DEPT MEETING, 30/09/2014, M. Umezaki

Derivation and validation of simple equations to predict total muscle mass from simple anthropometric and demographic data

Al-Gindan et al. (in press)

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Background: Muscle mass reflects and influences health status. Its reliable estimation would be of value for epidemiology. **Objective**: The aim of the study was to derive and validate anthropometric prediction equations to quantify whole-body skeletal muscle mass (SM) in adults. **Design**: The derivation sample included 423 subjects (227 women) aged 18–81 y with a body mass index (BMI; in kg/m2) of 15.9–40.8. The validation sample included 197 subjects (105 women) aged 19–83 y with a BMI of 15.7–36.4. Both samples were of mixed ethnic/racial groups. All underwent whole-body magnetic resonance imaging to quantify SM (dependent variable for multiple regressions) and anthropometric variables (independent variables). **Results**: Two prediction equations with high practicality and optimal derivation correlations with SM were further investigated to assess agreement and bias by using Bland-Altman plots and validated in separate data sets. Including race as a variable increased R2 by only 0.1% in men and by 8% in women. For men: SM (kg) =39.5 + 0.665 body weight (BW; kg) - 0.185 waist circumference (cm) - 0.418 hip circumference (cm) - 0.08 age (y) (derivation: R2 = 0.76, SEE = 2.7 kg; validation: R2 = 0.79, SEE = 2.7 kg). Bland-Altman plots showed moderate agreement in both derivation and validation analyses. For women: SM (kg) = 2.89 + 0.255 BW (kg) - 0.175 hip circumference (cm) - 0.038 age (y) + 0.118 height (cm) (derivation: R2 = 0.58, SEE = 2.2 kg; validation: R2 = 0.59, SEE = 2.1 kg). Bland-Altman plots had a negative slope, indicating a tendency to overestimate SM among women with smaller muscle mass and to underestimate SM among those with larger muscle mass. **Conclusions**: Anthropometry predicts SM better in men than in women. Equations that include hip circumference showed agreement between methods, with predictive power similar to that of BMI to predict fat mass, with the potential for applications in groups, as well as epidemiology and survey settings.

Important Indicators in this paper

R^2: correlation evaluating the variability explained by the model;

SEE (Standard Error of the Estimates): measures how different the actual value is from the prediction line;

$$s_{est} = \sqrt{\frac{\sum (Y - Y')^2}{N - 2}}$$

CV (Coefficient of Variation): the ratio of the SEE to the mean of the dependent variable and measures the relative closeness of the prediction to the actual value.

95% PI (Prediction interval): an estimate of an interval in which future observations will fall with a probability of 95%.

INTRODUCTION

Quantification of Skeletal Muscle Mass (SM) in Epidemiology

- Sarcopenia study
- Cardiovascular disease risk study
- ADL (activity of Daily Living) study

Quantification of Skeletal Muscle Mass (SM)

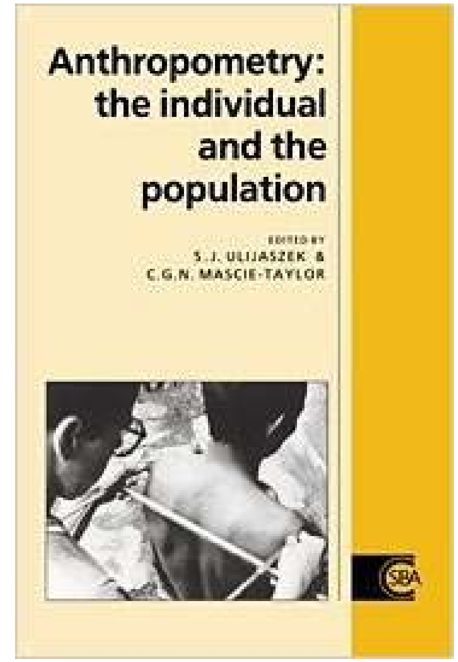
MRI (Magnetic Resonance Imaging)

Anthropometric Prediction Equations

Height, weight,

Circumference of chest/waist/hip/upper arm/thigh/calf,

Skinfold thickness at subscaplar/triceps



Accurate! but expensive

Simple, quick, safe, noninvasive, cheap, need only low skill levels, give immediate results

Anthropometric Prediction Equations

Systematic Review: Al-Gindan et al (2014). Predicting muscle mass from anthropometry, using magnetic resonance imaging (MRI) as reference: a systematic review. Nutr Rev 72(2):113–26.

Cochrane Review methodology, Medline (1946–2012), Embase (1974–2012), Web of Science (1898–2012), PubMed, and the Cochrane Library (to 08/2012)

Prediction equations (from anthropometric measurements) to estimate muscle mass by magnetic resonance imaging (MRI) in adults.

Of 257 papers identified from primary search terms, 12 studies met the inclusion criteria.

Only one published anthropometric method to estimate whole-body muscle mass as measured by MRI: Lee et al. (2000) Total body skeletal muscle mass: development and cross-validation of anthropometric prediction models. Am J Clin Nutr 2000;72:796–803.

Lee et al. (2000) Total body skeletal muscle mass: development and cross-validation of anthropometric prediction models. Am J Clin Nutr 72:796–803.

SM (kg) =0.244 × body weight (BW; kg) + 7.80 × height (m) - 0.098 × age (y) + 6.6 × sex + race* - 3.3.

$R^2 = 0.86$, $P < 0.0001$, SEE = 2.8 kg(non-obese subjects)

$R^2 = 0.79$, $P < 0.0001$, SEE = 3.0 kg (obese subjects)

*race = 1.2 for Asian, 1.4 for African American, and 0 for white and Hispanic

Problems:

1. The term of race is specific to US categories
2. Exaggerated R^2, because of wide ranges afforded by combining the sexes

The aim of the study

To derive/evaluate anthropometric Prediction Equations for whole-body SM.

The authors also validated the equation derived by Lee et al (2000) in an independently measured sample.

Subjects and Methods

Data collected by New York Obesity Nutrition Research Center's Body Composition Unit, St Luke-Roosevelt Hospital, New York.

1. Derivation study sample

   N=423 (227 women; Age: 18–81y; BMI: 15.9–40.8)

2. Validation study sample

   N=197 (105 women; Age: 18-83y; BMI: 15.7-36.4)

No known or diagnosed any health conditions that would affect body composition or fat distribution

Subjects

TABLE 1
Subject characteristics and variables used in this study for derivation and validation studies[1]

	Derivation sample		Validation sample	
	Men (n = 196)	Women (n = 227)	Men (n = 92)	Women (n = 105)
Age (y)	39.2 ± 13.9[2]	44.4 ± 16.2	43.3 ± 15.9	44.1 ± 16.4
BW (kg)	79.8 ± 12.7	67.1 ± 15.1	77.4 ± 14.1	66.3 ± 10.7
Height (cm)	176.0 ± 6.8	162.0 ± 7.2	174.5 ± 7.3	162.2 ± 5.9
BMI (kg/m^2)	25.4 ± 3.7	25.6 ± 5.5	25.4 ± 4.0	25.2 ± 4.1
MRI (kg)				
SM	31.8 ± 5.5	19.7 ± 3.4	28.8 ± 5.8	20.0 ± 3.4
Fat	18.4 ± 7.9	25.6 ± 12.4	—	—
Hip circumference (cm)	99.7 ± 7.5	101.2 ± 11.9	97.5 ± 7.9	99.6 ± 8.5
Waist circumference (cm)	87.6 ± 10.7	80.1 ± 13.4	88.3 ± 12.1	82.0 ± 11.1
White (%)	41.4	42.9	36.6	33.6
African American (%)	29	31.9	26.9	36.4
Hispanic (%)	15	14.5	16.1	14.5
Asian (%)	14.5	11.1	20.4	15.5

[1] BW, body weight; SM, skeletal muscle mass; —, MRI fat mass not measured in validation studies.
[2] Mean ± SD (all such values).

Methods

MRI

Whole-body multislice MRI (1.5-T Scanner: 6X Horizon; General Electric); 30–40 cross-sectional images; Sliceomatic software (TomoVision, Inc); assumed density of 1.04 kg/L for skeletal muscle; Reperted readings CVs of SM volume=1.4%, r=0.99.

Anthropometric measurements

- BW: to the nearest 0.1 kg by using a balance beam scale (Weight Tronix).
- Height: A wall-mounted stadiometer (Holtain), to the nearest 0.1 cm.
- Circumferences (waist, hips, midarm, midthigh): a heavy-duty inelastic plastic fiber tape measure (Gulick II Tape Measure; Fischer Scientific)

Statistical analysis

Multiple linear regressions generated equations separately for men and women:

Y: MRI-estimated Skeletal Muscle Mass

X: Age, weight, height, and hip, waist, thigh, arm, and calf circumferences

Stepwise analysis for the following sets of independent variables:

(1) age, BW, height, hip, and waist;

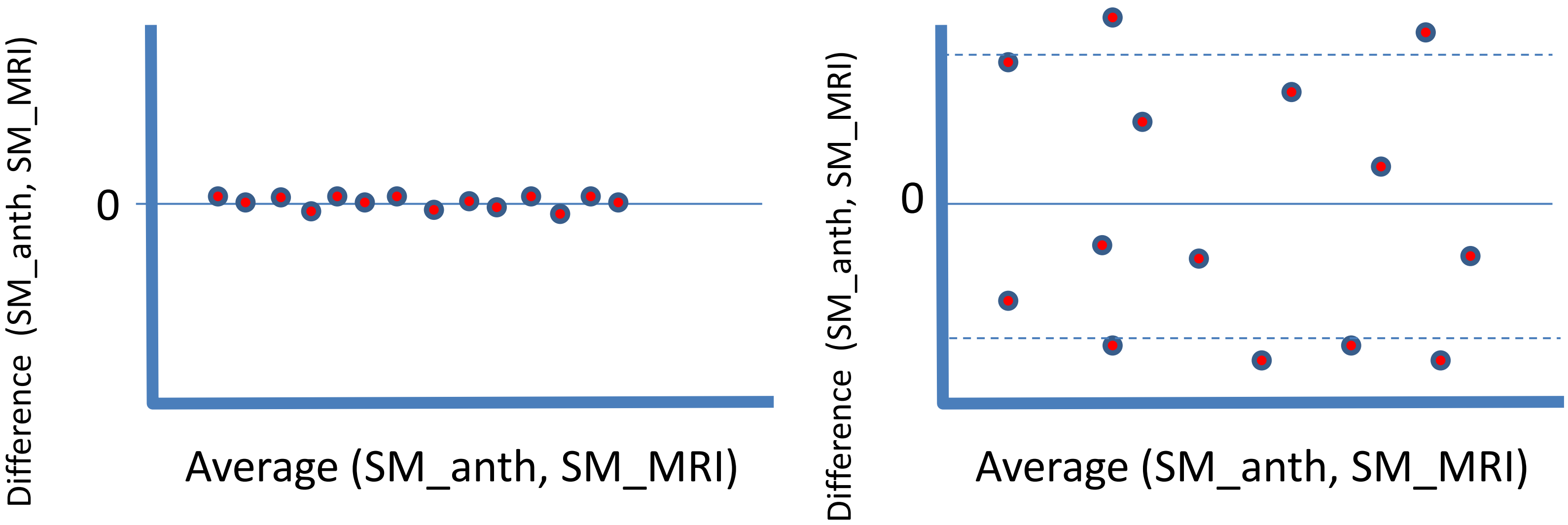
(2) age, BW, height, hip, waist, and midthigh;

(3) age, BW, height, hip, waist, midthigh, and midarm;

(4) age, BW, height, hip, waist, midthigh, midarm, and midcalf.

The effect of the variable “race” was investigated by ANCOVA

Bland-Altman plots (e.g., Altman DG, Bland JM (1983). "Measurement in medicine: the analysis of method comparison studies". *The Statistician* 32: 307–317.)



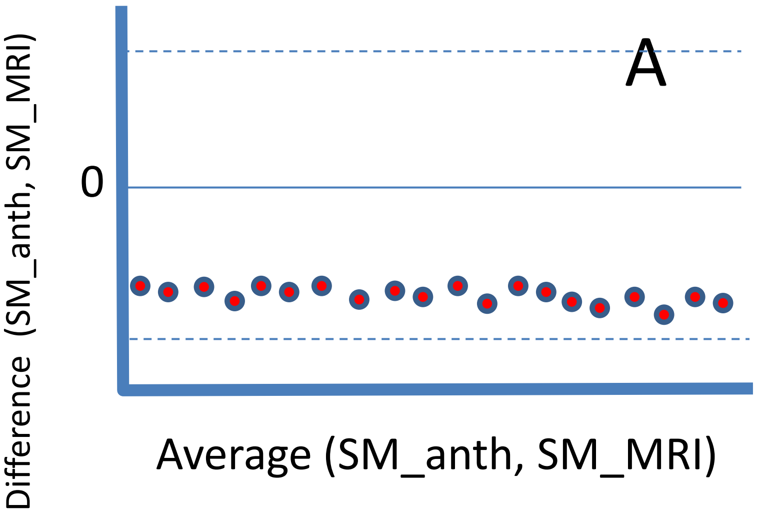
SM_Anth, validated by SM_MRI

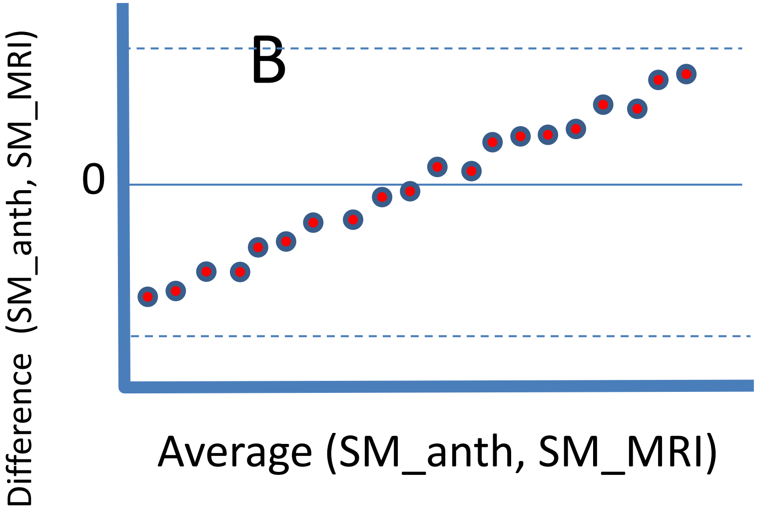
Systematic Errors

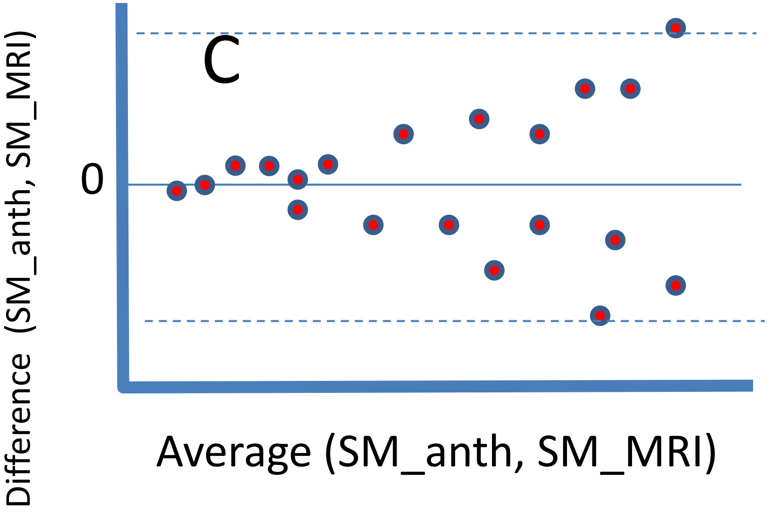
A: Underestimation

B: Underestimation in the lower range and overestimation in the higher range

C: More deviation in the higher range







Results: Deviation Study

Table 2: Bivariate regression between MRI SM and anthropometric and demographic variable

TABLE 2

Explained variance (R^2) in MRI whole-body skeletal muscle mass from linear regressions in the derivation study

Variable	R^2 Men		R^2 Women
		%	
Age	5.2		1.9
Body weight	53.9		38.8
Height	22.3		30.4
BMI	31.4		18.8
Race[1]	15.7	>	15.3
Waist circumference	11.6		16.7
Hip circumference	27.9		22.6
Midarm circumference	51.6		25.1
Midthigh circumference	36.9		27.7
Midcalf circumference	44.5		13.2

[1] Race included 4 categories as defined among the US population: white, African American, Asian, and Hispanic.

Results: Deviation Study

Table 3: Bivariate regression between MRI SM and anthropometric and demographic variable

TABLE 3
Prediction equations derived from stepwise regression analyses to estimate whole-body SM as measured by using MRI[1]

	Prediction equations	R^2 No race	R^2 Including race
		%	
Men			
PE1m[2]	MRI (SM) = 39.5 + 0.665 BW (kg) − 0.185 waist (cm) − 0.418 hip (cm) − 0.0805 age (y)	76	77.1[3]
PE2m	MRI (SM) = 38.4 + 0.581 BW (kg) − 0.194 waist (cm) − 0.387 hip (cm) − 0.0738 age (y) − 0.0222 Ht (cm) + 0.279 midarm (cm)	75.8	76.2
PE3m	MRI (SM) = 5.4 + 0.355 BW (kg) − 0.406 hip (cm) − 0.108 age (y) + 0.0998 Ht (cm) + 0.410 midarm (cm) + 0.299 midcalf (cm)	75.6	76.0
PE4m	MRI (SM) = 40.0 + 0.710 BW (kg) − 0.394 hip (cm) − 0.294 waist (cm)	73.0	74.1
Women			
PE1w[4]	MRI (SM) = 2.89 + 0.255 BW (kg) − 0.175 hip (cm) − 0.0384 age (y) + 0.118 Ht (cm)	58	61.5[5]
PE2w	MRI (SM) = −1.51 + 0.219 BW (kg) − 0.217 hip (cm) − 0.0252 age (y) + 0.136 Ht (cm) + 0.133 midthigh (cm)	57.5	60.0
PE3w	MRI (SM) = −4.33 + 0.214 BW (kg) − 0.231 hip (cm) + 0.153 Ht (cm) + 0.148 midthigh (cm)	56.3	58.0

[1] BW, body weight; Ht, height; PE1m, prediction equation 1 for men; PE2m, prediction equation 2 for men; PE3m, prediction equation 3 for men; PE4m, prediction equation 4 for men; PE1w, prediction equation 1 for women; PE2w, prediction equation 2 for women; PE3w, prediction equation 3 for women; SM, skeletal muscle mass.

[2] Prediction equation chosen for further analysis.

[3] Prediction equation: MRI = 38.809 + 0.62855 BW (kg) − 0.17843 waist (cm) − 0.38782 hip (cm) − 0.08351 age (y) − 1.13176 (Asian) + 0.56004 (African American) + 0.21902 (Hispanic) − 0.3527 (white).

[4] Prediction equation chosen for further analysis.

[5] Prediction equation: MRI = 3.995 + 0.22249 BW (kg) − 0.15890 hip (cm) − 0.045317 age (y) + 0.11523 Ht (cm) − 0.79309 (Asian) + 1.34820 (African American) − 0.50311 (Hispanic) + 0.052003 (white).

Equations derived in the present study

Women

SM (kg) = 2.89 + 0.255 BW (kg) - 0.175 hip (cm) - 0.0384 age (y) + 0.118 Ht (cm)

Men

SM (kg) = 39.5 + 0.665 BW (kg) - 0.185 waist (cm) - 0.418 hip (cm) - 0.0805 age (y)

Equations derived in Lee's study

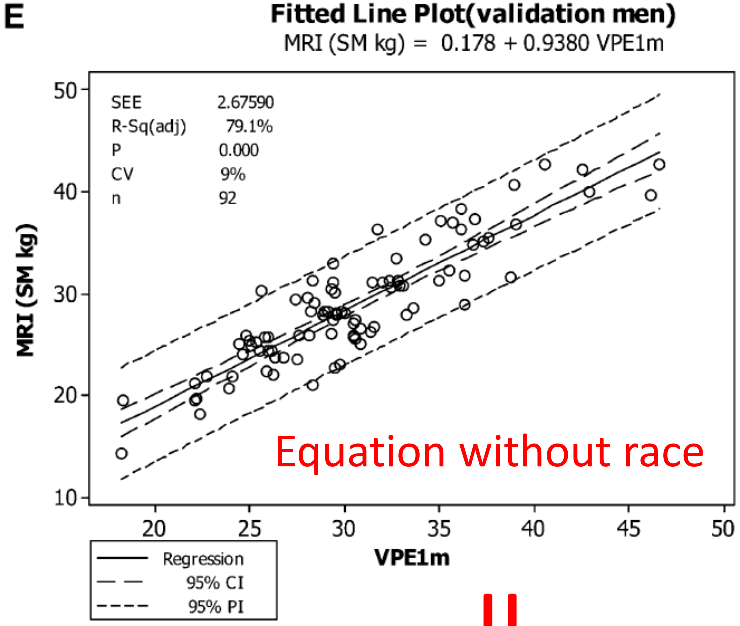
SM (kg) =0.244 × body weight (BW; kg) + 7.80 × height (m) - 0.098 × age (y) + 6.6 × sex + race - 3.3.

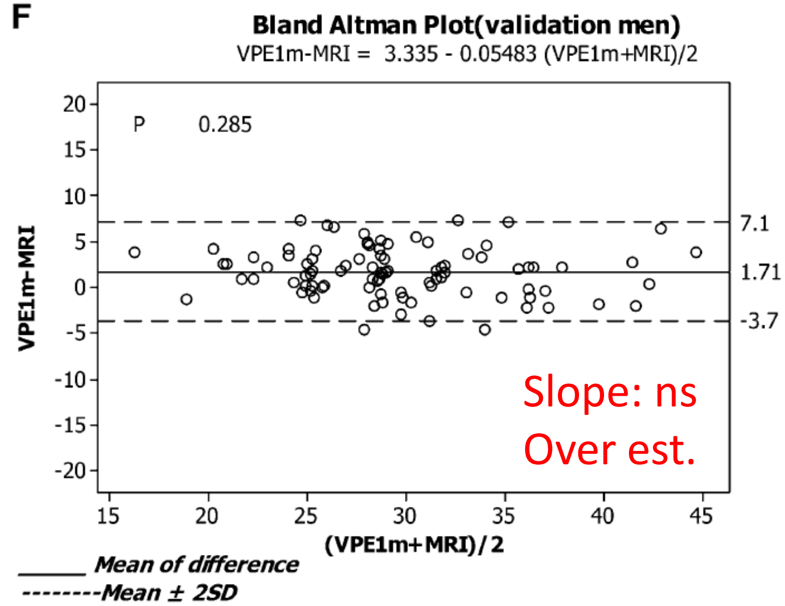
Results of validation study

FIGURE 1. Men: Panels A, C, E, G, and I show scatterplots of MRI-measured SM values (y-axis) against estimated SM values from prediction equations, whereas panels B, D, F, H, and J show Bland-Altman plots of difference between predicted and MRI-measured SM values (y-axis) against their mean (x-axis). Plots A and B and C and D represent results from the derivation of our PE without race (PE1m) and with race (PE1Rm), respectively. Plots E and F and G and H represent results from the validation of our equation without race (VPE1m) and with race (VPE1Rm), respectively. Plots I and J represent the validation of Lee et al's equation (11) (VPELm). For the plots with no significant slope, Bland-Altman plots show the mean difference with limits of agreement around the mean difference as a test for bias (mean difference significantly different from 0) with the use of the 1-sample t test. For the plots with a significant slope, Bland-Altman plots show the PI around the regression line. P values represent a test of significance of the slope. PE, prediction equation; PI, prediction interval; SM, skeletal muscle mass.

Men, Validation sample, the present equation

> Deviation sample





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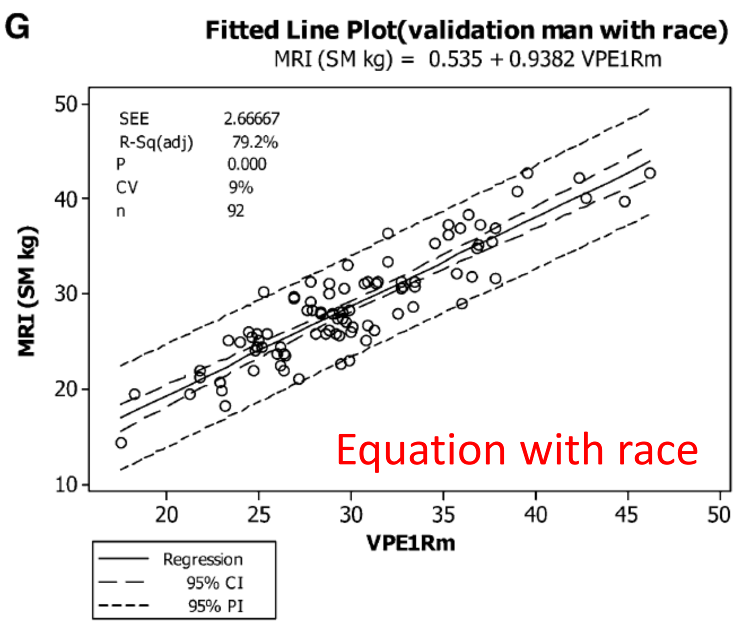
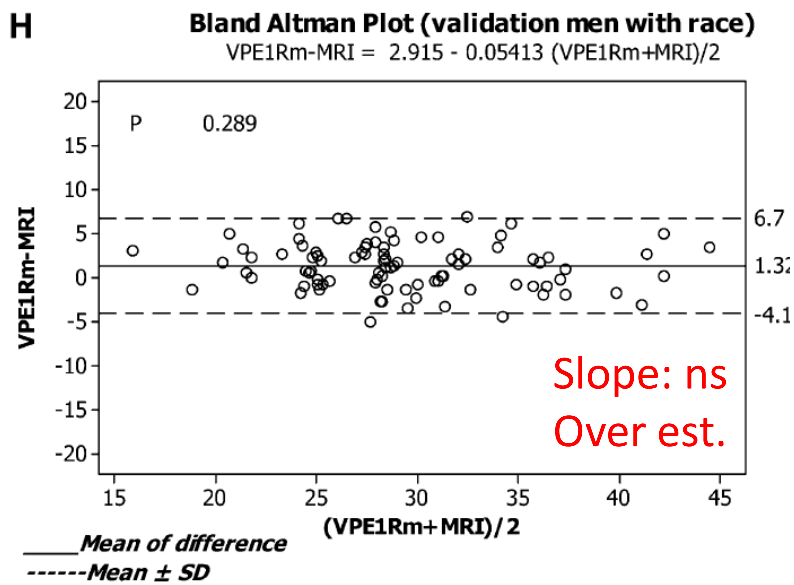
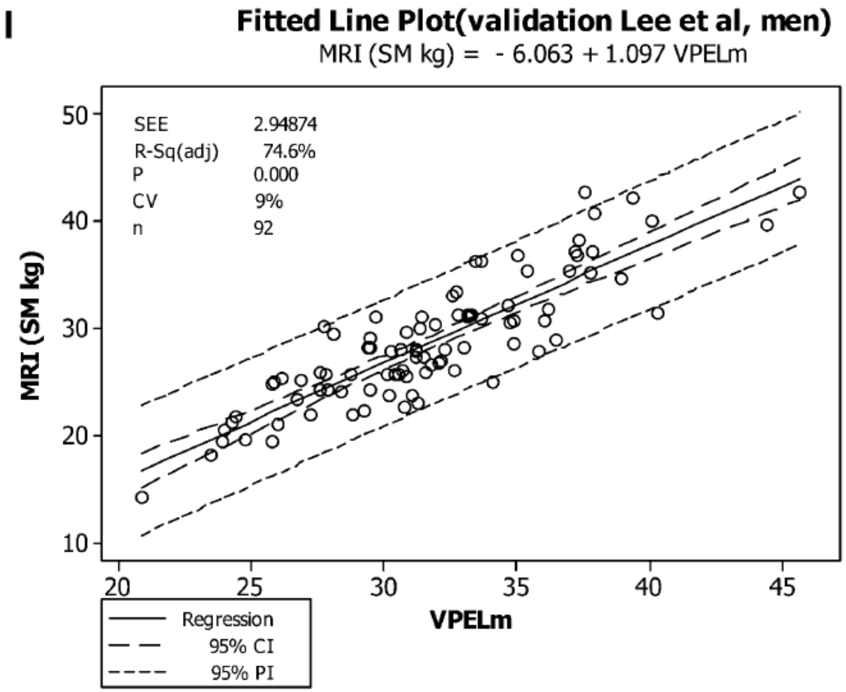
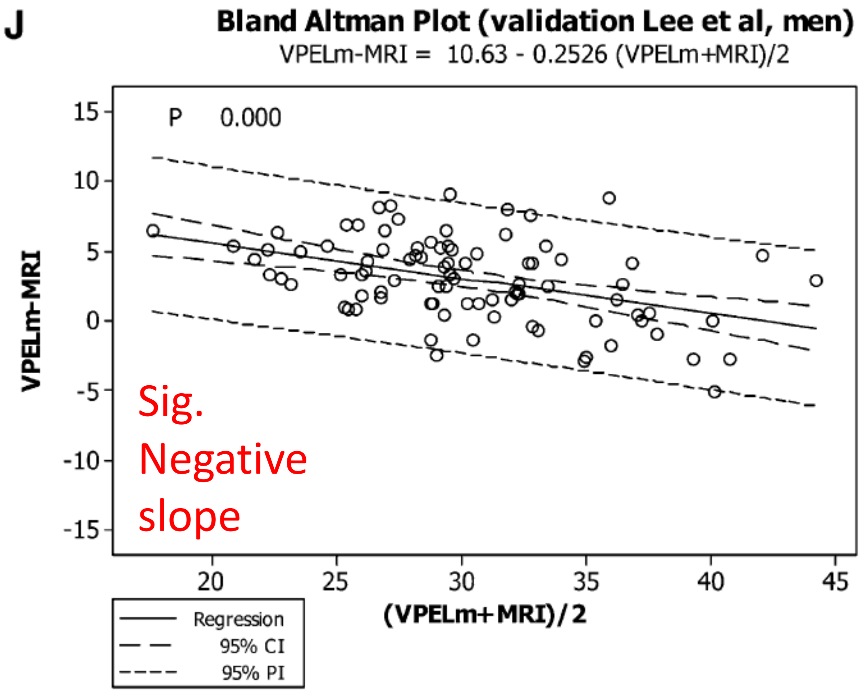




Men, Validation sample, Lee's equation





Lower R2 than the authors' equation

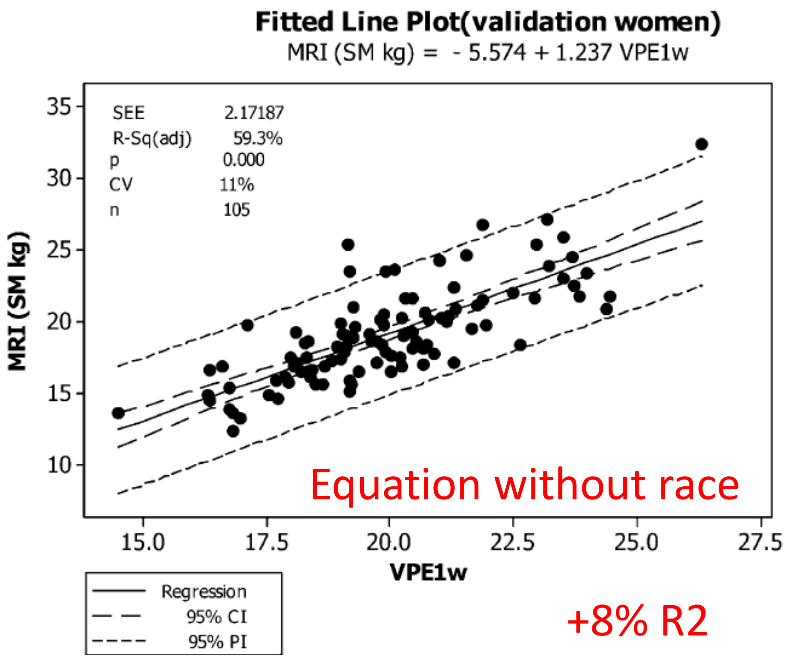
Results of validation study

FIGURE 2. Women: Panels A, C, E, G, I, and K show scatterplots of MRI-measured SM values (y-axis) against estimated SM values from prediction equations, whereas panels B, D, F, H, J, and L show Bland-Altman plots of difference between predicted and MRI-measured SM values (y-axis) against their mean (x-axis). Plots A and B and C and D represent results from the derivation of our PE without race (PE1w) and with race (PE1Rw), respectively. Plots E and F and G and H represent results from the validation of our equation without race (VPE1w) and with race (VPE1Rw), respectively. Plots I and J represent validation of Lee et al's equation (11) for women (VPELw), and plots K and L represent validation of Lee et al's equation for men and women combined (VPELm1w). For the plots with no significant slope, Bland-Altman plots show the mean difference with limits of agreement around the mean difference as a test for bias (mean difference significantly different from 0) with the use of the one-sample t test. For the plots with a significant slope, Bland-Altman plots show the PI around the regression line. P values represent a test of significance of the slope. PE, prediction equation; PI, prediction interval; SM, skeletal muscle mass.

Women, validation sample, the present equation

> Deviation sample

E



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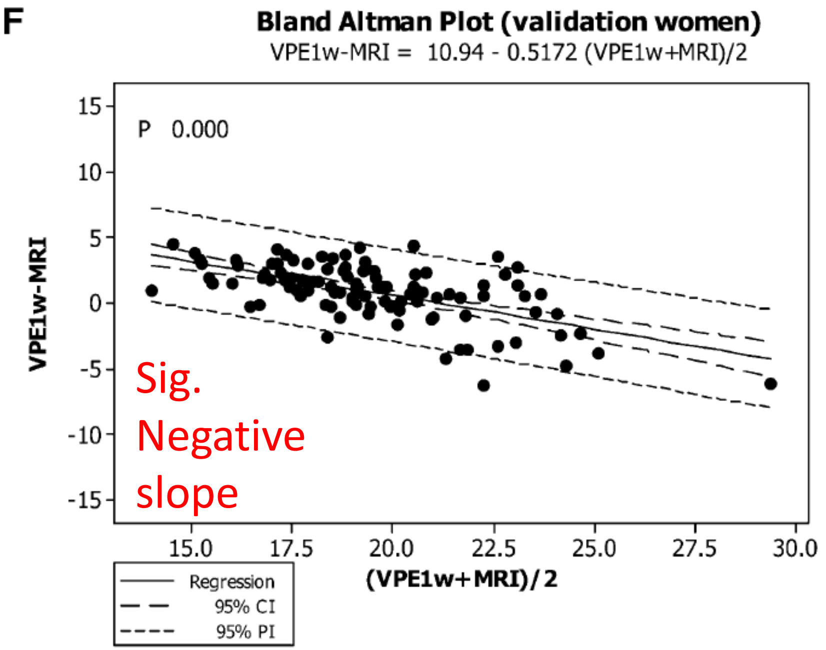

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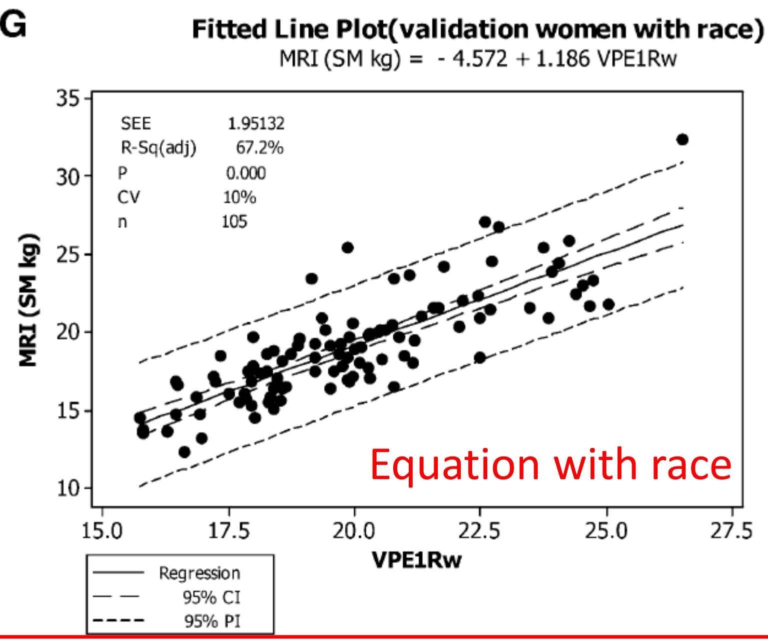

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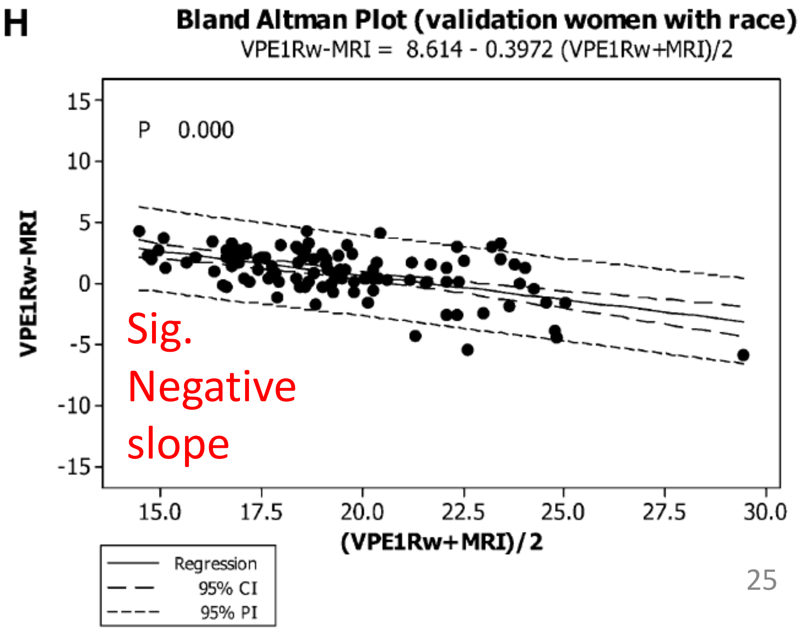
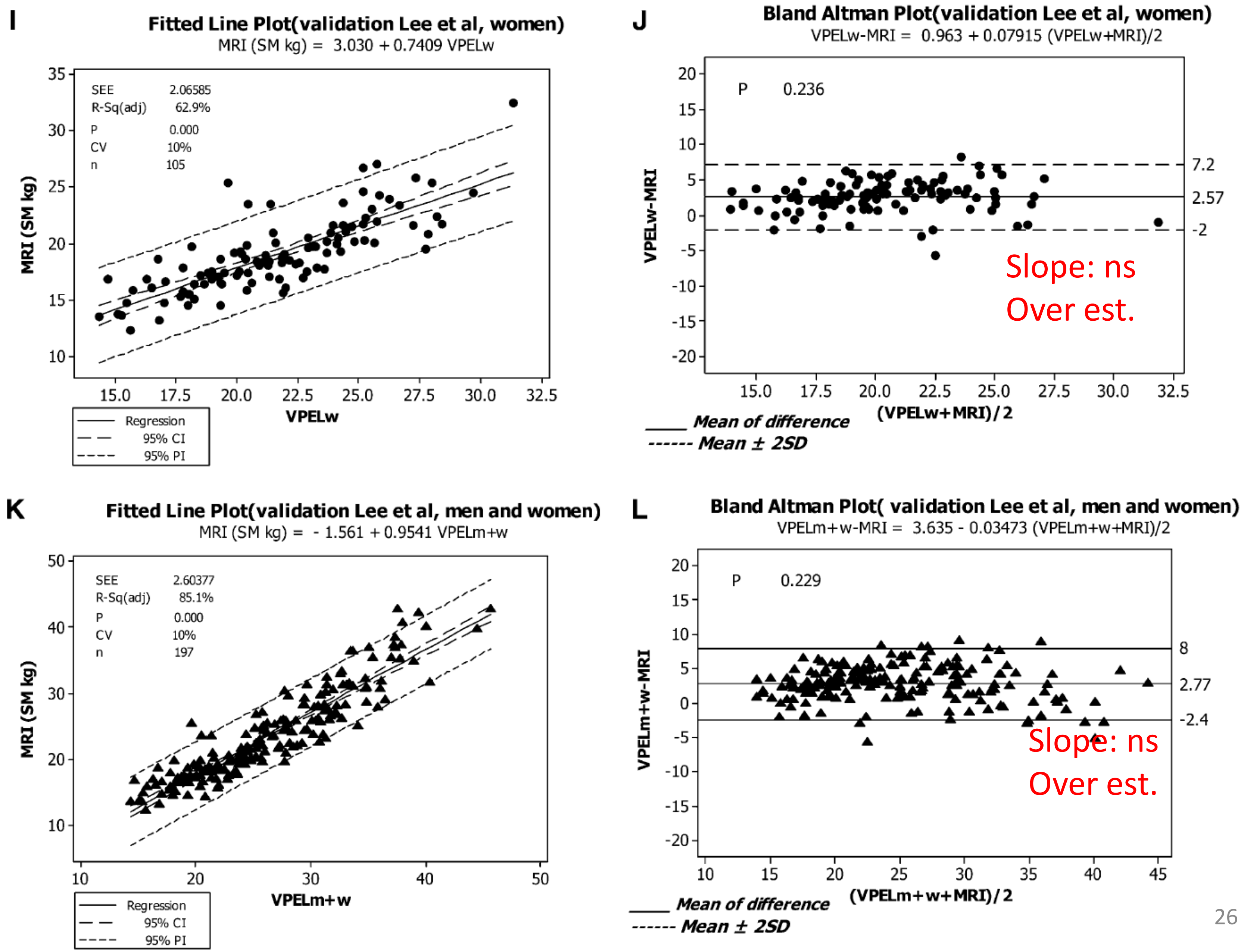


Lower R2 than the authors' equation

Women/Men and Women, Validation sample, Lee's equation



Equations derived in the present study

Men

SM (kg) = 2.89 + 0.255 BW (kg) - 0.175 hip (cm) - 0.0384 age (y) + 0.118 Ht (cm)

Women

SM (kg) = 39.5 + 0.665 BW (kg) - 0.185 waist (cm) - 0.418 hip (cm) - 0.0805 age (y)

Equations derived in Lee's study

SM (kg) =0.244 × body weight (BW; kg) + 7.80 × height (m) - 0.098 ×age (y) + 6.6 × sex + race - 3.3.

TABLE 4
Derivation and validation analysis summary of present prediction equations and summary of validation of Lee et al (11) prediction equations for men and women separately and combined[1]

Equation	Men				Women			
	R^2	SEE	CV for mean	Difference[2]	R^2	SEE	CV for mean	Difference[2]
		kg	*%*	*kg*		*kg*	*%*	*kg*
Derivation								
Prediction equation 1	0.76	2.7	8	NA	0.58	2.2	11	NA
Prediction equation 1 with race	0.77	2.6	8	NA	0.61	2.1	10	NA
Validation								
Prediction equation 1	0.79	2.7	9	1.7 ± 2.7	0.59	2.2	11	NA
Prediction equation 1 with race	0.79	2.7	9	1.3 ± 2.7	0.67	2.0	10	NA
Prediction equation of Lee et al (11)	0.75	2.9	9	NA	0.63	2.1	10	2.6 ± 2.3
Men and women combined								
Prediction equation of Lee et al (11), men + women	0.85	2.6	10			2.8 ± 2.6		

[1] R^2, correlation evaluating the variability explained by the model; SEE, measures how different the actual value is from the prediction line, sum of square error; CV, the ratio of the SEE to the mean of the dependent variable and measures the relative closeness of the prediction to the actual value. NA, not applicable.

[2] Mean (±SD) difference between SM values as predicted by using the equation and observed MRI values for skeletal muscle mass ± SD; equations with slope (significant relation between mean and difference) were not applicable.

1. Inclusion of the term of race in the equations?
2. Developing the equations for men and women separately?

Discussion

- Advantage of MRI the evaluation of whole-body muscle mass
- Limitation of relating regional muscle mass to whole-body muscle mass

Inclusion of the term of race in the equations?

The authors say:

"incorporating a term for race increased R2 by only 0.1% in men and by 7.9% in women, indicating that most of the variance associated with race was accounted for by simple anthropometric measurements, especially in men"

"attributing race to individuals in mixed populations can be potentially difficult and misleading, so there is a practical advantages for equations that do not require this term"

Developing the equations for men and women separately?

The authors say:

"the prediction of SM was substantially less accurate for women than for men. This was also the case for the published equations to predict lean body mass and SM"

"The sex difference probably reflects the much smaller muscle mass of women and a greater range of variability in fat mass"

"Combining men and women (in the equations) will increase the number of samples and the range of body composition, which contributes to heighten R2 but without improving the prediction of individual SM, as shown by CV and SEE (Fig 2: K, L)"

The best equations had hip circumference as a variable

Waist:hip ratio → risk of CVDs (cross sectional study)

W:H ratio is not a useful indicator of total body fat or fat distribution (Tothill et al., 1996; Burton et al., 2013)

W:H ratio increase among the people who have reduced H circumference (= SM) (due to illness or inactivity)

Limitations

- Applicability to group of subjects with restricted ranges of age, BMI or of a single racial type. e.g., obese, elderly groups, Asian and pacific Islanders
- Insufficient predictive power for clinical use or among individuals

Conclusion

- Anthropometric prediction equations for whole-body muscle mass
- Greater predictive power and less error in men than in women
- Equations included the term of hip circumference
- Equations will be useful for research/survey within mixed populations without the need to adjust for race