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Original Study

New Reference Values for Body Composition by Bioelectrical Impedance Analysis in the General Population: Results From the UK Biobank

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A B S T R A C T

Background: Low fat-free mass (FFM) is a risk factor for morbidity and mortality in elderly and patient populations. Therefore, measurement of FFM is important in nutritional assessment. Bioelectrical impedance analysis (BIA) is a convenient method to assess FFM and FFM index (FFMI; FFM/height^2). Although reference values have been established for individuals with normal body weight, no specific cutoff values are available for overweight and obese populations. Also, limited studies accounted for the age-related decline in FFM.

Objective: To determine BMI- and age-specific reference values for abnormal low FFM(I) in white-ethnic men and women free of self-reported disease from the general population.

Design: The UK Biobank is a prospective epidemiological study of the general population from the United Kingdom. Individuals in the age category 45 to 69 years were analyzed. In addition to body weight, FFM and FFMI were measured using a Tanita BC-418MA. Also, self-reported chronic conditions and ethnic background were registered, and lung function was assessed using spirometry.

Results: After exclusion of all individuals with missing data, nonwhite ethnicity, self-reported disease, body mass index (BMI) less than 14 or 36 kg/m^2 or higher, and/or an obstructive lung function, reference values for FFM and FFMI were derived from 186,975 individuals (45.9% men; age: 56.9 ± 6.8 years; BMI: 26.5 ± 3.6 kg/m^2; FFMI 18.3 ± 2.4 kg/m^2). FFM and FFMI were significantly associated with BMI and decreased with age. Percentiles 5, 10, 25, 50, 75, 90, and 95 were calculated for FFM, FFMI, and fat mass (index), after stratification for gender, age, and BMI.

Conclusions: Using the UK Biobank dataset, new reference values for body composition assessed with BIA were determined in white-ethnic men and women aged 45 to 69 years. Because these reference values are BMI specific, they are of broad interest for overweight and obese populations.

Determination of body composition is important in nutritional assessment. In the 2-compartment model, body weight is divided into fat mass (FM) and fat-free mass (FFM). FFM composes of all nonfat tissues and is commonly used as an indirect marker for skeletal muscle mass. Low FFM is an independent risk factor for functional impairment,[1] reduced quality of life, and increased mortality in the elderly.[2] Also in patients with chronic disease, low FFM is associated with morbidity and mortality, irrespective of body weight. In patients with chronic obstructive pulmonary disease (COPD),[3] chronic heart failure (CHF),[4] or cancer,[5] low FFM contributes to skeletal muscle weakness, exercise intolerance, poor health status,[6] and reduced survival.[7,8] Although there is a positive association between FFM and body weight,[9] FFM cannot adequately be predicted from weight or body mass index (BMI; weight/height^2). Therefore, FFM needs to be assessed both in clinical management of elderly and individuals with chronic disease, as well as in epidemiological studies.

Bioelectrical impedance analysis (BIA) is a noninvasive, easily applicable, safe, inexpensive and practical method[10] to assess FFM both in clinical practice[11,12] and in population studies.[13] BIA is based

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on the conductance of an electrical current through body fluids.[10] Reference values for whole-body FFM assessed by BIA have been established in healthy white populations of variable sizes (range: 500–3600 individuals) and with different age ranges (range: 18–98 years).[9,13–18] Most of these populations consisted of normal to slightly overweight individuals. Reference values commonly included a correction of FFM for height by calculating the FFM index (FFMI; FFM/height^2) and all were gender specific. However, study populations were not always representative of the general population, criteria for the absence of chronic disease were often lacking, and height-normalized indices for FFM were not always presented. In addition, not all studies reported age-specific reference values, although it is known that FFM declines in individuals older than 60.[19] Finally, reference values for FFMI in overweight and obese populations have not been reported. This is a relevant issue, because according to World Health Organization data, more than 35% of the adult worldwide population is overweight (BMI $\geq$25 kg/m^2) and 11% is obese (BMI $\geq$30 kg/m^2).[20] It is known that a substantial proportion of individuals with excessive body weight have a disproportional low FFM. This is also referred to as "sarcopenic obesity"[1] and is associated with greater disability. Because BMI is positively related to FFMI,[9] the currently available cutoff values are probably too low to detect an abnormal low FFMI in overweight and obese populations. Thus, the use of non–BMI-specific reference values probably results in underdiagnoses and undertreatment of low skeletal muscle mass in overweight and obese populations. Indeed, it was recently reported that in obese patients with COPD, low FFMI was not present when traditional cutoff values[21] were applied.[22,23]

The aim of the present study was to determine BMI-specific and age-specific reference values for abnormal low FFMI in white-ethnic men and women free of self-reported disease from the general population.

Methods

UK Biobank

UK Biobank is a prospective epidemiological study aimed at improving the prevention, diagnosis, and treatment of a wide range of serious and life-threatening illnesses. All people aged 40 to 69 years registered with a general practitioner through the National Health Service and living within a reasonable traveling distance of a UK Biobank assessment center were considered eligible. No further inclusion or exclusion criteria were defined. UK Biobank recruited 502,682 people from the general population between 2006–2010 from across the UK. The North West Multi-centre Research Ethics Committee approved the study. Detailed information about the study is available at the UK Biobank Web site: www.ukbiobank.ac.uk.

Study Participants

The present study is a cross-sectional analysis of the baseline data of the UK Biobank. Records from all white-ethnic participants aged 45 to 69 years with available data on body composition, lung function, and self-reported diseases were used. White ethnicity was defined as British, Irish, or any other white background. Because BIA is insufficiently validated in individuals with extreme underweight or severe obesity, participants with a BMI lower than 14 kg/m^2 or 36 kg/m^2 or higher were excluded.[24] Also, individuals with self-reported chronic diseases and conditions, as defined in Supplementary Figure 1, and individuals with objectified obstructive lung disease (OLD) were excluded.

Body Composition

Total body weight was measured after removal of shoes and heavy outer clothing, using a Tanita BC-418 MA (Tanita Corporation, Arlington Heights, IL). Standing height without shoes was measured using a Seca 202 (Seca, Hamburg, Germany). BMI was calculated as the ratio of weight to squared height. A priori, BMI was categorized into underweight (<18.50 kg/m^2), normal weight (18.50–24.99 kg/m^2), overweight (25.00–29.99 kg/m^2), and obese ($\geq$30.00 kg/m^2).[25] Bioelectrical impedance was measured using the Tanita BC-418 MA, with participants standing in bare feet on the analyzer's footpads, and holding its handles. It was used to estimate FFM and calculate FFMI thereafter, by using the prediction equation described by Jebb et al.[26] In addition, fat mass (FM) and fat mass index (FMI) were calculated.

Chronic Diseases and Conditions

Self-reported medical history was collected using standardized questions ("Has a doctor ever told you that…"), automatically coded and linked to the participants' past medical records. Supplementary Figure 1 shows an overview of the self-reported illnesses that were used as exclusion criteria for the definition of healthy individuals.

Lung Function

Lung function was measured by performing pre-bronchodilator spirometry using the Vitalograph Pneumotrac 6800 spirometer (Vitalograph, Buckingham, UK). Forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were assessed with a maximum of 3 measurements per participant. FEV_1/FVC was calculated after examining the data from all of the usable curves.[27] OLD was defined as FEV_1/FVC less than 0.70.[28]

Statistics

In the descriptive analyses, means and SDs were used for continuous variables, and frequencies and percentages for categorical variables, if appropriate. The Pearson product correlation coefficient was used to study associations. Percentiles 5, 10, 25, 50, 75, 90, and 95 were calculated for FFMI, after stratification for gender, age, and BMI in individuals without self-reported chronic illnesses (Supplementary Figure 1) and not fulfilling the criterion for OLD. Participants were stratified as younger than 60 years and 60 years or older, because FFM declines in those older than 60 years.[19] All statistics were performed by MTJG using STATA (version 12.1; Stata Corp LP, College Station, TX). The level of significance was set at P less than .01.

Results

Study Participants

The UK Biobank recruited 450,885 individuals in the age category 45 to 69 years. The study flowchart is presented in Supplementary Figure 1. Based on missing data for ethnicity, chronic diseases, BMI, body composition, or lung function, 23,639 individuals were excluded from current analyses. In addition, 240,271 individuals were excluded because of ethnicity, the presence of chronic disease or airflow limitation, or BMI of 36 kg/m^2 or higher. None of the individuals had a BMI lower than 14 kg/m^2. The final study population consisted of 186,975 healthy white-ethnic men and women (Table 1). Sixty-four percent of the study population had an overweight or obese BMI. The percentage of men per BMI category increased from 14.9% in underweight, 33.2% in normal weight, to 53.5% in overweight and 52.1% in obese individuals.

Table 1
General Characteristics of the Study Population (mean ± SD)

Characteristic	
Subjects, n (% men)	186,975 (45.9)
Age, y	56.9 ± 6.8
Height, cm	168.8 ± 9.1
Weight, kg	75.9 ± 13.6
BMI, kg/m^2	26.5 ± 3.6
BMI category	
Underweight, n (%)	784 (0.4)
Normal weight, n (%)	66,017 (35.3)
Overweight, n (%)	86,657 (46.3)
Obese, n (%)	33,517 (17.9)
FFM, kg	52.7 ± 11.2
FFMI, kg/m^2	18.3 ± 2.4
FM, kg	23.1 ± 7.4
FMI, kg/m^2	8.2 ± 2.8
Current smokers, n (%)	15,102 (8.1)
Overall health rating	
Excellent, good, fair, poor, %	23.5, 63.1, 12.3, 1.1

BMI, body mass index; FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index.

Reference Values for FFMI

Means and SDs for FFM(I) and FM(I) for men and women after stratification age and BMI are presented in Supplementary Tables 1 and 2. Percentiles 5, 10, 25, 50, 75, 90, and 95 were calculated for FFM (Tables 2 and 3) and FFMI (Tables 4 and 5), after stratifying for gender, age, and BMI. FFM and FFMI were consistently lower in women compared with men, were positively related to BMI (Figure 1), and decreased with age (Figure 2). Percentiles for FM and FMI are presented in Supplementary Tables 3–6.

Discussion

This is the first study presenting reference values for body composition assessed with BIA across all BMI categories, including overweight and obese populations. Using population-based data from the UK Biobank, BMI- and age-specific reference values for low FFM and FFMI were established in 186,975 male and female white-ethnic individuals free of chronic illness. Reference values were consistently lower in women and individuals aged 60 to 69 years. Also, reference values for FFM and FFMI increased with increasing BMI.

Assessment of Body Composition

It is well recognized that body weight and BMI are inadequate markers of underlying alterations in body composition in elderly and diseased populations. In fact, body composition, more than BMI, is a determinant of health and prognosis.[29] Thus, assessment of FFM is of considerable interest in the evaluation of nutritional status in epidemiological, clinical, and scientific settings. Low FFM is commonly observed in the elderly[2] and in patients with chronic conditions, including COPD,[21] CHF,[30] and lung cancer.[31] It is one of the diagnostic criteria for the diagnosis of cachexia[32] and is associated with significant morbidity and mortality. Importantly, low FFM is commonly observed in normal to overweight populations[1] and referred to as "sarcopenia." Also in these populations, low FFM is independently associated with adverse health outcomes and disabilities.[2] Thus, there is a need for methods to measure body composition in various settings. Several methods are available for the measurement of body composition, including deuterium dilution, whole-body counting of potassium, hydrodensitometry, and dual-energy X-ray absorptiometry (DXA). Although considered reference methods, these techniques are expensive, availability is limited, and they require skilled technicians in clinical practice. Therefore, use of these methods for clinical practice and population studies is limited. Alternatively, BIA is a well-validated, noninvasive, easy, and safe method to determine the lean and fat body compartments in normally hydrated individuals. BIA has been extensively validated against DXA.[33,34]

Table 3
Normative Values for FFM (in kg) for Healthy White-Ethnic Women

Age, y	BMI, kg/m^2	P5	P10	P25	P50	P75	P90	P95
45–59	<18.50	33.9	34.9	36.4	38.3	40.4	42.4	43.8
	18.50–24.99	37.0	38.0	40.0	42.2	44.5	46.7	48.1
	25.00–29.99	39.4	40.5	42.5	44.9	47.4	49.7	51.3
	≥30.00	42.5	43.7	45.8	48.3	51.1	53.8	55.6
60–69	<18.50	32.9	33.8	35.8	14.2	39.5	40.9	41.8
	18.50–24.99	35.9	37.0	38.8	40.9	43.1	45.1	46.5
	25.00–29.99	38.3	39.3	41.2	43.4	45.8	48.1	49.6
	≥30.00	41.1	42.3	44.3	46.8	49.5	52.0	53.7

BMI, body mass index; FFM, fat-free mass; P, percentile.

Previous Studies on Reference Values for Body Composition Using BIA

Obviously, the prevalence of low FFM in studied populations depends on the reference values that are used. Several epidemiological studies have been published on reference values for body composition using BIA. Although the populations included differed between studies and the criteria for lack of chronic disease were not always well defined, most of the studies presented gender- and age-specific reference values. However, few have reported reference values for height-corrected FFM and none presented BMI-specific cutoffs for FFMI.

Pichard et al[15] published percentiles for FFM in 3393 healthy white individuals aged 15 to 64 years. Although percentiles were gender and age specific, height-normalized indices for FFM were not presented and the authors did not provide BMI-specific reference values. Fewer than 20% of individuals in the study had a BMI higher than 25 kg/m^2,

Table 2
Normative Values for FFM (in kg) for Healthy White-Ethnic Men

Age, y	BMI, kg/m^2	P5	P10	P25	P50	P75	P90	P95
45–59	<18.50	41.5	43.8	46.6	49.4	52.9	56.1	58.5
	18.50–24.99	50.2	52.1	55.4	59.0	62.8	66.3	68.4
	25.00–29.99	55.4	57.2	60.5	64.2	68.2	72.1	74.4
	≥30.00	60.3	62.3	65.9	70.0	74.3	78.6	81.2
60–69	<18.50	40.6	41.2	47.3	50.0	52.0	55.3	56.5
	18.50–24.99	48.5	50.5	53.6	57.1	60.7	64.1	66.2
	25.00–29.99	53.1	54.9	58.0	61.7	65.6	69.3	71.6
	≥30.00	57.8	59.7	63.2	67.1	71.3	75.3	77.7

BMI, body mass index; FFM, fat-free mass; P, percentile.

Table 4
Normative Values for FFMI (in kg/m^2) for Healthy White-Ethnic Men

Age, y	BMI, kg/m^2	P5	P10	P25	P50	P75	P90	P95
45–59	<18.50	14.0	14.9	15.3	15.7	16.3	16.9	17.4
	18.50–24.99	17.0	17.5	18.1	18.9	19.5	20.1	20.5
	25.00–29.99	19.0	19.3	19.9	20.6	21.3	22.0	22.4
	≥30.00	20.9	21.3	21.8	22.6	23.3	24.0	24.5
60–69	<18.50	14.5	14.9	15.2	15.8	16.2	16.7	17.5
	18.50–24.99	16.8	17.2	17.9	18.6	19.2	19.9	20.2
	25.00–29.99	18.6	18.9	19.5	20.2	21.0	21.6	22.0
	≥30.00	20.4	20.7	21.3	22.1	22.8	23.6	24.0

BMI, body mass index; FFMI, fat-free mass index; P, percentile.

Table 5
Normative Values for FFMI (in kg/m^2) for Healthy White-Ethnic Women

Age, y	BMI, kg/m^2	P5	P10	P25	P50	P75	P90	P95
45–59	<18.50	12.9	13.3	13.7	14.1	14.6	15.1	15.4
	18.50–24.99	14.3	14.6	15.1	15.7	16.3	16.9	17.2
	25.00–29.99	15.5	15.8	16.3	16.9	17.5	18.1	18.5
	≥30.00	16.9	17.2	17.7	18.3	19.0	19.7	20.1
60–69	<18.50	12.7	13.0	13.6	14.2	14.6	15.0	15.4
	18.50–24.99	14.2	14.5	15.0	15.5	16.1	16.7	17.0
	25.00–29.99	15.4	15.7	16.1	16.7	17.3	17.9	18.3
	≥30.00	16.7	17.0	17.5	18.1	18.9	19.5	19.9

BMI, body mass index; FFMI, fat-free mass index; P, percentile.

indicating that the included population was not representative of the general population, where overweight and obesity are far more prevalent.[20] Furthermore, the exclusion criteria for chronic pathologies remained unclear. Schutz et al[14] published reference intervals for FFMI assessed by single-frequency BIA as a function of sex and age in 5635 white individuals aged 18 to 98 years without any self-reported known pathology or physical handicap. Although intervals were not BMI specific, the authors also determined the corresponding FFMI for classical BMI cutoff points. At a BMI of 25 kg/m^2, FFMI was 19.8 kg/m^2 in men and 16.7 kg/m^2 in women. Values corresponding to an obese BMI were not presented. In a subsequent publication, the same authors presented BMI-specific reference values for FFMI in 5629 healthy white individuals aged 18 to 98 years.[9] Using polynomial regression analyses, FFMI values corresponding to BMIs of 18.5, 20.0, 25.0, 27.3/27.8, and 30.0 kg/m^2 were determined for men and women without self-reported disease. In men, FFMIs corresponding to overweight and obesity were 19.8 kg/m^2 and 21.7 kg/m^2, respectively[9]; in women these were 16.8 kg/m^2 and 18.2 kg/m^2. Although FFMI was curvilinearly related to age, no age-specific values for FFMI in the different weight categories were presented. Also, 87% of individuals in the study were younger than 60 years, restricting the generalizability to older populations. In addition, the low number of obese individuals in the study and the absence of well-defined criteria for chronic disease were factors limiting the practical use of these criteria.

Dey et al[13] published reference values for FFM measured with BIA for 70- to 75-year-olds. Values were based on estimations of body composition in 823 self-declared healthy elderly from the general population in Sweden. Height-corrected FFM- and BMI-specific reference values were not presented.

Finally, using single-frequency BIA data from the Third National Health and Nutrition Examination Survey (NHANES III), Chumlea et al[17] presented estimates for FFM by sex and age for 3 racial-ethnic groups,

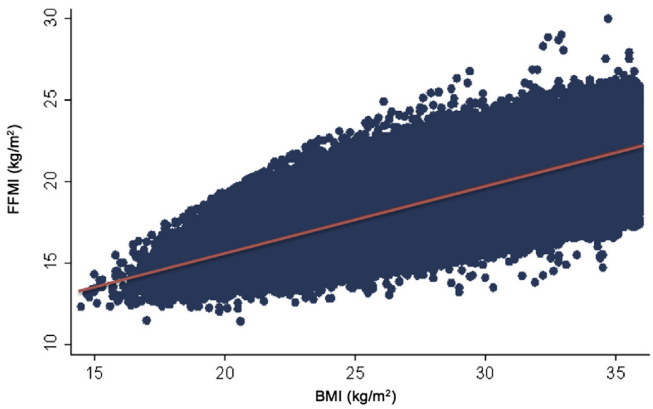

Fig. 1. Correlation between BMI and FFMI in 186,975 healthy white-ethnic individuals. $R = 0.6225$, $P < .001$.

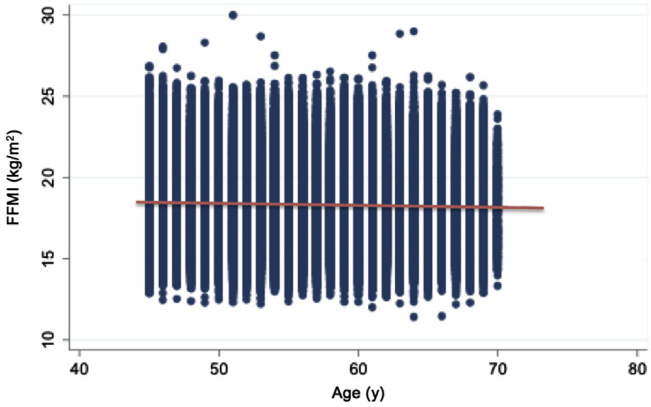

Fig. 2. Correlation between age and FFMI in 186,975 healthy white-ethnic individuals. $R = -0.0314$, $P < .001$.

including 3611 non-Hispanic whites aged 40 years and older. The clinical applicability of these data was limited, as no correction for height was done, FFM estimates were not BMI specific, and percentile ranges for FFM were lacking. Also, no information was provided about the presence of chronic health conditions.

The sample size of the present study is about 30 times larger than the largest of the previously discussed studies. Also, chronic diseases were well defined so as to include only healthy individuals. Furthermore, in addition to gender and age, BMI-specific cutoffs for FFM and FFMI were presented.

Future Perspective

The clinical implications of the presented reference values must be investigated. The application of BMI-specific reference values for FFM and FFMI to overweight and obese populations of elderly and/or chronically ill enables studying the true prevalence of abnormal body composition. For example, it was consistently reported that low FFMI is absent in obese patients with COPD,[22,23] when non–BMI-specific cutoffs were used. As a subsequent step, the clinical consequences and prognostic impact of low FFM(I) in these overweight and obese populations must be investigated.

Limitations

Although BIA is a reliable method for measuring FFM and FFMI in population studies,[35] no “gold standard” for body composition was available in the UK Biobank. The present data were derived from a prediction equation, incorporating gender, age, and a log-transformation of height, weight, and the measured impedance.[26] Although this equation was validated against a 4-compartment model, indirect assessments of body composition are subject to estimation errors.[9] However, given the advantages of BIA, it has great potential for measuring body composition in large populations, including UK Biobank. BIA works well in healthy individuals and in patients with stable water and electrolytes balance with a validated BIA equation that is appropriate with regard to age, sex, and race.[36] To ensure validity of the presented reference values, young adults and elderly individuals were excluded. However, because no individuals aged 70 and older were included, application of the reference values to this population would probably result in slight overestimation of the proportion of elderly with low FFMI. Also, all individuals with chronic disease that might affect fluid balance, including patients with COPD, CHF, and chronic renal failure, were excluded. Also, individuals with extreme underweight (BMI <14 kg/m^2) or severe

obesity (BMI $\geq$36 kg/m^2) were excluded[24] because of potential prediction errors.[35] Although it was previously shown that the use of generalized BIA equations results in overestimation of FFM in obese individuals, the applicability of BMI-specific equations is limited.[37] Thus, grade 2 (35 kg/m^2 $\leq$ BMI $<$ 40 kg/m^2) and grade 3 (BMI $\geq$40 kg/m^2) obesity are not represented in the current population. However, it was recently reported that most adult non-Hispanic white individuals with obesity in the general population have grade 1 obesity (30 kg/m^2 $\leq$ BMI $<$ 35 kg/m^2),[38] which is adequately represented in the present cohort. Finally, only white individuals were included because the use of general BIA equations across different ethnic groups results in bias.[39] Despite concerns regarding the validity of BIA when compared with more sophisticated techniques, it is the only method that is applicable in large populations such as the UK Biobank.

The presented reference values are applicable to FFM and FFMI values derived from BIA only. It is known that BIA may overestimate FFM and FFMI systematically compared with DXA.[40] Also for DXA, several investigators published reference values. Coin et al[41] presented gender- and age-specific reference ranges for FFMI measured by DXA in 1866 healthy Italian adults. No BMI-specific values were calculated. Li et al[18] published sex-, age-, and race-specific percentile cutoffs for FFM measured with DXA for different BMI categories in participants of NHANES III. Data included 4729 non-Hispanic whites aged 40 years and older, but again no height-corrected FFM was presented and data on the presence of chronic diseases among participants were lacking.

Conclusions

The percentile values for FFM and FFMI presented here can be used as reference values for healthy white individuals aged 45 to 69 years with a BMI of 14 to 36 kg/m^2. Although this is the first study to provide percentiles for FFM and FFMI in overweight and obese individuals, future studies are warranted to test the applicability and clinical impact of these reference values in individuals with chronic disease. Ultimately, the results of the present study will permit the optimization of management of abnormal body composition in elderly and diseased populations, including not only nutritional support but also exercise training modalities.

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Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jamda.2014.03.012.

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