Reviewer's report

Title: Various Appendicular Skeletal Muscle Cut-Points with Different Research Definitions Associated with Health-Related Quality of Life in Korean Elderly: Data from KNHANES 2008-2011

Version: 2 Date: 7 July 2014

Reviewer: Rachel Cooper

Reviewer’s report:

This paper compares the use of three different sets of cut-points to identify those people in the older Korean population with low levels of appendicular skeletal muscle mass index (ASMI). Prevalence estimates are compared and the associations of each of the 3 definitions of low ASMI with different domains of a self-reported measure of health-related quality of life are investigated.

As debates continue about how best to identify those older people in the population with clinically relevant age-related changes in muscle who may benefit from intervention, there is a need to explore the definitions that are being recommended in the literature in different populations and settings. This study, which draws on data from a large population sample, thus has the potential to contribute to this debate and provide useful empirical evidence. However, a number of recent developments in this ongoing debate are currently overlooked by the authors; if these were to be addressed the paper would be able to make a more useful contribution to the literature.

Major compulsory revisions

1) While the earliest definitions of sarcopenia focused on the age-related loss of muscle mass, there is now recognition that loss of muscle mass per se may not be the most clinically relevant age-related change in muscle and that perhaps other age-related changes in muscle structure and function are more important in terms of their impact on subsequent functional and clinical outcomes. There are a number of papers which discuss this and which the authors should draw on to place their work in the context of the current debates in this area (see for example, Visser M, Schaap LA. Consequences of sarcopenia. Clin Geriatr Med. 2011;27:387-399 and Correa-de-Araujo R, Hadley E. Skeletal muscle function deficit: a new terminology to embrace the evolving concepts of sarcopenia and age-related muscle dysfunction. J Gerontol A Biol Sci Med Sci 2014; 69(5):591-594). Did the authors also have the opportunity to investigate other characteristics of muscle e.g. strength, quality, performance?

2) The European Working Group on Sarcopenia in Older People (EWGSOP) consensus definition on sarcopenia is just one of a number of different consensus definitions that have been proposed in recent years (see for example, Dam TT, Peters KW, Fragala M, Cawthon PM, Harris TB, McLean R et al. An evidence-based comparison of operational criteria for the presence of
sarcopenia. J Gerontol A Biol Sci Med Sci 2014; 69(5):584-590). The authors should acknowledge that other definitions have been proposed and justify their focus on this one.

3) A potential challenge when operationalising the EWGSOP definition of sarcopenia, which I think the authors are trying to address, is that it is not entirely clear what the most appropriate cut-point for the identification of low ASMI is. Further, it is unclear whether any one cut-point suggested can be universally applied or whether this needs to be population-specific. If I have read this correctly and this is one of the challenges that the authors are trying to address they should make this clearer.

4) Most existing consensus definitions of sarcopenia include low ASMI, however, in addition to the debate about what cut-points for ASMI should be applied (see point 3), my understanding is that there is also an ongoing debate about whether ASMI (i.e. ASM/height2) is the most appropriate measure of muscle mass to use. Recommendations recently published by the FNIH Sarcopenia project, which the authors should refer to and place their work in the context of, (see Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci 2014; 69(5):547-558) include a measure of ASM adjusted for BMI (rather than height). This is because of growing evidence that it is important to take account of fat mass when trying to identify those people in the population most likely to have insufficient muscle mass to support movement (see for example, Newman et al, JAGS 2003 (already cited by the authors)). This may be more relevant in populations with higher prevalence of obesity but an interesting question that could be addressed using the KNHANES data is whether in a Korean population there is value when relating muscle mass to functional and clinical outcomes in using a measure of ASM that takes account of BMI or fat mass (rather than height).

5) My understanding is that in their paper, Newman and colleagues (2003) were not recommending a cut-point of 20% for use across different populations. They used a cut-point of 20% in their analyses (as we have also recently done, see Cooper R et al, J Gerontol Med Sci In press (2014)), to ensure that their models relating low levels of different characteristics of muscle to other variables were comparable. A cut-point of 20% is unlikely to be useful in other settings because by definition 20% of people will always be identified in any population examined even if their characteristics (e.g. age, gender, risk of subsequent outcomes etc.) differ markedly. I would recommend that the authors remove this definition from their analyses.

6) Have the authors any thoughts on why their ASMI data were not normally distributed? Does this suggest selection effects? Was a severe left skew observed in both the younger and older populations? The implications of this should be discussed; it suggests that it may not be valid to apply cut-points based on 1 or 2SDs below the mean of a younger population as these have been identified based on the assumption that data are normally distributed.
7) What was the justification for examining health-related quality of life as the main outcome? Was there any possibility to examine outcomes such as mobility limitations?

8) It would be very useful (from both a clinical perspective but also in order to understand the models and assess the impact of adjustment for covariates) to see a report of the unadjusted effect estimates as well as fully-adjusted estimates in tables 4 and 5 (and also in the abstract and results sections).

9) Please clarify the models used to test the associations between each of the three different definitions of low ASMI and the different EQ-5D outcome measures. The description of methods and the results presented (in the text and tables) are not very clear.

10) The first paragraph of the discussion should provide an overview of the main findings. It is not entirely clear, when 3 definitions have been investigated, why the authors focus on those older people in the bottom 2.28 percentile of SMI (if this is because it represents those who have ASMI 2SD below the mean value in a younger population this should be made clear).

Minor essential revisions

1) The term ‘elderly’ is best avoided in the title and throughout the paper as it has many negative connotations. It is common practice to refer to older people and populations.

2) On the first page of the methods (lines 90 onwards) it would be helpful to know what the target sample for KNHANES was and how many respondents there were in total (prior to the exclusion of those without DXA data). It would also be helpful if the authors could report how many people were excluded because they were pregnant, had a weight #136kg or height #196cm (lines 99-100). Were any sensitivity analyses undertaken to examine how those people included in analyses differed from those excluded? This would help establish how representative these data are and whether any biases are likely to have been introduced.

3) Please clarify how many people had missing DXA data because of prosthetic devices, implants or other objects.

4) In the abstract and the ‘definition of low SMI’ section (line 109 onwards) please could the authors make their description of how the 3 different definitions of low ASMI were operationalised clearer. I assume that the descriptive data on the younger population were used to identify cut-points that were then applied to the older population and that the prevalence estimates reported for the different definitions in the abstract refer to the older population but this is not sufficiently clear (and may be very confusing for readers not familiar with the literature on sarcopenia).

5) Abbreviations used in the abstract (e.g. SMI 2SD, SMI 20) need to be more clearly defined.
6) Please could the authors provide justification for their selection of covariates.

7) In their results section the authors refer to the range of values but then only present a mean and SD. Please change either the description or report the minimum and maximum values (i.e. the range). Given these data are not normally distributed it is questionable whether a mean and SD should be presented (both in the text and in table 1). At the very least it would be useful to see the median and inter-quartile range.

8) What is being referred to when the authors report on lines 174-175 ‘There was not a large difference in the male….but more of a difference was evident in the females…’?

9) It is very difficult to interpret the concluding statements of the paper (in the main text and abstract) and so please consider revising these.

10) What do the estimates in tables 4 and 5 represent and are these needed as well as the odds ratios?

Discretionary revisions

1) It is unclear what the value is of reporting in the abstract that the prevalence is 20% when using the SMI 20 definition as by definition it must be 20% (see point 5 of major compulsory revisions above).

2) Information on lines 158-160 is a repeat of information provided on lines 109-125.

3) Results in the text need only be reported to 2 decimal places.

4) As the appendicular skeletal muscle mass index has been used please refer to ASMI rather than SMI throughout the manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests