

Indexation of left ventricular mass in adults with a novel approximation for fat-free mass

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Background Indexation to fat-free mass (FFM) seems to be the best option for adjusting left ventricular (LV) mass. However, measurements of FFM are frequently not available.

Objectives To define the relation of FFM with commonly available anthropometric measures in order to derive an approximation formula of FFM that can be used for valid indexation of LV mass.

Subjects and methods A total of 1371 subjects from a community survey were examined by echocardiography to measure LV mass and by bioelectrical impedance analyses (BIA) for the determination of FFM. An approximation of FFM was generated in a healthy subgroup of 213 men and 291 women by non-linear regression techniques.

Results Compared with body height, height^{2.0}, height^{2.7}, (the superscripts following weight and height are raised powers used as a more appropriate method for indexing LV mass) or body surface area, FFM measured by BIA in the healthy subgroups was best predicted by gender-specific equations of the form:

$$\begin{aligned}\text{FFM} &= 5.1 \times \text{height}^{1.14} \times \text{weight}^{0.41} \text{ for men and} \\ \text{FFM} &= 5.34 \times \text{height}^{1.47} \times \text{weight}^{0.33} \text{ for women.}\end{aligned}$$

In the healthy reference group, indexation of LV mass for BIA-determined FFM and approximated FFM (FFMa), respectively, equally eliminated gender differences in LV mass and markedly reduced the influence of body mass index without affecting the associations between blood

pressure and LV mass. Validation of FFMa in two independent population-based samples, aged 52 to 67 years, of the same source population confirmed that LV mass indexed by FFMa produced results that were highly consistent with those obtained with indexation by BIA-determined FFM.

Conclusions We propose a novel approximation of FFM based on exponentials of body height and weight. It performed well in the indexation of LV mass in middle-aged men and women of this study. Evaluation of the equation in other populations should be awaited before its use is recommended in situations where direct determination of FFM is not possible. *J Hypertens* 19:135–142 © 2001 Lippincott Williams & Wilkins.

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Introduction

Increased left ventricular (LV) mass is an independent risk factor for congestive heart failure, myocardial infarction, cardiovascular death and total mortality [1–3]. To define normal values for LV mass, it is necessary to account for differences in body size. However, the methods used for indexing LV mass in the clinical setting are still controversial. Because indexation to body surface area (BSA) was suspected to underestimate the prevalence of LV hypertrophy associated with obesity, indexation to height has been proposed as the preferable method [4]. Furthermore, to account for

differences in dimensions between LV mass (three-dimensional) and height (one-dimensional), an allometric approach was used, and height raised to the power of 2.7 [5] or 2.0 [6] have been suggested as more appropriate methods for indexing LV mass. On the other hand, none of the investigations leading to the above recommendations had measurements of fat-free mass (FFM) available. Recent work, however, seems to suggest that accounting for FFM is the optimal method of LV mass indexation [5,7–10]. For example, indexation for FFM eliminates gender differences in LV mass indicating that heart sizes in men and women closely

reflect the metabolic demands of the fat-free body compartments rather than hormonal or genetic determinations [9–12].

Body impedance analysis (BIA) provides a validated [13–16] and easily applicable method for measuring fat-free mass. In this report, we examine the relationship of BIA-determined fat-free mass with body height and weight, and we derive a simple approximation equation, which we propose to use for LV mass indexation when BIA or other technical procedures of FFM determination are not available.

Methods

Study population

The third survey of the MONICA Augsburg Project took place from October 1994 to June 1995. The Augsburg Project is part of the international collaborative WHO MONICA Study (Monitoring of Trends and Determinants of Cardiovascular Disease) [17]. The study design, sampling frame and data collection have been described in detail elsewhere [17–20]. Briefly, 6640 individuals, aged 25 to 74 years, were randomly sampled by a two-stage, age–sex stratified cluster sampling from the population registry. A total of 4856 men and women (response rate 74.9%) participated. For logistic reasons, only 2376 participants residing within or close to the city of Augsburg were offered an additional echocardiographic examination. The 826 men and 852 women who agreed to be examined had the same sex distribution as the non-responders but they differed in that they were younger on average by 3.2 years; their BMI was lower by 0.7 kg/m²; and their systolic blood pressure was lower by 3.0 mmHg ($P < 0.001$).

After a detailed interview, body height and weight were measured in light clothing. Body mass index (BMI) was computed as weight divided by height squared (kg/m²). Body surface area (BSA) was computed according to the formula of Dubois [21]. Resting blood pressure was measured after subjects had been in a sitting position for a minimum of 30 min, using a random zero sphygmomanometer. Blood pressure was read three times in the right arm under the standardized conditions of the MONICA protocol [22] and the mean of the second and third measurement was used for this study.

Bioelectrical impedance analysis

Fat-free mass was determined by measurement of bioelectrical impedance (BIA) with a Body Composition Analyzer TVI-10 (Danziger Medical Technology, Heidelberg, Germany). Measurements were carried out under highly standardized conditions with all subjects being in a supine position [23,24]. All measurements were performed using an alternating current with a frequency of 50 kHz and an amplitude of 800 mA. A

tetrapolar placement of electrodes was used [14]. The method has been validated in former studies against a variety of other more laborious techniques [13–15]. Studies in children and adults have shown that BIA can be validly applied to assess body composition in epidemiological studies if proper consideration is given to population-specific characteristics [25]. As reported before [9,26], we used a formula derived by Heitmann [23,24]. Analysis of the intra- and inter-observer variability of BIA measurements indicated a high reliability with coefficients of variation consistently below 1% [23]. Body fat was calculated after subtraction of FFM from total body weight in kilograms.

Echocardiographic measurements

Two-dimensional guided M-mode echocardiograms were obtained by two expert sonographers using the Sonos 1500 of Hewlett Packard Inc. (Andover, Massachusetts, USA) M-mode tracings were recorded on stripchart paper at 50 mm/s. All M-mode tracings were analyzed by a single cardiologist who was blinded for clinical data. All measurements were made according to the Penn convention and left ventricular mass was calculated by the formula described by Devereux and Reichek [27]. The rank correlation for 144 duplicate measurements of the two sonographers was 0.91 and there was a mean difference (systematic bias) between observers of 0.9 g with a standard deviation of 10.8 g. Only M-mode tracings with optimal visualization of left ventricular inferences were allowed for this study. For the 825 men and 850 women with a complete examination, the echocardiographic recordings of 161 men and 110 women were considered as technically not adequate.

Three subsets of subjects were defined for the present investigation: firstly, to avoid unphysiological influences on the relationship between fat-free mass and LV shape, similarly to previous studies [5–7], a healthy reference group was generated. Secondly, to evaluate the performance of the approximation equations generated from the reference sample in unselected middle-aged adults, we applied them in two independent samples from the Augsburg study population.

Healthy reference sample

As previously described [26], a healthy reference group was generated by excluding all participants with evidence of cardiopulmonary disease by history, physical examination or electrocardiogram, echocardiographic evidence of heart valve disease, or a blood pressure ≥ 140 mmHg systolic and/or ≥ 90 mmHg diastolic. Furthermore, subjects taking medications for cardiopulmonary disease or being obese according to the criteria of the National Institutes of Health Consensus Development Panel [28] were excluded. The resulting

healthy reference group consisted of 213 men and 291 women.

Independent validation samples

Each sample encompassed men and women in the age range 52 to 67 years. Sample I consisted of all subjects fulfilling the age criteria, irrespective of disease and treatment status, of the echocardiographic substudy of the 1994/95 MONICA Augsburg survey from which the healthy reference group had also been selected (207 men and 231 women). Sample II (227 men and 293 women) were participants of the 1994 echocardiography reexamination of a part of the MONICA Augsburg survey of 1984/85 [29]. While BIA measurements of FFM were available for sample I, none had been done for sample II.

Statistical analyses

Non-linear regression analysis was performed to approximate BIA-determined FFM in the healthy reference group. Initially, we assessed which allometric power of height was most equivalent to fat-free mass by solving the following equation:

$$\text{FFMa}_1 = \alpha \times \text{height}^\beta,$$

where α is a regression coefficient reflecting the quantitative relation between variables and β is the exponent of height that produces the best fit of the data. Subsequently, a second equation was resolved taking height as well as weight into account:

$$\text{FFMa}_2 = \alpha \times \text{height}^\beta \times \text{weight}^\gamma.$$

All analyses were run separately for men and women. The non-linear regression analysis computes least square estimates of the parameters by an iterative computer technique so that the sum of squares of the deviations about the regression line reaches a minimum. The scatter of residuals of the regression between FFM and height, $\text{height}^{2.0}$, $\text{height}^{2.7}$, BSA, FFMa_1 and FFMa_2 was analyzed graphically. This plot indicates whether homoscedastic dispersion occurred about the zero line and for which approximation the least dispersion was achieved. The non-linear regressions were performed by the multivariant secant (DUD) method in the PROC NLIN program of the SAS[®] statistical analysis package [29].

Spearman correlation analyses assessed the congruity of ranking orders between the LV mass/FFM ratio as the reference method and unindexed as well as differently indexed LV mass in the healthy subgroup. Pearson correlations with body mass index and systolic blood pressure were used to evaluate the impacts of various indexations of LV mass. Finally, the averages of

differently indexed LV mass were compared between men and women using multivariate regression analyses controlling for age, BMI and systolic blood pressure.

The impacts of novel and established indexations on gender differences in LV mass were finally evaluated in samples I and II. Multivariate analyses allowed for comparisons of men and women independent of the effects of age, BMI and systolic blood pressure. All analyses were carried out with the SAS[®] System for Windows Release 6.11 (Cary, North Carolina, USA).

Results

Characteristics of healthy referents

The healthy reference group was substantially younger, taller, less heavy and with lower systolic and diastolic blood pressures than subjects in samples I and II. However, the values for FFM did not differ between the healthy reference group and sample I (Table 1).

Approximation of fat-free mass

The equations obtained by non-linear regression analysis that provided the best approximation of FFM taking only height into consideration were:

$$\text{FFMa}_1 = 20.5 \times \text{height}^{1.86} \text{ for men and}$$

$$\text{FFMa}_1 = 16.5 \times \text{height}^{1.94} \text{ for women.}$$

By simultaneously using body weight and body height to approximate FFM, we attained the following equations:

$$\text{FFMa}_2 = 5.1 \times \text{height}^{1.14} \times \text{weight}^{0.41} \text{ for men and}$$

$$\text{FFMa}_2 = 5.34 \times \text{height}^{1.47} \times \text{weight}^{0.33} \text{ for women.}$$

The computed values for FFMa_1 and FFMa_2 in each sample are also shown in Table 1. The scatter of residuals of the regression between FFM and height, $\text{height}^{2.0}$, $\text{height}^{2.7}$, BSA, FFMa_1 and FFMa_2 is shown in Figure 1. It indicates that FFM is only insufficiently predicted by BSA and height, regardless of the allometric signal applied. Plotting residuals against FFMa_1 resulted in a more stable, i.e. homoscedastic dispersion about the zero line while the least dispersion was observed with FFMa_2 . Spearman rank correlation coefficients varied accordingly: they were highest with FFMa_2 ($r = 0.985$) and less with FFMa_1 ($r = 0.965$) or with height ($r = 0.90$), $\text{height}^{2.0}$ ($r = 0.90$), $\text{height}^{2.7}$ ($r = 0.90$), and BSA ($r = 0.94$).

Table 2 shows that indexing LV mass to FFM and to FFMa_2 diminished the correlation with BMI by about the same amount. Indexation to BSA but not to FFMa_1 had similar impacts. The difference of correlation coef-

Table 1 Characteristics (mean values and standard deviations) of the healthy reference group, and samples I and II

	Healthy subgroup		Sample I		Sample II	
	Men (n = 213)	Women (n = 291)	Men (n = 207)	Women (n = 222)	Men (n = 227)	Women (n = 293)
	Mean $\pm$ SD		Mean $\pm$ SD		Mean $\pm$ SD	
Age (years)	42 $\pm$ 12	42 $\pm$ 12	59 $\pm$ 5 [†]	59 $\pm$ 5 [†]	58 $\pm$ 4 [†]	58 $\pm$ 4 [†]
Height (cm)	176 $\pm$ 6	164 $\pm$ 6	173 $\pm$ 6 [†]	160 $\pm$ 6 [†]	173 $\pm$ 6 [†]	160 $\pm$ 6 [†]
Weight (kg)	76 $\pm$ 8	62 $\pm$ 7	84 $\pm$ 11 [†]	71 $\pm$ 12 [†]	82 $\pm$ 11 [†]	69 $\pm$ 11 [†]
Body mass index (kg/m ²)	24.6 $\pm$ 2	23.0 $\pm$ 2	27.9 $\pm$ 3	27.8 $\pm$ 4 [†]	27.3 $\pm$ 3 [†]	27.1 $\pm$ 4 [†]
Fat-free mass (FFM) (kg/m ²)	58.9 $\pm$ 5	43.2 $\pm$ 4	59.2 $\pm$ 5	43.3 $\pm$ 4	—	—
Predicted FFMa ₁ (kg/m ²)	58.9 $\pm$ 5	43.0 $\pm$ 4	57.1 $\pm$ 5	41.3 $\pm$ 4	57.9 $\pm$ 5	42.9 $\pm$ 4
Predicted FFMa ₂ (kg/m ²)	57.6 $\pm$ 5	42.9 $\pm$ 4	57.6 $\pm$ 5	42.9 $\pm$ 4	56.9 $\pm$ 5	41.0 $\pm$ 5
Body surface area (m ²)	1.93 $\pm$ 0.1	1.67 $\pm$ 0.1	1.97 $\pm$ 0.1 [†]	1.74 $\pm$ 0.1 [†]	1.95 $\pm$ 0.1 [†]	1.72 $\pm$ 0.1 [†]
Systolic BP (mmHg)	124 $\pm$ 9	116 $\pm$ 11	141 $\pm$ 20 [†]	137 $\pm$ 20 [†]	147 $\pm$ 18 ^{*†}	146 $\pm$ 20 ^{*†}
Diastolic BP (mmHg)	77 $\pm$ 7	71 $\pm$ 8	84 $\pm$ 12 [†]	81 $\pm$ 10 [†]	92 $\pm$ 10 ^{*†}	90 $\pm$ 11 ^{*†}

$P < 0.001$ versus healthy subgroup; $^*P < 0.001$ sample II versus sample I; comparing men and women of the respective samples separately. FFM, fat-free mass; FFMa, approximate fat-free mass; BP, blood pressure; SD, standard deviation.

ficients to those obtained with traditional indexations was significant mostly at the 10% level only. On the other hand, the associations with systolic blood pressure were largely independent of the type of indexation.

Gender differences in relation to various methods of indexation

The healthy reference group

Table 3 demonstrates the large differences between men and women in unindexed LV mass (164 ± 2.3 versus 121 ± 1.9 g; $P < 0.0001$). The statistical significance of the differences persisted after indexing LV mass to height, height^{2.0}, height^{2.7}, or BSA. By contrast, correcting LV mass for FFM resulted in elimination of the gender differences. Similarly, indexing of LV mass to FFMa₁ as well as FFMa₂ eliminated the differences in heart size between men and women. Furthermore, the absolute values of LV mass indexed to FFM, FFMa₁, and FFMa₂ were very similar and not significantly different.

The two independent validation samples

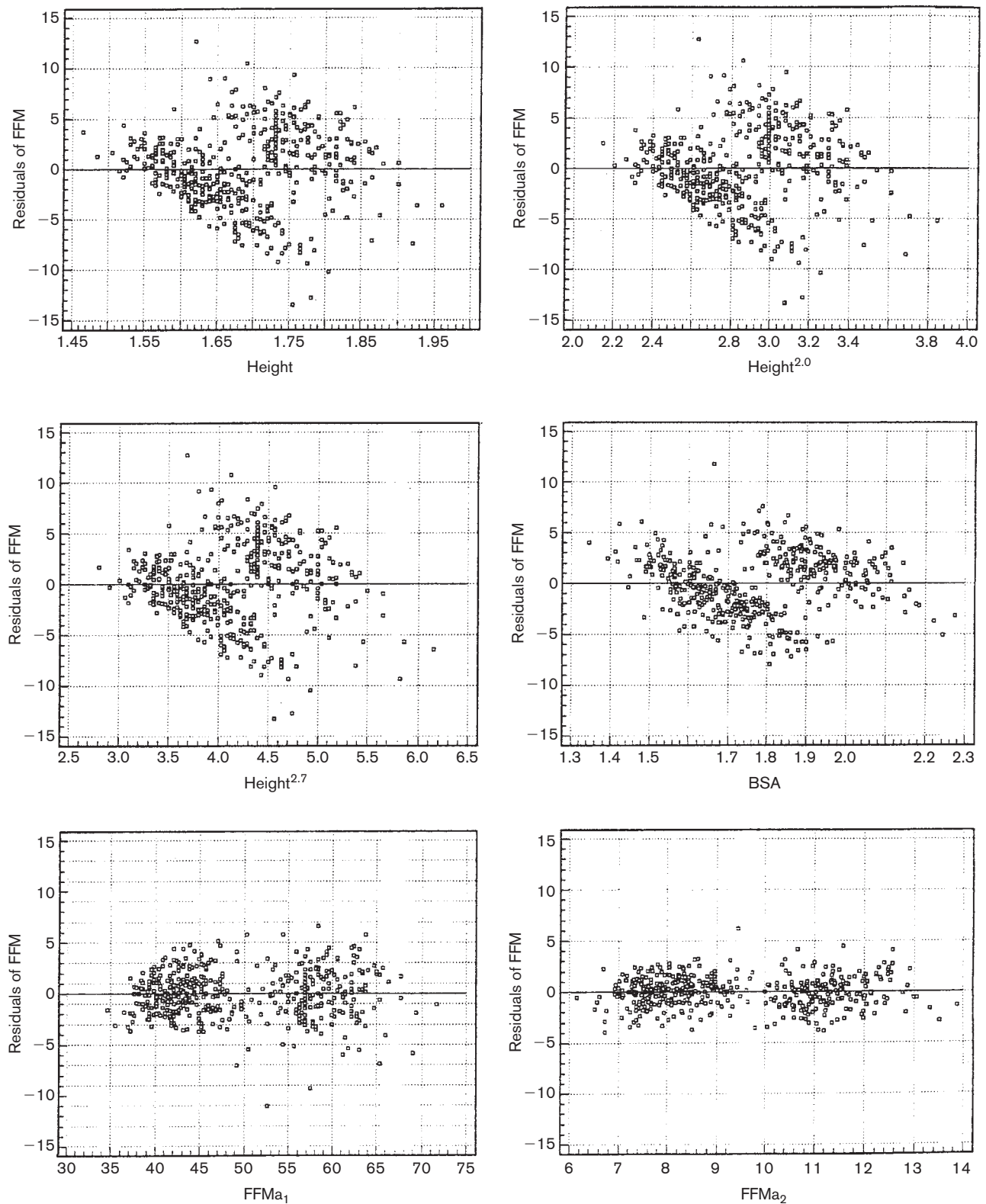
Despite the higher age of subjects in samples I and II, and irrespective of the inclusion of subjects with various risk factors and diseases, FFM, FFMa₁ and FFMa₂ produced consistent results regarding the reduction of gender differences displayed with other indexations (Table 4). A significant overindexation occurred with FFMa₁ in women. A comparison with measured FFM was not possible in sample II, however, application of the equations for FFMa₁ and FFMa₂ resulted in very similar values for indexed LV mass in comparison with sample I. An overindexation with FFMa₁ was also seen in women of sample II. The use of FFMa₂ produced results highly consistent with BIA-determined FFM (Table 4).

Discussion

Absolute LV mass is determined by age, gender, blood pressure and body stature. In order to be able to validly distinguish subjects with morbidly increased LV mass from those with physiological cardiac adaptation, it is necessary that LV mass is normalized to a measure of body size. To date, the problem was how to identify an appropriate variable or algorithm for indexing LV mass. It should, for example, not introduce a putative 'forgiveness of obesity', as was claimed for BSA-indexations [4]. On the other hand, one had to resolve the complexities of relating LV mass or body mass, i.e. three-dimensional objects, to strictly one-dimensional variables such as height. Hence, more sophisticated proposals of allometric signals were suggested [5–7]. More recently, fat-free mass has been suggested as the optimal method to normalize LV mass for body size and to account for the physiological adaptations of the heart in response to the rising metabolic demands of bigger human bodies [7,8,11].

In the present study FFM was determined by bioelectrical impedance analysis (BIA), a reliable, validated and easily applicable method [13,23,24]. In a recent report from this study involving the entire sample of 653 men and 718 women, differences in LV mass between men and women were completely eliminated after indexation for FFM [9] and resulted in identical criteria for the determination of LV hypertrophy [26]. The present analyses using approximated FFM values obtained from commonly available anthropometric variables confirmed this in healthy adults and in two independent samples of men and women aged 52 to 67 years that originated from the same source population. These consistent findings support our previously expressed view [9,26] that the variation in heart sizes

Fig. 1



Residuals of fat-free mass (FFM) after non-linear regressions of FFM on height, height^{2.0}, height^{2.7}, body surface area (BSA), approximate fat-free mass FFMa₁, and FFMa₂.

Table 2 Correlation of crude and indexed left ventricular mass with body mass index and systolic blood pressure

	Healthy subgroup		Sample I		Sample II	
	Men (n = 213)	Women (n = 291)	Men (n = 207)	Women (n = 222)	Men (n = 227)	Women (n = 293)
Coefficients of correlation with BMI						
LVM (g)	0.36	0.42	0.47	0.52	0.35	0.44
LVM/height (g/m)	0.38	0.44	0.47	0.54	0.36	0.47
LVM/height ^{2.0} (g/m ^{2.0})	0.40	0.45	0.47	0.55	0.36	0.49
LVM/height ^{2.7} (g/m ^{2.7})	0.40	0.46	0.46	0.56	0.36	0.50
LVM/BSA (g/m ²)	0.24* [‡]	0.30	0.32 [‡]	0.38 [‡]	0.20* [‡]	0.30 [‡]
LVM/FFM (g/kg)	0.25* [‡]	0.35	0.28 [‡]	0.38 [‡]	—	—
LVM/FFMa ₁ (g/kg)	0.40	0.45	0.47	0.55	0.36	0.49
LVM/FFMa ₂ (g/kg)	0.25* [‡]	0.35	0.33* [‡]	0.43	0.21* [‡]	0.36 [‡] *
Coefficients of correlation with systolic blood pressure						
LVM (g)	0.16	0.25	0.31	0.32	0.31	0.43
LVM/height (g/m)	0.17	0.26	0.33	0.32	0.31	0.44
LVM/height ^{2.0} (g/m ^{2.0})	0.17	0.26	0.34	0.33	0.31	0.46
LVM/height ^{2.7} (g/m ^{2.7})	0.17	0.25	0.35	0.33	0.31	0.46
LVM/BSA (g/m ²)	0.17	0.24	0.33	0.33	0.31	0.42
LVM/FFM (g/kg)	0.21	0.26	0.34	0.34	—	—
LVM/FFMa ₁ (g/kg)	0.17	0.26	0.34	0.33	0.31	0.45
LVM/FFMa ₂ (g/kg)	0.17	0.24	0.34	0.33	0.29	0.43

Statistically significant differences between correlation coefficients: $P < 0.1$ versus LVM/height; * $P < 0.1$ versus LVM/height^{2.0} or LVM/height^{2.7}.
[‡] $P < 0.05$ versus LVM/height; [‡] $P < 0.05$ versus LVM/height^{2.0} or LVM/height^{2.7}. BMI, body mass index; LVM, left ventricular mass; BSA, body surface area; FFM, fat-free mass; FFMa₁, equation including height only; FFMa₂, equation including height and weight.

Table 3 Mean values (± standard errors) of LV mass using different indexation methods in the healthy reference group. Gender differences are expressed as percentage of mean values

	Men (n = 213)	Women (n = 291)	Gender difference	P-value
LVM (g)	164 ± 2.3	121 ± 1.9	26.2%	0.0001
LVM/height (g/m)	93.0 ± 1.3	74.0 ± 1.1	20.4%	0.0001
LVM/height ^{2.0} (g/m ^{2.0})	52.7 ± 0.8	45.2 ± 0.6	14.2%	0.0001
LVM/height ^{2.7} (g/m ^{2.7})	35.5 ± 0.5	32.1 ± 0.4	9.6%	0.0001
LVM/BSA (g/m ²)	86.2 ± 1.2	71.7 ± 1.0	16.8%	0.0001
LVM/FFM (g/kg)	2.81 ± 0.04	2.78 ± 0.04	1.0%	0.68
LVM/FFMa ₁ (g/kg)	2.77 ± 0.04	2.82 ± 0.04	−1.8%	0.44
LVM/FFMa ₂ (g/kg)	2.87 ± 0.04	2.79 ± 0.04	2.8%	0.19

LVM, left ventricular mass; BSA, body surface area; FFM, Fat-free mass; FFMa₁, equation including height only; FFMa₂, equation including height and weight. P-values are given for differences between means after adjustment for age, body mass index and blood pressure.

Table 4 Mean values (± standard errors) of left ventricular mass using different indexation methods. Two independent samples of men and women, ages 52 to 67 years from the same source population

	Sample I			Sample II		
	Men (n = 207)	Women (n = 222)	P-value	Men (n = 227)	Women (n = 293)	P-value
LVM	213 ± 3.3	161 ± 3.1	< 0.0001	216 ± 3.7	164 ± 3.2	< 0.0001
LVM/height (g/m)	123 ± 1.9	100 ± 1.8	< 0.0001	125 ± 2.1	102 ± 1.9	< 0.0001
LVM/height ^{2.0} (g/m ^{2.0})	71 ± 1.1	63 ± 1.1	< 0.0001	72 ± 1.3	64 ± 1.1	< 0.0001
LVM/height ^{2.7} (g/m ^{2.7})	49 ± 0.8	45 ± 0.8	0.002	49 ± 0.9	46 ± 0.8	0.02
LVM/BSA (g/m ²)	108 ± 1.6	92 ± 1.6	< 0.0001	110 ± 1.9	95 ± 1.7	< 0.0001
LVM/FFM (g/kg)	3.60 ± 0.06	3.70 ± 0.06	0.33	—	—	—
LVM/FFMa ₁ (g/kg)	3.75 ± 0.06	3.90 ± 0.06	0.08	3.77 ± 0.07	3.98 ± 0.06	< 0.03
LVM/FFMa ₂ (g/kg)	3.64 ± 0.06	3.67 ± 0.06	0.73	3.70 ± 0.07	3.78 ± 0.06	0.42

LVM, left ventricular mass; BSA, body surface area; FFM, Fat-free mass; FFMa₁, equation including height only; FFMa₂, equation including height and weight. P-values are given for gender differences between means after adjustment for age, body mass index and blood pressure.

between men and women reflects mostly differences in metabolic demand.

FFM measurements are frequently not available in the clinical setting. To identify a novel approximation formula we reiterated the allometric approaches suggested by other investigators before [5,6,30]. Specifically, we used an approach similar to Daniels *et al.* [7], employing non-linear regression modelling of FFM. In models restricted exclusively to body height as predictor variable, height raised to the power of 1.86, in men, and 1.94, in women, were identified as the best approximators of FFM. Interestingly, these exponents are strikingly close to previously determined allometric signals. Thus, Lauer *et al.*, investigating the relation between body height and LV mass in a larger group of adults, suggested that height raised to the power of 2.0 (2.12 in men, 1.91 in women) would best be suited for indexing LV mass [6]. Separate analysis of children and adults in the study of de Simone *et al.* resulted in an estimated allometric power of body height^{2.13} in adults [30].

Of note, these studies had no FFM measurements at their disposition and derived allometric signals of body height by directly assessing their impacts on LV mass. However, while the relation between LV mass and body height to its allometric powers is quite close among children and adolescents, it becomes clearly more scattered in adults and bigger subjects [30]. The scatter of the regression residuals of FFM found in this study (Fig. 1) demonstrates convincingly that body height, even when raised to different powers, is unable to sufficiently predict FFM. This was evident through the entire range of body heights found in this study. FFM prediction by body surface area was similarly ineffective; and our own approach of non-linear equations including only height (FFMa₁) turned out also to be less predictive than expected. These observations may reflect the fact that variables other than body height alone gain increasing influences on fat-free mass in adults [30,31]. To create a better fitting prediction model, body weight was included together with body height in the same non-linear regressions. The resulting gender-specific variable FFMa₂ displayed by far the best approximation of FFM. Moreover, like FFM determined by BIA, but in contrast to the various allometric height corrections and to BSA, indexation of LV mass to FFMa₂ also eliminated gender differences.

We reported before that indexing LV mass to BIA-determined FFM results in a marked attenuation of the strength of the association with adiposity in an unrestricted sample of the general population [9]. This finding was now confirmed in the healthy reference group also for approximated FFM. Our results are consistent with observations of Hammond *et al.*; and may, at least

in part, be due to the higher values of FFM in the obese [31,32]. Moreover, indexation to the FFMa₂ did not affect the strength of the association between systolic blood pressure and LV mass. This supports our previously expressed view that the latter relation is widely invariant to the type of indexation selected [9].

Limitations of the study

The present study is cross-sectional by design and, therefore, lacks the ability to prospectively look at outcomes in relation to different indexation methods. While LV mass indexed to BSA, height or height^{2.7} have been identified as independent predictors of cardiovascular risk [3,30,33] similar evidence pertaining to indexations to FFM is presently missing. For example, it would be of interest to know whether gender differences in clinical outcome of LV hypertrophy [34] persist after normalization of LV mass to FFM. Our novel approximation of FFM does easily allow such calculations from original data. On the other hand, our approximation formula of FFM was derived and applied in a specific population of Central Europe and it cannot be assumed to be directly applicable in populations of different ethnic composition. Third, it may be argued, that our new formula FFMa₂ is based on weight and height measurements which are already used in the determination of BIA-estimated FFM from which the new formula is derived and, therefore, causes some tautology. However, applying FFMa₂ to an independent sample of middle-aged subjects missing direct fat-free mass determination (sample II), resulted in findings that were highly consistent with those obtained in sample I using BIA determination of FFM. Nevertheless, the presented formula is probably specific for the Augsburg population and needs confirmation or modification in other settings or for other methods of FFM measurement.

Conclusions

A novel equation encompassing exponentials of height and weight approximated FFM much better and it performed well in the indexation of LV mass when evaluated in independent middle-aged samples from the general population. Approximations of FFM may be helpful in situations where no direct FFM measurements are available.

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