Osteoporosis and Sarcopenia 7 (2021) S1–S2

Contents lists available at ScienceDirect

Osteoporosis and Sarcopenia

journal homepage: http://www.elsevier.com/locate/afos

Review article

Summary of the special issue of the meta-analyses of lean mass with mortality in multiple perspectives

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ARTICLE INFO

Article history:
Received 10 March 2021
Accepted 11 March 2021
Available online 23 March 2021

Keywords:
Sarcopenia
Mortality
Lean mass
Association
Cancer

Sarcopenia was previously used to describe deficiency of muscle mass. However, decrease in muscle strength is now the principal determinant of sarcopenia, instead of muscle mass [1]. This prompts a question of what the role of low muscle mass is. Given that direct measurement of muscle mass is technically difficult, lean mass, which is composed of primarily muscle mass, is the most commonly used surrogate of muscle mass.

In this special issue, we primarily evaluated the role of lean mass in mortality from different perspectives [2]. The robust association of lean mass with mortality suggests that it could be a predictor of mortality [3]. Yet, the accuracy of the prediction was not evaluated in the meta-analysis, as it was out of the scope of our study. Although we provide robust evidence on the association of lean mass with mortality, we did not independently assess the effect of muscle strength and function out of lean mass, as they are expected to be highly correlated. In our previous study using the data from the continuous NHANES [4], we stratified the population based on whether the study participants have normal gait speed and/or lean mass or not. We observed a consistent association with mortality in people with normal lean mass but slow gait speed. However, the association was inconsistent in people with normal gait speed but low lean mass. This is in line with the recent consensus that muscle strength overtakes the role of muscle mass as the principal determinant of sarcopenia [1,5,6]. Nevertheless, given that lean mass can be measured easily using digital scale with built-in bioelectrical impedance analysis (BIA) function, whether measuring lean mass alone is sufficient for assessment of sarcopenia is of clinical importance.

Loss of lean mass could be due to primary (age-related) and secondary causes (other than age-related cause). Lee et al [3] in this special issue showed that the association of low lean mass due to primary cause was significantly associated with increased risk of mortality. When compared with low lean mass due to secondary causes, the hazard ratio observed in the elderly population was the lowest when compared with the hazard ratio observed for other clinical conditions. This is not surprising, as low lean mass due to secondary causes could be a marker of disease progression and body catabolism, which are known to be associated with increased risk of mortality. As aforementioned, BIA is now commonly used even in the household digital scale. Thus, the usefulness of measuring lean mass using BIA is of public health significance. Among all commonly used modalities in assessing lean mass, BIA was used as the least preferred. Li et al [7] in this special issue, we showed that BIA-measured lean mass was indeed robustly associated with mortality. This is a clear message showing that measuring

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Peer review under responsibility of The Korean Society of Osteoporosis.

https://doi.org/10.1016/j.afos.2021.03.005

lean mass using the BIA function in the digital scale could be a simple way in health monitoring.

Au et al [8] in this special issue, we examined the relationship between lean mass and cancer. Lean mass is again robustly associated with cancers. Notably, the number of studies included in the meta-analyses of several types of cancers was small, such as breast cancer (n = 1). Thus. no definite conclusion can be drawn. As this systematic review and meta-analysis searched for literature up to end of 20,17[2], and many studies have been published since then, an updated meta-analysis will be important. Computed tomography (CT) is commonly used in cancer management, with lumbar L3 skeletal muscle index and psoas muscle commonly used to quantify muscle mass. However, the usefulness of psoas muscle has been controversial [1,9,10], since it is a small muscle, despite its high correlation with overall muscle mass [11]. Au et al [8] in this issue, we observed that both L3 skeletal muscle index and psoas muscle were both significantly associated with mortality. These observations provide further evidence on the validity of using psoas muscle to ascertain sarcopenia status.

Different cutpoints have been adopted in defining low lean mass for primary sarcopenia [1], but whether such cutpoints are useful in cancer-related sarcopenia is unclear. Thus, several cutpoints have been derived specifically for cancer-related sarcopenia, including the International Consensus of Cancer Cachexia [12,13], Martin [14], or Prado [15]. The relationship of different cancer-specific cutpoints with mortality were evaluated by Li et al [16] in this issue, and they showed a similar estimate. In summary, the meta-analyses included in this issue provide not only evidence on the relationship between low lean mass and mortality in different perspectives, but also propose several areas for further investigations.

Although the research community has been advocating the diagnosis and management of sarcopenia in clinical practice, multiple problems are still left to be solved. Examples include the perspectives investigated in the meta-analyses in this special issue, such as measurement modalities, site of measurement, cutpoints used in special population. These problems are indeed also present in the measurement of other sarcopenia components, such as grip strength. Grip strength would be affected by speed of twisting, use of dominant vs non-dominant hand, positioning of arms, and rest time between each test. Optimizing these factors could potentially enhance the predictive power of grip strength further. Moreover, to the best of our knowledge, we are the first group who derived an age-related loss of muscle strength (namely dynapenia) using a T-score that was derived from the normative data from the local Chinese population in Hong Kong [17,18], which is similar to the T-score calculation for bone mineral density. Given that grip strength is ethnic- and population-specific due to difference in genetics, diet, and lifestyle, deriving a population-specific T-score may be more accurate in reflecting the loss in muscle strength than using a specific cutoff point derived from a consensus based on studies from different ethnicities and populations. Nevertheless, in addition to performing studies such as dual-energy X-ray absorptiometry for measuring bone mineral density, a standard protocol in assessing sarcopenia is highly recommended.

In conclusion, this special issue provides not only a clearer picture about the role of lean mass in mortality, but also proposes several areas for further study. Development of a standard protocol in guiding measurement of sarcopenia related phenotypes is important. Such development requires further investigations. Regional and global collaborations are expected to facilitate the whole development process.

CRediT author statement

Ching-Lung Cheung: Conceptualization, Writing - Original Draft, Writing - Review & Editing, Supervision. **Gloria Hoi-Yee Li**: Writing - Original Draft, Writing - Review & Editing.

Conflicts of interest

All authors declare no competing interests.

Acknowledgements

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