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Review

Equation models developed with bioelectric impedance analysis tools to assess muscle mass: A systematic review

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SUMMARY

Background & aims: This systematic review aims to systematically assess and summarize the equation models developed to estimate muscle mass with bioelectric impedance analysis (BIA) instruments against a reference instrument (DXA, MRI, CT-scan, Ultrasonography), in order to help researchers and clinicians choose the most adapted equation, depending on the device and the population in question.
Methods: The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement was followed. Medline (via Ovid) and Scopus were searched in January 2019 for observational (transversal, longitudinal, retrospective) studies developing an equation prediction model to validate BIA against another reference method for the assessment of muscle mass. Study selection and data extraction was performed independently by two researchers. Methodological quality of the included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.
Results: 25 studies matched the inclusion criteria and were included in the present systematic review. Among them, 10 studies proposed an equation for subjects aged 65 years and older, 9 for adults, 4 for infants and 2 did not report the age of the population. A large heterogeneity was observed regarding the brand and type of BIA as well as the administration protocol (mode, frequency, number of electrodes, administration position and empty bladder/stomach or not). Most of the studies used DXA as the reference instrument, except 4 that used MRI. In each of the included papers authors provided, through simple or multiple regression, a predictive equation for muscle mass. BIA resistance index, sex, weight, age, BIA reactance and height were most frequently included as predictive variables. The majority of the equations developed explained more than 80% of the variance between both instruments. Out of the 25 equations available, only 9 were also validated in another population within the same paper.
Conclusion: This systematic review of the literature offers clinicians and researchers the opportunity to verify the existence of a prediction equation when using a BIA device for estimating muscle mass. This will help them to obtain a valid estimation of muscle mass in a specific population and with a specific instrument. If the equation exists and has been validated by a study free of high risk of bias, it's use is recommended because the development of a new equation in the same context seems redundant and undesirable. If a validation has not been carried out for a specific brand of BIA, reference method or population, we recommend the development and cross-validation of a new equation.

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Introduction

It is widely accepted that body composition can independently influence health [1]. The loss of muscle mass and muscle function associated with the aging process – called sarcopenia – is related to an increased risk of cardiovascular disease, mobility disorders, impaired ability to perform activities of daily living, risk of falls and fractures, and loss of independence [2–5]. Moreover, a lower amount of skeletal muscle mass is considered to be directly correlated with a higher risk of mortality [6–8]. Therefore, body composition measurement, and specifically muscle mass measurement is considered valuable both from a clinical and an epidemiological point of view. There is often confusion regarding body composition terminology and several models exist for describing body composition. At the compartment level, Total Body Mass (TBM) is composed of Fat Mass (FM) and Fat Free Mass (FFM). FFM is itself divided into Lean Body Mass (LBM) and Bone Mineral Compartments (BMC). Lean Body Mass (LBM), or Lean Tissue Mass (LTM) is the sum of body water, total body protein, carbohydrates, non-fat lipids and soft tissue, excluding FM and BMC. Since LBM consist of skeletal muscle mass, alongside a small and relatively constant amount of skin and underlying connective tissue, it is often assumed to represent Skeletal Muscle Mass (SMM) [9]. Finally, Appendicular Lean Mass (ALM), therefore also called Appendicular Skeletal Muscle Mass (ASM) is the sum of the lean mass in the arms and legs [10].

Besides anthropometric measurements, five main techniques are commonly used to estimate skeletal muscle mass: Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Dual energy X-ray Absorptiometry (DXA), Ultrasonography and Bioelectric Impedance Analysis (BIA) [11–14]. Each technique relies on different technologies and estimates different aspects of muscle mass [15]. CT-scan and MRI are considered as reference tools because of their high level of accuracy and capacity of differentiating tissue types. However, major disadvantages of CT are the limited access to the radiological departments that operate it, the high cost and radiation exposure [14]. Limitations in the use of MRI in clinical and research settings are largely related to its high cost, the technical expertise required for analysis and the limited access. Because of the high cost of the equipment, its operation and maintenance, and its non-portable nature, the use of DXA may also be limited [16]. Finally, a major problem with Ultrasonography is the lack of reference and cut-off values, as is also the case for MRI and CT-scan. Moreover, the measurement performed with ultrasonography is limited to a local area. Therefore, the estimation of whole-limb or whole-body muscle mass is difficult to obtain. Because BIA is a safe, inexpensive and reliable technique [17–23], it could be considered as a very good compromise between cost, ease of administration and precision.

The principle of BIA is to determine the electric impedance of an electric current passing through the body [24]. The electrical impedance consists of two components: reactance – a measure of body cell mass [25] -, and resistance – a measure of total body water (TBW) [24]. In subjects without fluid and electrolyte status abnormalities, BIA measures of resistance and impedance are proportional to body water volume and to the length of the conductor or stature [25]. From the determined impedance a number of body composition parameters can be estimated, such as FM, FFM, TBW [25]. However, compared to reference methods, BIA tends to overestimate muscle mass [16,26–28]. This is an important issue to address when using BIA for clinical and research purposes. To fill this gap, equations have been generated allowing to estimate muscle mass based on factors including age, sex, height, weight and resistance and/or reactance estimated by BIA. The purpose of these formulas is to obtain the most accurate estimation of muscle mass, close to that estimated by reference methods [16]. Because BIA has become more popular in the last 2 decades, a large number of prediction equation models have been generated through different validation studies.

This systematic review aims to systematically assess and summarize BIA equation models for the estimation of muscle mass against other reference methods (DXA, MRI, CT-scan, Ultrasonography). The results of this review will help researchers and clinicians to choose and use the most appropriate equation for their target population, using a reference method that corresponds to their muscle mass estimator of interest.

Materials and methods

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [29] has been followed throughout the whole procedure of this systematic review (completed PRISMA available in Appendix 1). Our research project can be summarized by the following PICOS strategy: *Population or disease*: All type of populations; *Intervention*: BIA; *Comparator*: DXA, MRI, CT-scan or Ultrasonography; *Outcome*: equation model for the assessment of muscle mass; *Study design*: observational transversal and longitudinal studies. A protocol has been developed prior the conducting the study which was approved by all the authors (unpublished but available as Appendix 2).

Literature search

The electronic database Medline (via Ovid) and Scopus have been searched from inception to January 2019 for observational (transversal, longitudinal, retrospective) studies providing an equation prediction model to validate BIA against another tool (DXA, CT-scan, MRI or ultrasonography) for the assessment of muscle mass. No restriction of date was applied but the search was limited to papers published in English or French. The search strategy used for the Medline search is available in Appendix 2. Additionally, a manual search within the bibliography of relevant papers was also performed in order to complete the bibliographic search.

Study selection

The list of articles provided by the search strategy was first reviewed independently by two investigators by reading their titles and abstracts. The choice of keeping or rejecting articles was based on strict inclusion/exclusion criteria summarized in Table 1. We only included studies that developed an original BIA-equation (i.e. we excluded studies using a predefined manufacturer's equation) for estimating muscle mass (i.e. we included all terminologies, such as lean tissue mass, lean body mass, appendicular lean mass, skeletal muscle mass, appendicular skeletal muscle mass and skeletal muscle volume)). Any discrepancies between both investigators were resolved through discussion and consensus. If needed, the opinion of a third reviewer was asked. Once an article was selected based on title and abstract review, the full-text was then screened for final eligibility by the two same investigators. Once again, any discrepancies were resolved by discussion and consensus.

Data extraction

Data were extracted independently by two investigators using a standardized extraction form, previously pre-tested on a sample of 3 studies. A third investigator was called to resolve difference of

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Table 1
Inclusion and exclusion criteria.

Inclusion criteria	
Design	Observational studies including transversal studies, longitudinal studies, retrospective studies
Participants	- Both men and women - No age restriction - No restriction regarding ethnicity
Tools	Muscle mass (total lean mass or restricted to appendicular lean mass) should be assessed by BIA and by another tool (DXA, BIA, CT-scan, MRI or ultrasonography)
Outcome	An equation prediction model should be proposed to validate BIA against DXA, MRI, CT-scan or ultrasonography
Exclusion criteria	
Design	- Animal studies - Genetic studies - Study protocol - Systematic reviews, MA, case report, etc.
Outcome	Equations provided by the manufacturer of BIA instrument.

extraction between both investigators. The following data were extracted:

- *Article characteristics*: first author, journal, year of publication, title, objectives, funding, conflict of interest;
- *Study characteristics*: study design, country, BIA characteristics (frequency, mode, electrode placement, number of electrodes, BIA procedure), and reference instrument;
- *Population*: sample size, gender distribution, ethnicity, age range, description of population;
- *Study results*: regression model specifications, variables in equation, full equation, quality of the model (R^2, p-value, SEE) for each muscle mass parameter;

Quality assessment

Methodological quality of each included study was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool [30], independently by 2 investigators (disagreement was resolved by consensus). The tool consists of four key domains namely: 1) patient selection, 2) index test, 3) reference standard and 4) flow and timing. For each domain, the risk of bias can be graded as “low risk” of bias, “unclear risk” of bias or “high risk” of bias based on the appraisal of the reviewers. QUADAS-2 evaluates the “risk of bias” per domain but also “concerns about applicability”.

Data synthesis

Because the objective of our research was to provide a comprehensive overview of existing equations, a meta-analysis was not relevant.

Results

Studies characteristics

After removing duplicates, the search yielded 2101 references which were screened on title and abstract. After excluding unappropriate references based on title/abstract screening, 686 references were estimated as potentially relevant by both reviewers and were further screened for in/exclusion criteria based on full-text review. Finally, 25 studies [16,31–54] were included in the systematic review (Fig. 1). In 9 out of the 25 papers [31,37,40,43,44,47,49,50,54], authors developed an equation based on one study sample and validated this equation on another study sample. All remaining papers described the development of the equation only and did not report on further validation of their equation. The number of participants ranged from n = 16 [34] to n = 1125 [44], who were mainly Caucasian (Table 2). Regarding the participants' age, 10 studies proposed an equation for subjects aged 65 years and older [35,41,45–48,51–53], 9 for adults (age range 24–53 years) [16,31,36–39,42,50,54], 4 for children [32,33,43,49] and 2 did not report the age of the study population [34,40]. Most studies included healthy participants, except for some specific populations such as obese children [32,33], adults with chronic kidney diseases [41,42], healthy adults but at risk of osteopenia [38], and older subjects presenting sarcopenia or frailty [51,53].

Muscle mass assessment

Regarding BIA devices used, it is observed that: 1) *Different brands* of BIA have been used throughout the studies: among them, 5 studies reported using the Inbody device [16,39,42,44,46], 8 used the RJL systems [35,37,38,43,47,49,52,53], 4 studies reported using the Tanita system [32,33,45,50], 3 used the Xitron devices [40,41,51] and the 5 last ones used other devices [31,34,36,48,54]. However, among the same brand of BIA devices a large diversity is also observed regarding the version of the devices used. For example, Inbody model version 3.0 has been used by three authors [39,42,44] while others used Inbody 720 and Inbody S10 models have been used by others [16,46]. 2) *Different frequencies* were used for the assessment: most of the studies used single frequency at 50 kHz with one study using single frequency at 250 kHZ [44] and 9 other studies using multifrequency [16,34,36,39,42,45,46,50,51]. 3) *Different modes* were used for the assessment: 9 studies used segmental analysis [16,32,33,35,36,39,42,46,50], 5 used whole-body analysis [37,49,51–53], 1 study used both types [31] and 10 studies did not reported the mode chosen [34,38,40,41,43–45,47,48,54]. 4) *Difference regarding the number of electrodes and their placement* (if the mode is segmental): For all of the studies using a segmental mode, the electrode placement was hand-to-foot. The number of electrodes varies between 4 electrodes (reported in 6 studies [31,38,40,43,51,53]), 6 electrodes (reported in one study [36]), 8 electrodes (reported in 10 studies [16,32,33,35,39,42,44–46,50]) and 16 electrodes (reported in one study [50]). The other studies did not report the number of electrodes used. 5) *Different assessment positions*: in 11 studies, assessment was performed in supine position [31,34,35,37,38,40,43,48,51–53],and in 9 other ones it was performed standing [32,33,39,42,44–46,50,54]. The other studies did not report the information. 6) *Different assessment conditions*: empty bladder or stomach in 15 out of the 25 studies [31,34–36,38,39,41,42,46,47,49–53]. This information was not reported in the 10 other study.

Regarding the reference standard instrument used to compare BIA-data and to compute an equation, only 4 studies [31,34,37,54] used MRI as reference method for the measurement of muscle mass. Two of these four studies measured skeletal muscle volume (SMV) [31,34] and the two other ones measured skeletal muscle mass (SM) [45,51]. All the other validation studies used DXA (half of them using Lunar technologies and half of them using Hologic technologies) (Table 3). Different parameters of muscle mass have been assessed throughout these studies: lean body mass (LBM) (reported in 8 studies [33,35,41,42,44,47,48,51]), sometime assessing only a part of the body (arms, legs, trunk), skeletal muscle mass (SM) (reported in 1 study [50]), appendicular lean mass (ALM) or appendicular skeletal muscle mass (ASM) (reported in 11 studies [33,35–38,48,49,51–54]) and appendicular lean mass divided by height^2 (ALM/ht^2) (reported in 1 study [16]).

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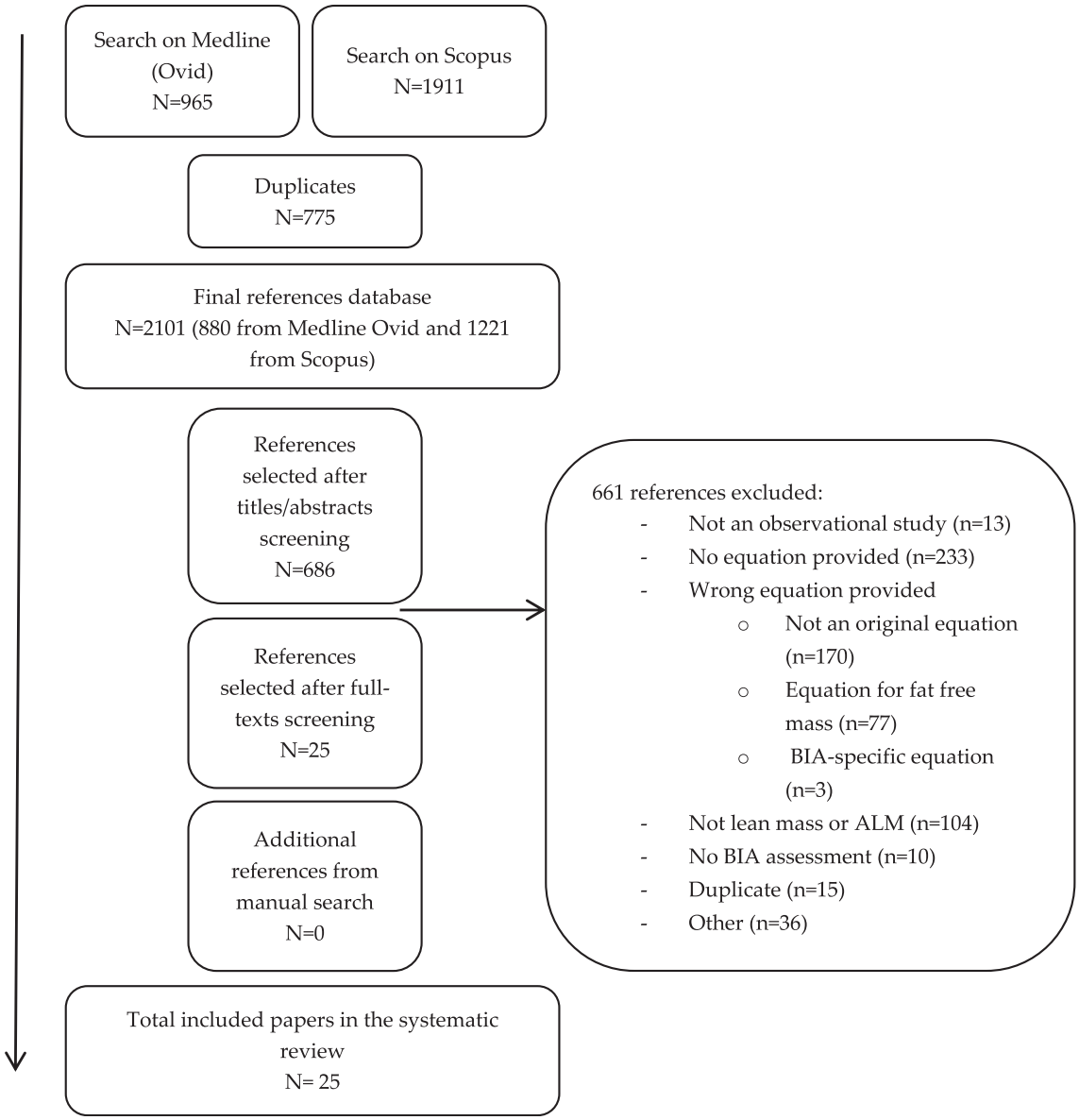

Fig. 1. Flow of the search strategy.

Development of equations

To develop the prediction equations of BIA versus the reference standard, authors performed mainly multiple linear regressions (20/25 studies) including sometimes stepwise procedures (10/20 studies). So, from BIA assessment, they developed a predictive equation to obtain a value of muscle mass that will be as close as possible to the value obtained with the reference standard measurement. For this purpose, authors included in the equation, through a multiple regression, different variables (between 1 and 11 variables, depending on the equation developed):

- BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)), which is included in 22 (88%) of the equations;
- Sex which is included in 18 (72%) of the equations;
- Weight (in kg), which is included in 13 (52%) of the equations;
- Age (in years), which is included in 9 (36%) of the equations;
- BIA reactance (Ohm), which is included in 7 (28%) of the equations;
- Height (in cm), which is included in 5 (20%) of the equations;
- ALM_{BIA}, which is included in 3 (12%) of the equations;
- Other specific parameters such as body surface area, BMI, chest circumference, length of arms, etc. were used in only 1 equation.

The full equations developed in each study are available in Table 3. The majority of the equations explained more than 80% of the variance (R^2 above 0.8) with the highest R^2 provided by the equation of Colica et al. [49] which explained 96.2% of the variance of lean body mass measured by BIA versus DXA in 155 children aged 5–14 years. The lowest R^2 has been found in the study of Yamada et al. [50] for assessing appendicular lean mass in women aged 47 ± 18 years (R^2 = 0.757). This last equation only included, as variables of the equation, BIA resistance index and impedance at difference frequencies but no clinical characteristics of the subjects. Some authors also reported the standard error of measurement (SEE) between BIA-prediction and reference-standard assessment to inform about the measurement error of the predicted values.

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Table 2
Studies' characteristics.

First author, year, country	Population		Equation		
	General description INclusion criteria EXclusion criteria	1) Sample size 2) Gender distribution 3) Ethnicity 4) Age range	Development of the equation/ validation of the equation	BIA Brand; frequency; mode; number of electrodes, placement of electrodes (if segmental); administration position; empty bladder/ stomach?	Gold standard (complete reference)
Bolanowski, 2001, Sweden [38]	IN: Subjects undergoing bone density DEXA examination because of increased risk of osteopenia or as part of an epidemiological study	1) 100 participants 2) Male 41 (41.0%)/female 59 (59.0%) 3) Ethnicity NR 4) 38 ± 17.5 years	Development only	RJL Systems BIA-103; single frequency (50 kHz); 4 electrodes (hand-to-foot position); supine administration position; empty bladder.	DXA Lunar DPX-L
Buckinx, 2015, Belgium [16]	IN: adult volunteers. EX: electronic implant, BMI >50, limb amputation, pregnancy	1) 219 participants 2) Male 106 (48.4%)/female 113 (51.6%) 3) White: 216 (98.6%)/Black: 3 (1.4%) 4) 43.7 ± 19.1 years	Development only	InBody S10; multi frequencies (1−5−50−250−500 −1000 kHz); segmental mode; 8 electrodes.	DXA Hologic QDR Discovery
Colica, 2018, Italy [49]	IN: Children aged 5−14 years recruited through elementary and junior high urban schools.	1) 155 participants (35 for validation study) 2) Male 72 (46.5%)/female 83 (53.5%) 3) Ethnicity NR 4) Male: 9.03 (8.00−11.00) years, female: 8.51 (8.00 −11.00) years for development study; male: 9.00 (7.00−11.00), female: 8.00 (7.00−10.25) years for validation study	Development & validation	RJL systems BIA-101 Akern, single frequency (50 kHz), whole body mode, empty stomach.	DXA GE Medical i-DXA
De Rui, 2017, Italy [35]	IN: older subjects over 60 years EX: skeletal deformities that affect height, significant cardiovascular or lung diseases, uncontrolled metabolic disease, electrolyte abnormalities, cancer or inflammatory conditions in the last 5 years & drugs that might interfere with body composition	1) 244 participants 2) Male 110 (45.0%)/female 134 (55.0%) 3) Caucasian 4) 70.95 ± 5.6 years	Development only	RJL systems BIA 101; single frequency (50 kHz); segmental mode; 8 electrodes; supine administration position; empties stomach and bladder.	DXA Hologic QDR Discovery A
Fuller, 1999, UK [34]	IN: Healthy subjects	1) 16 participants 2) Male 8 (50.0%)/female 8 (50.0%) 3-4) Ethnicity and age NR	Development only	Model SFB2, SEAC; multi frequencies but only 50 kHz used; electrodes in hand-to-foot position; supine administration position; empty stomach.	MRI General Electic Signa 0.5 T

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Table 2 (*continued*)

First author, year, country	Population		Equation		
	General description INclusion criteria EXclusion criteria	1) Sample size 2) Gender distribution 3) Ethnicity 4) Age range	Development of the equation/ validation of the equation	BIA Brand; frequency; mode; number of electrodes, placement of electrodes (if segmental); administration position; empty bladder/ stomach?	Gold standard (complete reference)
Janssen, 2000, Canada [37]	IN: Healthy adults who had participated in a variety of body composition studies.	1) 388 participants (119 for validation study) 2) Male 230 (59.3%), female 158 (40.7%) 3) Caucasian 269 (69.3%), African−American (13.6%), Asian 40 (10.3%), Hispanic 26 (6.7%) 4) Caucasian 41.5 ± 12.8 years, African−American 36.6 ± 11.6 years, Asian: 31.8 ± 9.8 years, Hispanic: 33.5 ± 11.1 years	Development & validation	RJL systems BIA 101B; single frequency (50 kHz); whole body mode; electrodes in hand-to-foot position; supine administration position.	MRI General Electric 1.5-T Scanner
Kim, 2014, South Korea [44]	IN: Two ongoing community-dwelling cohorts, the Ansung cohort and the Korean Longitudinal Study of Healthy Aging (KLoSHA). IN: men and women over 65 years of age	1) 1125 participants (405 for validation study) 2) Male 483 (42.9%), female 642 (57.1%) 3) Ethnicity NR 4) 73.5 ± 5.6 years for development study; 70.1 ± 3.8 years for validation study	Development & validation	InBody 3.0; single frequency (250 kHz); 8 electrodes (hand-to-foot position); standing administration position.	DXA Lunar Corporation, Madison, WI
Kim, 2015, Japan [46]	IN: noninstitutionalized, community-dwelling Japanese adults aged between 65 and 87 years	1) 551 participants 2) Male 241 (43.7%)/female 310 (56.3%) 3) Ethnicity NR 4) 73.6 ± 2.4 years	Development only	InBody 720; multi frequencies (1−5−50−250−500 −1000 kHz); segmental mode; 8 electrodes (hand-to-foot position); standing administration position; empty stomach.	DXA Hologic QDR-4500 A
Kyle, 2003, Switzerland [40]	Development: IN: healthy ambulatory Caucasians / EX: active medical treatment or hospitalization within 3 months prior, physial handicap that interferes with body composition Validation: IN: pre- and posttransplant patients/ EX: ascites or other fluid abnormalities requiring correction	1) 770 participants (326 for validation study) 2) Male 459 (59.6%)/female 311 (40.4%) 3) Caucasian 4) Age NR	Development & validation	Xitron 4000B; single frequency (50 kHz); 4 electrodes (hand-to-foot position); supine administration position.	DXA Hologic QDR4500A with enhanced 8.26 whole-body software
Luque, 2014a, Spain [33]	IN: All children from the Spanish subsample of the EU Childhood Obesity Project who took part in the study at 7 years of age	1) 171 participants 2) Male 84 (49.1%)/female 87 (50.9%) 3) Caucasian 4) 7 years old (±1 month)	Development only	Tanita BC-418; single frequency (50 kHz); segmental mode; 8 electrodes (hand-to-foot position); standing administration position.	DXA General Electric Lunar Prodigy Advance

Luque, 2014b, Spain [32]	IN: All children from the Spanish subsample of the EU Childhood Obesity Project who took part in the study at 7 years of age	1) 171 participants 2) Male 84 (49.1%)/female 87 (50.9%) 3) Caucasian 4) Age NR	Development only	Tanita BC-418; single frequency (50 kHz); segmental mode; 8 electrodes (hand-to-foot position); standing administration position.	DXA General Electric Lunar Prodigy Advance (Madison, Wisc., USA)
Macdonald, 2006, Wales [41]	Non-diabetic subjects attending pre-dialysis clinics. IN: adult, confirmed chronic kidney disease. EX: current dialysis or renal transplant, diabetes, significant uncontrolled edema, medications affecting secretion of creatinine, previous reaction to inulin, severe asthma, inability to lie flat, cardiac pacemakers	1) 75 participants 2) Male 49 (65.3%), Female 26 (34.7%) 3) Ethnicity NR 4) 65.1 ± 12.0 years	Development only	Xitron Hydra ECF/ICF 4200; single frequency (50 kHz); electrodes in hand-to-foot position; empty stomach.	DXA Hologic QDR1500, software version 5.72
Malavolti, 2003, Italy [39]	IN: caucasian, ≥18 years, BMI ≥ 18.5 kg/m^2, menstrual cycle between 6th and 10th day. EX: presence of chronic or acute disease, use of drugs influencing body water	1) 110 participants 2) Male 42 (38.2%)/female 68 (61.8%) 3) Caucasian 4) Male: 54 ± 15 years/female 53 ± 17 years	Development only	InBody 3.0; multi frequencies (5−50−250−500 kHz); segmental mode; 8 electrodes (hand-to-foot position); standing administration position; empty stomach.	DXA Lunar DPX-L with adult software version 3.6
Medici, 2005, Italy [42]	PD: patients with chronic kidney disease treated by continuous ambulatory peritoneal dialysis. Control: healthy individuals recruited among university personnel	1) 97 participants (PD: 20, Control: 77) 2) Male 45 (46.3%)/female 52 (53.7%) 3) Ethnicity NR 4) PD: 53 ± 19 years/control: 53 ± 17 years	Development only	InBody 3.0; multi frequencies (5−50−250−500 kHz); segmental mode; 8 electrodes (hand-to-foot position); standing administration position; empty stomach.	DXA Lunar DPX-L & adult software version 3.6
Nielsen, 2007, Sweden [43]	IN: Children from 4 schools in Malmo situated in homogeneous middle-class areas EX: non-European ethnicity, growth hormone treatment	1) 101 participants 2) Male 52 (51.5%), female 49 (48.5%) 3) Caucasian 4) 9.9 (9.4−10.5) years	Development & validation	RJL Systems BIA-103; single frequency (50 kHz); 4 electrodes (hand-to-foot position); supine administration position.	DXA Lunar DPX-L version 1.3z
Oshima, 2010, Japan [54]	IN: Healthy adult Japanese volunteers	1) 244 participants (81 for validation study) 2) Male 106 (43.4%)/Female 138 (56.5%) 3-4) Ethnicity and age NR	Development & validation	HBF-354 prototype (Omron Healthcare Co)); single frequency (50 kHz); electrodes hand-to-foot position; standing administration position.	MRI VISART EX 1.5-T scanner (Toshiba Medical systems Co., Tochigi, Japan)
Peniche, 2015, Mexico [47]	IN: healthy older individuals >60 years of age with normal blood results, stable body weight for 3 months, free of medication, physically independent and without cognitive problems. EX: abnormal blood results for TSH, glucose, urea, creatinine, creatine phosphokinase, gamma glutamyl transpeptidase; edema, hypertension	1) 213 participants (106 for validation study) 2) Male 55 (25.8%)/female 158 (74.2%) 3) Ethnicity NR 4) 68.7 ± 5.9 years	Development & validation	RJL systems quantum X; single frequency (50 kHz); empties stomach and bladder.	DXA Hologic explorer QDR-4500W

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Table 2 (*continued*)

First author, year, country	Population		Equation		
	General description INclusion criteria EXclusion criteria	1) Sample size 2) Gender distribution 3) Ethnicity 4) Age range	Development of the equation/ validation of the equation	BIA Brand; frequency; mode; number of electrodes, placement of electrodes (if segmental); administration position; empty bladder/ stomach?	Gold standard (complete reference)
Pietrobelli, 1998, USA [36]	IN: Healthy men and women recruited from hospital center employees and students. EX: medical conditions affecting body composition, participation in structured exercise regime, <20 years of age	1) 49 participants 2) Male 19 (38.8%)/female 30 (61.2%) 3) Caucasian 4) 31.5 ± 9.9 years	Development only	Human-IM DIP, DS-Medigroup; multi frequencies (1−5−10−25 −50−100−300 kHz), segmental mode; 6 electrodes (hand-to-foot position); empties stomach and bladder.	DXA Lunar DPX, Madison, WI, software version 3.6
Scafoglieri, 2017, Belgium, Germany, Ireland, Italy, Sweden, UK [53]	Older persons with functional limitations and sarcopenia. IN: age ≥ 65 years, BMI between 20 & 30. EX: chronic disease or cognitive impairment	1) 291 participants 2) Male 87 (29.9%)/female 204 (70.1%) 3) Ethnicity NR 4) 77.6 ± 6.9 years	Development only	RJL systems BIA 101 AKERN; Single frequency (50 kHz); whole body mode; 4 electrodes (hand-to-foot position); supine administration position; empties stomach and bladder.	DXA * Hologic Apex software version 4.0.2 * Ge Medical Systems Lunar enCORE software version 14.10.022
Sergi, 2015, Italy [52]	IN: older subjects over 60 years. EX: skeletal deformities that affect height, significant cardiovascular or lung diseases, uncontrolled metabolic disease, electrolyte abnormalities, cancer or inflammatory conditions in the last 5 years & drugs that might interfere with body composition were grounds for exclusion	1) 296 participants 2) Male 117 (39.5%)/female 179 (60.5%) 3) Caucasian 4) 71.4 ± 5.4 years	Development only	RJL systems BIA 101 AKERN; single frequency (50 kHz); whole body mode; supine administration position; empties stomach and bladder.	DXA Hologic QDR Discovery A
Tanaka, 2007, Japan [31]	IN: healthy Asian males (19−34 years of age), both athletes and sedentary/mildly active	1) 30 participants (10 for validation study) 2) Male 30 (100.0%) 3) Asian 4) 24.4 ± 3.2 years	Development & validation	Muscle α, Art Haven 9; single frequency (50 kHz); whole body AND segmental modes; 4 electrodes for whole-body mode; 16 electrodes for segmental mode (hand-to-foot position); supine administration position; empty stomach	MRI Hitachi Airis
van Baar, 2015, The Netherlands [51]	IN: community-dwelling, ≥65 years, (pre-)frail. EX: diagnosis of cancer, COPD, diabetes or renal insufficiency	1) 106 participants 2) Male 45 (42.4%)/female 61 (57.5%) 3) Ethnicity NR 4) 78.7 ± 8.1 years	Development only	Xitron Hydra 4200 Bio-impedance Spectrum Analyzer; Multi frequencies (between 5 kHz and 1 mHz); whole body mode; 4 electrodes (hand-to-foot position); supine administration position; empty stomach.	DXA GE Lunar Prodigy
Vermeiren, 2018, Belgium [48]	IN: 80 years of age and older, community-dwelling, mentally fit. EX: recent diagnosis of cancer; surgery or radio- or chemotherapy in last 6 months; planned surgery or radio- or chemotherapy in near future	1) 174 participants 2) Male 91 (52.3%)/female 83 (47.7%) 3) Ethnicity NR 4) 83.3 ± 3.0 years	Development only	Bodystat Quadscan 4000; single frequency (50 kHz); electrodes in hand-to-foot; supine administration position.	DXA Hologic 4500 QDR upgraded to Discovery

Yamada, 2017, Japan [50]	IN: Japanese employees of Tanita Co. undergoing a company health examination. Able to walk >10 m with or without help. EX: indication of dementia, joint arthroplasty, artificial pacemaker	1) 756 participants (233 for validation study) 2) Male 319 (42.2%)/female 437 (57.8%) 3) Asian 4) Male 46 ± 17 years for development study, 49 ± 18 years for validation study/female: 47 ± 18 years for development study, 44 ± 18 years for validation study	Development & validation	Tanita, MC-780A-N; Multi frequencies (5, 50, 250 kHz); segmental mode; 8 electrodes (hand-to-foot position); standing administration position; empties stomach and bladder.	DXA GE Lunar DPX-L with software version 1.35
Yoshida, 2014, Japan [45]	Subjects recruited from earlier cohort study IN: 65 year or older; living in Oby city Japan. EX: participation in other study; need for long-term care or impairment of ADL; severe visual or hearing impairment; medical history; depression; pacemaker; MMSE < 18	1) 250 participants 2) Male 141 (56.4%)/female 109 (43.6%) 3) Ethnicity NR 4) 73.5 ± 5.6 years	Development only	Tanita MC-980A; multi frequencies (1−5−50−250 −500−1000 kHz); 8 electrodes; standing administration position.	DXA Hologic QDR-4500 A with software version 9.03D

NR = not reported; IN = inclusion criteria; EX = exclusion criteria.
Note: any unavailable information about BIA procedures means that the information was not reported in the original article.

In 9 of the 25 papers proposing a predictive equation for BIA, authors also proposed a validation of this equation in another sample of participants. Authors used very heterogeneous statistics for the validation of their equations: mean difference between instruments, correlation between instruments, SEE between instruments, etc. (*data not shown*).

Quality assessment

The overall quality of studies was moderate as graphically displayed in Fig. 2. Indeed, only a limited number of studies present with a low risk of bias and a considerable number of articles did not provide enough information to decide either way on the risk of bias. For “Reference standard”, no study was scored at high risk of bias, 16 (64%) were scored with an unclear risk of bias and 9 (36%) with a low risk of bias. For “Flow and timing” and “Patient selection”, 2/25 studies (8%) were scored at high risk of bias. For “Flow and timing”, one study did not provide any flowchart and/or explanation to understand why 2 subjects were excluded from the analyses [16] and, in the other study, BIA and MRI were not performed on the same day [31]. Therefore, these studies were scored high risk of bias. For “Patient selection”, one study used such strict inclusion criteria whereby only subjects with a good health were included although the authors described their population as “older adults” and considered the equation valid for assessing ALM in elderly with acute or chronic illness [35]. For the other study [50], the inclusion criteria used for the development study were unclear. For “Patient selection” and “Flow and timing”, a low risk of bias was found in 10 (40%) and in 13 studies (52%) respectively. The rest of studies were scored as unclear risk of bias. The highest proportion of high risk of bias has been found for “Index test” for which 3/25 (12%) studies [38,45,50] were scored at high risk of bias because unappropriated procedure regarding meal ingestion before BIA assessment. For “Index test”, 17 studies (68%) were scored with an unclear risk of bias and 5 (20%) with a low risk of bias. The individual quality assessment of each study is available in Appendix 3.

Discussion

In the literature, many different BIA prediction equations are available to estimate various elements of muscle mass. Thus, to help researchers and clinicians to choose the most appropriate equation, this systematic review provides a comprehensive overview of the available equation models developed for BIA to predict muscle mass estimates according to the reference method used (c.q. muscle mass outcome) and target population. Overall, the results show a large heterogeneity regarding both the brand of BIA and the BIA procedure (e.g. frequencies, modes, number of electrodes, conditions of administration). The reference method is also found to vary according to the studies. Most studies used DXA as reference (Lunar or Hologic technologies) and a few studies used MRI. For elaborating a high-quality prediction equation, we expected authors to choose the most accurate reference method. Even if MRI has been recognized as a more accurate method for measuring muscle mass as compared to DXA, it is likely the higher feasibility and safety, and the lower cost of DXA have influenced the choice of authors for using this reference technique for their validation equation. Finally, the studied population as well as the other predictors included in the equation differ from one study to another. This is in line with the study of Sergi et al. showing that the reliability of BIA measurements is influenced by various factors related to the instrument itself, including electrodes, operator, subject, and environment [55]. Our study is consistent with Sergi et al. suggesting that the BIA prediction models differ according to the characteristics of the population in which they have been derived

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Table 3
Overview of existing BIA-Equations to estimate muscle mass.

First author, year	Reference method	Muscle mass parameter measured	Age of the population	BIA frequency	Regression model	Variables in equation	Full equation	R^2	p-value	SEE
Buckinx, 2015 [16]	DXA	ALM/ht^2	43.7 ± 19.1 years	Multi (1−5−50−250 −500−1000 kHz)	M	* Sex: female = 1, male = 0 * BMI (kg/m^2) * ALM/ht$^2_{BIA}$: appendicular lean mass/height^2 as measured by BIA	ALM/ht$^2_{DXA}$ (kg) = 0.04*BMI − 0.58*sex + 0.69*ALM/ht$^2_{BIA}$	0.89	<0.001	NR
Yamada, 2017 [50]	DXA	ALM_{MEN} (kg) ALM_{WOMEN} (kg)	46 ± 17 years (Males)/47 ± 18 years (Females)	Multi (5, 50, 250 kHz)	M	* RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) AT 50 kHz * Z_5 = impedance at 5 kHz (Ohm) * Z_{50} = impedance at 50 kHz (Ohm) * Z_{250} = impedance at 250 kHz (Ohm)	ALM_{MEN} = (0.6947*(RI_{50})) + (−55.24*(Z_{250}/Z_5)) + (−10940* ($1/Z_{50}$)) + 51.33 ALM_{WOMEN} = (0.6144*RI_{50}) + (−36.61*(Z_{250}/Z_5)) + (−9332* ($1/Z_{50}$)) + 37.91	ALM_{MEN}: 0.851 ALM_{WOMEN}: 0.757	NR	ALM_{MEN}: 1.46 kg ALM_{MEN}: 1.22 kg
Macdonald, 2006 [41]	DXA	ALM (kg)	65.1 ± 12.0 years	Single (50 kHz)	MS	* Sex: female = 1, male = 0 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Xc: BIA reactance (Ohm) * Height (cm) * Age (years)	ALM (kg) = −11.626 + (0.292*RI) + (0.06983*Xc) + (0.08553*height) + (−2.092*sex) + (−0.05*age)	0.921	<0.001	1.57 kg
Kim, 2015 [46]	DXA	ALM (kg)	73.6 ± 2.4 years	Multi (1−5−50−250 −500−1000 kHz)	M	* Sex: female = 1, male = 0 * Age (years) * Weight (kg) * ALM_{BIA} (kg): appendicular lean mass as measured by BIA	ALM (kg) = (0.710*ALM_{BIA}) + (−0.002*age) + (0.964*sex) + (0.070*weight) + 1.931	0.943	NR	0.88 kg
Scafoglieri, 2017 [53]	DXA	ALM (kg)	77.6 ± 6.9 years	Single (50 kHz)	MS	* Sex: female = 1, male = 0 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Weight (kg) * Xc: BIA reactance (Ohm)	ALM_{LUNAR} = 1.821 + (0.168*RI) + (0.132*weight) + (0.017*Xc) − (1.931*sex) $ALM_{HOLOGIC}$ = 4.957 + (0.196*Ht^2/R) + (0.060*weight) − (2.554*sex)	ALM_{LUNAR}: 0.86 $ALM_{HOLOGIC}$: 0.90	<0.001	ALM_{LUNAR}: 1.391 kg $ALM_{HOLOGIC}$: 1.322 kg
Vermeiren, 2018 [48]	DXA	ALM (kg)	83.3 ± 3.0 years	Single (50 kHz)	MS	* RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Weight (kg) * Sex: female = 0, male = 1	ALM = 0.827 + (0.19RI) + (2.101*sex) + (0.079*weight)	0.888	<0.001	1.45 kg
Peniche, 2015 [47]	DXA	ASM (kg)	68.7 ± 5.9 years	Single (50 kHz)	MS	* Sex: female = 0, male = 1 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Weight (kg)	ASM (kg) = −0.05376 + (0.2394*RI) + (2.708*sex) + (0.065*weight)	0.91	<0.001	
Sergi, 2015 [52]	DXA	ASM (kg)	71.4 ± 5.4 years	Single (50 kHz)	MS	* Sex: female = 0, male = 1 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Xc: BIA reactance (Ohm) * Weight (kg)	ASM (kg) = −3.964 + (0.227*RI) + (0.095*weight) + (1.384*sex) + (0.064*Xc)	0.923	NR	1.143 kg
Kim, 2014 [44]	DXA	ASM (kg)	73.5 ± 5.6 years	Single (250 kHz)	M	* RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Age (years) * Weight (kg)	ASM (kg) = [(RI*0.104) + (age*−0.050) + (sex*2.954) + (weight*0.055)] + 5.663	0.88	NR	1.35 kg

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Yoshida, 2014 [45]	DXA	ASM_{MEN} (kg) ASM_{WOMEN} (kg)	73.5 ± 5.6 years	Multi (1−5−50−250 −500−1000 kHz)	M	* RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) AT 50 kHz * Weight (kg)	ASM_{MEN} (kg) = 0.197*(RI) + 0.179*weight − 0.019 ASM_{WOMEN} (kg): 0.221*(RI) + 0.179*weight + 0.881	ASM_{MEN}: 0.87 ASM_{WOMEN}: 0.89	NR	ASM_{MEN}: 0.98 kg ASM_{WOMEN}: 0.81 kg
van Baar, 2015 [51]	DXA	ASM (kg)	78.7 ± 8.1 years	Multi (between 5 kHz and 1 mHz)	MS	* Sex: NR * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Xc: BIA reactance (Ohm) * Weight (kg) * Age: years	ASM_{50kHz} = −6.296 + (RI*0.227) + (Xc*0.072) + (sex*9.909) + (weight*0.072) + (sex*age* −0.098) + (age*0.054)	Adj: 0.923	NR	1.19 kg
Kyle, 2003 [40]	DXA	ASM (kg)	NR	Single (50 kHz)	MS	* Sex: female = 0, male = 1 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Xc: BIA reactance (Ohm) * Weight (kg) * Age (years)	ASM (kg) = −4.211 + (0.267*RI) + (0.095*weight) + (1.909*sex) + (−0.012*age) + (0.058*Xc)	0.953	NR	1.12 kg
Luque, 2014a [33]	DXA	LM (kg)	7.00 years old (±1 month)	Single (50 kHz)	M	* Sex: female = 0, male = 1 * Weight (kg) * Height (cm) * impedance (ohm)	LM (kg) = −4.740 − (0.010 × impedance) + (0.110 × weight) + (0.251 × height) − (1.020 × sex)	0.776	<0.001	NR
Colica, 2018 [49]	DXA	LM (kg)	9.03 (8.00−11.00) years (males), 8.51 (8.00−11.00) years (females)	Single (50 kHz)	S	* RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * HC (cm): hip circumference * WHR: waist-to-hip ratio * Age (years) * Height (cm)	LM = −27.597 + 0.337*RI + 0.094*HC + 9.593*WHR + 0.360*Age + 0.164*height	0.962	<0.0001	NR
Nielsen, 2007 [43]	DXA	LM (kg)	9.9 (9.4−10.5) years	Single (50 kHz)	M	* RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Xc: BIA reactance (Ohm) * Height (cm) * Weight (kg)	LM (kg) = −3.97 {±2.11} + (RI)*0.52 {±0.05} + Xc*0.04 {±0.02} + Height*0.06 {±0.02} + Weight*0.08 {±0.03} + sex*0.93 {±0.19}	adj: 0.94	NR	NR
Bolanowski, 2001 [38]	DXA	LM (kg)	38 ± 17.5 years	Single (50 kHz)	S	* LM_{BIA} (kg) = lean body mass as predicted by BIA	LM_{MEN} = 9.07 + 0.78*LM_{BIA} LM_{WOMEN}12.54 + 0.59*LM_{BIA}	NR	NR	NR
Medici, 2005 [42]	DXA	LM_{ARM-PD} in PD LM_{LEG-PD} in PD LM_{ARM-CO} in controls LM_{LEG-CO} in controls	53 ± 19 years (PD)/ 53 ± 17 years (controls)	Multi (5−50−250 −500 kHz)	S	* RI_{ARM500} = BIA resistance index in arms (mean of left and right) = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) AT 500 kHz * RI_{LEG500} = BIA resistance index in arms (mean of left and right) = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) AT 500 kHz	LM_{ARM-PD} = −0.362 + (RI_{ARM500}*0.025) LTM_{LEG-PD} = 3.023 + (RI_{LEG500}*0.030) LTM_{ARM-CO} = −0.643 + (RI_{ARM500}*0.029) LM_{LEG-CO} = 0.095 + (RI_{LEG500}*0.060)	LM_{ARM-PD}: adj: 0.91 LM_{LEG-PD}: adj: 0.85 LM_{ARM-CO}: adj: 0.93 LM_{LEG-CO}: adj 0.75	<0.001	NR
Malavolti, 2003 [39]	DXA	LM_{ARM} (kg) LTM_{LEG} (kg)	54 ± 15 years (males)/53 ± 17 years (females)	Multi (5−50−250 −500 khHz)	S	* RI_{ARM500} = BIA resistance index in arms (mean of left and right) = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) AT 500 kHz * RI_{LEG500} = BIA resistance index in arms (mean of left and right) = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) AT 500 kHz	LM_{ARM} = −0.6 + 0.03*RI_{ARM500} LTM_{LEG} = −0.06 + 0.06*RI_{LEG500}	LM_{ARM}: adj: 0.93 LM_{LEG}: adj: 0.86	NR	NR

(continued on next page)

Table 3 (*continued*)

First author, year	Reference method	Muscle mass parameter measured	Age of the population	BIA frequency	Regression model	Variables in equation	Full equation	R^2	p-value	SEE
De Rui, 2017 [35]	DXA	LM_{ARMDOM} (kg) $LM_{ARM-NONDOM}$ (kg) $LM_{LEG-DOM}$ (kg) $LM_{LEG-NONDOM}$ (kg)	70.95 ± 5.6 years	Single (50 kHz)	MS	* Sex: female = 0, male = 1 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Weight (kg)	$LM_{ARM-DOM} = -0.081 + 0.016*RI_{ARM-DOM} + 0.010*weight + 0.299*sex$ $LM_{ARM-NONDOM} = -0.026 + 0.014*RI_{ARM-NONDOM} + 0.009*weight + 0.352*sex$ $LM_{LEG-DOM} = -0.462 + 0.027*RI_{LEG-DOM} + 0.047*weight + 0.639*sex + 0.026*Xc_{LEG-DOM}$ $LM_{LEG-NONDOM} = -0.522 + 0.029*RI_{LEG-NONDOM} + 0.045*weight + 0.569*sex + 0.025*Xc_{LEG-NONDOM}$	$LM_{ARM-DOM} = 0.86$ $LM_{ARM-NONDOM} = 0.88$ $LM_{LEG-DOM} = 0.81$ $LM_{LEG-NONDOM} = 0.88$	NR	NR
Luque, 2014b [32]	DXA	LM_{TRUNK} LM_{ARM} LM_{LEG}	NR	Single (50 kHz)	M	* Sex: female = 2, male = 1 * Height (cm) * Impedance (ohm) * Chest circumference (cm) * Triceps skinfold (cm) * Mid-thigh circumference * Mid-thigh skinfold	LM_{TRUNK} (kg) = −4.774 − (0.004 × impedance) + (0.129 × height) − (0.559 × sex) + (0.031 × chest circumference) LM_{ARM} (kg) = −0.173 − (0.001 × impedance) + (0.024 × weight) + (0.008 × height) − (0.029 × sex) − (0.008 × triceps skinfold) LM_{LEG} (kg) = −1.723 − (0.003 × impedance) + (0.051 × weight) + (0.032 × height) + (0.026 × mid-thigh circumference) − (0.023 × mid-thigh skinfold)	LM_{TRUNK}: 0.82 LM_{ARM}: 0.8 LM_{LEG}: 0.8	<0.001	NR
Pietrobelli, 1998 [36]	DXA	SM_{ARM} (kg) SM_{LEG} (kg)	31.5 ± 9.9 years	Multi (1−5−10−25 −50−100−300 kHz)	M	* Sex: NR * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Age (years)	SMARM1 kHz = 1.025 + RI*0.042 + age*−0.026 + sex*1.426 SMARM10 kHz = −0.560 + RI*0.065 + age*−0.029 + sex*−0.058 SMARM50 kHz = −0.253 + RI*0.055 + age*−0.027 + sex*−0.162 SMARM300 kHz = −0.588 + RI*0.052 + age*−0.023 + sex*−0.247 SMLEG1 kHz = 6.087 + RI*0.098 + age*−0.075 + sex*5.171 SMLEG10 kHz = −0.297 + RI*0.179 + age*−0.108 + sex*2.071 SMLEG50 kHz = −0.997 + RI*0.162 + age*−0.092 + sex*1.549 SMLEG300 kHz = −4.166 + RI*0.195 + age*−0.095 + sex*0.235	* $SM_{ARM1kHz}$: 0.82 * $SM_{ARM\ 10kHz}$: 0.91 * $SM_{ARM\ 50kHz}$: 0.93 * $SM_{ARM\ 300kHz}$: 0.93 * $SM_{LG1\ kHz}$: 0.75 * $SM_{LEG\ 10\ kHz}$: 0.81 * $SM_{LEG50\ kHz}$: 0.84 * $SM_{LEG300\ kHz}$: 0.88	NR	NR
Janssen, 2000 [37]	MRI	SM (kg)	41.5 ± 12.8 years (Caucasian)/ 36.6 ± 11.6 years (African−American)/ 31.8 ± 9.8 years (Asian/33.5 ± 11.1 years (Hispanic)	Single (50 kHz)	MS	* Sex: female = 0, male = 1 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Age (years)	SM = [(RI*0.401) + (sex*3.825) + (age*−0.071)] + 5.102	0.86	NR	2.7 kg (9%)
Oshima, 2010 [54]	MRI	SM (kg)	NR	Single (50 kHz)	MS	* Sex: female = 2, male = 1 * RI: BIA resistance index = Ht^2/R (height^2 (in cm^2)/resistance (Ohm)) * Age: years * BSA (body surface area): NA	SM (kg) = (0.126 × RI) + (1.937 × BSA) + (−0.062 × age) + (−2.186 × sex) − 2.881	0.893	NR	1.65 kg

Tanaka, 2007 [31]	MRI	SMV (cm^3)	24.4 ± 3.2 years	Single (50 kHz)	Whole body: S Segmental:M	* L_{TR} = trunk length (cm) * $Z_{TR\text{-}WHOLE}$ = impedance in whole trunk (Ohm) * $L_{UPPER\ LEG}$ = length upper leg (cm) * $Z_{UPPER\ LEG}$ = impedance upper leg (Ohm)	SMV (cm^3) = 116.1*[$(L_{TR})^2/Z_{TR\text{-}WHOLE}$ + 1220.8*$(L_{UPPER\ LEG})^2/Z_{UPPER\ LEG}$] − 4913.1	0.842	NR	1693.8 cm^3
Fuller, 1999 [34]	MRI	SMV_m (liter)	NR	Multi but, only 50 kHz used	NR	* L^2 (cm*100) = section (thigh or calf) length * R (Ohm) = impedance at 50 kHz * V (l) = limb volume (circumference^2/4π)*length (in cm) * ρ_{at} = resistivity of adipose tissue 50 kHz (16 Ω m) * V_b = bone cross-sectional area*length of limb section (6 cm^2*length (in cm)) * V_s = skin cross-sectional area (cm^2)*length (cm) * V_n = neurovascular cross-sectional area (cm^2), multiplied by limb section length (cm) * ρ_n = resistivity of neurovascular tissue 50 kHz (1.6 Ω m) * ρ_b = resistivity of bone 50 kHz (>100Ω m) * p_s = resistivity of skin 50 kHz (5.5Ω m) * ρ_m = resistivity of human muscle 50 kHz (1.49Ω m)	Full equation: $SMV_m = [(L^2/R) - (V/\rho_{at}) + (V_n/\rho_{at}) + (V_b/\rho_{at}) + (V_s/\rho_{at}) - (V_n/\rho_n) - V_b/\rho_b) - (V_s/\rho_s)]^*[(\rho_m{}^*\rho_{at})/(\rho_{at} - \rho_m)]$ Simplified equation: $SMVm = [(L^2/R) - (V/\rho at)]^*$ $[(\rho m^*\rho at)/(\rho at - \rho m)]$	NR	NR	NR

LM: lean mass; ALM: appendicular lean mass; ALM/ht^2: appendicular lean mass divided by $height^2$; SM: skeletal muscle mass; ASM: appendicular skeletal muscle mass, SMV: skeletal muscle volume; MS: stepwise multiple regression; M: multiple linear regression; S: simple linear regression; adj: adjusted; NR: not reported.

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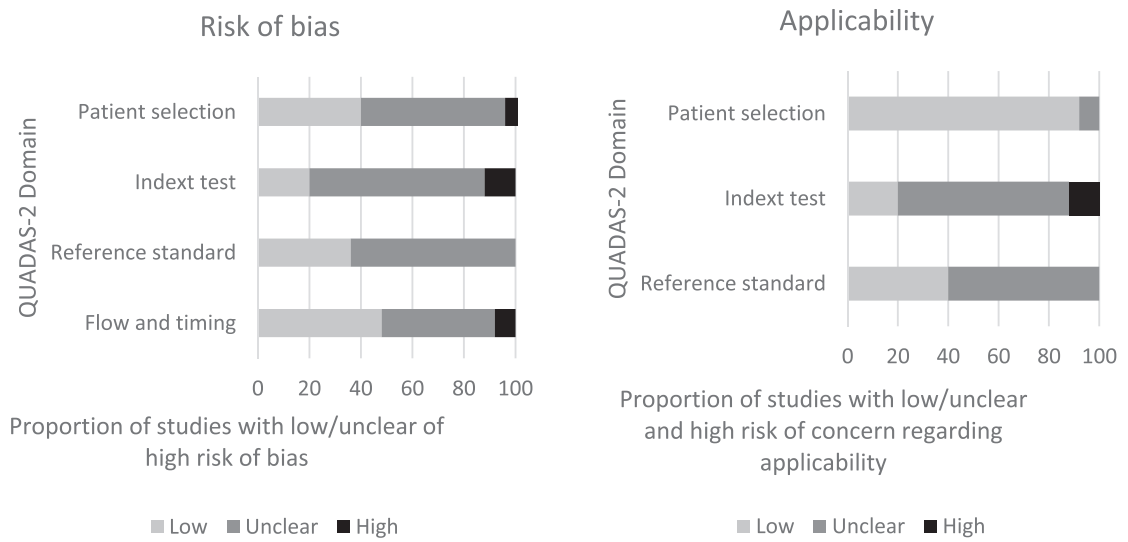

Fig. 2. Quality assessment by QUADAS-2.

[55]. Therefore, as described by Kyle et al., an adequate equation is of great importance for a valid estimation of a patient's body composition [24].

The review findings demonstrate that the parameters most frequently included in the equations are BIA resistance index, socio-demographic (sex and age) and anthropometric (weight and height) variables. The choice of these parameters (i.e. type and number of parameters) is heterogeneous between studies, ranging between 1 and 11. However, this choice can greatly influence the R^2 of the equation (i.e. the percentage of the response variation that is explained by the linear model). In general, we observed that equations including a larger number of variables explain a larger part of the variance of lean body mass measured by BIA versus DXA. For example, the studies of Colica et al. and Kim et al., both including 4 variables, present an R^2 above 0.90 whereas, the studies of Buckinx et al. and Janssen et al., including 3 variables present an R^2 below 0.90 [16,37,46,49]. Thus, the addition of complementary variables in the regression model, if well chosen, seem to bring more precision to the prediction equation. Nevertheless, the addition of complementary variables implies a great workload for the researcher and the clinician during the data collection and could, therefore, limit the feasibility. In the case of already designed studies (i.e. for other purposes), the need of a large number of variables may similarly limit the use of the equation. It is therefore necessary to find a balance between avoiding using too many variables (and unsuitable variables) in order to guarantee the maximum use of the equation and putting too few variables to get the best R^2 possible.

Most of the prediction equations have been developed in European or North American non-Hispanic white subjects. More limited data is available for Hispanics, non-Hispanic Blacks, Asians, and Native Americans. Moreover, the equations were mainly developed in older or adult populations and in generally healthy populations. In choosing BIA equations, it is very important to consider the characteristics of the sample in which it has been developed and validated (e.g. age, ethnicity). Indeed, it may lead to predictive errors when an equation is applied to a population with divergent characteristics from those of the population in which the equation was developed. Equations are only valid for a similar population as in the validation study and using the same BIA device. Ideally, prediction equations should be cross-validated on independent samples. Only a minority of the studies in our review provided cross-validation data in the development article itself (9 studies out of 25). It is possible that, in some cases, the validation has been published in a later article. We invite the reader to search for validation studies when they are considering using a specific equation. However, it is important to emphasize that the validation studies are often limited to a few specific populations and therefore unlikely to be applicable and helpful in clinical settings, where patients are more heterogeneous with different health and clinical conditions. Moreover, the methods used to validate and the statistics used are very different between studies which brings additional confusion. Identifying the existence of validations of the equations in other types of population was not the aim of this work, and therefore, results of validations that happened separately from the development have not been presented in this manuscript.

The quality of most of the included studies was moderate, and in a substantial proportion of them, items with an unclear risk of bias were observed. The results must be interpreted with caution because these items could have influenced the results. It is disappointing that so few studies report in sufficient detail on BIA procedures, which is what led to the high number of unclear risk of bias ratings, and complicates the interpretation of the obtained results. A significant risk of Selection bias was observed in 2 studies, De Rui [35] et al. and Yamada et al. [50]. As mentioned above, the study population has a considerable influence on the validation results so participant's selection is of huge importance. In their study, De Rui et al. found r^2 values from 0.81 to 0.88 according to the regions of the body that were measured, which is within the range of the other studies identified in this review. However, Yamada et al. found a lower value of r^2, as compared to other equations, which could be the result of the risk of bias observed in the participant's selection. Other studies also reported high risk of bias with regards to the Index test, and thus, the procedure of the BIA assessment. “Special attention should be given to the fact that not all studies took into account the hydration status of their participants. In 1998, Gallagher et al. already demonstrated the importance of being in a fasting state to ensure consistency in the interpretation of BIA for body composition analysis [56,57]. In this systematic review, only 15/25 of the included studies provided adequate information about empty stomach and/or bladder. The other studies did not report this information and we therefore cannot ensure that hydration status was well respected before measurements”. In their study, Colica et al. [49] found the highest r^2

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value of 0.96 for their equation developed for estimating body lean mass in children. However, this study was classified as high risk of bias for Index Test (participant not fasted, no bladder voiding, no information about BIA calibration).

From a practical point of view, this systematic review of the literature allows clinicians and researchers to verify the existence of a prediction equation for a valid estimation of muscle mass in a specific population and with a specific tool. If the equation exists, it's use is recommended because the development of new equations in the same context would be redundant and undesirable. However, we advise clinicians and researchers to be mindful of the following points so they can make the best choice with regards to the equations they will use: 1) they should select an equation depending on the reference method used/chosen by the authors. For example, if the purpose is to diagnose sarcopenia with BIA, while most muscle mass cut-offs are based on DXA, choosing a BIA equation that has been validated against DXA would be preferable. 2) they need to question themselves about the relevance of the muscle parameters that they want to measure (ALM/ASM, ALM/ht^2, SM, TLM, etc.) since equations will differ for these different parameters. For example, if they are interested in sarcopenia, they should privilege equations that have been developed for ASM; 3) they need to select an equation that has been developed in a similar population of interest (e.g. sex, age, ethnicity, health condition, etc.); 4) they need to select an equation that has been developed with the same BIA device as the one they will use in their clinic/research, and that also operates at the same frequency (e.g. 50 Hz); 5) they need to select the equation that led to the highest r^2 value, taking into account the variables included in the equation and the possibility to collect these variables; 6) they need to ensure that the study that developed this equation is free from high risk of bias (selection bias, bias in the procedures of assessment such as no empty stomach, inadequate positioning of the electrodes, reference method not applied at the same time, etc.); 7) finally, they need to ensure that this equation has been validated. If validation has not been done, we recommend developing a study to validate the equation.

In conclusion, this systematic review provides a comprehensive overview of the available equation models developed for BIA to predict muscle mass estimates according to the reference method used. The results highlight that there is a large heterogeneity in BIA predictive equations to obtain a value of muscle mass that will be as close as possible to the value obtained with the reference method. Overall, the heterogeneity concerns both the brand of BIA and the BIA procedure, but also the studied population and the confounding variables included in the equation. Important factors that could influence the choice between equations are made available in this review.

Author contribution

The protocol was developed by CB in collaboration with all the members of the BAMS working group on BIA equation model and under the supervision of OB. Search strategy was performed by CB as well as studies exportation in an Excel document. Study selection was performed by CB and FB for the phase of title/abstract selection and by AG/MH in the phase of full text screening. Data extraction was performed by AG and MH with FB as third reviewer. Results analysis was performed by CB. The manuscript was written by both CB and FB and critically approved by all members of the working group.

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Declaration of competing interest

The authors declared they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2019.09.012.

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