Reference standards for lean mass measures using GE dual energy x-ray absorptiometry in Caucasian adults

Mary T. Imboden[1]*, Ann M. Swartz[2], Holmes W. Finch[1], Matthew P. Harber[1], Leonard A. Kaminsky[1]

1 Ball State University, Muncie, Indiana, United States of America, 2 University of Wisconsin-Milwaukee, Milwaukee, Wisconsin, United States of America

* Mstuttle2@bsu.edu

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Abstract

Body composition assessments commonly focus predominantly on fat mass, however lean mass (LM) measurements also provide useful information regarding clinical and nutritional status. LM measurements help predict health outcomes and diagnose sarcopenia, which has been associated with frailty. Dual energy x-ray absorptiometry (DXA) is an established technique used in clinical and research settings to assess body composition including total and regional LM. Currently, there are no reference values available that were derived from GE-Healthcare DXA systems directly for US adults for LM, LM index (LMI), percent LM (%LM), and appendicular lean mass index (ALMI) and it is known that whole-body and regional LM measures differ by DXA manufacturer.

Objective

To develop reference values by age and sex for LM measures using GE-Healthcare DXA systems.

Methods

A de-identified sample was obtained from Ball State University's Clinical Exercise Physiology Laboratory and University of Wisconsin-Milwaukee's Physical Activity & Health Research Laboratory. DXA scans of 2,076 women and 1,251 men were completed using a GE Lunar Prodigy or iDXA. Percentiles (%ile) were calculated for all variables of interest (LM, LMI, %LM, and ALMI) and a factorial ANOVA was used to assess differences for each variable between 10-year age groups and sex, as well as the interaction between age and sex.

Results

Men had higher mean total LM, %LM, LMI, and ALMI than women (p<0.01), across all age groups. All LM variables decreased significantly over the 5 decades in men, however in women only total LM, %LM, and ALMI decreased from the youngest to oldest age groups (p<0.01).

Conclusion

These reference values provide for a more accurate interpretation of GE-Healthcare DXA-derived LM measurements offering clinicians and researchers with an initial resource to aid in the early detection and assessment of LM deficits.

Introduction

Body composition assessments commonly focus on fat mass measurements, however lean mass (LM) also provides useful information regarding an individual's health and nutritional status. LM plays an important role in helping to maintain bone density, improve metabolic health, preserve strength, and reduces the risk of injury and falls [1]. Additionally, significant reductions in LM with age or accompanying disease, known as sarcopenia and cachexia, have been associated with decreased function and quality of life, as well as the development of frailty [1, 2]. Therefore, body composition assessments across the life span that measure LM are valued in clinical and research settings, to aid in the identification and diagnosis of sarcopenia and cachexia. Computed tomography (CT) and magnetic resonance imaging (MRI) are considered gold standards for measuring whole body LM, as they have shown excellent measurement accuracy when compared to cadaver analysis (r = 0.99) [3]. However, they are impractical in most clinical and research settings due to their high cost and radiation exposure. LM measured by dual energy x-ray absorptiometry (DXA) is a composite of non-fat and non-bone tissue and is highly associated with LM measured using CT and MRI technology (r^2 = 0.86–0.96) [4–6]. DXA is also less expensive and time-consuming than CT and MRI scans, and therefore is considered the best alternative method for measuring LM [4, 7].

DXA is a three-compartment method that distinguishes total bone mineral content from soft tissue with high precision and accuracy, dividing the latter into fat and lean body mass. DXA is also advantageous over other body composition methods due to its ability to assess both total and regional body composition. This allows the assessment of whole-body and site specific LM. From these measurements total LM, LM index (LMI), percent LM (%LM), and appendicular LM index (ALMI) can be determined, all of which have been used previously in research and clinical settings to diagnose sarcopenia or identify those at risk of physical disability [1, 7–11]. However, since there are no universally recognized standards for these key LM variables using GE-Healthcare DXA systems in healthy US adults (Total LM, LMI, %LM, and ALMI) it makes the interpretation of results challenging.

In 2009, Kelly et al. used data from the National Health and Nutrition Examination Survey (NHANES) to develop reference values for measures of LM specific to DXA measurement obtained with the Hologic QDR 4500A fan beam densitometer [12]. Hologic and GE-Healthcare are the two dominant DXA manufacturers, which have been validated against criterion 4-compartment models [13, 14]. However these devices have been shown to produce different body composition results, including differences in whole-body and regional LM measurements [15]. These discrepancies in measurements between manufacturers may be due to differences in instrumentation, fan beam angle, calibration standards, and manufacturer derived algorithms used to calculate the body composition measurements. Shepherd et al. compared the body composition results from the Hologic and GE-Healthcare Lunar DXA systems and found significant differences between the Hologic and GE-Healthcare devices for total LM and ALMI (23.2 vs. 21.8 kg and 9.5 vs. 8.7 kg, respectively p<0.01) measured in adults [15]. Similar differences in LM measurements between DXA manufacturers have been reported in the literature [16, 17].

Fan et al. used cross-calibrated equations between the Hologic and GE-Healthcare models to convert whole-body and regional bone and soft tissue measurements from the NHANES 1999–2004 dataset to reference values for the GE-Healthcare models [18]. Although this study provided an initial set of reference values for body composition measures, including total LM, LMI, and ALMI for GE-Healthcare DXA models, these are estimates and therefore it is important to develop body composition reference values obtained directly from whole-body scans using the GE-Healthcare models [15]. These standards are needed to appropriately determine values for body composition measurements that are associated with LM deficits that can predict poor health-outcomes and lead to decreased physical function.

Other DXA-derived measures of LM are useful in predicting health-risks associated with body composition. LMI is a measure of total skeletal muscle LM (kg) scaled to height (m^2). This index allows for the comparison of LM body composition in individuals of different height, as it is not confounded by fat mass, making it a useful tool for assessing LM deficits. Additionally, ALMI, calculated as the sum of arm LM and leg LM scaled to height (m^2), is thought to be a surrogate of skeletal muscle mass and therefore is another important measure used to identify and assess the development of sarcopenia [1]. Reference values for LMI and ALMI have been developed in Australian and Mexican adult populations using direct measurement from GE-Healthcare DXA models, however these LM reference values may not be consistent for US adults as a result of differences in geographical regions [7, 19].

As GE-Healthcare is one of the two major DXA manufacturers [15] widely used by researchers and clinicians, reference values are needed to guide interpretation of body composition results obtained with this instrument. The purpose of this study was to develop reference values for LM variables including total LM, LMI, %LM and ALMI for a US population using the GE-Healthcare DXA models.

Methods

A de-identified sample of 3,327 participants (2,076 women, 1,251 men; 95% of which were Caucasian), was obtained from Ball State University's Clinical Exercise Physiology Laboratory (2,218 scans) and University of Wisconsin-Milwaukee's Physical Activity & Health Research Laboratory (1,109 scans). Participants were either self-referred, residents of the surrounding communities, or research subjects or participants at one of the two laboratories, all of which were considered apparently healthy. All participants were ≥20 and <80 years old (mean age 45.8 ± 18.3 years (**Table 1**)). Only the first scan was used in analysis for individuals with repeat

Table 1. Descriptive characteristics of participants by gender (Mean ± SD).

	Men (n = 1,251)	Women (n = 2,076)
Age (yr)	46.1 ± 19.1	45.6 ± 17.9
Ethnicity	92.2% Caucasian	96.1% Caucasian
Height (cm)	177.8 ± 7.6	164.8 ± 6.9*
Weight (kg)	89.1 ± 18.6	70.9 ± 18.4*
BMI (kg m^{-2})	28.0 ± 5.3 Distribution • Underweight 0.5% • Normal 31.5% • Overweight 41.2% • Obese 26.8%	26.4 ± 6.7* Distribution • Underweight 0.7% • Normal 47.0% • Overweight 27.0% • Obese 25.3%
Total body fat (%)	28.3 ± 8.3	38.6 ± 8.9*

* Significantly different from Men (p<0.01).

BMI distribution based on the World Health Organization classification.

scans. Participants were excluded if their width exceeded the scanner field or their body weight exceeded the limits of the scanner bed (159 kg (350 lbs) for Prodigy or 204 kg (450 lbs) for iDXA). The study was declared exempt by the Ball State University and University of Wisconsin-Milwaukee Institutional Review Boards as all data was de-identified. Additionally, prior to all DXA scans participants signed an informed consent agreeing that their data from the scan could be used for research purposes.

A whole-body DXA scan was performed on all participants. The GE-Healthcare Lunar Prodigy was used at the Clinical Exercise Physiology Laboratory at Ball State University from 2003 to 2010 and the GE-Healthcare iDXA was used from 2010 to October 2015. All scans performed at the Physical Activity & Health Research Laboratory at the University of Wisconsin-Milwaukee used the GE Lunar Prodigy from 2005 to October 2015. Both the GE-Healthcare Lunar Prodigy and iDXA are narrow fan-beam densitometers that use the enCORE software platform that has been updated as GE-Healthcare releases new versions (Ball State University: 13.40.038, University of Wisconsin-Milwaukee: 13.31.016). These two GE-Healthcare DXA models have been shown to have high agreement between systems ($R^2 = 0.85–0.99$) for both total and regional lean mass measurements, thus are suitable for intra-subject comparisons [20, 21, 22].

Procedure

A full explanation of the procedures have been described previously [23]. In summary DXA scans were administered by trained research technicians using standardized procedures recommended by GE-Healthcare. All technicians were trained over a period of 1 to 3 months at each laboratory. Prior to each testing session, the GE-Healthcare DXA systems at both laboratories were operated following manufacturer guidelines, passing the recommended quality assurance procedure. Participants were asked to remove all metal, as well as shoes prior to the scan and their height was measured using a wall-mounted stadiometer and mass using a calibrated scale. The participant was then positioned according to manufacturer specifications within the scanner field on the DXA table. Automatic scan mode and automatic analysis mode were used as the default setting at both sites and one trained technician at each site analyzed the DXA scans. Technicians modified the ROI only if determined to be significantly off. Variables of interest from the scan that were used in this analysis included LM, leg LM, and arm LM [24]. Leg LM and arm LM were summed to calcuate appendicular lean mass.

Statistical analysis

All statistical analyses were performed using SPSS (version 24.0), with descriptive measures reported as means ± standard deviation. Sex- and age-specific body composition measurements were analyzed, with participants classified into age groups by decade (20–29, 30–39, 40–49, 50–59, 60–69, and 70–79 years). The distribution of men and women between decades was checked for normality using the Kolmogorov-Smirnov test. This distribution was found to be non-normal ($p<0.05$). The LM, LMI (LM (kg) height (m^{-2})), %LM, ALMI ((arm LM + leg LM) (kg) height (m^{-2})) [25] were calculated from scan measurements. Percentiles were calculated for each outcome variable specific to sex and age groups. A factorial ANOVA was used to determine potential differences in mean LM, LMI, %LM, ALMI, between sex- and age-specific groups. Finally, reference curves were created using LMS regression (S1 Fig–S8 Fig), where for each variable of interest, the model was fit using a B-spline with a difference penalty. The curves were fit to the 3rd, 50th, and 97th percentiles superimposed upon the raw data values [26]. The median values from the NHANES cohort were also added to these curves for comparison. An alpha level was set at 0.05 to determine statistical significance.

Results

The demographic information from the sample is shown in **Table 1**. The mean age of the sample was 45.8 ± 18.3 years. Mean BMI, weight, height, and percent body fat were significantly different between sexes (p<0.05). Mean BMI, Weight, and percent body fat significantly increased from the youngest (20–29 years) to oldest (70–79 years) age groups in women (23.8 to 27.2 kg m^{-2}; 66.2 to 70.3 kg; 31.4 to 40.4%, respectively; p<0.05). In men, BMI significantly increased between the youngest (20–29 years) and the 2nd to oldest age group (60–69 years) (26.5 to 28.8 kg m^{-2}, p<0.05). Whereas weight significantly decreased, but percent body fat significantly increased from 20–29 to the 70–79 year age group in men (87.1 to 83.4 kg; 21.1 to 31.1%, respectively; p<0.05).

Mean (± SD) and percentiles of LM from the GE-Healthcare models by age for both women and men are displayed in **Table 2**. Men had a greater mean LM than women (men: 60.8 kg, women: 42.3 kg; p<0.01), across all age groups. The mean LM decreased significantly with increasing age in both men and women from the youngest to oldest age groups (p<0.05). In men it was observed that mean LM decreased with increasing age up until 70–79 years, however in women mean LM remained constant until the 5th decade, after which it starts to decline (p<0.05).

LMI means (±SD) and percentiles by age group for both women and men are presented in **Table 3**. Mean LMI was higher in men than women at all age groups (men: 19.2 ±2.4 kg m^{-2}; women: 15.7± 2.2 kg m^{-2}, p < 0.05). Additionally, it was observed that the mean LMI decreased across each decade in men, whereas in women mean LMI appeared to increase up until 40–49 years of age after which a decrease was observed.

Mean (± SD) and percentiles of %LM from the GE-Healthcare models by age for both women and men are displayed in **Table 4**. Men had a greater mean %LM than women

Table 2. Sex-specific percentiles of total lean body mass (kg) measured with DXA.

	Women										
AGE (YR)	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th
20–29	562	43.0± 6.1	35.7	37.6	39.3	41.0	42.5	43.7	45.5	47.7	51.1
30–39	196	43.6± 6.8	36.3	38.3	39.6	41.3	42.5	43.8	45.9	48.7	52.4
40–49	258	42.9±7.0	35.4	36.9	38.4	39.9	41.6	43.0	44.8	47.5	51.8
50–59	437	42.3±6.9 C	34.4	36.4	38.1	39.7	41.5	43.1	45.1	47.2	51.5
60–69	440	40.8± 5.5 B	34.9	36.5	37.9	39.1	40.8	42.1	43.6	45.4	48.2
70–79	183	39.0± 5.0 A	32.9	34.9	36.2	37.9	39.1	40.4	41.6	43.1	45.1
	Men										
AGE (YR)	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th
20–29	384	65.0±11.0 D	53.5	57.0	59.1	61.4	63.9	66.2	69.5	73.6	82.0
30–39	104	60.9±9.0 E	52.1	55.1	56.5	59.8	61.8	63.7	67.3	69.8	74.1
40–49	145	60.2±8.5 E	51.4	53.9	56.8	58.4	60.2	62.1	64.0	67.9	73.2
50–59	214	59.3±8.1	50.5	53.0	55.3	57.5	60.5	61.8	63.8	65.8	70.2
60–69	236	58.9±6.9	50.2	53.2	55.7	57.5	58.5	60.2	61.9	63.9	67.9
70–79	168	54.3±6.0	47.6	49.8	51.4	52.9	54.2	56.0	57.4	59.8	62.3

A Significantly different than 20–29, 30–39, 40–49, 50–59, 60–69; p<0.05.

B Significantly different than 20–29, 30–39, 40–49, 70–79; p<0.05.

C Significantly different than 30–39, 60–69, 70–79; p<0.05.

D Significantly different than 30–39, 40–49, 50–59, 60–69, 70–79; p<0.05.

E Significantly different than 20–29, 50–59, 60–69, 70–79; p<0.05.

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Table 3. Sex-specific percentiles of lean mass index (kg m⁻²) measured with DXA.

	Women											
AGE (YR)	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th
20–29	562	15.5± 1.8 A	13.4	14.0	14.5	14.9	15.3	15.6	16.2	17.0	18.0
30–39	196	15.8± 2.2	13.3	14.1	14.6	15.0	15.4	16.1	16.7	17.6	18.8
40–49	258	15.9±2.5 B	13.2	13.8	14.4	14.9	15.3	15.9	16.5	17.3	19.0
50–59	437	15.8±2.2	13.2	13.9	14.4	15.0	15.5	16.0	16.6	17.3	18.7
60–69	440	15.4±2.1	13.3	13.9	14.4	14.8	15.3	15.7	16.4	17.0	18.2
70–79	183	14.9±1.8 C	13.2	13.8	14.2	14.4	14.9	15.3	15.8	16.7	17.7
	Men											
AGE (YR)	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th
20–29	384	19.8± 2.7 D	16.9	17.8	18.3	19.0	19.5	20.3	21.4	22.3	23.8
30–39	104	19.0±2.2	16.8	17.4	18.2	19.0	19.3	19.7	20.2	21.2	22.2
40–49	145	18.9±2.2	16.7	17.4	17.9	18.6	19.2	19.6	20.3	21.0	22.1
50–59	214	18.7±2.1	16.3	17.2	17.8	18.3	18.8	19.4	20.1	20.8	21.6
60–69	236	18.9±2.0	16.8	17.3	17.8	18.3	18.9	19.3	19.8	20.4	21.3
70–79	168	17.8±1.7 C	16.2	16.8	17.1	17.4	17.7	18.0	18.4	19.0	19.9

A Significantly different than 30–39, 40–49, 50–59; p<0.05.
B Significantly different than 20–29, 60–69, 70–79; p<0.05.
C Significantly different than 20–29, 30–39, 40–49, 50–59, 60–69; p<0.05.
D Significantly different than 40–49, 50–59, 60–69, 70–79; p<0.05.

(69.6 ± 8.8% vs. 59.3 ± 9.3%, respectively; p<0.01), across all age groups. The mean %LM decreased with increasing age in men until the 60–69 year age group (p<0.05), where it then remained steady. In women, mean %LM decreased up until the 50–59 year age group

Table 4. Sex-specific percentiles of % lean body mass measured with DXA.

	Women											
AGE (YR)	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th
20–29	562	65.7± 8.1 A	54.4	59.4	62.3	65.4	67.4	69.3	71.1	72.9	76.1
30–39	196	61.0±10.3 B	47.7	51.6	54.2	57.2	60.6	63.6	67.9	70.9	75.1
40–49	258	58.6±9.0 C	46.4	49.3	52.8	54.8	57.4	59.8	62.8	65.6	71.5
50–59	437	56.3±8.1	46.5	49.2	51.4	53.3	55.3	57.5	59.7	63.1	66.8
60–69	440	56.2±7.2	46.5	49.2	51.4	53.3	55.6	57.1	59.2	62.1	64.9
70–79	183	58.6±7.5 C	48.1	50.3	53.0	55.1	57.1	58.9	60.6	63.8	67.6
	Men											
AGE (YR)	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th
20–29	384	75.7±7.8 A	65.3	68.7	71.8	74.3	77.0	78.6	80.4	83.1	86.4
30–39	104	72.6±9.9 B	58.2	62.2	64.3	67.4	71.0	73.8	77.2	80.2	85.2
40–49	145	69.1±8.1	57.5	61.0	64.1	66.0	67.5	69.1	71.7	74.6	80.2
50–59	214	67.2±7.3	57.6	59.8	62.0	63.8	65.6	67.5	70.1	72.4	76.6
60–69	236	66.8±7.3	57.1	60.6	63.0	64.3	64.9	67.6	69.7	72.0	75.5
70–79	168	67.0±6.2	58.2	60.5	62.5	64.4	66.1	68.3	69.3	72.1	74.3

A Significantly different than 30–39, 40–49, 50–59, 60–69, 70–79; p<0.05.
B Significantly different than 20–29, 40–49, 50–59, 60–69, 70–79; p<0.01.
C Significantly different than 20–29, 30–39, 50–59, 60–69; p<0.01.

(p<0.05) and then remained steady in the 60–69 year age group, where thereafter mean %LM significantly increased from the 60–69 to70-79 year age group (p<0.05).

ALMI means (±SD) and percentiles by age group for both women and men are presented in Table 5. Mean ALMI was higher in men than women (8.8± 1.4 kg m^{-2} vs. 6.8 ±1.1 kg m^{-2}; p< 0.05) across all age groups. Additionally, in both sexes ALMI decreased over the 5 decades, as the mean for men and women aged 20–29 years decreased from 9.47 and 6.96 to 7.94 and 6.33 for age 70–79 years, respectively (p<0.05). The decrease in ALMI can be attributed to a reduction in arm LM of 4.1% and 2.6% and reductions in leg LM of 5.2% and 2.8% in men and women, respectively.

Discussion

The current research represents the first reference values for total LM, LMI, %LM, and ALMI using measures obtained directly from GE-Healthcare DXA systems for adults in the United States. The only other known reference values for these LM variables measured directly from DXA were derived from the 1999–2004 NHANES dataset [12], which used the Hologic QDR 4500A system that is known to differ from GE-Healthcare systems [15], as well as in reference datasets from Mexican [19] and Australian [7] adult populations.

Total LM is an important indicator of muscle mass and has been found to be associated with muscular strength and dependency in activities, as well as predictive of health outcomes [4, 9]. The sex-specific data from this study cohort with DXA measures concurs with known literature showing mean and median values for total LM in men are higher than seen in women across all age groups [7, 12, 19]. The current results showed a reduction in mean LM from the 20–29 year age group through the 70–79 year age group of approximately 2% and 3% per decade in women and men, respectively. The greater reduction per decade in men causes the difference in total LM between sexes to narrow with age, from a mean sex difference of

Table 5. Sex-specific percentiles of appendicular lean mass index (kg m^{-2}) measured with DXA.

AGE (YR)	Women											
	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th	
20–29	562	6.96±0.97	5.8	6.1	6.4	6.7	6.9	7.1	7.4	7.8	8.3	
30–39	196	6.95±1.10	5.7	6.1	6.4	6.6	6.8	7.1	7.4	7.8	8.4	
40–49	258	6.88±1.20	5.7	5.9	6.1	6.3	6.7	7.0	7.2	7.6	8.2	
50–59	437	6.71±1.10 [A]	5.5	5.8	6.1	6.3	6.6	6.8	7.1	7.4	8.0	
60–69	440	6.62±1.00 [A]	5.6	5.9	6.1	6.3	6.5	6.8	7.1	7.4	8.1	
70–79	183	6.33±0.87 [B]	5.3	5.7	5.9	6.1	6.3	6.5	6.7	7.1	7.5	
AGE (YR)	Men											
	n	X ± SD	10th	20th	30th	40th	50th	60th	70th	80th	90th	
20–29	384	9.47±1.56 [C]	7.9	8.3	8.6	9.0	9.3	9.6	10.2	10.9	12.1	
30–39	104	8.94±1.20	7.7	8.1	8.6	8.9	9.1	9.3	9.6	10.0	10.6	
40–49	145	8.75±1.17	7.3	8.0	8.3	8.5	8.7	9.0	9.2	9.8	10.5	
50–59	214	8.53±1.11 [A]	7.4	7.8	8.1	8.4	8.6	8.9	9.2	9.5	10.1	
60–69	236	8.48±1.01 [A]	7.4	7.7	8.0	8.3	8.5	8.8	9.0	9.3	9.7	
70–79	168	7.94±0.86 [B]	7.1	7.4	7.6	7.8	8.0	8.2	8.3	8.6	9.1	

[A] Significantly different than 20–29, 30–39, 40–49, 70–79; p<0.05.
[B] Significantly different than 20–29, 30–39, 40–49, 50–59, 60–69; p<0.05.
[C] Significantly different than 30–39, 40–49, 50–59, 60–69, 70–79; p<0.05.

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21.9 kg (percent difference: 33.5%) in the youngest age group to a mean sex difference of 15.5 kg (percent difference: 27.9%) in the oldest age group. Compared to the Mexican and Australian cohorts the women in the current study had higher mean total LM at each age group [7, 19]. The mean total LM in men from the current study was higher at each age group compared to men in the Mexican cohort and was higher up until the 70–79 year age group compared to men of the Australian cohort. The reduction in total LM across each decade was also different between the cohorts. Men in this cohort had a greater reduction per decade than both the Mexican and Australian men [7, 19]. The reductions in total LM per decade in women were similar between our cohort and the Australian women (both cohorts showed reductions of approximately 2% per decade) but was higher than that reported in Mexican women (0.5% reduction per decade) [7, 19].

DXA is capable of separating soft tissue into fat and lean mass components, thereby permitting the evaluation of LM without the confounding influence of other tissue constituents, such as excess fat. As a result, LMI has been a useful measure in identifying those with LM deficits and at risk of sarcopenia and/or physical disability [27]. Data from our study sample reveal that median LMI is significantly reduced from the youngest (20–29 years) to oldest (70–79 years) age groups in both men and women. Although no formal statistical analysis was performed, it was observed that the median values from the current study for LMI were lower across all age groups in women and in all age groups after the youngest age group (20–29 years) in men compared to the NHANES dataset [12]. Although these differences could have stemmed from differences in the recruitment processes, both study samples provided a large distribution of US adults across a wide age-range, however the NHANES cohort was recruited from a larger geographical compared to the current study. That being said, these comparisons are consistent with the results reported by Shepherd et al. who found that whole-body LM measurement results from GE-Healthcare DXA systems were lower than Hologic systems [15]. However, our LMI reference values were higher than those proposed by Fan et al. using the cross-calibrated prediction equation between Hologic and GE-Healthcare models [18]. The observed differences between sex and age-group reference values using the GE-Healthcare DXA systems compared to those created using Hologic or prediction equations are not meant to downplay the use of these references values when appropriate, but instead emphasize the need for instrumentation specific and directly measured reference values.

Using the LMI classification ranges developed by Janssen et al. to help diagnose sarcopenia, there were no men or women from the current cohort that were identified as having sarcopenia or at risk for physical disability (< 10.75 kg m^{-2} and 5.75 kg m^{-2}, respectively) [9], which may be a result of the difference in the body composition method used in deriving these cut-points, and/or the current study sample being apparently healthy men and women.

Median %LM was significantly higher in men across all age groups. In both men and women, median %LM decreased with age up until the 50–59 year age group, after which there was an increasing trend in %LM. This increasing trend in the older age groups (60–69 and 70–79), may again be due to the apparently healthy study sample, rather than a clinical population.

Reference values for ALMI were developed as this measure is a good indicator of skeletal muscle mass and is commonly used in defining sarcopenia [8, 10, 27]. In both men and women, there was a decreasing trend in mean ALMI with age with a mean absolute difference between the youngest and oldest age groups of 1.53 and 0.63 kg m^{-2}, respectively. Similar to median LMI values, the median values for ALMI were higher than those proposed by Fan et al. using the cross-calibrated equations in both men and women. Additionally, the median values for ALMI were lower in the men and women across all age groups in this study sample, compared to the NHANES cohort [12]. Again, this may be attributed to the differences in the specific instrumentation used.

Diagnostic criteria to define sarcopenia have used cutoff points for ALMI of > 2SD below the young reference population (18–39 years of age) [8, 12, 27], as well as below the 20th percentile in an older adult population of similar age (≥70 years) [10]. Cutoff points for ALMI using the established diagnostic criteria of >2SD below the young reference population, were 6.35 kg m^{-2} for men and 4.92 kg m^{-2} for women in this study cohort. These cutoff points are lower than those derived from the Australian adult cohort (6.94 kg m^{-2} men, 5.30 kg m^{-2} women) and cutoff points from a different US non-Hispanic white population (7.26 kg m^{-2} men, 5.45 kg m^{-2} women), both of which were measured using GE-Healthcare DXA systems [7, 8]. The current study's cutoff points may differ from the Australian cohort due to geographical differences between the two study samples [7]. The higher cutoff points reported in the other US non-Hispanic white population may be due to their smaller sample size and/or representativeness of their young adult sample which the authors declare as "unknown" [8]. When using the criteria of ALMI >2SD below the young reference standard to define sarcopenia (6.35 kg m^{-2} in men, 4.92 kg m^{-2} in women), 17 men and 24 women would be classified as sarcopenic, of which only included 3 men and 2 women from the 70–79 year age group. However when using the criteria of ≤ 20th percentile for ALMI in an older adult population (defined as over age 70 years) higher cutoff points for defining sarcopenia were found in the current study (7.40 kg m^{-2} in men, 5.60 kg m^{-2} in women). These cutoff points using the ≤ 20th percentile criteria are similar to those derived from Delmonico et al. who studied 2,976 US adults and reported cutoff points of 7.25 and 5.67 kg m^{-2} in men and women for defining sarcopenia [10]. When the current study's cutoff points using ≤20th percentile were applied, 34 men and 32 women in the 70–79 year age group were classified as sarcopenic. The discrepancy in the amount of individuals classified as sarcopenic by criteria used highlights the importance of developing standardized diagnostic criteria for defining sarcopenia (Table 6 provides a comparison of different measurable LM variables and their cut-points used in defining sarcopenia).

This study is not without limitations. First, the current study cohort was 95% white. Ethnic variation in body composition has been documented in the literature [30, 31], and therefore these reference ranges may not be an accurate representation for all ethnic groups. All participants in this cohort were apparently healthy and therefore reference values for specific clinical populations are needed. Additionally, the GE lunar prodigy and iDXA have weight limits of 159 (350 lb.) and 204 kg (450 lb.), respectively and therefore these data may not be representative of morbidly obese that weigh ≥159 kg (350 lb.) or ≥204 kg (450lb.). Additionally, we could not statistically compare our population sample to the NHANES cohort and therefore we cannot rule out that differences between the current reference values using the GE-Healthcare DXA systems compared to those created using Hologic or prediction equations were not in part due to population differences. This study had several strengths including using pooled data from two laboratories with standardized procedures and a subject group with a wide-range of characteristics including age, BMI, and physical activity levels.

Conclusion

Body composition measurements are recognized as an important tool in research and clinical settings to assess health and nutritional status. DXA scans provide a high-quality measure of both whole-body and regional body composition measures, however, the interpretation of DXA data has been limited by lack of reference values. The results from this study provide directly measured reference values for total LM, LMI, %LM, and ALMI using the GE-Healthcare models. These reference values will provide GE-Healthcare DXA system users with the ability to derive meaningful interpretation of the results obtained from whole-body and

Table 6. Measurable lean mass variables and cut-off points used for the diagnosis of sarcopenia.

Criterion Method	Reference	Measurement Method	Established cut-points by gender	*New cut-points by gender	Participants meeting established cut-points (n, %)	*Participants meeting new cut-points (n, %)
Lean mass (kg)	Castillo et al [11]	Bioelectrical Impedance: (Valhalla Med., Model 1990B) $\geq$ 2 SD below mean of young reference population (18-39y)	**Men:** $\leq$ 47.9 kg **Women:** $\leq$ 34.7 kg	**Men:** $\leq$43.5 **Women:** $\leq$30.5	**Men:** (55, 4.4%) **Women:** (178, 8.6%)	**Men:** (16, 1.3%) **Women:** (12, 0.6%)
Lean Mass Index	Janssen et al [9, 28]	Bioelectrical Impedance: Valhalla Med., Model 1990B ROC analysis was used to develop cut-points associated with moderate and high physical disability	**Men** Moderate: 10.75 kg m^{-2} High: 8.50 kg m^{-2} **Women** Moderate: 6.75 kg m^{-2} High: 5.75 kg m^{-2}	+	**Men:** (0, 0%) **Women:** (0, 0%)	+
Percent Lean Mass	Janssen et al [28]	Bioelectrical Impedance: (Valhalla Med., Model 1990B) Class I: 1–2 SD below reference population (18-39y) Class II: > 2 SD below reference population	**Men** Class I: 37% Class II: 31% **Women** Class I: 28% Class II: 22%	**Men** Class I: 56.4% Class II:47.4% **Women** Class I:46.0% Class II: 36.8%	**Men** Class I: (0, 0%) Class II: (0, 0%) **Women** Class I: (0, 0%) Class II: (0, 0%)	**Men** Class I: (69, 5.5%) Class II: (11, 0.9%) **Women** Class I: (136, 6.6%) Class II: (1, 0.1%)
Appendicular Lean Mass Index	Baumgartner et al Melton et al [8, 29] Delmonico et al [10]	DXA: (Lunar DPX [8], Hologic QDR 2000[29], Hologic QDR 4500 A [10]) $\geq$ 2 SD below mean young reference population (18-39y) Or > 20th % ile of specific gender and aged population	**Men:** 7.26 kg m^{-2} **Women:** 5.50 kg m^{-2} **Men:** 7.25 kg m^{-2} **Women:** 5.67 kg m^{-2} (70–79 years of age)	**Men:** 6.35 kg m^{-2} **Women:** 4.92 kg m^{-2} **Men:** 7.40 kg m^{-2} **Women:** 5.60 kg m^{-2} (70–79 year age group)	**Men:** (95, 7.6%) **Women:** (162, 7.8%) **Men:** (27, 2.2%) **Women:** (35, 1.6%)	**Men:** (17, 1.4%) **Women:** (24, 1.2%) **Men** $\geq$ **70 y:** (34, 2.7%) **Women** $\geq$ **70 y:** (32, 1.5%)

*New cut-points were generated using the same measurement criteria as the established cut-points, but using the current study population.

+ New cut-points were unable to be generated for lean mass index using the current study population.

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regional DXA scans. As a result, the proposed reference values will also help in the early detection of those at an increased risk of sarcopenia, frailty, and/or physical disability, and lead to early and appropriate interventions to minimize LM deficits.

Supporting information

S1 Fig. Lean mass (kg) vs. age in women. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S2 Fig. Lean mass (kg) vs. age in men. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S3 Fig. Lean mass index (kg m^{-2}) vs. age in women. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S4 Fig. Lean mass index (kg m^{-2}) vs. age in men. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S5 Fig. Percent lean mass (%) vs. age in women. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S6 Fig. Percent lean mass (%) vs. age in men. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S7 Fig. Appendicular lean mass index (kg m^{-2}) vs. age in women. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S8 Fig. Appendicular lean mass index (kg m^{-2}) vs. age in men. Lines indicate 3rd (black), 50th (red), and 97th (green) percentiles.
(TIF)

S1 Table. Lean mass vs. age-group in women. 3rd, 50th, and 97th percentile values for total lean mass in women for smoothed age-group values.
(PDF)

S2 Table. Lean mass vs. age-group in men. 3rd, 50th, and 97th percentile values for total lean mass in men for smoothed age-group values.
(PDF)

S3 Table. Lean mass index vs. age-group in women. 3rd, 50th, and 97th percentile values for lean mass index in women for smoothed age-group values.
(PDF)

S4 Table. Lean mass index vs. age-group in men. 3rd, 50th, and 97th percentile values for lean mass index in men for smoothed age-group values.
(PDF)

S5 Table. Percent lean mass vs. age-group in women. 3rd, 50th, and 97th percentile values for percent lean mass in women for smoothed age-group values.
(PDF)

S6 Table. Percent lean mass vs. age-group in men. 3rd, 50th, and 97th percentile values for percent lean mass in men for smoothed age-group values.
(PDF)

S7 Table. Appendicular lean mass index vs. age-group in women. 3rd, 50th, and 97th percentile values for appendicular lean mass index in women for smoothed age-group values.
(PDF)

S8 Table. Appendicular lean mass index vs. age-group in men. 3rd, 50th, and 97th percentile values for appendicular lean mass index in men for smoothed age-group values.
(PDF)

Author Contributions

Conceptualization: MTI AMS MPH LAK.

Data curation: MTI AMS HWF MPH LAK.

Formal analysis: MTI HWF.

Investigation: MTI AMS MPH LAK.

Methodology: MTI AMS MPH LAK.

Project administration: MTI AMS MPH LAK.

Resources: AMS MPH LAK.

Supervision: AMS MPH LAK.

Validation: MTI AMS MPH LAK.

Visualization: MTI AMS MPH LAK.

Writing – original draft: MTI AMS MPH LAK.

Writing – review & editing: MTI AMS HWF MPH LAK.

References

1. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. JAMDA. 2011; 12(4):249–56. https://doi.org/10.1016/j.jamda.2011.01.003 PMID: 21527165

2. Rizzoli R, Reginster JY, Arnal JF, Bautmans I, Beaudart C, Bischoff-Ferrari H, et al. Quality of life in sarcopenia and frailty. Calcif Tissue Int. 2013; 93(2):101–20. https://doi.org/10.1007/s00223-013-9758-y PMID: 23828275

3. Lustgarten MS, Fielding RA. Assessment of analytical methods used to measure changes in body composition in the elderly and recommendations for their use in phase II clinical trials. JNHA. 2011; 15 (5):368–75.

4. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010; 39(4):412–23. https://doi.org/10.1093/ageing/afq034 PMID: 20392703

5. Fuller NJ, Hardingham CR, Graves M, Screaton N, Dixon AK, Ward LC, et al. Assessment of limb muscle and adipose tissue by dual-energy X-ray absorptiometry using magnetic resonance imaging for comparison. Int J Obes Relat Metab Disord. 1999; 23(12):1295–302. PMID: 10643687

6. Visser M, Fuerst T, Lang T, Salamone L, Harris TB. Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Health, Aging, and Body Composition Study—Dual-Energy X-ray Absorptiometry and Body Composition Working Group. J Appl Physiol. 1999; 87 (4):1513–20. PMID: 10517786

7. Gould H, Brennan SL, Kotowicz MA, Nicholson GC, Pasco JA. Total and appendicular lean mass reference ranges for Australian men and women: the Geelong osteoporosis study. Calcif Tissue Int. 2014; 94(4):363–72. https://doi.org/10.1007/s00223-013-9830-7 PMID: 24390582

8. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol. 1998; 147(8):755–63. PMID: 9554417

9. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. Am J Epidemiol. 2004; 159(4):413–21. PMID: 14769646

10. Delmonico MJ, Harris TB, Lee JS, Visser M, Nevitt M, Kritchevsky SB, et al. Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women. J Am Geriatr Soc. 2007; 55(5):769–74. https://doi.org/10.1111/j.1532-5415.2007.01140.x PMID: 17493199

11. Castillo EM, Goodman-Gruen D, Kritz-Silverstein D, Morton DJ, Wingard DL, Barrett-Connor E. Sarcopenia in elderly men and women: the Rancho Bernardo study. Am J Prev Med. 2003; 25(3):226–31. PMID: 14507529

12. Kelly TL, Wilson KE, Heymsfield SB. Dual energy X-Ray absorptiometry body composition reference values from NHANES. *PloS One*. 2009; 4(9):e7038. https://doi.org/10.1371/journal.pone.0007038 PMID: 19753111

13. Wells JC, Haroun D, Williams JE, Wilson C, Darch T, Viner RM, et al. Evaluation of DXA against the four-component model of body composition in obese children and adolescents aged 5–21 years. *Int J Obes* (Lond). 2010; 34(4):649–55.

14. Van Der Ploeg GE, Withers RT, Laforgia J. Percent body fat via DEXA: comparison with a four-compartment model. J Appl Physiol. 2003; 94(2):499–506. https://doi.org/10.1152/japplphysiol.00436.2002 PMID: 12531910

15. Shepherd JA, Fan B, Lu Y, Wu XP, Wacker WK, Ergun DL, et al. A multinational study to develop universal standardization of whole-body bone density and composition using GE Healthcare Lunar and Hologic DXA systems. J Bone Miner Res. 2012; 27(10):2208–16. https://doi.org/10.1002/jbmr.1654 PMID: 22623101

16. Gillette-Guyonnet S, Andrieu S, Nourhashemi F, Cantet C, Grandjean H, Vellas B. Comparison of bone mineral density and body composition measurements in women obtained from two DXA instruments. Mech Ageing Dev. 2003; 124(3):317–21. PMID: 12663129

17. Guo S. Inter-machine and inter-method differences in body composition measures from dual energy x-ray absorptiometry. Age Nutr. 1997; 8(1):12–21.

18. Fan B, Shepherd JA, Levine MA, Steinberg D, Wacker W, Barden HS, et al. National Health and Nutrition Examination Survey whole-body dual-energy X-ray absorptiometry reference data for GE Lunar systems. JCD. 2014; 17(3):344–77.

19. Clark P, Denova-Gutierrez E, Ambrosi R, Szulc P, Rivas-Ruiz R, Salmeron J. Reference Values of Total Lean Mass, Appendicular Lean Mass, and Fat Mass Measured with Dual-Energy X-ray Absorptiometry in a Healthy Mexican Population. Calcif Tissue Int. 2016.

20. Kirschner MM, Ozemek C. Hargens T.A., Kaminsky L.A. Comparison of body composition measures between the Lunar Prodigy and iDXA. Med Sci Sports Exerc. 2011; 43(5).

21. Morrison SA, Petri RM, Hunter HL, Raju D, Gower B. Comparison of the Lunar Prodigy and iDXA Dual-Energy X-ray Absorptiometers for Assessing Total and Regional Body Composition. J Clin Densitom. 2016; 19(3):290–7. https://doi.org/10.1016/j.jocd.2015.06.003 PMID: 26209017

22. Hull H, He Q, Thornton J, Javed F, Allen L, Wang J, et al. iDXA, Prodigy, and DPXL dual-energy X-ray absorptiometry whole-body scans: a cross-calibration study. J Clin Densitom. 2009; 12(1):95–102. https://doi.org/10.1016/j.jocd.2008.09.004 PMID: 19028125

23. Imboden MT, Welch WA, Swartz AM, Montoye AHK, Harber MP. Kaminsky LA. Reference standards for body fat measures using GE dual energy x-ray absorptiometry in caucasian adults. PloS one. 2017.

24. Stults-Kolehmainen MA, Stanforth PR, Bartholomew JB, Lu T, Abolt CJ, Sinha R. DXA estimates of fat in abdominal, trunk and hip regions varies by ethnicity in men. Nutr Diabetes. 2013; 3:e64. https://doi.org/10.1038/nutd.2013.5 PMID: 23507968

25. Heymsfield SB, Smith R, Aulet M, Bensen B, Lichtman S, Wang J, et al. Appendicular skeletal muscle mass: measurement by dual-photon absorptiometry. Am J Clin Nutr. 1990; 52(2):214–8. PMID: 2375286

26. Pan H, Cole TJ. A comparison of goodness of fit tests for age-related reference ranges. Stat Med. 2004; 23(11):1749–65. https://doi.org/10.1002/sim.1692 PMID: 15160406

27. Bijlsma AY, Meskers CG, Ling CH, Narici M, Kurrle SE, Cameron ID, et al. Defining sarcopenia: the impact of different diagnostic criteria on the prevalence of sarcopenia in a large middle aged cohort. Age. 2013; 35(3):871–81. https://doi.org/10.1007/s11357-012-9384-z PMID: 22314402

28. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc. 2002; 50(5):889–96. PMID: 12028177

29. Melton LJ 3rd, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, Riggs BL. Epidemiology of sarcopenia. J Am Geriatr Soc. 2000; 48(6):625–30. PMID: 10855597

30. Wagner DR, Heyward VH. Measures of body composition in blacks and whites: a comparative review. Am J Clin Nutr. 2000; 71(6):1392–402. PMID: 10837277

31. Hong S, Oh HJ, Choi H, Kim JG, Lim SK, Kim EK, et al. Characteristics of body fat, body fat percentage and other body composition for Koreans from KNHANES IV. J Korean Med Sci. 2011; 26(12):1599–605. https://doi.org/10.3346/jkms.2011.26.12.1599 PMID: 22147997