Special Article

NUTRITION REVIEWS

Predicting muscle mass from anthropometry using magnetic resonance imaging as reference: a systematic review

Yasmin Y Al-Gindan, Catherine R Hankey, Wilma Leslie, Lindsay Govan, and Michael EJ Lean

Identification and management of sarcopenia are limited by lack of reliable simple approaches to assess muscle mass. The aim of this review is to identify and evaluate simple methods to quantify muscle mass/volume of adults. Using Cochrane Review methodology, Medline (1946–2012), Embase (1974–2012), Web of Science (1898–2012), PubMed, and the Cochrane Library (to 08/2012) were searched for publications that included prediction equations (from anthropometric measurements) to estimate muscle mass by magnetic resonance imaging (MRI) in adults. Of 257 papers identified from primary search terms, 12 studies met the inclusion criteria. Most studies (n = 10) assessed only regional/limb muscle mass/volume. Many studies (n = 9) assessed limb circumference adjusted for skinfold thickness, which limits their practical applications. Only two included validation in separate subject-samples, and two reported relationships between whole-body MRI-measured muscle mass and anthropometry beyond linear correlations. In conclusion, one simple prediction equation shows promise, but it has not been validated in a separate population with different investigators. Furthermore, it did not incorporate widely available trunk/limb girths, which have offered valuable prediction of body composition in other studies.

INTRODUCTION

Muscle is important for physical activity, social functioning, and metabolic health. Measuring muscle mass is of interest for various reasons, such as evaluating the effects of weight loss or gain, assessing the effects of disease on body composition, determining the effects of physical activity, and predicting frailty and falls. The term "sarcopenia" has been used for over two decades to describe loss of muscle mass, strength, and/or quality.[1] Low muscle mass or loss of muscle function has major effects on quality of life, contributes to frailty, and is related to chronic illnesses like diabetes and heart disease.[2,3] Low muscle mass may thus affect physical, mental, and social aspects of health through a range of functional, nutritional, endocrine, and metabolic consequences[4] of particular importance to aging.[5] Recognition of the clinical and public health consequences of sarcopenia[6,7] has attracted some research interest in evaluating approaches to assess muscle mass and its quality and functional capacity. Progress, however, is hampered by a lack of agreement on simple approaches to estimate muscle mass[6,8] and provide unified criteria for diagnosis, clinical application, and epidemiological practice.[9]

Sarcopenia can result from a primary disease of muscle, such as myasthenia, or occur as disuse atrophy secondary to a primary cause, such as metabolic disease, inflammation, neurological disease, or physical inactivity (as a result of any condition).[10,11] Overweight and obesity, which now affect well over half of all adults in postindustrialized societies, are generally associated with increased muscle mass to support greater weight; however,

Affiliations: *YY Al-Gindan*, *CR Hankey*, *W Leslie*, and *MEJ Lean* are with Human Nutrition, College of Medical, Veterinary & Life Sciences, School of Medicine, University of Glasgow, Glasgow, UK. *L Govan* is with Institute of Health and Well Being, College of Medical, Veterinary & Life Sciences, University of Glasgow, Glasgow, UK.

Correspondence: *MEJ Lean*, Human Nutrition, MVLS, School of Medicine, University of Glasgow, Glasgow G4 0SF, UK. E-mail: Mike.Lean@glasgow.ac.uk, Phone: +44-141-211-4686, Fax: +44-141-211-4844.

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the extent of muscle hypertrophy may be insufficient to maintain metabolic and physical capacities. A relatively low muscle mass in obese people, termed "sarcopenic obesity," is difficult to identify clinically but appears to be increasing in prevalence[12] and presents limitations to mobility and function, promoting diabetes and cardiovascular disease.[13]

The European Working Group on Sarcopenia in Older People suggests three measurable variables: mass, strength, and/or physical performance.[14] Muscle strength can be measured by grip strength and physical performance by gait-speed, the 6-minute walk test, the stair-climbing test, the short physical performance battery.[14] The International Sarcopenia Consensus Conference Working Group proposed including both muscle mass and physical function in the definition of sarcopenia.[15] To estimate muscle mass, they suggest an index (whole-body fat-free mass to height^2), applying cutoff points used in other epidemiological studies: ≤7.23 kg/m^2 for men and ≤5.67 kg/m^2 for women.[16] They propose that functional capacity be indicated by gait speed. Janssen et al.[17] recommended a quantitative definition based on the muscle mass index or ratio, derived by dividing appendicular skeletal muscle (SM) mass by height.[2] Individuals with ratios between −1 and −2 standard deviations of young controls of the same gender would be considered to have class I sarcopenia (men, 8.51–10.75 kg/m^2; women, 5.76–6.75 kg/m^2). Individuals with ratios below −2 would be categorized as class II sarcopenia (men, ≤8.51 kg/m^2; women, ≤5.75 kg/m^2).

There is a need for a standardized quantitative definition of sarcopenia that can be related to morbidity, mortality, and physical disability.[18] Such a definition is likely to be based on total SM mass, possibly with additional measures of strength and/or physical performance. It would be helpful if muscle mass could be estimated, and sarcopenia identified, from simple measures that can be made routinely, both clinically and epidemiologically, in large health surveys.

Approaches to assessment of muscle mass and sarcopenia

Reference methods for body composition analyses have historically included cadaver dissection, underwater weighing (using a simple two-compartment model) and, more recently, three-dimensional computed tomography (CT) and magnetic resonance imaging (MRI). Prediction equations from these reference methods have been developed for use in field methods of anthropometric measurement, such as dual-energy X-ray absorptiometry (DEXA) and bioelectrical impedance analysis (BIA).

Before sophisticated imaging methods were available, skeletal muscle was most commonly estimated from circumferences of the upper arm[19] and/or lower leg[20] (sometimes corrected for skinfold thickness) and from simple tests of strength or endurance, such as hand grip, stair climbing, and chair rise.[21,22] Measurement now includes the use of imaging methods such as MRI, DEXA, CT, and BIA,[23] the assessment of muscle metabolites, the calculation of 3-methylhistidine and creatinine excretion, and anthropometry.[24] MRI and CT scanning are generally considered accurate and reliable for quantification of muscle mass, based on validations against cadaver dissections.[25] They permit simpler field measurements using techniques such as anthropometry and enable validation of prediction equations in the variety of clinical and epidemiological settings where such measurements are needed.[25–28] Even with modern imaging, problems remain: 1) Limb muscle groups are separated by nonmuscular components and covered by variable amounts of fat[29]; 2) obesity, aging, and some illnesses lead to fat infiltration of muscle, complicating the identification and quantification of muscle[30]; 3) sophisticated scanning instruments and trained staff are costly[31]; 4) high-quality reference data have not been defined for individuals of different sex, age, race, and body fat content[32]; and 5) there may still be confounding effects from smoking, nutrition, occupation, alcohol use, and physical activity.

DEXA has been used to estimate body fat and muscle mass in clinical and epidemiological settings,[15] but its accuracy depends on having prediction equations validated against reference-method measurements, and conflicting results have been reported when compared with underwater weighing,[33] total body nitrogen,[34] CT scanning,[35,36] and MRI.[26] DEXA has many limitations: 1) Muscle is not quantified directly, and several crude assumptions are made to calculate muscle mass; 2) patients are exposed to radiation; 3) there is potential interference from fluid, dehydration, or edema; 4) it is relatively costly; and 5) it requires skilled technicians.[6,31] Nonetheless, the 1993–1995 New Mexico Elderly Health Survey, one of the most-cited studies that measured SM mass and quantified sarcopenia, used DEXA to estimate total lean soft tissue of the arm and leg.[16] The best predictive equation, from stepwise regression, included weight, height, hip circumference, grip strength, and gender ($R^2 = 0.91$, standard error of estimate [SEE] = 1.58). Sarcopenia, defined as SM mass (kg)/height^2 (m^2) below two standard deviations from the mean in a young reference group, increased with age, ranging 13–24% in subjects >70 years of age and exceeding 50% in subjects 80 years of age.

BIA has been used in many large-scale health surveys. As with DEXA, there is a huge conflict in the literature over its validity.[37–39] Nevertheless, it has been used in epidemiological studies, such as the National Health and Examination Survey III, in which sarcopenia,

defined arbitrarily as a low "muscle mass index" (skeletal muscle mass index [SMI] = skeletal muscle mass/body mass × 100; sarcopenia was considered present in subjects whose SMI was below −1 standard deviation) was associated with disability and functional impairment in 4,504 adults over 60 years of age.[2] Many factors, however, introduce error and limit the value of BIA, including the size and type of electrodes used and the calibration of the equipment, the need for a multifrequency signal, and the effects of hydration, edema, temperature variations, and sweating on electrical impedance.[24] BIA has not been found superior to anthropometry for estimating body composition.

There are many advantages of anthropometric measurement. It is simple, quick, safe, noninvasive, and inexpensive, requiring only a low level of skill to perform and providing immediate results. It is essential, however, that anthropometry be practical, sensitive, and specific for the quantification of muscle mass.[31]

Interestingly, rather few studies have compared predictions between anthropometry and "black-box" methods like DEXA and BIA, and most of the literature has focused on body fat, with little attention given to whole-body muscle mass, although limb muscle mass has been widely examined in the sports science field. No studies have developed prediction equations for whole-body muscle mass from anthropometry using CT as the reference method.

Efforts to economize and save time by using a single cross-sectional MRI slice or a limited number of MRI slices, rather than using contiguous scans of the whole body, raise questions about three steps in the prediction of whole-body muscle mass: 1) Does limited cross-sectional muscle area of limbs represent the whole muscle mass of the region (limb) examined? If so, how many slices are needed? 2) Does regional muscle mass, e.g., of limbs, quantitatively reflect whole-body muscle mass? 3) Which single or contiguous imaging (thigh, arm, or calf) best represents whole-body muscle mass or volume? No study appears to have drawn comparisons between the three limb areas, although the thigh was used most frequently.

The validity of estimating thigh muscle volume (quadriceps) using a single MRI image was examined by Morse et al.[40] in 18 active young men. A single MRI scan taken at 60% of the femur length from the distal end of the femur estimated muscle volume, with $R^2 = 0.90$ and SEE = 10%. Similarly, Tothill and Stewart[41] showed strong correlation between the area of a single mid-thigh MRI muscle image and the volume of thigh muscle obtained from contiguous scans ($R^2 = 0.96$, SEE = 207 cm^3) (see Table S1 in the Supporting Information for this article, available online).

Lee et al.[42] related MRI measurement of thigh SM mass to whole-body SM mass and reported the correlation coefficients between a single MRI measurement and multiple MRI images in 387 white men and women. The findings, perhaps unsurprisingly, indicated that a seven-slice estimate of thigh muscle mass had a higher correlation with whole-body SM mass ($R^2 = 0.84$, SEE = 5.4% in men; $R^2 = 0.90$, SEE = 5.1% in women) than the muscle area on a single thigh image ($R^2 = 0.77$, SEE = 6.5% in men; $R^2 = 0.79$, SEE = 7.4% in women). Both measurements, however, showed sufficient correlation to provide useful prediction for many purposes (Table S1).

With these limitations accepted, a systematic review approach was used to explore the published literature for simple anthropometric equations to predict the muscle mass of adults, as measured by MRI.

METHODS

Selection of studies

A search strategy was conducted according to Cochrane Review criteria,[43] using the key words in Table 1. MeSH

Table 1 **Key words used to search the published literature.**

Search term	No. of results				
	Medline	PubMed	Embase	Web of Science	Cochrane Library
Sarcopenia & anthropometry & MRI	1	1	5	5	0
Muscle mass & anthropometry & MRI	14	22	31	15	1
Muscle volume & anthropometry & MRI	14	18	14	13	0
Mid-arm circumference & MRI	1	1	1	0	0
Arm circumference & MRI	7	9	14	8	2
Mid-thigh circumference & MRI	0	0	0	0	0
Thigh circumference & MRI	8	11	8	9	4
Mid-calf circumference & MRI	0	0	0	0	0
Calf circumference & MRI	4	5	5	3	3
Total	49	67	78	53	10

Abbreviations: MRI, magnetic resonance imaging.

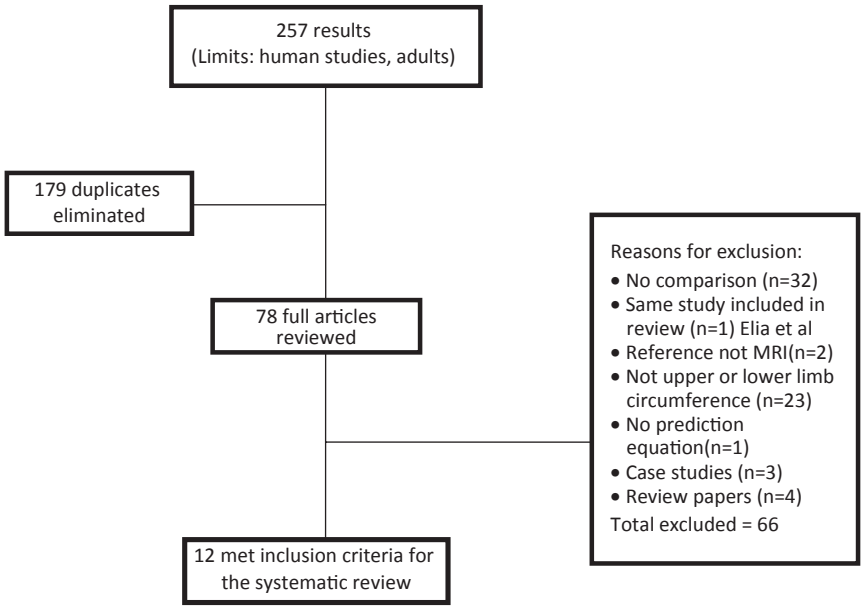

Figure 1 **Flow chart of selection of studies.**

terms were used in Medline (1946–2012), Embase (1974–2012), Web of Science (1898–2012), PubMed, and the Cochrane Central Register of Clinical Trials (to 08/2012). Limits were "human" and "adults." In the primary search, irrelevant articles were eliminated first, on the basis of title and abstract. The remaining articles were read and eliminated if they did not meet the inclusion criteria. Reference lists of relevant papers were checked. Reference Manager® version 12 was used to manage articles.

Studies were included if they were conducted in adult humans (>18 years), if they used MRI as a reference method to measure lean or muscle mass/volume, and if they used anthropometric measurements with prediction equations of lower or upper limb circumferences and/or skinfold thickness.

Studies were excluded if they did not use prediction equations, if they used reference methods other than MRI, and if they used comparator methods other than simple anthropometric measurements commonly available in health surveys, e.g., DEXA, BIA (Figure 1).

Quality assessment

Studies were checked for relevance by two reviewers (YA, WL) independently, using the same search strategy in Table 1; both reviewers agreed on the included studies. Technical and critical quality assessment was completed using a critical review form[44] and QUADAS, a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews[45] (Tables 2 and 3).

RESULTS

Altogether, 257 studies were identified by the primary search terms (Table 1). After eliminating the duplicates (n = 179), 78 studies were identified by title and abstract as potentially relevant. Of these, 12 studies met all inclusion criteria and were included in the review (Figure 1).

Quality assessment

Critical quality assessment. The purpose of the study was stated clearly in all papers (Table 2 and Table S2 available in the Supporting Information online). All studies with the exception of one were cross-sectional. Nakamura et al.[46] was a longitudinal study that lasted 3 years, with measurements taken once annually. However, the time points used to compare reference and index methods were not specified. Sample size justification was not reported in all studies. Sample size was below 69 subjects in all studies except one,[47] which had 324 subjects (Table 4). Reliability and validity were assessed in most studies (Table 2). Studies that used limb circumference corrected for skinfold thickness, employing the method of Jelliffe and Jelliffe[19] to obtain the prediction equation, were considered validation studies because this equation has been already validated.[20,48] Limitations and biases were reported only in three studies.[46,49,50] The Bland-Altman method to assess agreement and distributions of errors was used by Lee et al.[47] and Mathur et al.[51] Overall, there were no major concerns about the quality of papers included in this study, although all contained some type(s) of weakness (Table 2).

Table 2 **Critical quality assessment of studies included in the review.**

	Chen et al. (2011)[49]	Mathur et al. (2008)[51]	Tonson et al. (2008)[54]	Nakamura et al. (2006)[46]	Tothill & Stewart (2002)[41]	Lee et al. (2000)[47]	Bamman et al. (2000)[53]	Fuller et al. (1999)[55]	Knapik et al. (1996)[58]	Ross et al. (1994)[50]	Housh et al. (1995)[29]	Baumgartner et al. (1992)[52]
Study purpose stated	✓	✓	✓	✓[a]	✓	✓	✓[a]	✓	✓	✓[a]	✓	✓
Literature reviewed	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Design												
Cross-sectional	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓
Longitudinal				✓								
Sample												
Described	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Justified												
Outcomes												
Reliability	✓	✓			✓	✓	✓	✓	✓	✓	✓	
Validated		✓	✓		✓	✓	✓	✓	✓		✓	✓
Prediction equation described	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Statistical significance of results reported	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Limitations and bias reported	✓			✓						✓		
Appropriate conclusion drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[a] Developing or validating prediction equation not main purpose of study (see Table S2 for aim of each study).

Technical quality assessment. Several points of criticism emerged from the technical assessment of the included studies (Table 3). First, the period between performing the reference and index tests was not reported in most studies (n = 9 studies). Since they were cross-sectional studies, it was assumed that measurements were made close together, but this information would increase confidence in the conclusions (question 4, Table 3). Second, none of the studies mentioned whether the test results were analyzed or interpreted with or without (i.e., blinded) knowledge of the other test (questions 10 and 11, Table 3). Third, Nakamura et al.[46] was the only study that mentioned withdrawals, as that study was longitudinal. All male subjects withdrew for varying reasons, so the authors focused their study on the female subjects. Baumgartner et al.[52] used data from New Mexico Aging Process Study and mentioned a dropout rate of 5.8/year and a death rate 4.9/year (question 14, Table 3). Finally, the response rate was not mentioned in any of the studies, although selection criteria were clearly explained in all cases. Each study represented a specific age group of interest (questions 1 and 2, Table 3).

Magnetic resonance imaging

All studies except two[47,50] attempted to use regional muscle mass as a marker of whole-body muscle mass (Table 5). Ten studies used T1-weighed spine echo sequences (Table 6), which are optimal for representing anatomy.[30]

MRI machines ranged from 0.5 to 1.5 tesla: 7 of the 12 studies used 1.5 tesla. One study[53] used whole-body imaging and 4.1 tesla spectroscopy. MRI scanning methodologies varied (Table 6), described as follows: 1) The strength of the magnetic field varied between 0.5 and 1.5 tesla, affecting scanning time and thus image quality. Not all studies reported scanning times. The length of reported scans ranged between 2 min and 90 min, the main difference being the longer time required for whole-body versus single cross-sectional measurements. 2) Considerable variation in repetition time and echo time was found. 3) Variation in the number and thickness of images (5 mm or 10 mm) also was noted. 4) Gap thickness ranged 2.5–50 mm. 5) In most studies, cross-sectional areas were totaled and converted to volumes, and then muscle mass/volume was calculated. Different software program were used for these calculations.

Anthropometric variables and subject characteristics

In all studies except three[46,49,50] and the study of Lee et al.,[47] who used skinfold thickness and simple anthropometric measurements, a combination of regional skinfold thicknesses and circumferences was used in anthropometric

Table 3 **Technical quality assessment of studies included in the review, as determined by QUADAS.**

Question	Chen et al. (2011)[49]	Mathur et al. (2008)[51]	Tonson et al. (2008)[54]	Nakamura et al. (2006)[46]	Tothill & Stewart (2002)[41a]	Lee et al. (2000)[47]	Bamman et al. (2000)[53]	Fuller et al. (1999)[55]	Knapik et al. (1996)[58]	Ross et al. (1994)[50]	Housh et al. (1995)[29]	Baumgartner et al. (1992)[52]
1. Was the spectrum of participants representative of the patients who will receive the test in practice?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
2. Were selection criteria clearly described?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
3. Was the reference standard likely to classify the target condition correctly?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
4. Was the period between performance of the reference standard and the index test short enough to be reasonably sure that the target condition did not change between the two tests?	~	~	~	~	✓	~	~	✓	✓	~	~	~
5. Did the whole selection of the sample receive verification using the reference standard?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
6. Did participants receive the same reference standard regardless of the index test result?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
7. Was the reference standard independent of the index test? (that is, the index test did not form part of the reference standard)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
8. Was the execution of the index test described in sufficient detail to permit its replication?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
9. Was the execution of the reference standard described in sufficient detail to permit its replication?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
10. Were the index test results interpreted without knowledge of the results of the reference standard?	~	~	~	~	~	~	~	~	~	~	~	~
11. Were the reference standard results interpreted without knowledge of the results of the index test?	~	~	~	~	~	~	~	~	~	~	~	~
12. Were the same clinical data available when the test results were interpreted as would be available when the test is used in practice?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
13. Were un-interpretable, indeterminate or intermediate test results reported?	~	~	~	~	~	~	~	~	~	~	~	~
14. Were withdrawals from the study explained?	~	~	~	✓	~	~	~	~	~	~	~	✓

Abbreviations: N/A, not applicable; ~, not reported; ✓, reported.
[a] Not all participants underwent anthropometric measurement.

Table 4 **Subject characteristics of studies included in the review.**

Reference	Sex	Age (years)	No. of subjects	BMI or weight
Chen et al. (2011)[49]	W	76 ± 6.0	36	24.5 ± 3.0 kg/m^2
	M		33	
Mathur et al. (2008)[51]	W/M healthy	56–78	11/9	24.3 ± 2.2 kg/m^2
	W/M COPD		11/9	26.6 ± 4.7 kg/m^2
Tonson et al. (2008)[54]	M (boys, adolescents, men)	11.3 ± 0.8	14	16.4 ± 1.0 kg/m^2
		13.3 ± 1.4	16	18.3 ± 3.7 kg/m^2
		35.4 ± 6.4	16	22.7 ± 2.5 kg/m^2
Nakamura et al. (2006)[46]	W	<60	9	20.5 ± 4.3 kg/m^2
		>60	7	21.0 ± 3.7 kg/m^2
Tothill et al. (2002)[41]	W	23–49	10	19.6 ± 0.4 – 29.5 ± 4.8 kg/m^2
	M		9	24.3 ± 1.4 – 34.0 ± 1.5 kg/m^2
Fuller et al. (1999)[55]	W	41–60	8	25.1 ± 5.4 kg/m^2
	M	43–62	8	28.6 ± 5.4 kg/m^2
Lee et al. (2000)[47]	W	41 ± 15	109	23.8 ± 3.4 kg/m^2
	M	38 ± 12	135	25.2 ± 3.1 kg/m^2
	W	43 ± 10	41	34.8 ± 3.5 kg/m^2
	M	42 ± 13	39	33.8 ± 2.7 kg/m^2
Bamman et al. (2000)[53]	W (trained)	34 ± 5	7	55.6 ± 5.0 kg
	W (untrained)	36 ± 8	32	67.6 ± 8.8 kg
Knapik et al. (1996)[58]	W (trained)	21 ± 2.3	9	59.6 ± 7.0 kg
	M (trained)	25.2 ± 5.5	9	81.6 ± 7.0 kg
Ross et al. (1994)[50]	W	35.9 ± 7.8	40	33.4 ± 5.5 kg/m^2
	M	39.1 ± 10.5	17	32.0 ± 3.6 kg/m^2
Housh et al. (1995)[29]	M	25 ± 5	43	81.1 ± 12.8 kg
Baumgartner et al. (1992)[52]	W	80.5 ± 6.2	17	23.3 ± 3.8 kg/m^2
	M	77.0 ± 3.8	8	26.8 ± 3.6 kg/m^2

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; F, females; M, males.

measurement (Table 5). Ten used thigh circumference, three used arm circumference,[47,52,54] and three used calf circumference[47,53,55] (Table 5).

All studies included in this review recruited healthy adults except that of Mathur et al.,[51] which included adults with chronic obstructive pulmonary disease. That study validated the prediction equations developed by Housh et al.,[29] and results showed very low correlations $R^2 = 0.01–0.2$ (Tables 3 and 7).

It was difficult to assess variations in anthropometric prediction by age, because age varied widely between studies (range, 18–92 years) and within samples; for example, Tothill and Stewart[41] had an age range of 23–49 years. Tonson et al.[54] validated the Jones and Pearson equation in children and adolescents, as well as in adults (Table 4), and reported that – compared with MRI – anthropometry tends to overestimate muscle mass. The overestimation was higher in children and adolescents than in adults (43.1%, 38.5%, and 20.5%, respectively).

Nakamura et al.,[46] when assessing thigh muscle mass, included underweight elderly subjects (BMI = 21.0 ± 3.7). The remaining studies did not use BMI as an inclusion criterion, hence BMI ranges were wide, from 18 kg/m^2 to 39 kg/m^2 (Table 4), with the exception of the study by Lee et al.,[47] who cross-validated equations derived in nonobese subjects separately in obese (BMI > 30 kg/m^2) and nonobese groups. In general, more bias was seen in obese subjects than in nonobese subjects when either the skinfold-corrected model (SEE = 2.9 and 2.5, respectively) or the body weight and height model (SEE = 3.0 and 2.6, respectively) was used. This study concluded that the equation with limb skinfold circumference was more robust for use in obese subjects than the simple equation that included body weight, height, sex, age, and race (Table 7).

Method reproducibility

Whether single or multiple observers were used was reported in most studies. A detailed explanation of method reproducibility was given by Fuller et al.[55] and by Tothill and Stewart,[41] while other authors provided only limited data (Table S3, available in the Supporting Information online). In general, limb circumference measurement resulted in the least variability and skinfold thickness measurement in the greatest variability (Table S3).

Prediction equations

Prediction equations are listed in (Table 7). Four studies used a simple anthropometric approach, and nine

Table 5 **Anthropometric and MRI measurements included in the prediction equations of studies.**

Reference	Derivation	Validation	Circumferences					SFT	Wt	Ht	Age	Sex	Race	MRI		
			Arm	Thigh	Calf	Hip	Waist							Region	Image	Muscle
Chen et al. (2011)[49]	✓			✓			✓		✓		✓	✓		Thigh	Continuous slices	Muscle (cm^3)
Mathur et al. (2008)[51]		✓		✓				✓						Thigh	Mid-thigh CSA	Muscle (cm^3)
Tonson et al. (2008)[54]		✓	✓					✓						Arm	Continuous (5 mm thickness, 10 mm gap) and cross-sectional scans of the highest area measured	Muscle (cm^3)
Nakamura et al. (2006)[46]	✓			✓									–[a]	Thigh	Continuous cross-sectional scans at intervals of 1 cm	Muscle (cm^3)
Tothill et al.& Stewart (2002)[41]		✓		✓				✓						Torso to feet	Institution 1: continuous scans (10 mm thick, gap of 2 mm) Institution 2: continuous scans (10 mm thick, gap)	Muscle (cm^3)
Lee et al. (2000)[47]	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓	WB	Continuous scans (10 mm thick, 40 mm gap)	Muscle (kg)
Bamman et al. (2000)[53]		✓			✓			✓						Calf	Continuous scans (5 mm thick, 10 mm gap). Image with anatomically largest cross-section was used	Lean (cm^2)[b]
Fuller et al. (1999)[55]		✓		✓	✓			✓						Leg	Continuous scans (1 cm slices at 5 cm intervals)	Muscle (cm^3)
Knapik et al. (1996)[58]	✓	✓		✓				✓						Thigh	Cross-sectional image	Lean (cm^3)
Ross et al. (1994)[50]	✓			✓		✓	✓		✓					WB	Continuous (10 mm thick, every 50 mm)	Lean (L)
Housh et al. (1995)[29]	✓	✓		✓				✓						Thigh	Cross-sectional image	Muscle (cm^2)
Baumgartner et al. (1992)[52]		✓	✓	✓				✓						Arm, thigh	Cross-sectional images	Lean (cm^2)

Abbreviations: CSA, cross-sectional area; Ht, height; MRI, magnetic resonance imaging; SFT, skinfold thickness; WB, whole body; Wt, weight.
[a] All subjects Asian.
[b] Muscle × bone cross-sectional area, lean: muscle + bone.

Table 6 **MRI characteristics of studies included in the review.**

Reference	MRI tesla	Axial images	Matrix (pixel)	Repetition time (ms)	Echo time (ms)	Scan time	Field of view	Gap thickness	Slice thickness (mm)
Chen et al. (2011)[49]	1.5	T1-weighed	512 × 384 × 1	136	4.8	20 min	380 × 285 mm^2	2.5 mm	5
Mathur et al. (2008)[51]	1.5	T1-weighed	512 × 384	650	8	–	40 cm^2	2–2.5 cm	5
Tonson et al. (2008)[54]	1.5	T1-weighed	512 × 512	490	12	122 s	200 mm	10 mm	5
Nakamura et al. (2006)[46]	0.5	T1-weighed	–	530	15	–	–	–	–
Tothill & Stewart (2002)[41a]	1	T1-weighed	128 × 256	570	15	–	500 × 500 mm	2 mm	10
	0.95	T1-weighed	–	1,150	12	–	–	50 mm	10
Fuller et al. (1999)[55]	0.5	T1-weighed	256 × 192 × 2	TE/TR = 17	–	–	48 × 36 cm	–	10
Lee et al. (2000)[47a]	1.5	T1-weighed	256 × 256	210	17	25 min	48 × 36 cm	40 mm	10
Bamman et al. (2000)[53b]	4.1	–	–	1,000	14.5	–	256 mm	10 mm	5
Knapik et al. (1996)[58]	1.4	T1-weighed	–	200	22	5 min	–	–	–
Ross et al. (1994)[50c]	1.5	T1-weighed	–	500/210	20/15	1 h 30 min	–	50 mm	10
Housh et al. (1995)[29]	1.5	–	–	600	20 ms	–	–	–	–
Baumgartner et al. (1992)[52]	1.5	T1-weighed	256 × 256	1,500	TE/TI = 20	–	20–60 cm	–	10

Abbreviations: MRI, magnetic resonance imaging; TE/TI, echo time/inversion time; TE/TR, echo time/repetition time; –, not reported.

[a] Scans were done in two different centers.

[b] Spectroscopy.

[c] MRI was upgraded.

studies used local skinfold thickness measurements and employed existing equations in the adjusted skinfold thickness approach. The following measurements or characteristics were found to offer useful prediction of whole-body muscle mass: body weight, height, hip circumference, waist circumference, thigh circumference, age, sex, and race.

Reporting results

Not all studies reported SEE and/or percent error. There was a wide range in the strength of correlations, from very low ($R^2 = 0.01$) to very high ($R^2 = 0.95$) (Table 7). The agreement between methods and the distribution of errors, calculated using the Bland-Altman method,[56] were reported only by Mathur et al.[51] (who showed overestimation) and Lee et al.,[47] who showed reasonably good agreement for measurements in very similar, nonobese subject samples of the same population made by the same investigators, and less than good agreement for measurements in obese subjects of the same population and made by the same investigators (Table 7).

Validation studies

Validation is an important step in developing prediction equations for general use. The equations of Ross et al.[50] and Chen et al.[49] were practical and provided moderate-to-high correlations, but they were not validated, and agreement between methods has not been investigated. Ross et al.[50] assessed lean body mass, and Chen et al.[49] assessed thigh muscle mass, not whole-body muscle mass.

Lee et al.[47] divided their subjects into three subject samples.[47] Nonobese subjects were randomized into groups A and B. Group A ($n = 122$ nonobese subjects) was used to develop the following equation: SM (kg) = 0.226 × body weight × 13.0 × height − 0.089 × age × 6.3 × sex × race − 11.0, where $R^2 = 0.85$ and SEE = 3.0 kg. This equation was cross-validated in group B ($n = 122$ nonobese subjects), where $R^2 = 0.86$ and SEE = 2.6 kg. The final equation was developed with subjects from both groups, A and B: SM (kg) = 0.244 × body weight × 7.80 × height − 0.098 × age × 6.6 × sex × race − 3.3, where $R^2 = 0.86$, $P < 0.0001$, and SEE = 2.8 kg. This equation was then evaluated in the third group, which consisted of obese subjects ($n = 80$, 39 men), where $R^2 = 0.79$, $P < 0.0001$, and SEE = 3.0. The mean muscle mass of the obese group, however, was significantly overestimated (approx. 10%), and significant skewing was seen, with correlation found between the difference of measured and predicted muscle mass and measured muscle mass ($R^2 = 0.18$, $P < 0.001$). The significant correlation means that, for lower values of SM mass, the equation overesti-

Table 7 **Prediction equations included in the systematic review, along with reported results.**

Reference	Prediction equation	R^2 value	SEE	Percent error
Ross et al. (1994)[50]	M: Lean tissue (L) = 0.990 × BW (kg) − 0.542 × waist (cm) − 0.881 × thigh (cm) × 73.12	D: 0.89	2.1 L	3.6
	W: Lean tissue (L) = 0.501 × BW (kg) − 0.379 × hip (cm) × 43.01	D: 0.62	2.8 L	6.5
Lee et al. (2000)[47]	SM (kg) = 0.244 × BW (kg) × 7.80 × ht (m) − 0.098 × age (years) × 6.6 × sex × race − 3.3	D: 0.86	2.8 kg	–
		V: 0.79	3.0 kg	–
Nakamura et al. (2006)[46]	Thigh muscle volume (cm^3) = 21 × thigh (cm) × 979	D: 0.12		–
Chen et al. (2011)[49]	M: SM (cm^3) = 7,168.8 − 52.1 × age (years) × 96.5 × BW (kg) − 67.4 × waist (cm) × 47.3 thigh (cm)	D: 0.68	608.1 cm^3	–
	W: SM (cm^3) = 1,719.3 − 29.9 × age (years) × 53.5 × BW (kg) × 39.8 × thigh (cm)	D: 0.62	496.0 cm^3	–
	C: SM (cm^3) = 4,226.3 − 42.5 × age (years) − 955.7 × gender (1 for men, 2 for women) × 45.9 × BW (kg) × 60.0 × thigh (cm)	D: 0.74	581.6 cm^3	–
Mathur et al. (2008)[51]	Quadriceps muscle CSA = (2.52 × mid-thigh [cm]) − (1.25 × anterior thigh skinfold [mm]) − 45.13	V: 0.057	–	–
	Hamstring muscle CSA = (1.08 × mid-thigh [cm]) − (0.64 × anterior thigh skinfold [mm]) − 22.69	V: 0.078	–	
Tonson et al. (2008)[54a]	Volume 1 = ⅓ ht (area of wrist × [area of wrist × area of mid-forearm]$^{0.5}$ × area of mid-forearm Volume 2 = ⅓ ht (area of mid-forearm × [area of mid-forearm × area of elbow]$^{0.5}$ × area of elbow Total volume = volume 1 × volume 2	V: 0.90		20.5
Lee et al. (2000)[47]	SM (L) = ht × (0.00744 × CAG^2 × 0.00088 × CTG^2 × 0.00441 × CCG^2) × 2.4 × sex − 0.048 × age × race × 7.8	D: 0.91	2.2 kg	–
		V: 0.83	2.9 kg	–
Tothill & Stewart (2002)[41]	Area of the lean tissue (AL) = (circumference of inner tissue − 2π × thickness of superficial adipose tissue)^2/4π Lean volume = (A_1 × A_2 × [A_1 × A_2]$^{0.5}$) × ht/3	V: 0.95	288 cm^3	30
Fuller et al. (1999)[55]	Muscle CSA (cm^2) = (girth^2/4 × 3.14) − (girth × SFT/2) − 6[b]	VT: 0.35	–	40
		VC: 0.69	–	22
Bamman et al. (2000)[53c]	Right calf skinfold thickness and maximum circumference	V: 0.45		
Knapik et al. (1996)[58]	Thigh muscle CSA = 0.649 × ([thigh circumference/π − fat plus skin thickness]^2 − [0.3 × bone]^2)	V: 0.92	10.1 cm^2	22 CSA
Housh et al. (1995)[29]	Quadriceps muscle CSA = (2.52 × mid-thigh [cm]) − (1.25 × anterior thigh skinfold [mm]) − 45.13	D,V: 0.72, 0.64	5.4, 7.3	–
	Hamstring muscle CSA = (1.08 × mid-thigh [cm]) − (0.64 × anterior thigh skinfold [mm]) − 22.69	D,V: 0.52, 0.29	3.2, 3.7	–
	Total thigh muscle CSA = (4.68 × mid-thigh [cm]) − (2.09 × anterior thigh skinfold [mm]) − 80.99	D,V: 0.74, 0.77	9.6, 12.5	–
Baumgartner et al. (1992)[52]	Muscle plus bone area = (limb circumference − πskinfold thickness/2)^{2}4π	VT: 0.43	–	41.5
		VC: 0.69	–	46.8

Abbreviations: A_1 and A_2, area at the top and bottom of section; BW, body weight; C, combined men and women; CAG, corrected arm girth; CSA, cross-sectional area; CTG, corrected thigh girth; D, derivation; ht, height; L, lean tissue; M, men; SEE, standard error of the estimate; SFT, skinfold thickness; SM, skeletal muscle; V, validation; VC, validation calf; VT, validation thigh; W, women; –, not reported.

[a] Jones and Pearson method.

[b] For thigh and calf bone with its constituents, marrow assumed to be 6 cm^2.

[c] Method developed by Gurney et al.[71] in 16 men.

mates SM mass, but for larger values it underestimates. The same method was used for their skinfold circumference model, which gave higher correlations, especially for the obese subjects (Table 7).

DISCUSSION

Total body mass and its major constituents (total body fat, muscle mass, etc.) vary with age, sex, race, and lifestyle but can, in principle, be correlated with height, weight, and circumferences, from which prediction equations can be derived that will, to some extent, account for variations in factors such as race and lifestyle, which can be hard to define. Anthropometry is susceptible to errors, depending on the assumptions and specific characteristics of the derivation and validation populations (which mainly introduce bias) and on observer error in measurements,[57,58] which may be random or systematic.

As long ago as 1921, Mateiga[59] measured circumferences of the forearm, the upper arm, the calf, and the thigh and corrected for skinfold thickness in order to estimate whole-body muscle mass anthropometrically; through this, he derived a value for muscle limb radius. The value was squared and multiplied by height and a constant of 6.5. This equation was not validated by Mateiga[59] or later investigators. This work was expanded, however, by Doupe et al.[60] and Martin et al.,[61] who developed whole-body anthropometric SM mass prediction models from two equations of the Brussels Cadaver Study of 12 elderly men.[24,47] In the first equation, SM (g) = height × (0.0553 × [thigh girth, corrected for skinfold thickness]^2 × 0.0987 × [forearm girth (cm), uncorrected for skinfold thickness]^2 × 0.0331 × [calf girth, corrected for skinfold thickness]^2 − 2445), where R^2 = 0.97 and SEE = 1.53 kg. In the second equation, SM = height × (0.031 × [modified upper thigh girth]^2 × 0.064 × [calf girth, corrected for skinfold thickness]^2 × 0.089 × [arm girth, corrected for skinfold thickness]^2) − 3006. These equations were either never validated or were based on small sample sizes and proved too complicated for wide application.

In adults, most skeletal muscle (30%) is found in the lower limbs, with lesser amounts located in the upper limbs, the head, and the trunk.[6] In an honors thesis published in the UniSA Research Archives, Hellmanns[62] measured whole-body muscle mass using contiguous MRI scans in healthy adults and estimated the torso muscle mass to be 11.43 ± 3.39 kg, the upper appendicular muscle mass to be 3.27 ± 1.23 kg, the lower appendicular muscle mass to be 10.45 ± 3.27 kg, and the whole-body muscle mass to be 25.14 ± 7.11 kg. Recently. the thigh has generated the most interest as a predictor of whole-body muscle mass.[49,51] Thigh muscles are major determinants of total muscular physical activity, and quadriceps and hamstrings are the most powerful muscles of humans.[41] In addition to their volume/mass, their maximal power production can be measured in anaerobic capacity tests and related to functional capacity and independence at older age.[41,63,64]

Calf circumference has also been considered a predictor of whole-body mass, but it showed only moderate correlation (R^2 = 0.48) with regional MRI muscle mass.[53] Lee et al.[47] found skinfold-corrected arm circumference to have a higher correlation (R^2 = 0.77) than skinfold-corrected thigh and calf circumferences (R^2 = 0.61 and 0.67, respectively). Rolland et al.,[65] using DEXA in elderly women, reported R^2 = 0.40 for the correlation between calf circumference and appendicular muscle mass. Hip circumference, which is closely related to gluteal muscle mass, has received relatively little interest for whole-body muscle mass estimation, despite suggestions that it may be relevant on the basis of associations with chronic diseases.[66,67]

The present review sought all previous studies that used MRI, which is the most accurate method for measurement of muscle mass, and derived and/or validated predictive equations from anthropometry. Two anthropometric approaches were identified in the literature: simple anthropometric measurements that included limb circumferences, weight, height, age, sex, and/or race; and circumferences and corresponding skinfold thicknesses to correct for subcutaneous fat, i.e., mid-arm circumference and triceps skinfold thickness, mid-thigh circumference and thigh skinfold thickness, and mid-calf circumference and calf skinfold thickness.

The equation adopted (limb muscle mass = limb circumference − π × skinfold thickness) and employed extensively in studies of chronic disease and protein energy malnutrition[31,61] depends on several simplifying assumptions. First, skinfold measurement by calipers gives an estimation of the thickness of superficial adipose tissue. Second, for estimation of muscle mass, fat and bone are a negligible or are a constant proportion of the nonsuperficial adipose tissue. Third, the limb is cylindrical, and the superficial adipose tissue structures form an annulus. Finally, limited measurement sites can be used to predict muscle volume.[41] These assumptions are relatively crude and introduce error. Knapik et al.[58] suggested that errors in predicting MRI measurements from the thigh muscle area reflect an underestimation of fat and skin by excessive skinfold calliper tension and an overestimation of the total thigh area due to the assumption that the thigh is cylindrical. Taking skinfold thickness measurements is time-consuming, requires undressing, which compromises practicality for large-scale survey work, and can increase measurement errors (Table S3). Another approach in regional muscle mass estimation was introduced in 1969 by Jones and Pearson,[68] who

proposed dividing leg volume into six segments of a truncated cone. Their equation, applied in 32 young men and 15 women and validated against a water displacement method, showed correlation coefficients for the total leg muscle mass of 0.98 in men and 0.99 in women. Tonson et al.[54] used the same method to estimate forearm lean (muscle × bone) volume. Compared with correlations of MRI results, correlations were as high as 0.90.

In the studies that used simpler measurements without skinfolds, body weight was included in all but one,[46] along with different combinations of age, height, sex, race, hip circumference, waist circumference, and/or thigh circumference, and correlations remained relatively high, with R^2 ranging from 0.86 to 0.62[47,49,50] (Table 7). Only one study explored hip circumference,[50] but that study predicted lean tissue mass – including bone, SM, and organs – rather than muscle mass. The relationship of hip circumference to body composition is complicated by the dominating effect of obesity on all circumferential measurements, but outside the context of obesity, hip circumference does have a close relationship with the gluteal muscles. It has been hypothesized that the strong association of chronic illnesses with high waist/hip ratios may reflect small hip circumference (indicating reduced muscle mass) rather than greater waist circumference (indicating increased body fat).[66,67,69,70]

The limitations of the studies in the present review restrict the use of anthropometric prediction equations to estimate muscle mass. It was surprising to find only two studies that used whole-body MRI scans for the development of prediction equations.[47,50] All other studies used regional muscle mass as a marker of whole-body muscle mass. Many studies did not consider gender differences and used the same equation for both genders. Previous research has reported that women have 25% less muscle mass than men.[50]

Another approach found by this review was to distinguish between the muscle groups of the thigh in order to avoid including non-muscle tissue like adipose, nerves, vessels, and fascia in the cross-sectional area measurement.[29] However, Mathur et al.,[51] who attempted to validate this equation in patients with chronic obstructive pulmonary disease and in healthy elderly subjects, found very low correlation with MRI measurements (Table 7).

It is clear that whole-body muscle mass can, in principle, be predicted from simple anthropometric measures, but the existing literature does not provide a method that can be applied generally with confidence, and variable methodological approaches present problems. The studies included in the present review had small sample sizes, which is not surprising because the high cost of MRI, which is considered the best reference method, restricts its use. Nevertheless, small sample sizes limit study power. Heterogeneity between relatively small studies (measurement of different limbs, of whole body versus regions, of total thigh versus components of thigh, of circumferences versus skinfold thicknesses, of different age groups, and of different ethnicities) made it difficult to make direct comparisons between equations or to form a unified conclusion. Bland-Altman analysis is considered the best method to assess agreement and distribution of errors between two methods[56] but was used in only two studies in the present review.[47,51] All other studies depended on linear correlations alone to assess the accuracy of prediction equations. The use of prediction equations to monitor change in muscle mass across time, or with interventions, has not been explored. Although one study was longitudinal,[46] its main purpose was not muscle mass estimation but rather longitudinal assessment of nutritional status of elderly women ($n = 16$) in a nursing home over a period of 3 years. The authors used only simple linear regression from thigh circumference as determined by MRI (thigh muscle volume $[cm^3] = 21 \times$ thigh circumference $[cm] \times 979$). Thigh circumferences decreased significantly during the 3-year observation period ($P < 0.05$), but correlation between the two measurements, i.e., thigh circumference and MRI estimate of thigh muscle volume using the previously mentioned equation, was very low ($R^2 = 0.12$).

CONCLUSION

This systematic review identified only two studies that developed prediction equations for estimation of whole-body muscle mass or lean body mass, as measured by MRI, from simple anthropometric measures. Several studies have generated anthropometric prediction equations for regional/limb muscle mass, which mostly include limb circumferences and local skinfold thicknesses, but evidence is insufficient that limb muscle mass can be used to estimate whole-body muscle mass.

Studies differed in participant characteristics, BMI, age, gender, and measurement methodology and do not provide enough evidence to propose an anthropometric method that could be applied routinely as a reliable indicator to estimate muscle mass or to diagnose sarcopenia. Some of the regression equations, however, show promise and warrant further investigation, particularly through validation in separate populations and by assessment of changes across time and during illness. The variables included in the simpler anthropometric approaches (body weight, height, age, sex, race, and limb circumferences) are readily available in population health surveys, with the R^2 value of the best published equations ranging from 0.62 to 0.86. Though the practical equations retrieved from this systematic review were encouraging, especially those of Lee et al.,[47] the validations conducted

have not involved separate populations using measurements by independent investigators, and the equations do not take advantage of trunk or limb girths, which are widely available in health surveys and offer valuable prediction of muscle mass.

Development of a simple, clinically friendly definition of sarcopenia with unified criteria for diagnosis would aid in the detection and management of this disease.[9] Reliable prediction of muscle mass in ill people is not currently possible with the available literature. The only study that included ill subjects was that of Mathur et al.,[51] which validated the Housh et al. equation.[29] Early identification of muscle loss in order to target disease management could be of great clinical benefit in combating frailty and falls and in improving quality of life during chronic illnesses and aging.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 **Regional versus whole-body images, and continuous versus discontinuous images.**
Table S2 **Purpose of studies included in the review.**
Table S3 **Reliability and observer error of studies included in the review.**