip dynamometer (Kern MAP 80K1, Kern & Sohn GmbH Co., Balingen, Germany) by the same trained observer, along with body composition using bioimpedance assessment, as part of the standard dietetic clinical assessment. Patients were first taught how to use the strength gauge, holding the dynamometer at a right angle with the elbow by the side of the body, and adjusted to ensure their fingers rested on the handle to perform the maximal voluntary exertion. The highest value of three measurements was recorded [5].

Bioimpedance assessment measurements were made after voiding, using 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 [6]. Patients with implantable cardiac devices, amputations, infected foot ulcers and those with limb atrophy were excluded.

In addition to the 2018 EWGSOP guidelines, we also used their previous 2010 guidelines [7], and those from the Foundation for the National Institutes for Health (FNIH) [8], Asian Working Group for Sarcopenia (AWGS) [9], and the International Working Group on Sarcopenia (IWGS) [10].

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, Chi square), with adjustments for small numbers and multiple testing, as required (Prism 8.4. Graph Pad, San Diego and IBM SPSS version 25, IBM Armonk, New York, USA).

Our prospective 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),

Results

Contemporaneous data was available for 146 patients (table 1), 4.1% with CKD stage 3b, 50% stage 4 and 45.9% stage 5 non-dialysis, and just over 30% screened positive using the Sarc-F questionnaire with a score of 4 or more. Patients screened positive for sarcopenia had greater weight, but this was fat mass, and lower HGS (table1). Relatively more non-white patients screened positive; 12 of 25 (48%) of Black ethnicity and 15 of 45 (33.3%) Asian patients, compared to 23% of those of white ethnicity. We recorded the results of physical examination and 22 patients (15.1%) were note to have some peripheral oedema, this included 13 (8.9%) with minimal to mild oedema, limited to the ankle, .and 9 (6.2%) as moderate (to mid-shin or below).

Using the cut-off values proposed by the different guideline groups for sarcopenia, then more patients had muscle weakness compared to loss of

appendicular muscle mass (Figure 1), More patients had appendicular muscle loss using the EWGSOP 2018 appendicular muscle mass, and the EWGSOP 2019 cut offs compared to the EWGSOP 2018 appendicular mass index cut off (Figure 1).

The prevalence of sarcopenia fell from 31.5% using the Sarc-F screening questionnaire to around 22% when HGS criteria were added, and then down to around 3% after adding the appendicular muscle mass index cut offs (Figure 2). If we excluded the screening Sarc-F questionnaire, and simply applied the different HGS criteria, and then the appendicular muscle index cut offs, compared to when using the Sarc-F screening questionnaire, then the prevalence of sarcopenia increased for EWGSOP 2018 appendicular mass index (2.8 to 7.5%, p=0.065), appendicular mass (4.8 to 13.7%, p=0.009), FNIH (4.8 to 17.1%, p=0.001), IWGS (4.8 to 16.4%, p=0.004), and AWGS (2.8 to 6.8%, p=0.10).

Discussion

Patients with CKD and those treated by dialysis are at greater risk of sarcopenia. Several specialist national and international interest groups have advocated different approaches to the diagnosis of sarcopenia, but these have generally been developed for different populations [1, 7-10]. The revised EWGSOP guidelines now advocate a 3-stage screening algorithm, which includes both a cut-off value for appendicular muscle and another for appendicular muscle indexed for height. The advantage of any such step-wise approach is that it reduces the number of patients who have to be assessed at each stage, and so reducing the impact on clinical resources.

Taking each of the criteria recommended by the EWGSOP independently, then more of our patients with CKD had muscle weakness, as defined by the HGS cut offs by the different guidelines, followed by those with an increased Sarc F screening questionnaire score, and then finally loss of appendicular muscle mass.. It has been suggested that muscle tissue in patients with CKD may contain increased amounts of fat or water, and so appear to maintain muscle bulk but lose function [2] We found no difference in appendicular muscle mass, either as the absolute amount of appendicular muscle mass or after indexing for height in those with low and high Sarc-F scores. To exclude an increase in water, we reviewed both the clinical assessments which showed that only 6.2% had peripheral oedema above the ankle to the mid-shin, and we also measured intracellular (ICW) and extracellular water (ECW), and although there were no absolute differences, the ECW/total body water (TBW) ratio was increased in those with a high Sarc-F score, but this was due to a loss of cell mass (ICW), as the ratio of ECW to height was not different, so excluding an increased ECW. We did however note that those patients who screened positive with the Sarc-F questionnaire were heavier, and this was due to increased body fat, and there has been increased interest in the concept of sarcopenic obesity and the association between obesity and fat infiltration into muscle [1,2]. This finding requires further investigation, as patients with CKD and kidney dialysis patients may require different cut-off values when screening for sarcopenia compared to other patient groups.

Using the EWGSOP three step approach, then the prevalence of sarcopenia fell from around 32% using the Sarc-F screening questionnaire to

just over 20% after then adjusting for HGS, and then down to <5% with the addition of appendicular mass. However, when we excluded the Sarc-F questionnaire and simply combined HGS measurements and cut offs and then added the appendicular muscle mass and cut offs, then the prevalence increased to between 7 and 17%, depending on which guideline cut offs were used, with the smallest difference observed with and without the Sarc-F screening tool when using the AWGS and 2018 EWGSOP appendicular mass index guidelines [1,9]. The Sarc-F questionnaire is a simple screening tool, that can readily be used in clinical practice and although this is based on patient self-reporting of 5 questions, it has been reported to be valid in different ethnic populations world-wide, providing consistent identification of patients at risk of developing adverse outcomes associated with sarcopenia [1].

Although by starting with the Sarc-F screening tool, a number of our patients with CKD would then have been excluded from subsequent investigation for sarcopenia, the main differences observed when applying or not using the Sarc-F questionnaire were when we used older guideline cut-offs derived from European studies published a decade ago [7], or North American studies published in 2011 and 2014, respectively [8,10].

We report on a relatively small cohort of predominantly older male patients with CKD, and as such our findings may not be comparable to other patient groups, with different demographics or co-morbidities. We aimed to minimised inter-observer error by using the same trained dietitian, and employing bioimpedance equipment regularly serviced and calibrated by the manufacturer.

In our multi-ethnic population of patients with CKD, thenusing the revised EWGSOP three stage approach to establishing the diagnosis of sarcopenia, we observed very similar prevalences for sarcopenia, when compared to using the cut off criteria for muscle strength and appendicular muscle mass indexed for height advised by different national and international guidelines.

No author has any conflict of interest

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Figure 1. Prevalence of sarcopenia based on cut offs of hang grip strength and appendicular muscle mass index of the guidelines published by the European Working Group on Sarcopenia in Older People (EWGSOP) 2018 and 2010, Foundation for the National Institutes of Health (FNIH), Asian Working Group for Sarcopenia (AWGS). EWGSOP* appendicular muscle mass. * p<0.05, *** <0.001 vs EWGSOP-2018

Figure 2. Prevalence of sarcopenia based on cut off of the Sarc-F questionnaire, and then step wise according to hang grip strength and then appendicular muscle mass index using the guidelines published by the European Working Group on Sarcopenia in Older People (EWGSOP) 2018 and 2010, Foundation for the National Institutes of Health (FNIH), Asian Working Group for Sarcopenia (AWGS). EWGSOP* appendicular muscle mass.