



Original article

Bio-impedance analysis for appendicular skeletal muscle mass assessment in (pre-) frail elderly people



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SUMMARY

Background & aims: Screening populations for skeletal muscle mass (SMM) is important for early detection of sarcopenia. Our aim was to develop an age specific bio-impedance (BI) prediction equation for the assessment of appendicular skeletal muscle mass (ASMM) in (pre-) frail elderly people aged 65 and older.

Methods: Anthropometric, BI and dual-energy X-ray absorptiometry (DEXA) measurements from 106 (pre-) frail elderly subjects (61 females and 45 males, aged 65–96 years) were used to derive three ASMM prediction equations using multiple regression analysis: one for single frequency BI measurements at 50 kHz (ASMM_{50kHz}), one for measurements at the characteristic frequency (ASMM_{FC}) and one for bioelectrical impedance spectroscopy (ASMM_{BIS}). The same data was used to evaluate an existing prediction equation.

Results: ASMM_{50kHz} had the best fitting model ($r^2_{adj} = 0.923$, SEE = 1.19 and a PRESS value = 163.4), followed by ASMM_{FC} ($r^2_{adj} = 0.915$, SEE = 1.25 and a PRESS value = 175.9) and ASMM_{BIS} ($r^2_{adj} = 0.915$, SEE = 1.26 and a PRESS value = 177.1). Average ASMM measured by DEXA and both ASMM_{50kHz} and ASMM_{FC} were comparable. ASMM_{BIS} tended to underestimate ASMM slightly. An existing prediction equation had a tendency to underestimate ASMM in people with a lower amount of ASMM and overestimate ASMM in people with a higher amount of ASMM.

Conclusions: ASMM_{50kHz} was able to measure average ASMM within our population of (pre-) frail elderly in a valid way. However, its predictive power on both individual and population level needs to be confirmed in an independent and larger (pre-) frail elderly population and across multiple institutions and ethnic groups.

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1. Introduction

Sarcopenia is the age-related loss of skeletal muscle mass, strength and/or physical performance [1]. It increases the risk for adverse outcomes such as the onset of disability [2,3], morbidity, and institutionalization [2,4,5]. Sarcopenia has been operationalized as the appendicular skeletal muscle mass index (ASMM/Height²) or skeletal muscle mass index (SMM/Height²) two standard deviations lower than the gender-specific mean of young healthy adults [1,6] accompanied by poor handgrip strength and/or slow gait speed [1]. While handgrip strength and gait speed are relatively easy to

measure, an easy-to-use method to assess ASMM within a large population is needed for future sarcopenia screenings.

Dual-energy X-ray absorptiometry (DEXA) is a frequently used and validated method to assess appendicular skeletal muscle mass [6–8]. A drawback of DEXA, however, is that it is neither widespread available nor a mobile device, making large-scale screening of muscle loss in the elderly no common practice. An alternative method to use is bio-impedance (BI) [9]. Because BI is a quick, safe, non-invasive, easy to use, inexpensive and portable method to estimate body composition, it has the potential to become a valuable screening tool for sarcopenia. Unfortunately, BI's weak point is the uncertain reliability of its prediction equations when it is applied in populations other than where its validity was derived from. For example, one factor known to affect the accuracy of prediction equations is hydration status [10], a condition that fluctuates and

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which can be commonly found in the elderly [11]. Therefore, it is not advisable to use a BI prediction equation that has not been validated for the target population. Thus, for a sarcopenia screening tool, the BI prediction equations need to be age specific. Two prediction equations have been developed for the assessment of whole body skeletal muscle mass in elderly [12,13], but to our knowledge only one BI prediction equation was developed to assess ASMM in elderly. This equation [14] ($ASMM_{KYLE}$) was developed in a population of 444 healthy Caucasians (246 male and 198 female), aged 22–94 years. As this $ASMM_{KYLE}$ prediction equation was developed in a large age range population, it is uncertain how valid the equation is in a frail elderly population aged 65 and older. Therefore, we aimed to develop a new prediction equation for the assessment of appendicular skeletal muscle mass in (pre-) frail elderly people aged 65 and older.

2. Material and methods

2.1. Subjects

For this study, data collected from 106 pre-frail and frail elderly subjects who participated in the 2010 ProMuscle study [15,16] were used. In the ProMuscle study the impact of protein on muscle mass and physical performance in (pre-) frail elderly people was studied. Community-dwelling elderly participants, ≥ 65 years, were recruited between December 2009 and September 2010 for participation. Potentially eligible subjects were screened for pre-frailty and frailty using the Fried criteria [17]. These criteria were: 1) unintentional weight loss of more than 4.5 kg in the preceding year by self-report, 2) measured handgrip strength below 20th percentile by gender and body mass index, 3) self-reported exhaustion based on two questions in the CES-D depression scale [18], 4) 15 feet distance walking speed below 20th percentile by gender and height, 5) weekly physical activity measured with the Minnesota Leisure Time Activity questionnaire < 383 kcal (men) or < 270 kcal (women) [19]. Furthermore, subjects who were diagnosed with any form of cancer, chronic obstructive pulmonary disease (COPD), diabetes type 1 and 2 (≥ 7 mmol/L), or renal insufficiency (eGFR < 60 mL/min/1.73 m²) were excluded. The baseline dataset included 127 pre-frail and frail elderly subjects. Due to missing BI data ($n = 11$), missing DEXA data ($n = 9$), or both ($n = 1$), we excluded twenty-one subjects. Thus the final dataset included data collected from 106 subjects (61 females and 45 males, age 78.7 ± 8.1 years; range 65–96 years). This dataset was used to develop the prediction equations.

The Wageningen University Medical Ethical Committee approved the study and subjects gave their written informed consent.

2.2. Anthropometry and body composition

During the ProMuscle study, anthropometric, BI and DEXA measurements and physical performance tests were performed at baseline, after 3 and after 6 months. All anthropometric, BI and DEXA measurements were carried out when subjects were in a fasting state.

Height was measured with a wall-mounted stadiometer to the nearest 0.1 cm. Body weight was measured to the nearest of 0.1 kg with a calibrated digital scale (ED-6-T; Berkel, Rotterdam, The Netherlands).

BI measurements were carried out using a Xitron Hydra 4200 Bio-Impedance Spectrum Analyzer (Xitron Technologies, San Diego, CA, USA) following the whole body wrist-ankle measurement protocol of the manufacturer. All but 4 baseline BI measurements were carried out before the DEXA measurements were done. With

these 4 measurements it was made sure that the participants were in an upright position for at least 15 min after the DEXA measurement. BI was assessed using the tetra polar surface electrode technique, where one current-injection electrode was attached to the dorsal side of the right hand near the metacarpal-phalangeal joints and one on the dorsal side of the right foot near the metatarsal-phalangeal joints. One voltage-detection electrode was placed on the mid-line between the notable ends of the right radius and ulna of the wrist, and one voltage-detection electrode was placed on the midline between the medial and lateral malleoli of the right ankle. The BI measurement was performed after the participant was in a supine position for 4–6 min.

DEXA measurements were carried out using a Lunar Prodigy Advanced DEXA scanner (GE Health Care, Madison, WI). Each morning a quality assurance test was performed to ensure system suitability and precision of the scanner. Whole body scans were performed according to the manufacturer's protocol and identical scan protocols were used for all subjects. DEXA's appendicular lean soft tissue (ALST) output was used for our analyses. ALST was defined as the sum of lean soft tissue (i.e. water + proteins + glycogen + non-bone minerals + residue) of both the left and right arms and legs. Since ALST consists of skeletal muscle mass, alongside a small and relatively constant amount of skin and underlying connective tissue, it is assumed to represent ASMM [14,20]. The precision of the DEXA-ALST measurements was estimated from repeated measurements within two days in 9 subjects. Within subject coefficient of variation (precision) of the ALST measurement was 1.7%.

2.3. Development and evaluation of bio-impedance ASMM prediction equations

Baseline data were used to derive three ASMM prediction equations: one for single frequency BI measurements at 50 kHz ($ASMM_{50kHz}$), one for measurements at the characteristic frequency ($ASMM_{Fc}$) and one for bioelectrical impedance spectroscopy ($ASMM_{BIS}$). The characteristic frequency (F_c) is the frequency where the body's reactance is at its maximum. Most single-frequency BI analyzers measure at 50 kHz, but it has been suggested that measurements at the F_c could lead to a more accurate prediction of body composition [21].

Baseline data of the subjects were also used to evaluate the ASMM prediction equation developed by Kyle [14] ($ASMM_{KYLE}$). $ASMM_{KYLE}$ was developed for single-frequency BI measurements at 50 kHz:

$$ASMM_{KYLE} = -4.211 + (\text{Height}^2 / \text{Resistance} \times 0.267) + (\text{Weight} \times 0.095) + (\text{Sex} \times 1.909) + (\text{Age} \times -0.012) + (\text{Reactance} \times 0.058)$$

where height is in centimeters, resistance and reactance are in Ω , weight is in kilograms and for sex 1 is for men and 0 is for female.

2.4. Statistical analyses

All analyses were performed using IBM SPSS Statistics software version 20.0. Level of significance was set at $p = 0.05$. All descriptive analyses are presented as mean and standard deviation (SD).

Stepwise-regression analyses were performed to derive the best fitting regression equations to predict ASMM. ASMM measured by DEXA ($ASMM_{DEXA}$) was set as dependent variable. A correlation matrix was generated from BI parameters, anthropometric and subject data to see if the correlation between $ASMM_{DEXA}$ and each variable was significant. Because the correlation between $ASMM_{DEXA}$ and "age" was only significant for men ($r = -0.421$, $p = 0.003$)

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