LETTERS TO THE EDITOR

SENSITIVITY AND SPECIFICITY OF THE HANDGRIP STRENGTH IN THE PREDICTION OF LOW MUSCLE MASS IN HOSPITALIZED OLDER PATIENTS

To the Editor: In the article entitled “Potential prognostic value of handgrip strength in older hospitalized patients” published in the first issue of The Journal of Frailty & Aging (1), Savino and colleagues presented the handgrip strength as a predictor of hospitalization length of stay in older patients admitted to an acute care unit. Authors reported an inverse association between muscle strength at the admission and subsequent duration of the hospital stay, even after adjustment for potential confounders.

The relationship existing between handgrip strength and the risk of major health related events (including disability and hospitalization) is well established in literature (2). The proposal of adopting the handgrip strength in the clinical setting supports the growing request of implementing physical function measures in the routine evaluation of geriatric patients.

To date, the handgrip strength test is mainly used in clinical research as a marker of global muscular strength. Poor results at the handgrip test (together with the simultaneous presence of low muscle mass) have recently been proposed in the definition of sarcopenia (3). Sarcopenia is a geriatric syndrome and an important matter of research, due to its close relationship with physical impairment and disability (2). An intense debate is currently ongoing about the proper operational definition able to capture the age-related decline of skeletal muscle quantity and quality. In these last years, several groups of experts have released recommendations to adequately identify sarcopenia in older persons (3-6). Although each consensus paper provides different algorithms, the common element shared by all the propositions was the combined adoption of a bidimensional approach, measuring at the same time the amount of skeletal muscle (using different body composition techniques, e.g., dual energy X-ray absorptiometry, bioelectrical impedance analysis, computed tomography, or magnetic resonance imaging) together with a marker of muscle function (adopting physical performance or muscle strength measures, e.g., gait speed, handgrip strength)(3-6).

Given the relevance of sarcopenia in geriatric research as the most evident phenomenon of aging, it is possible that a growing number of studies will be planned in the future to specifically target this condition. However, screening of participants by evaluating both quantitative and qualitative parameters of skeletal muscle might be unfeasible due to the costs and time needed to conduct the imaging techniques. Having an easy-to-administer, well-accepted, validated, and cheap parameter that might replace the assessment of muscle mass in the screening phase of a sarcopenia trial might be important.

In this context, we recently conducted secondary analyses aimed at exploring the sensitivity and specificity of poor handgrip strength for low skeletal muscle mass in older patients admitted to an acute care setting. Results of this study were presented at the 56th Annual Meeting of the Italian Society of Gerontology and Geriatrics (7).

We recruited 162 patients, admitted during a period of 4 months to Division of Geriatrics (University of Verona, Italy). All patients were tested for their handgrip strength using a hand-held dynamometer (model Jamar® 2A, JA Preston Corp., Clifton, NJ, USA) at their hospital admission. Patients were asked to repeat three times the assessment with their dominant hand; the best of the three values was considered for the present analyses. Poor muscle strength was defined by the gender-specific cut-points of <30 kg and <20 kg for men and women, respectively (8).

Body composition was estimated by a bioelectrical impedance analysis (BIA) device (Soft-Tissue-Analyzer-STA, Akern, Florence, Italy). The skeletal muscle mass index was defined as appendicular skeletal muscle mass (in kilograms) divided by the square of height (in meters). Patients with metallic implants, mechanical protheses, or diseases associated with fluid retention (e.g., nephrotic syndrome, dysproteinemia, untreated heart failure) were excluded from the analyses to avoid biasing the body composition results. Patients unable to complete the handgrip test due to serious medical conditions were also excluded.

To define a dichotomous variable of low muscle mass, we also recruited a reference group of 98 apparently healthy Caucasian individuals aged between 25 and 39 years (body mass index, BMI, ranging between 18 e 26 Kg/m2). Based on the of skeletal muscle mass index value identified at -2 standard deviations (SDs) in this referent group, we set the critical cut-point defining low muscle mass at ±0.44 kg/m2 and ±0.32 kg/m2 in women and men, respectively. Interestingly, such cut-points are very similar to others previously reported in other studies (9-11).

Participants (prevalence of women: 37%) had a mean age of 81.6 (SD 7.0) years old, and mean BMI of 25.7 (SD 4.8) kg/m2. In our study sample, 65.4% of patients presented poor muscle strength, and 27.1% had low muscle mass. Analyses were stratified in two different subgroups according to the capacity (n=118) or incapacity (i.e., bedridden patients, n=44) to walk. In the first group, 61.8% had poor results at the handgrip test, whereas such prevalence was higher in the second group (75%). At the same time, 22.8% of patients with no mobility disability and 38.6% of bedridden patients had low muscle mass.

In the group of participants with no mobility disability, poor handgrip strength had high sensitivity (100%) and low specificity (55.5%) to identify individuals with low muscle mass. Similar results were obtained in the bedridden group.
In other words, all the participants with low muscle mass also presented poor handgrip strength. Differently, almost half of those having normal muscle mass had abnormal results at the handgrip test (explained by third factors, e.g. malnutrition, weakness, poor cognition and clinical conditions).

We believe that our data might be of interest for researchers planning to conduct clinical trials in older persons on sarcopenia. Our findings demonstrate that the presence of normal handgrip strength might efficiently discriminate individuals highly unlikely to be sarcopenic (also consistently with the current operational definitions proposed by consensus papers). Therefore, the assessment of body composition and the specific quantification of muscle mass could be limited to only those individuals presenting abnormal values of muscle strength.

The body composition assessment (especially when the most accurate and reliable techniques are used) is often difficult for older persons, and almost impossible to be conducted in bedridden individuals. The possibility of preselecting individuals which might be more likely to present sarcopenia on the basis of results from an easy test as the handgrip test might significantly facilitate researchers in the area.

Our analyses were conducted stratifying results according to their mobility capacity. This choice was justified by the worse results at both the handgrip test and appendicular lean mass assessment reported in bedridden patients compared to those able to walk. After all, it is well-know that immobility and disuse are important factors involved in the loss of muscle mass and strength in the elderly (12). However, results in the two groups were very similar, showing in both that poor muscle strength reported the maximum specificity for low muscle mass.

Although taking into account the major limitation residing in the cross-sectional nature of our data, we might speculate that our findings may suggest a temporal sequence in the development of the two defining component of sarcopenia. In fact, while low muscle mass was always present in the presence of poor muscle strength, the opposite occurred just in half of the cases. Therefore, it is possible that the decline of muscle mass may precede the decrease of muscle strength.

Finally, it is also noteworthy that the preliminary use of physical performance and muscle strength measures has been suggested in consensus papers as the first approach towards the diagnosis of sarcopenia. After all, since the two conditions (poor quality and low quantity) of skeletal muscle health needs to be simultaneously present to define sarcopenia, it makes sense to start assessing them from the easiest and cheapest. Our data may provide statistical support and justification to such reasonable approach.

Our study sample was relatively small and characterized by hospitalized older patients in an acute geriatric setting. Therefore, our findings might not be directly applicable to other populations and/or in other settings. In this context, we cannot exclude that our results might have been biased by third factors (such as acute clinical conditions) able to negatively affect the two dimensions of the skeletal muscle. It is also important to mention that our definition of low muscle mass was based on results from the BIA. Other techniques measuring muscle mass (as well as muscle strength) might provide different results, thus potentially modifying our conclusions. For these reasons, the present report should be considered as a preliminary step in the attempt of optimizing the design of clinical trials on sarcopenia. Further studies on this topic are needed to confirm and extend our findings.

In conclusion, our results show that having normal handgrip test seems to quite automatically exclude the presence of low muscle mass. These data imply that an easy evaluation of muscle strength (as the one adopted in our study) may indeed efficiently serve to better identify subjects at risk of presenting sarcopenia.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Patients with low muscle mass</th>
<th>Patients with normal muscle mass</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants with no mobility disability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor handgrip test</td>
<td>27</td>
<td>46</td>
<td>73</td>
</tr>
<tr>
<td>Normal handgrip test</td>
<td>0</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>27</td>
<td>91</td>
<td>118</td>
</tr>
<tr>
<td><strong>Bedridden participants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor handgrip test</td>
<td>17</td>
<td>16</td>
<td>33</td>
</tr>
<tr>
<td>Normal handgrip test</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>17</td>
<td>27</td>
<td>44</td>
</tr>
</tbody>
</table>

(sensitivity 100%, specificity 40.7%; Table 1).
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FRAILTY AND COGNITION: NOT AS STRAIGHT-FORWARD AS IT MIGHT APPEAR

To the Editor: In a previous issue of the Journal of Frailty & Aging, Houles and colleagues (1) presented a review paper entitled “Frailty and cognition”. The association between frailty and cognitive impairment was proposed, and Authors discussed a large amount of evidence. However, a number of conceptual and methodological issues should be taken into account as potentially affecting the possibility to include cognition in the operational definition of frailty (as suggested by Authors). Frailty should be considered as a construct under development and several concepts are still intensely discussed (2). We think the paper fails to fully cover the vast amount of on-going debate in this field. In particular:

1) Frailty has been defined as an insufficient capacity of the organism to react to stressors, consequently leading to an increased risk of adverse outcomes (e.g., falls, disability, death) (3). Several attempts have been made in order to operationalize its theoretical definition, with the criteria proposed by Fried and colleagues (3) and the Frailty Index designed by Rockwood and colleagues (4-5) among the others. A still open issue in the field is represented by the different conceptual and structural design of these definitions, giving rise to inconsistencies of data and difficulties in the interpretation of findings. Such problem has been described by Collard and colleagues (6) when discussing the too large variability of frailty prevalence (ranging from 4 to 59.1%) in a recent systematic review. Consistently, Houles and colleagues present a number of studies characterized by a great heterogeneity. For example, only 58.3% of the considered studies adopt the same method to assess cognition (without a unique clear definition of impairment or clinically relevant thresholds) and only 16.7% used a similar definition of frailty. Therefore, the comparability and the representativeness of the studies included in the paper might be argued.

2) If we consider the so-called “geriatric syndromes” (such as urinary incontinence, falls, depression, malnutrition…), growing evidence shows that their addition to the construct of frailty increases the capacity to predict the risk of adverse outcomes (7, 8). So, the questions are: why should not these other conditions be added as well among the defining frailty criteria? Why this special consideration for the only cognitive impairment? To improve the predictive capacity of frailty variables? (9)

3) A further point of concern is due to the different approaches that can be used to describe frailty. Frailty is an extremely complex condition resulting from the derangement of multiple physiological dynamics. Experiments by Goldberger and colleagues (10) have shown that the heart rhythm entropy (i.e., R-R variability) is lower in frail subjects in comparison to healthy older persons. They hypothesized the existence of an underlying mechanism that could generate frailty as a result of a derangement of a complex action (such as heart rate) which in turn gives rise to the lack of response to stressors. Although a review by Drachman points out to a possible loss of complex physiological tasks in Alzheimer’s disease (12), this has not been clearly demonstrated for cognitive impairment.
However, this does not automatically imply the existence of a parsimonious approach (in contrast to more complex ones). Related to the same aging process” (1) is an appealing and cognition have obvious interrelationships, at least as both being to be definitive. The final statement suggesting that “frailty and available definitions are still too ambiguous and controversial sufficient evidence that cognitive impairment shares the same parameter versus a dynamic physiological response (4). It is obvious that hospitalized or institutionalized subjects are from comparing studies of very different populations, such as community dwelling, acute care, and institutionalized subjects. Therefore, the reported findings might be simply explained by not considered third factors. Potential bias may also derive to influence both the dependent and independent variables. Therefore, the reported findings might be simply explained by not considered third factors. Potential bias may also derive from comparing studies of very different populations, such as community dwelling, acute care, and institutionalized subjects. It is obvious that hospitalized or institutionalized subjects are more likely to simultaneously present cognitive and physical problems (16).

In conclusion, we agree with the Authors about the need for additional research with specifically designed studies. It is particularly important to explore the direction of the two conditions (i.e., does frailty produce cognitive impairment or vice versa?), although the typical synergistic interaction existing within geriatric syndromes should also be considered. We believe that frailty should not include cognitive impairment among its defining criteria, at least at this moment. There is not sufficient evidence that cognitive impairment shares the same underlying pathophysiological processes with frailty and available definitions are still too ambiguous and controversial to be definitive. The final statement suggesting that “frailty and cognition have obvious interrelationships, at least as both being related to the same aging process” (1) is an appealing and parsimonious approach (in contrast to more complex ones). However, this does not automatically imply the existence of a "cognitive frailty" condition.

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