Research Article

Association of Low Lean Mass With Frailty and Physical Performance: A Comparison Between Two Operational Definitions of Sarcopenia—Data From the Berlin Aging Study II (BASE-II)

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Abstract

Background. For prevention and treatment of sarcopenia, defined as a decline in lean mass, reliable diagnostic criteria and cutpoints reflecting a clinically relevant threshold are indispensable. As of yet, various parameters have been proposed but no gold standard exists. The aim of this study was to compare cutpoints of appendicular lean mass related to body mass index (ALM\textsubscript{BMI}) or height (ALM/height\textsuperscript{2}) regarding their association with self-reported physical limitations and frailty status in a sample of community-dwelling older adults.

Methods. A total of 1,343 participants from the Berlin Aging Study II were included. ALM index was assessed with dual-energy X-ray absorptiometry. Limitations in physical performance were assessed via questionnaire and frailty status was defined according to the Fried criteria.

Results. In a risk factor-adjusted analysis, participants with an ALM\textsubscript{BMI} below the cutpoints had 1.4–2.8 times higher odds of difficulties in several domains of physical activity (\(p = .031\) to \(p < .0001\)) compared with participants with normal ALM\textsubscript{BMI}. In participants with low ALM/height\textsuperscript{2}, no associations with physical limitations were found. Moreover, the odds of being prefrail/frail were statistically significant for the low ALM\textsubscript{BMI} group only (odds ratio = 2.403, 95% confidence interval: 1.671–3.454, \(p < .0001\)) and not for the low ALM/height\textsuperscript{2} group.

Conclusions. This study showed striking differences between the two operational criteria ALM/height\textsuperscript{2} and ALM\textsubscript{BMI} concerning their association with physical limitations and prefraility/frailty. The low ALM\textsubscript{BMI} cutpoints seem suitable to detect patients at risk for negative outcomes such as frailty who might benefit from interventions targeted at improving lean mass.

Key Words: Sarcopenia—Frailty—Functional performance.

Decision Editor: Dr. Stephen Kritchevsky

The age-associated loss of lean mass is a defining parameter of sarcopenia and may lead to various negative health outcomes such as impairment of physical performance and disability (1). Furthermore sarcopenia is considered to be one of the main factors in the pathogenesis of the frailty syndrome (2,3). However, for clinical use and for treatment and prevention strategies, reliable diagnostic criteria
and cutpoints based on clinically relevant thresholds are indispensable. This topic has recently been addressed by the Foundation for the National Institutes of Health Sarcopenia Project which identified cutpoints for appendicular lean mass (ALM) below which older adults had a higher likelihood of clinically relevant weakness reflected by low grip strength (4,5). Moreover, a low ALM-to-body mass index (BMI) ratio (<0.789 men and <0.512 women) was found to be associated with increased likelihood for mobility impairment (6). However, the last years showed an abundant use of ALM corrected by height squared (ALM/height²) as the defining parameter of low muscle mass in the context of sarcopenia, using cutpoints of the New Mexico Elder Health Study (<7.26 kg/m² in men and <5.45 kg/m² in women) (7) alone or in conjunction with low strength or slow gait speed (8,9). This approach has been widely adopted by other studies. In an attempt to validate the recently published cutpoints (4,6), we studied both cutpoints of the parameters ALM-to-BMI ratio (ALM/BMI) and ALM/height² and their association with self-reported physical limitations as well as compared their ability to predict the frailty syndrome in a cross-sectional sample of community-dwelling older adults of the Berlin area in Germany.

Methods
Participants
Altogether 1,343 participants from the Berlin Aging Study II (BASE-II) recruited between 2009 and 2013 were included in this cross-sectional analysis. BASE-II is a prospective epidemiological study to investigate factors associated with “healthy” or “unhealthy” aging in the residents of the greater metropolitan area of Berlin, Germany which has been described previously in detail (10). Briefly, participants were community-dwelling, comparably well-functioning older participants aged between 60 and 82 years. All participants gave written informed consent and the Ethics Committee of the Charité—Universitätsmedizin Berlin approved the study (approval number EA2/029/09).

Anthropometric Measurements
Body weight was measured in light clothes with a portable electronic scale to the nearest 0.1 kg and height was determined to the nearest 0.1 cm by using an electronic weighing and measuring station (Seca 764; Seca, Hamburg, Germany). Weight and height were used for calculating the BMI (weight [kg]/height [m]²).

Body Composition and Lean Mass Cutpoints
Body composition was assessed with dual-energy X-ray absorptiometry (Hologic QDR Discovery; Hologic Inc., Bedford, MA) with a trained technician performing the dual-energy X-ray absorptiometry measurement protocol. Total nonbone lean mass was determined from the difference between total lean mass and bone mineral content; and ALM in kilograms was calculated as the sum of the regional lean mass of the four limbs. From this ALM/height² (kg/m²) and ALM-to-BMI (ALM/BMI) ratio were derived. ALM/height² ≤7.26 kg/m² in men and ≤5.45 kg/m² in women were chosen as cut-off values according to the definition proposed by Baumgartner and colleagues (7) which is based on the assumption that a value 2 SDs below the mean value of a young reference cohort reflects sarcopenia. Participants with an ALM/height² below these cutpoints were characterized as the low ALM/height² group. As cut-off values for ALM/BMI <0.789 in men and <0.512 in women were chosen according to the lean mass thresholds for higher likelihood of weakness as identified within the Foundation for the National Institutes of Health Sarcopenia Project (4). Participants with an ALM/BMI below these cutpoints were characterized as the low ALM/BMI group.

Frailty
Frailty was defined according to the validated definition proposed by Fried and colleagues based on the five criteria unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity (11,12). Some minor adjustments compared with the original methodology had to be made since not all assessment methods used by Fried and colleagues were also available in the BASE-II study. In detail

1. Weight loss was defined as unintentional loss of at least 5% of the body weight in the last year.
2. Self-reported exhaustion was identified by two questions from the “Center for Epidemiological Studies Depression Scale” (13).
3. Weakness was assessed by measuring hand grip strength with a Smedley Dynamometer (Scandidact, Denmark). Participants were instructed to perform a maximal isometric contraction and the test was performed three times for each hand and the highest value was chosen. The cut-off values stratified by gender and BMI as suggested by Fried and colleagues were used to identify reduced grip strength reflecting weakness.
4. Slow walking speed was judged by using the timed “Up&Go” test (14). The time in seconds taken to stand up from a chair, walk a distance of 3 m, turn, walk back to the chair, and sit down again was measured for the participants. Participants unable to complete the test in less than 10 seconds were considered to have a slow walking speed.
5. Low physical activity was based on the question “Are you seldom or never physically active?” If answered “Yes” the criterion was fulfilled.

According to how many criteria were met, participants were ranked as frail (3–5), prefrail (1–2), or not frail (0). For statistical analysis, prefrail and frail were combined into one variable.

Self-Reported Physical Limitations
Participants were asked whether they had difficulties performing certain physical tasks such as lifting or carrying, bending or kneeling, bathing or getting dressed, climbing several flights of stairs, walking (>1 km), or performing exhausting activities such as lifting heavy objects, walking fast, or running (severe/moderate/no difficulties).

Confounders
In the regression models, age and sex were included as potential confounders as well as comorbidities such as depression or depressive symptoms, chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, congestive heart failure, diabetes, and arterial hypertension as they all may have an effect on either strength or mobility. Comorbidities were either taken from the medical history recorded by a study physician or determined via laboratory tests (glomerular filtration rate in case of chronic kidney disease and oral glucose tolerance test in case of diabetes). Depressive symptoms were assessed via Center for Epidemiological Studies Depression scale or taken from medical history.

Statistics
Statistical analyses were carried out using the software package IBM Statistics SPSS 21. Data are given in percentage or as mean and standard deviation. Student’s t test was performed to compare means
between groups. Chi² test was used to compare percentages between groups in relation to categorical variables. A binary logistic regression controlling for potential confounders was performed to calculate odds ratios (95% confidence interval interval) of being prefrail/frail (combined variable) or experiencing moderate to severe physical limitations according to low ALM/height² and low ALM_BMI. An acceptable level of statistical significance was established a priori at p < .05.

**Results**

One thousand three hundred and forty-three participants with a mean age of 68.2 ± 3.6 ranging from 60 to 82 years were included in this analysis. A low ALM/height² was found in 25.5% of the participants, whereas a low ALM_BMI was less frequent and found in 15.8% of the participants. Only 4.3% of the women and 7.3% of the men showed a low lean mass according to both definitions as can be seen in **Figure 1**.

Overall more men than women had low lean mass according to both criteria but these differences were significant only for ALM_BMI (p < .001). Only 0.9% of the participants were diagnosed as frail but 30.7% met the criteria for being prefrail. As can be seen in **Table 1**, comparison of individuals with lean mass above or below the cutoffpoints of the two respective criteria (ALM/height² and ALM_BMI) revealed the differential impact of these definitions. Participants with low ALM/height² were significantly leaner than those with normal ALM/height², whereas individuals with low ALM_BMI had a higher BMI despite lower ALM.

**Low Lean Mass and Physical Limitations**

Both parameters of low lean mass were investigated with regard to associations with self-reported physical limitations (moderate or severe) in a logistic regression model adjusted for age, sex, and comorbidities with possible impact on muscle mass, strength, or aerobic capacity (ie, depressive symptoms, chronic kidney disease, chronic...
obstructive pulmonary disease, coronary artery disease, congestive heart failure, diabetes, and arterial hypertension). Participants with a low \( \text{ALM}_{\text{BMI}} \) roughly had 1.4–2.8 times higher odds of experiencing limitations in all of the examined domains of physical activity. These results, shown in Table 2, were all statistically significant (<0.0001) in comparison to the group with normal lean mass according to \( \text{ALM}_{\text{BMI}} \). For those with a low \( \text{ALM}/\text{height} \), no statistically significant associations with physical limitations in any of the categories were found, except for “kneeling and bending” where low \( \text{ALM}/\text{height} \) was even associated with no limitations.

### Table 1. Characteristics of the Study Population, Stratified According to the Different ALM Criteria (\( \text{ALM}/\text{height} \) and \( \text{ALM}_{\text{BMI}} \)) and Their Cutpoints

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>( \text{ALM}/\text{Height} )</th>
<th>( \text{ALM}_{\text{BMI}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>&gt;Cutpoint</td>
<td>&lt;Cutpoint</td>
</tr>
<tr>
<td>Age (y)</td>
<td>994 (74.5)</td>
<td>340 (25.5)</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>68.0 ± 3.5</td>
<td>68.7 ± 3.8</td>
</tr>
<tr>
<td>ALM (kg)</td>
<td>27.7 ± 4.2</td>
<td>24.1 ± 2.8</td>
</tr>
<tr>
<td>Grip strength (kg)</td>
<td>34.6 ± 9.8</td>
<td>32.8 ± 8.4</td>
</tr>
<tr>
<td>TUG time (s)</td>
<td>7.8 ± 1.6</td>
<td>8.1 ± 1.9</td>
</tr>
<tr>
<td>Frailty (N/%)</td>
<td>8 (0.8)</td>
<td>4 (1.2)</td>
</tr>
</tbody>
</table>

Notes: Variables are presented as mean and standard deviation or in N and percent. ALM = appendicular lean mass; BMI = body mass index; TUG = timed “Up&Go” test.

*Data available for 1,288 participants.

### Table 2. Risk Factor-Adjusted Logistic Regression Displaying the Association of Low Lean Mass According to the Criteria Low \( \text{ALM}/\text{Height} \) and Low \( \text{ALM}_{\text{BMI}} \) With Self-Reported Physical Limitations

<table>
<thead>
<tr>
<th>Moderate/Severe Self-Reported Limitations in...</th>
<th>Low ( \text{ALM}/\text{Height} )</th>
<th>Low ( \text{ALM}_{\text{BMI}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Exhausting activities</td>
<td>1.086</td>
<td>0.807–1.462</td>
</tr>
<tr>
<td>Lifting or carrying</td>
<td>1.116</td>
<td>0.825–1.549</td>
</tr>
<tr>
<td>Climbing several flights of stairs</td>
<td>0.973</td>
<td>0.709–1.337</td>
</tr>
<tr>
<td>Kneeling and bending</td>
<td>0.728</td>
<td>0.537–0.987</td>
</tr>
<tr>
<td>Walking (&gt;1 km)</td>
<td>0.659</td>
<td>0.406–1.071</td>
</tr>
<tr>
<td>Bathing and/or dressing</td>
<td>0.537</td>
<td>0.254–1.11</td>
</tr>
</tbody>
</table>

Notes: Logistic regression adjusted for age, sex, and comorbidities (presence of COPD, CKD, CAD, CHF, hypertension, diabetes, and depressive symptoms). ALM = appendicular lean mass; BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; CI = confidence interval; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; OR = odds ratio.

### Table 3. Risk Factor-Adjusted Logistic Regression Displaying the Association of Low Lean Mass According to the Criteria Low \( \text{ALM}/\text{Height} \) and Low \( \text{ALM}_{\text{BMI}} \) With Frailty Status

<table>
<thead>
<tr>
<th>Frailty criteria</th>
<th>Low ( \text{ALM}/\text{Height} )</th>
<th>Low ( \text{ALM}_{\text{BMI}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>1.243</td>
<td>0.472–3.269</td>
</tr>
<tr>
<td>Exhaustion</td>
<td>0.881</td>
<td>0.535–1.452</td>
</tr>
<tr>
<td>Weakness</td>
<td>1.183</td>
<td>0.597–2.434</td>
</tr>
<tr>
<td>Slow walking speed</td>
<td>1.239</td>
<td>0.775–1.980</td>
</tr>
<tr>
<td>Low physical activity</td>
<td>0.800</td>
<td>0.477–1.344</td>
</tr>
<tr>
<td>Prefrail/frail</td>
<td>0.997</td>
<td>0.722–1.376</td>
</tr>
</tbody>
</table>

Notes: Logistic regression adjusted for age, sex, and comorbidities (presence of COPD, CKD, CAD, CHF, hypertension, diabetes, and depressive symptoms). ALM = appendicular lean mass; BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; CI = confidence interval; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; OR = odds ratio.

### Low Lean Mass and Frailty

Of those participants with a low \( \text{ALM}/\text{Height} \), 31.6% were prefrail and 1.2% were frail, whereas 48.5% of participants with a low \( \text{ALM}_{\text{BMI}} \) were prefrail and 2.0% were frail. The odds of being prefrail/frail were positive and statistically significant for the low \( \text{ALM}_{\text{BMI}} \) group but not for the low \( \text{ALM}/\text{height} \) group. These results are shown in Table 3. Regarding the individual frailty criteria, low \( \text{ALM}_{\text{BMI}} \) was significantly associated with weakness, slow walking speed, and low physical activity, whereas low \( \text{ALM}/\text{height} \) was not significantly associated with the individual frailty criteria. No statistically significant
Table 4. Logistic Regression Showing the Association Between Frailty Status and Low ALM/Height and Low ALM BMI Stratified to Sex

<table>
<thead>
<tr>
<th></th>
<th>Low ALM/Height²</th>
<th></th>
<th></th>
<th>Low ALM BMI</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>p</td>
<td>OR</td>
<td>95% CI</td>
<td>p Value</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prefrail/frail</td>
<td>0.806</td>
<td>0.506–1.283</td>
<td>.364</td>
<td>3.708</td>
<td>2.157–6.373</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Men</td>
<td>1.207</td>
<td>0.764–1.907</td>
<td>.419</td>
<td>1.720</td>
<td>1.045–2.830</td>
<td>.033</td>
</tr>
</tbody>
</table>

Notes: ALM = appendicular lean mass; BMI = body mass index; CI = confidence interval; OR = odds ratio.

association was, however, seen between low ALM BMI and exhaustion or weight loss. When stratifying the regression analysis according to sex (Table 4), it emerged that women with an ALM BMI below the cut-off had a higher risk of being frail than men with a lower ALM BMI.

Discussion

This study demonstrated striking differences between the two operational criteria for defining lean mass, ALM/height² versus the recently suggested ALM BMI, and their respective association with physical limitations and prefrailty/frailty. Fewer participants had a low ALM BMI than a low ALM/height² (25.5% vs 15.8% of the study population). Clearly, different criteria for low lean mass and the use of diverse correction factors for lean mass such as height, total body mass or fat mass, leads to a different selection of participants and therefore a varying prevalence of sarcopenia (15–19).

Participants with an ALM BMI below the cut-off had significantly higher odds of limitations in all domains of activities of daily living investigated here which was not the case for the low ALM/height² group. It has to be considered that adjusting lean mass for body mass or BMI instead of height reflects an individual’s lean-to-fat mass ratio and evidently accounts better for the unfavorable effect of proportionally higher fat mass (20). In order to be clinically relevant, thresholds for low lean mass need to reliably predict weakness and impaired function. The cutpoints for low ALM BMI were derived to intentionally discriminate between the absence or presence of weakness which may explain the physical performance deficits found in our study (4). We also considered the implementation of the weakness criterion according to the Foundation for the National Institutes of Health (21) in our analysis but had to dismiss this since only 0.7% of our study participants fulfilled this criterion.

Remarkably, in BASE-II community-dwelling old people with a low ALM BMI were approximately twice as likely to be prefrail/frail compared with those with normal ALM BMI. To the best of our knowledge this is the first study to provide evidence for the impact of low ALM BMI cutpoints on prefrailty/frailty. In regard to the individual frailty criteria, the strongest association was with weakness, that is, poor grip strength, which supports the discriminative power of low ALM BMI for weakness. Even more importantly, the impact of low ALM-to-BMI ratio remained after adjusting for potential confounders such as age, sex, and comorbidities. Women with low ALM BMI showed a higher risk of being frail than men with low ALM BMI which indicates gender differences in the association between lean mass and frailty. On the other hand, low ALM/height² showed no increased odds for any of the individual frailty criteria and prefrailty/frailty at all. Hence, our results encourage further use of the ALM BMI instead of ALM/height² cutpoints as they are highly indicative of prefrailty/frailty.

Since low lean mass alone might not be determinative of reduced strength and impaired function (22), a combination of this parameter with low strength or low gait speed (reflecting function) has been proposed by various consensus definitions of sarcopenia (8,9). However, it has to be considered that grip strength and gait speed in particular are prone to impairments independent of lean mass such as osteoarthritis, peripheral arterial occlusive disease, or cardiorespiratory disease. This has to be respected in the diagnostic process of sarcopenia should these definitions be used in a clinical setting.

Our results, although only cross-sectional, support the idea that the low ALM BMI cutpoints suggested by the Foundation for the National Institutes of Health are superior to low ALM/height² cutpoints and might be suitable to select appropriate patients for treatment studies. Further longitudinal studies are, however, necessary to confirm whether low ALM/BMI also predicts the development of frailty over time. Whether an improvement in lean mass in participants with a lean mass below the ALM BMI cut-off leads to improved strength and function as well remains to be seen in future studies.

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Responsibility for the contents of this publication lies with the authors.

Conflict of Interest

The authors have no conflict to declare.

References


