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Ethnic differences in fat and muscle mass and their implication for interpretation of bioelectrical impedance vector analysis

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Abbreviations:

BCC, body composition chart; BIA, bioelectrical impedance analysis; BIVA, bioelectrical impedance vector analysis; ECW, extracellular water; FFM, fat free mass; FFMI, fat free mass index; FM, fat mass; FMI, fat mass index; Ht, body height; mBCA, medical Body Composition Analyzer; R, resistance; SMI, skeletal muscle index; SMM, skeletal muscle mass; TBW, total body water; VAT, visceral adipose tissue; Xc, reactance

Abstract

According to the WHO Expert Consultation, current BMI cut-offs should be retained as an international classification. There are, however, ethnic differences in BMI associated health risks that may be due to differences in body fat or skeletal muscle mass and also impact the interpretation of phase angle and bioelectrical impedance vector analysis (BIVA). Therefore the aim of this study was to compare body composition measured by bioelectrical impedance analysis between 1048 German, 1026 Mexican and 995 Japanese adults with a wide range of age and BMI (18-78years, BMI 13.9–44.3kg/m²). Regression analyses between body composition parameters and BMI were used to predict ethnic-specific reference values at the standard BMI cut-offs of 18.5, 25 and 30kg/m². German men and women had a higher fat free mass per fat mass compared to Mexicans. Normal weight Japanese were similar to Mexicans but approached the German phenotype with increasing BMI. The skeletal muscle index (SMI, kg/m^2) was highest in Germans whereas in BIVA the Mexican population had the longest vector, and the Japanese population had the lowest phase angle and the highest extracellular/total body water ratio. Ethnic differences in regional partitioning of fat and muscle mass at the trunk and the extremities contribute to differences in BIVA and phase angle. In conclusion, not only the relationship between BMI and adiposity is ethnic-specific but also fat distribution, SMI and muscle mass distribution vary at the same BMI. These results emphasize the need for ethnic-specific normal values in the diagnosis of obesity and sarcopenia.

Keywords: fat mass, fat free mass, ethnicity, bioelectrical impedance analysis, body composition, body mass index, skeletal muscle index, phase angle, bioelectrical impedance vector analysis

Introduction

Obesity associated health risks differ greatly across ethnic groups (Gasevic et al. 2015; Ntuk et al. 2014). Proposed BMI cut-off points used to predict clinical outcomes are manifold and even vary between Asian populations (WHO/IASO/IOTF 2000; James et al. 2002). The WHO Expert Consultation recommended that the current WHO BMI cut-off points should be retained as the international classification (WHO expert consultation 2004). Despite a growing debate on the need for ethnic-specific BMI cut-off points, the rationale for population specific health risks at the WHO BMI thresholds remains insufficiently justified. The percentage of body fat varies significantly even at the same BMI (Buffa et al. 2017). Differences across populations due to genetic and environmental effects not only concern the relationship between BMI and percentage of body fat but also the associations between BMI and body fat distribution, skeletal muscle mass (SMM) or composition of lean mass (Heymsfield et al. 2016). BMI has limitations as an index of body composition in certain diseases that contribute to a loss in FFM, whereas FM may be unchanged or even elevated (Cederholm et al. 2015). Hence, it is not sufficient to introduce ethnic-specific BMI cut-off points that are solely based on adiposity as the reference. It is also important to consider ethnic differences in other clinically meaningful body composition parameters at these cut-offs. Beyond BMI, waist circumference is recommended for health risk assessment (NIH 2000). However, at the same waist circumference there are ethnic differences in VAT (Sumner et al. 2011); it is therefore important to consider ethnic differences in VAT.

To facilitate this, there is a need for practical phenotypic measures beyond BMI, which are reliable, non-invasive, easy to perform, cost-effective and can be applied in clinical routine.

Bioelectrical impedance analysis (BIA) not only meets these requirements, but it also offers body composition phenotyping that is related to physiologic function and is of prognostic value in patients. Clinical outcome parameters by BIA include total and regional SMM for diagnosis of sarcopenia (Chien et al. 2008; Cruz-Jentoft et al. 2010), phase angle as a predictor of mortality (Wirth et al. 2010; Norman et al. 2010), and bioelectrical impedance vector analysis (BIVA) that can be used to assess hydration status and catabolic states e.g. in critically ill patients, malnutrition and wasting diseases (Piccoli et al. 1994; Fassini et al. 2016; Castillo-Martínez et al. 2012; Nicoletti et al. 2014). Ethnic differences in body composition may impact the interpretation of these important clinical outcome parameters.

The aim of this observational study was to analyze ethnic differences in BIA outcome measures that assess body fat and SMM at the standard BMI cut-offs of 18.5, 25 and 30 kg/m² between Caucasian (German), Mexican (Mexican-mestizos) and Asian (Japanese) adults.

Since body composition differs between these ethnicities, differences can also be expected for the phase angle and the BIVA, which are derived from the raw data of the BIA measurement. Therefore, as a secondary objective of this study, normal ranges for the phase angle and the BIVA where compared between the three ethnicities.

Materials and methods

Body composition was measured in a cross-sectional study in 3069 healthy adults from three study centers in Germany, Japan and Mexico between 2011 and 2016.

996 healthy Japanese adults (497 women and 499 men) aged 21-87 years (BMI 13.9 – 41.2 kg/m²) were examined at the University of Tokyo Hospital (Japan) on a seca medical Body Composition Analyzer (mBCA) 515 with a handrail height adjusted for an Asian population, from March until May 2014. Measurements were carried out in the morning between 10 am and 12:30 pm and in the afternoon between 2 pm and 5 pm. Data from one subject with an age of 87 years were excluded due to the high age being an outlier in the study population with an age range of 21-78 years.

1026 healthy Mexican-Mestizos (503 women and 523 men) aged 18-67 years (BMI 17.1 – 44.3 kg/m²) were measured at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (National Institute of Medical Sciences and Nutrition Salvador Zubirán; Mexico) from April 2015 until April 2016. Healthy adults with Mexican ancestors back to the second generation (all four grandparents) were considered Mexican-Mestizo and were eligible for the study. Only subjects that qualified for blood donation according to the Mexican official guidelines for blood donors (Norma Oficial Mexicana NOM-253-SSA1-2012 2012) were included. Measurements were carried out between 8 am and 1 pm.

1050 healthy Germans (518 women and 532 men) aged 18-65 years (BMI 18.2 – 42.6 kg/m²) were measured at the Institute for Transfusion Medicine at the University Hospital Hamburg-Eppendorf (Germany) from October 2011 until January 2012. All adult blood donors under the age of 65 years were generally eligible for the study. Subjects were included in the study and considered as healthy if they qualified as blood donors according to the German guidelines for blood donors (Bundesärztekammer 2010). All BIA measurements were performed before blood donation to avoid fluid shifts. Measurements were carried out between 7:30 am and 7 pm. Data

from two subjects (1 woman, 1 man) were omitted, due to missing waist circumference values. Normal values for BIA-outcome parameters in the German study population were previously published (Peine et al. 2013).

Blood donors in Germany and Mexico were expected to be healthy and were obliged to answer an extensive questionnaire regarding their health and chronic and acute disease. Blood donors in Germany were strongly advised not to perform vigorous physical activity, to drink about half a liter, and take a small meal 1 to 2 hours before donation; in Mexico they were advised to drink, but an 8 hour fast was required. Female donors in Germany were strongly advised not to donate during or within one week after menstrual bleeding - however if the hemoglobin level was above 12.5 g/dl Germans and Mexicans were allowed irrespective of their menstrual cycle.

Further exclusion criteria were chronic diseases that impact fluid homeostasis (e.g. hypertension, heart or kidney failure, patients treated with diuretics), amputation of limbs, implants such as cardiac pacemaker, insulin pumps, artificial joints, metallic implants (except tooth implants), pregnancy or breastfeeding period, subjects who cannot provide an informed consent form by themselves and subjects who might be dependent from the sponsor or the investigation site. In Germany and Mexico additional exclusion criteria were extensive tattoos and ankle edema that were assessed by inspection. All subjects provided their fully informed and written consent before participation. The studies were approved individually by the responsible ethical committee in each institution and were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Anthropometry

Body weight was measured using the devices seca mBCA 514/515 (seca gmbh & co. kg, Hamburg, Germany). In Germany and Japan the device seca 515 was used, that includes an approved scale with an accuracy of 50 g up to 100 kg. In Mexico the device seca 514 was used that includes a scale with an accuracy of ±0.3 %. Body height (Ht) in Germany was obtained with a seca 217 stadiometer with an accuracy of ±5 mm. In Japan and Mexico a digital stadiometer seca 274 with an accuracy of ±2 mm was used. BMI was calculated by BMI = weight / Ht^2 and classified as underweight (BMI <18.5 kg/m^2), normal weight (BMI ≥18.5, <25 kg/m^2), overweight (BMI ≥25, <30 kg/m^2) and obesity (BMI ≥30 kg/m^2). Waist circumference was measured midway between the lowest rib and the uppermost boarder of the iliac crest in the medial axillary line and at the end of normal expiration using a non-stretchable measurement tape seca 201.

Bioelectrical impedance analysis (BIA)

The seca mBCA 514/515 consists of a platform with an integrated scale and a handrail system. Each side of the ascending handrail carries six electrodes, of which two were chosen depending on the person's height. To get the right choice of grip position, the subject had to stand upright with outstretched arms. Another two pairs of electrodes contact the feet. This eight-electrode technique enables segmental impedance measurement. Details of the device were previously described (Bosy-Westphal et al. 2013). The devices mBCA 514 and mBCA 515 are of identical construction and differ only in the approval of the integrated scale, which is required by law in Germany and Japan and explains the different accuracy specifications of the scales. The

accuracy for measurements of the right and left body side at frequencies of 5 and 50 kHz is 5 Ω for the impedance and 0.5° for the phase angle. The prediction equation for fat free mass (FFM), total body water (TBW) and extracellular water (ECW) were validated by Bosy-Westphal et al. (2013) and fat mass (FM) was calculated as the difference between body weight and FFM. The reproducibility of FM measurement is 0.221 kg (Bosy-Westphal et al. 2013). The prediction equations for SMM and visceral adipose tissue (VAT) were validated by Bosy-Westphal et al. (2017). Resistance (R) and reactance (Xc) values obtained at 5 and 50 kHz for different body segments are used in the prediction equations. Corrections for ethnical differences of prediction equations are implemented in the devices as described by Bosy-Westphal et al. (2017). Listed values for R_{50kHz}/Ht, Xc_{50kHz}/Ht and the phase angle are mean values of both sides of the body. The mBCA device used in Japan was a device for the Asian market which has a 10 cm lower handrail compared to the devices used in Germany and Mexico. A comparison of both devices in a subgroup of 199 subjects in Japan (102 women and 97 men) aged 21-78 years (BMI 15.9 – 32.7 kg/m²) showed a higher resistance of the arms for the device with the low handrail due to the slightly different positioning of the arms. This leads to higher impedance measurements (R_{50kHz}/Ht: +0.077 ± 0.036 Ω/cm, $p < 0.0001$ and Xc_{50kHz}/Ht: +0.0011 ± 0.0041 Ω/cm, $p < 0.001$) and a lower phase angle (-0.086° ± 0.067°, $p < 0.0001$), which explains 11% - 23% of the differences in these raw data between Japanese and Germans shown in **Table 1**. The BIA-prediction equations include corrections for these differences.

Statistics

Data analyses were performed with R software, version 3.0.1 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics are presented as means ±SD. For the calculation of the 95% confidence intervals of regression lines, normal distribution and homoscedasticity were assumed. Differences between independent samples of three ethnic groups were analyzed using ANOVA with Bonferroni post hoc tests. Differences between Pearson correlation coefficients r were evaluated by using a ż-transformation according to R.A. Fischer (Hedderich and Sachs 2012). A p-value <0.05 was considered significant.

Fat mass index (FMI), fat free mass index (FFMI), skeletal muscle index (SMI) and VAT in **Tables 2 and 3** were calculated by a linear regression versus BMI. The percentage value of FM was calculated from the FMI by $FM = 100\% \cdot FMI/BMI$ using the respective BMI value. Negative results for VAT at a BMI of 18.5 kg/m² were omitted. Calculations in **Table S2** were performed for subgroups with at least 25 subjects; results for subgroups with fewer subjects were omitted.

For BIVA graphs, the 50% tolerance ellipses were calculated from R_{50kHz}/Ht and Xc_{50kHz}/Ht as explained in detail by Piccoli et al. (1994). The ellipses describe the area in which the measurements of 50% of all subjects fall. Vector displacements parallel to the major axis indicate tissue hydration (less TBW leading to longer vectors) and vector displacements parallel to the minor axis indicate cell mass (less cell mass leading to a down-sloping of the vector) (Piccoli and Pastori 2002). The three indices FMI, FFMI and SMI represent the FM, FFM and SMM normalized by body height square:

$$FMI = \frac{FM}{Ht^2} \qquad FFMI = \frac{FFM}{Ht^2} \qquad SMI = \frac{SMM}{Ht^2}$$

FMI vs. FFMI is displayed in the body composition chart (BCC), which is based on a chart from Hattori (1991) and uses 50% tolerance ellipses that indicate the area that contains 50% of the measurements. These ellipses were calculated similar to the BIVA according to Piccoli et al. (1994).

Percentile curves for phase angle were calculated with the R package "VGAM" using LMS quantile regression with a Box-Cox transformation to normality (lms.bcn). The M value was modelled with two degrees of freedom (df) for age dependency. The L and S values were modeled as intercept only. When one df for height dependency was added for the M value, values of -0.0197°/cm and -0.0223°/cm were found for German women and men as well as -0.0196°/cm and -0.0189°/cm for Japanese and -0.0261°/cm and -0.0236°/cm for Mexican.

Results

A characterization of the study population stratified into the three ethnic groups is given in **Table 1**. The Japanese population was slightly older compared with Germans (in men and women) and Mexicans (in men only). Larger differences between subpopulations were observed in BMI with the lowest values in Japanese and the highest in Mexicans. Dividing each subpopulation in two age groups (<40 and ≥40 years) revealed that the majority of the younger populations were normal weight with the exception of Mexican men who had a greater proportion of overweight subjects similar to Mexican men and women ≥40 years and German men ≥40 years. The Japanese population had the greatest prevalence of underweight and the lowest prevalence of obesity.

Gender and ethnic-specific body composition for different WHO BMI cut-offs is given in **Table 2** for the whole study population and in **Table 3** stratified by age groups. Adults of the same BMI but differing in ethnic group have different levels of adiposity with the lowest values for FM percentage, FMI and VAT in Germans and the highest in Mexicans. As an exception to this rule, underweight Japanese subjects had the highest amount of VAT. However, this is not statistically significant for underweight Japanese men ≥40 years. Further exceptions were not significant. An inverse pattern was observed for FFMI and total SMI with highest values in Germans and lowest in Mexicans.

Partitioning of fat and lean mass therefore differs between ethnicities. For a given BMI, Germans have a higher FFMI and a lower FMI than Mexicans. For normal weight Japanese, the partitioning is comparable with Mexicans and approaches the partitioning of Germans with increasing BMI resulting in more similar obese phenotypes in Japanese and German populations **(Table 2, Figure S1)**. These patterns are also observed in subgroups of younger and older adults (**Table 3**).

The regional distribution of SMM differs between ethnicities as well. The SMI of the trunk and the arms was highest in Germans and lowest in Japanese (**Table 2**). In contrast, SMI of the legs is lowest in Mexicans and similar in Germans and Japanese with a stronger BMI dependency in Japanese women and to a smaller extent in Japanese men (**Figure S2**).

Differences in body composition between ethnic populations are displayed in **Figure 1** in form of a BCC. Next to the highest BMI, Mexican men and women have the highest FMI, whereas the FFMI is comparable to Germans. Japanese men and women have the lowest FMI and FFMI.

Phase angle percentiles are lower in Japanese compared to German and Mexican populations (**Figure 2**). This is also reflected by higher extracellular/total body water ratio (ECW/TBW) in Japanese compared to Germans and Mexicans (**Table 4**), and is also consistent with a lower SMI in the Japanese compared to the German population.

The BIVA reveals further between-ethnic differences in body composition related to tissue composition (hydration and cellularity). In **Figure 3**, BIVA-tolerance ellipses for normal weight subjects are compared between ethnic groups. Consistent with the low FFM, the longest vectors are observed in Mexicans. Vector length was however similar between German and Japanese populations despite a lower FFMI and higher FMI and VAT in Japanese compared to German subjects (**Table 2**). The lower phase angle of the Japanese population (**Figure 2**) is represented by a shift of the ellipses to the bottom right of the graph. Data bases for BCC and BIVA charts are given in Supplemental **Tables S1** and **S2**.

Discussion

The primary aim of the present study was to analyze differences in clinically relevant outcome parameters of body composition at standard BMI cut-offs across three ethnic groups. We found profound differences in percentage FM at the same BMI between ethnicities. Therefore ethnic differences significantly contribute to the well-known inter-individual variance in percentage FM at the same BMI. We have shown that ethnic-specific relationships between BMI and body composition depend on weight status. For a given BMI, Mexicans have higher FM and VAT than Germans. Normal weight Japanese are similar to Mexicans, whereas overweight Japanese are

more similar to Germans (**Table 2**, **Figure S1**).The relationship between FMI and BMI had a similar pattern and slope in younger (<40 years) and older (≥40 years) subpopulations (**Table 3**). By contrast, results from NHANES (National Health and Nutrition Examination Survey) have shown that ethnic differences in body shape and composition were less apparent in older (≥70 years) Mexican American and non-Hispanic white and black populations (Heymsfield et al. 2016).

The lower increase of the fat-to-lean partitioning with increasing BMI in Japanese compared to German and Mexican populations is unlikely to be explained by ethnic differences in body proportions, i.e. a higher trunk mass in the Japanese population. With weight gain, a disproportional higher gain in fat mass at the trunk in men and at the extremities in women was observed in Germans (Schautz et al. 2012). A lower increase in total body fat with weight gain would therefore have required longer legs in men and a gynoid fat distribution in women, both are however unlikely phenotypes in the Japanese population and disagree with the finding of a lower ratio of leg length to trunk length in Asian populations (Deurenberg et al. 2002).

The results of the present study demonstrate ethnical differences in the raw data of BIA presented as phase angle (**Figure 2**) and BIVA charts (**Figure 3**). The lower phase angle in Japanese compared with Germans in all age groups is likely due to a higher ECW/TBW (**Table 4**) and is also compatible with a lower SMM/FFM (i.e. 0.41 vs. 0.45 in underweight and 0.45 vs. 0.47 in obese Japanese vs. German women or 0.46 vs 0.48 in underweight and 0.49 vs. 0.50 in obese Japanese vs. German men, as calculated from data in **Table 2**). In addition, the lower phase angle and the higher ECW/TBW in the Japanese population are explained by ethnic differences in partitioning of fat and lean mass with a lower FFMI and higher FMI in

underweight and normal weight BMI groups (**Table 2**). A higher phase angle for Mexicans in comparison to Germans is in accordance with differences in body height (**Table 1**) and height dependency of the phase angle in all groups. Phase angle measured with the seca mBCA 515 is lower in comparison to values measured by BIA 2000-S, Data Input (Bosy-Westphal et al. 2006) due to differences between devices, the measurement in standing vs. supine position and due to different type and placement of electrodes (unpublished data).

In BIVA analysis, longer vectors at the same BMI were observed in Mexicans compared to Germans. This is in accordance with a lower FFMI at the same BMI for Mexicans compared to Germans (**Table 2, Figure S1**), which results in lower TBW per weight for the same BMI (data no shown) and therefore in higher impedances per body length. This result is supported by NHANES data showing less FFM and muscle mass per BMI with a concomitant higher FM percentage in Mexican American men and women compared with the corresponding groups of non-Hispanic whites or blacks (Heymsfield et al. 2016; Heo et al. 2012).

Besides a lower phase angle with the corresponding down-sloping of the BIVA vector, Japanese men and women have slightly longer vectors compared to Germans. A lower FFMI and SMI for normal weight Japanese (**Table 2**) can explain longer vectors due to lower TBW per weight. Compared to Mexicans, mean BIVA vectors were however shorter in the Japanese population despite a similarly low FFMI and high FMI for normal weight subjects (**Table 2, Figure S1**). This result is likely due to a higher SMI_{legs} in relation to SMI_{trunk} in Japanese men and women (**Table 2, Figure S2**) and a lower ratio of leg length to trunk length (Deurenberg et al. 2002). After normalization of sex and BMI, differences in body shape (i.e. the distribution of lean mass) are often overlooked as an important additional confounder for the interpretation of BIVA.

Because legs have a small diameter relative to their length, when compared with the trunk, they contribute to approximately half the total body resistance, whereas the trunk only contributes 9% (Foster and Lukaski 1996). A higher SMI_{leg} in Japanese men and women compared to Mexicans as well as shorter leg length therefore leads to a better conductivity of the legs and hence a shortening of vectors (**Figure 3, Table S2**).

When compared with Germans, for a given BMI a lower SMM at the trunk and a similar SMM at the legs were found for Japanese (**Table 2, Figure S2**). This leads to a higher SMI_{legs}/SMI_{trunk} ratio and therefore, together with shorter legs, to a shortening of vectors which counteracts longer vectors due to lower FFMI. This finding is in accordance with a higher leg/trunk ratio of muscle thickness measured with ultrasound in Japanese compared to American women (Ishida et al. 1992).

The relationship between SMM at the legs and trunk was also slightly lower in Mexican men and women when compared to Germans (**Table 2, Figure S2**). This adds to the longer vectors in Mexicans. By contrast, no significant differences in the ratio of leg length to trunk length were found between American Whites (who are assumed to be similar to Germans) and Mexicans (Heymsfield et al. 2005).

In summary, longer vectors in Mexicans compared to Germans may be explained by a higher FMI and lower FFMI per BMI and lower SMI_{leg} in relation to SMI_{trunk} (**Table 2**) whereas the shorter vectors in the Japanese population compared to Mexicans might be explained by (i) a higher SMI_{legs} in relation to SMI_{trunk}, (ii) a higher trunk length/height and (iii) a lower leg

length/height that were unfortunately not measured in the present study. Differences in vector length between Japanese and Germans are small due to opposing effects.

It has been shown by Marini et al. (2013) in elderly Italians and Buffa et al. (2013) in US adults that classic BIVA, in contrast to specific BIVA, does not recognize differences in the percentage of fat mass. Classic BIVA has limitations in the interpretation of body composition because values are not corrected for cross sectional areas. For classic BIVA, a negative correlation between FM% by DXA and vector length was reported by Buffa et al. (2013), whereas we found a positive correlation between FM% and vector length at the same BMI. This discrepancy can be explained by the fact that we compared FM% at the same BMI. Because of negative correlations that were also found between BMI and vector length of classic BIVA (Buffa et al. 2013) and the correlation between BMI and FM%, the vector displacement due to higher BMI can counteract the displacement due to higher percentages of FM at the same BMI. Therefore, the comparison of subjects with the same BMI helps to avoid the limitations of classic BIVA.

As a limitation of our study, weight status differed between ethnic populations. Subgroups with underweight or obesity are underrepresented in certain ethnic groups (**Table 1**, **Figure 1**). These differences were accounted for by comparing subjects with similar BMI in the BMI range from 18.5 to 30 kg/m² that was represented in all groups. In order to get comparable groups for all three ethnicities, similar inclusion and exclusion criteria were applied and people who were eligible for blood donation were considered as healthy. In addition, a lower phase angle in the Japanese population as seen in the BIVA could be explained by the higher age in this group. However, adjusting Xc per height for age did not change the BIVA pattern (data not shown).

The consequences of the observed ethnic differences in the relationships between BMI and different body composition parameters for BMI-associated health risks deserve more attention. Of note, ethnic differences in body composition contribute to differences in metabolic clearance rate of insulin (i.e. lower clearance rate in Hispanics compared with non-Hispanic whites) and thus to differences in insulin sensitivity across ethnic groups (Lorenzo et al. 2013). Ethnic variations in adipokine levels and metabolic risk factors have been shown to persist after adjustment for BMI (Morimoto et al. 2014) and need to be investigated with regard to ethnicity-specifics in body composition in order to understand the etiology of these differences in obesity-associated health risk.

In conclusion, not only the relationship between BMI and adiposity is ethnic-specific but also fat distribution, SMI and muscle mass distribution vary at the same BMI according to ethnicity and lead to profound differences in BCC, phase angle and BIVA. Ethnic-specific normal values are therefore required for BCC, phase angle and BIVA. The developed ethnic-specific reference values for different WHO BMI cut-off points can serve as a useful research tool.

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Author contributions: B. Jensen and A. Bosy-Westphal designed research, analyzed data and wrote the paper. T. Moritoyo, A. Matsumoto, Y. Masui and the Trial Group of P1 Unit of the University of Tokyo Hospital conducted research for the Japanese population. M. Kaufer-Horwitz, A. Velázquez-González, J. Domínguez-García, E. Fonz-Enríquez and S. G. Salgado-Moctezuma conducted research for the Mexican population. S. Peine conducted research for the German population. K. Norman and M. J. Maisch contributed to the discussion of the data. T. Moritoyo and M. Kaufer-Horwitz contributed to the critical review and intellectual content of the manuscript. All authors read and approved the final manuscript.

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Table 1 Characterization of the study populations

	women			men		
	German n = 517	**Japanese** n = 497	**Mexican** n = 503	**German** n = 531	**Japanese** n = 498	**Mexican** n = 523
age, years	38.6 ±13.4	40.7 ±13.3[a]	39.5 ±11.9	39.3 ±13.2	42.1 ±15.9[a]	39.1 ±12.3[c]
weight, kg	69.6 ±12.2	52.7 ±7.8[a]	66.8 ±11.4[b,c]	86.4 ±12.5	67.3 ±11.5[a]	80.2 ±13.6[b,c]
height, cm	168 ±7	158 ±6[a]	157 ±6[b]	181 ±7	171 ±6[a]	170 ±7[b]
BMI, kg/m²	24.7 ±4.2	21.0 ±3.0[a]	27.0 ±4.5[b,c]	26.2 ±3.4	23.1 ±3.6[a]	27.8 ±4.1[b,c]
R_{50kHz}/Ht, Ω/cm	3.94 ±0.40	4.41 ±0.48[a]	4.39 ±0.50[b]	3.02 ±0.32	3.36 ±0.38[a]	3.33 ±0.37[b]
Xc_{50kHz}/Ht, Ω/cm	0.348 ±0.046	0.358 ±0.048[a]	0.399 ±0.050[b,c]	0.312 ±0.045	0.320 ±0.045[a]	0.352 ±0.048[b,c]
phase angle, °	5.05 ±0.47	4.65 ±0.44[a]	5.21 ±0.48[b,c]	5.88 ± 0.51	5.46 ± 0.58[a]	6.04 ± 0.50[b,c]
FMI, kg/m²	8.5 ±3.2	6.4 ±2.2[a]	10.7 ±3.4[b,c]	6.4 ±2.5	4.8 ±2.5[a]	8.1 ±2.9[b,c]
FFMI, kg/m²	16.3 ±1.4	14.6 ±1.3[a]	16.3 ±1.5[c]	19.8 ±1.5	18.3 ±1.7[a]	19.7 ±1.6[c]
SMI, kg/m²	7.50 ±0.82	6.16 ±0.80[a]	7.12 ±0.88[b,c]	9.80 ±0.83	8.66 ±1.02[a]	9.43 ±0.91[b,c]
VAT, l	1.11 ±0.83	1.40 ±0.39[a]	2.19 ±0.81[b,c]	2.54 ±1.45	2.27 ±1.09[a]	3.61 ±1.49[b,c]
age <40 years	n = 264	n = 248	n = 251	n = 265	n = 248	n = 265
BMI, kg/m²	23.9 ±3.6	20.8 ±3.1[a]	26.0 ±4.5[b,c]	25.2 ±3.2	22.4 ±3.5[a]	27.3 ±4.5[b,c]
underweight	2	41	0	0	16	3
normal weight	192	190	130	139	189	84
overweight	50	14	77	111	32	108
obesity	20	3	44	15	11	70
age ≥40 years	n = 253	n = 249	n = 252	n = 266	n = 250	n = 258
BMI, kg/m²	25.6 ±4.5	21.2 ±3.0[a]	28.0 ±4.2[b,c]	27.3 ±3.4	23.8 ±3.6[a]	28.4 ±3.6[b,c]
underweight	0	34	1	0	9	0
normal weight	133	191	65	66	159	38
overweight	82	19	112	153	69	144
obesity	38	5	74	47	13	76

Abbreviations: FMI, fat mass index; FFMI, fat free mass index; SMI, skeletal muscle index; VAT, visceral adipose tissue.

Significant differences between [a]Japanese vs. Germans, [b]Mexicans vs. Germans, [c]Mexicans vs. Japanese, ANOVA with Bonferroni post hoc test.

Prevalence of underweight: BMI <18.5 kg/m², normal weight: BMI ≥18.5, <25 kg/m², overweight: BMI ≥25, <30 kg/m², obesity: BMI ≥30 kg/m²

Table 2 Fat mass (FM), fat mass index (FMI), fat free mass index (FFMI), skeletal muscle index (SMI) and visceral adipose tissue (VAT) calculated from the WHO reference values for BMI (WHO expert consultation 2004)

		women			men		
BMI, kg/m²		**18.5**	**25**	**30**	**18.5**	**25**	**30**
Total population							
FM, %	Ge	20.6	34.6	41.3	6.6	22.3	29.8
	Ja	25.3[a]	36.2[a]	41.4	10.2[a]	23.9[a]	30.5
	Me	24.4[b]	37.1[b]	43.1[b,c]	9.7[b]	24.8[b,c]	32.0[b,c]
FMI, kg/m²	Ge	3.8	8.7	12.4	1.2	5.6	8.9
	Ja	4.7[a]	9.1[a]	12.4	1.9[a]	6.0[a]	9.1
	Me	4.5[b]	9.3[b]	12.9[b,c]	1.8[b]	6.2[b,c]	9.6[b,c]
FFMI, kg/m²	Ge	14.7	16.3	17.6	17.3	19.4	21.1
	Ja	13.8[a]	15.9[a]	17.6	16.6[a]	19.0[a]	20.9
	Me	14.0[b]	15.7[b]	17.1[b,c]	16.7[b]	18.8[b,c]	20.4[b,c]
SMI, kg/m²	Ge	6.56	7.55	8.30	8.34	9.57	10.51
	Ja	5.67[a]	6.93[a]	7.89[a]	7.67[a]	9.07[a]	10.15[a]
	Me	5.84[b]	6.82[b]	7.57[b,c]	7.76[b]	8.93[b,c]	9.82[b,c]
SMI_{trunk}, kg/m²	Ge	2.77	3.23	3.59	3.89	4.42	4.82
	Ja	2.29[a]	2.80[a]	3.19[a]	3.48[a]	4.04[a]	4.46[a]
	Me	2.55[b,c]	3.01[b,c]	3.38[b,c]	3.81[c]	4.30[b,c]	4.67[b,c]
SMI_{arms}, kg/m²	Ge	0.82	0.88	0.92	1.07	1.21	1.32
	Ja	0.64[a]	0.73[a]	0.81[a]	0.92[a]	1.08[a]	1.20[a]
	Me	0.73[b,c]	0.80[b,c]	0.86[b,c]	1.02[b,c]	1.14[b,c]	1.23[b]
SMI_{legs}, kg/m²	Ge	2.97	3.44	3.79	3.37	3.94	4.38
	Ja	2.75[a]	3.40	3.90	3.27	3.96	4.48[a]
	Me	2.57[b,c]	3.00[b,c]	3.33[b,c]	2.94[b,c]	3.49[b,c]	3.92[b,c]
VAT, l	Ge	0.16	1.15	1.92		2.12	3.83
	Ja	1.23[a]	1.67[a]	2.01	1.10[a]	2.74[a]	4.01
	Me	0.94[b,c]	1.90[b,c]	2.64[b,c]	0.75[c]	2.74[b]	4.28[b,c]

All values except for FM in % are calculated as linear regression to BMI.
FM in % is calculated from the FMI by 100% * FMI / BMI.
German (Ge), Japanese (Ja), Mexican (Me).
Negative results for VAT for BMI = 18.5 kg/m² are omitted.
Separate 95% confidence intervals indicate a statistically significant difference between [a]Japanese vs. Germans, [b]Mexicans vs. Germans and [c]Mexicans vs. Japanese.
Underweight: BMI <18.5 kg/m², normal weight: BMI ≥18.5, <25 kg/m², overweight: BMI ≥25, <30 kg/m², obesity: BMI ≥30 kg/m²

Table 3 Fat mass (FM), fat mass index (FMI), fat free mass index (FFMI), skeletal muscle index (SMI) and visceral adipose tissue (VAT) calculated from the WHO reference values for BMI (WHO expert consultation 2004) and given separately for younger (<40 years) and older adults (≥40 years)

		women			men		
BMI, kg/m²		**18.5**	**25**	**30**	**18.5**	**25**	**30**
age <40 years							
FM, %	Ge	20.0	33.4	39.8	4.9	21.6	29.6
	Ja	23.8[a]	35.3[a]	40.7	8.6[a]	22.4	28.9
	Me	22.8[b]	35.5[b]	41.6[b]	7.7[b]	23.7[b,c]	31.3[b,c]
FMI, kg/m²	Ge	3.7	8.4	11.9	0.9	5.4	8.9
	Ja	4.4[a]	8.8[a]	12.2	1.6[a]	5.6	8.7
	Me	4.2[b]	8.9[b]	12.5[b]	1.4[b]	5.9[b,c]	9.4[b,c]
FFMI, kg/m²	Ge	14.8	16.6	18.1	17.6	19.6	21.1
	Ja	14.1[a]	16.2[a]	17.8	16.9[a]	19.4	21.3
	Me	14.3[b]	16.1[b]	17.5[b]	17.1[b]	19.1[b,c]	20.6[b,c]
SMI, kg/m²	Ge	6.60	7.73	8.60	8.50	9.69	10.61
	Ja	5.83[a]	7.06[a]	8.01[a]	7.90[a]	9.39[a]	10.54
	Me	5.99[b]	7.04[b]	7.84[b]	7.98[b]	9.13[b,c]	10.00[b,c]
VAT, l	Ge	0.07	0.88	1.50		1.80	3.37
	Ja	1.07[a]	1.47[a]	1.78[a]	0.99[a]	2.39[a]	3.47
	Me	0.86[b,c]	1.74[b,c]	2.41[b,c]	0.61[c]	2.47[b]	3.91[b,c]
age ≥40 years							
FM, %	Ge	22.3	35.8	42.2	9.8	23.4	29.9
	Ja	27.0[a]	37.0[a]	41.8	12.8	25.2[a]	31.1
	Me	28.1[b]	39.0[b,c]	44.2[b,c]	13.4[b]	26.4[b,c]	32.6[b,c]
FMI, kg/m²	Ge	4.1	8.9	12.7	1.8	5.9	9.0
	Ja	5.0[a]	9.2[a]	12.5	2.4	6.3[a]	9.3
	Me	5.2[b]	9.7[b,c]	13.3[b,c]	2.5[b]	6.6[b,c]	9.8[b,c]
FFMI, kg/m²	Ge	14.4	16.1	17.3	16.7	19.1	21.0
	Ja	13.5[a]	15.8[a]	17.5	16.1	18.7[a]	20.7
	Me	13.3[b]	15.3[b,c]	16.7[b,c]	16.0[b]	18.4[b,c]	20.2[b,c]
SMI, kg/m²	Ge	6.40	7.38	8.14	7.98	9.38	10.46
	Ja	5.49[a]	6.82[a]	7.84	7.29[a]	8.81[a]	9.99[a]
	Me	5.47[b]	6.54[b,c]	7.36[b,c]	7.35[b]	8.66[b]	9.66[b,c]
VAT, l	Ge	0.44	1.41	2.16	0.48	2.51	4.06
	Ja	1.41[a]	1.84[a]	2.17	1.33[a]	3.00[a]	4.29
	Me	1.17[b,c]	2.09[b,c]	2.80[b,c]	1.04[b]	3.05[b]	4.60[b,c]

All values except for FM in % are calculated as linear regression to BMI.
FM in % is calculated from the FMI by 100% * FMI / BMI.
German (Ge), Japanese (Ja), Mexican (Me).
Negative results for VAT for BMI = 18.5 kg/m² are omitted.

Separate 95% confidence intervals indicate a statistically significant difference between [a]Japanese vs. Germans, [b]Mexicans vs. Germans and [c]Mexicans vs. Japanese.
Underweight: BMI <18.5 kg/m², normal weight: BMI ≥18.5, <25 kg/m², overweight: BMI ≥25, <30 kg/m², obesity: BMI ≥30 kg/m²

Table 4 Extracellular water (ECW) as a percentage of total body water (TBW) for subjects with normal weight (BMI ≥18.5, <25 kg/m²) stratified by age range and ethnicity

	women	**men**
age <40 years		
German	43.3 ± 1.3	39.8 ± 1.1
Japanese	44.9 ± 1.7[a]	40.2 ± 1.4[a]
Mexican	42.9 ± 1.6[b,c]	39.1 ± 1.2[b,c]
age ≥40 years		
German	45.0 ± 1.6	41.4 ± 1.2
Japanese	47.0 ± 2.0[a]	42.8 ± 1.9[a]
Mexican	45.3 ± 1.7[c]	41.1 ± 1.2[c]

Significant differences between [a]Japanese vs. Germans, [b]Mexicans vs. Germans, [c]Mexicans vs. Japanese, ANOVA with Bonferroni post hoc test.

Figure 1 Body Composition Chart with 50% tolerance ellipsis for Germans, Japanese and Mexicans. FMI, fat mass index; FFMI, fat free mass index. The dashed lines indicate BMI values of 18.5, 25 and 30 kg/m². Significance of differences are described in Table S1

Figure 2 Comparison of 5th, 50th and 95th percentiles of phase angle between Germans, Japanese and Mexicans

Figure 3 BIVA with 50% tolerance ellipsis for normal weight (BMI ≥18.5, <25 kg/m²) subpopulations (mean±SD in Ω/cm: **German** women R=4.07±0.36 Xc=0.356±0.045, men R=3.22±0.30, Xc=0.332±0.045, **Japanese** women R=4.37±0.42 Xc=0.355±0.046, men R=3.42±0.33, Xc=0.324±0.046, **Mexican** women R=4.72±0.42 Xc=0.416±0.046, men R=3.64±0.28, Xc=0.378±0.044). Significance of differences and correlation coefficients are described in Table S2

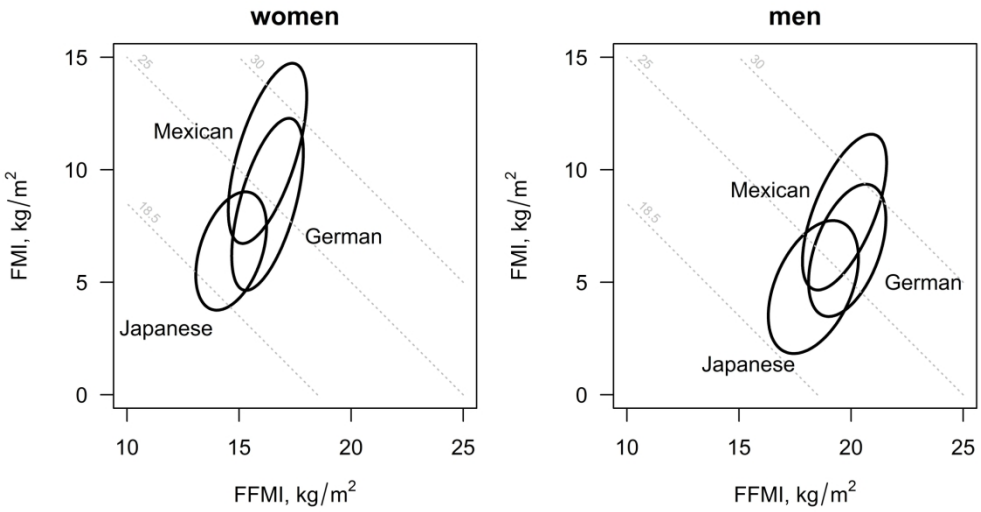

Figure 1 Body Composition Chart with 50% tolerance ellipsis for Germans, Japanese and Mexicans. FMI, fat mass index; FFMI, fat free mass index. The dashed lines indicate BMI values of 18.5, 25 and 30 kg/m². Significance of differences are described in Table S1

94x50mm (600 x 600 DPI)

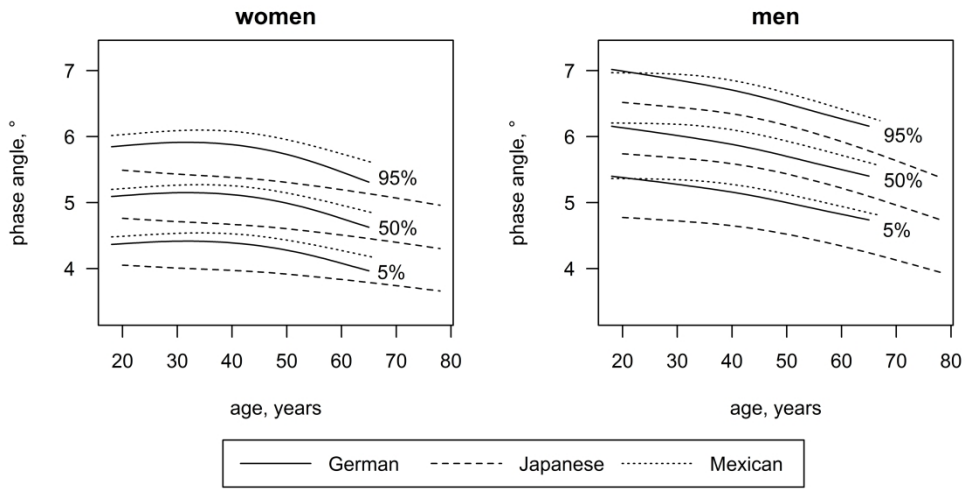

Figure 2 Comparison of 5th, 50th and 95th percentiles of phase angle between Germans, Japanese and Mexicans

179x89mm (600 x 600 DPI)

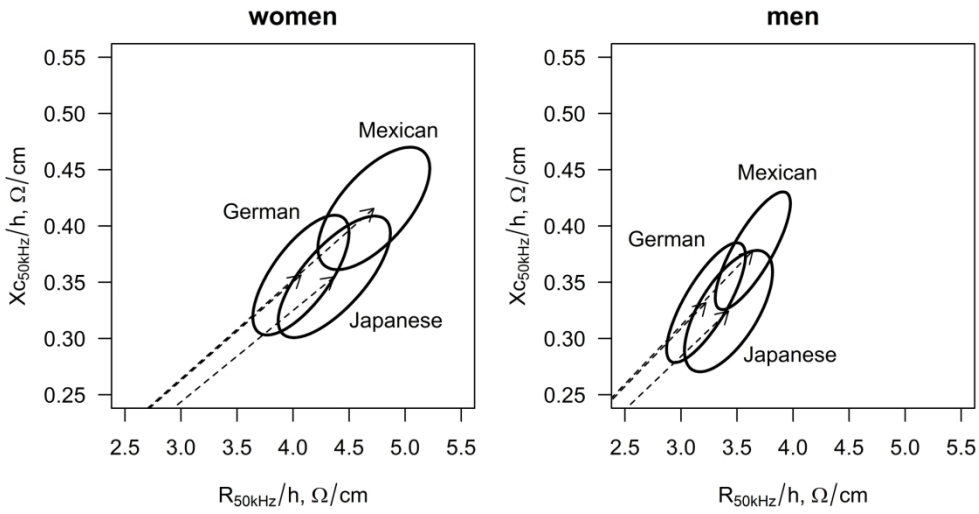

Figure 3 BIVA with 50% tolerance ellipsis for normal weight (BMI ≥18.5, <25 kg/m²) subpopulations (mean±SD in Ω/cm: German women R=4.07±0.36 Xc=0.356±0.045, men R=3.22±0.30, Xc=0.332±0.045, Japanese women R=4.37±0.42 Xc=0.355±0.046, men R=3.42±0.33, Xc=0.324±0.046, Mexican women R=4.72±0.42 Xc=0.416±0.046, men R=3.64±0.28, Xc=0.378±0.044). Significance of differences and correlation coefficients are described in Table S2

94x50mm (600 x 600 DPI)