Size Matters! Impact of Age, Sex, Height, and Weight on the Normal Heart Size

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Background**—**Therapeutic decisions in cardiology are determined frequently by cardiac chamber size. To decide whether cardiac dimensions are still in the normal range, reliable reference values are needed. However, published reference values mostly refer to historical cohorts using motion-mode measurements and have not been adjusted for sex or age. The impact of body size was only vaguely addressed. The importance of such adjustments is illustrated by studies, which show that smaller individuals and women are at risk of delayed treatment and impaired outcome when currently used reference values are applied. The aim of the present study was to assess the impact of body size, sex, and age on the normal heart size.

Methods and Results**—**We prospectively studied 622 individuals (52.7% women; 17–91 years; 143–200 cm; 32–240 kg) without cardiac disease by standard transthoracic echocardiography. Multivariable linear regression analyses of the impact of sex, age, height, and weight on cardiac chamber size were performed. By multivariable regression analysis (n=500), all 4 variables independently influenced cardiac chamber size. The validity of cardiac dimensions predicted by the regression model was tested prospectively in a validation cohort (n=122). A calculator is proposed that estimates cardiac dimensions on the basis of the regression analysis.

Conclusions**—**Sex, height, weight, and age significantly affect the normal heart size. These parameters need to be considered when cutoff values indicating the need for treatment or even surgery are established. **(*Circ Cardiovasc Imaging*. 2013;6:1073-1079.)**

Key Words: age ■ body size ■ echocardiography ■ sex

The judgment whether a heart is normally sized or enlarged is of enormous importance, particularly when patient management is determined by such estimates. Although it is generally accepted that cardiac cavity dimensions are determined by body size, this has not resulted in the widespread use of indexed values. The reason for this is the lack of reliable reference data, which could resolve the uncertainties related to the exclusive use of body surface area (BSA) as an indexing tool. Obese, but small individuals and slim, tall ones may present with similar BSAs but may presumably have different expected normal values concerning the normal size of their heart. Such questions, to date, have not been addressed systematically. Furthermore, the independent impact of sex and age on cardiac size is not well defined.

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This fact is surprising but has been recently highlighted in a review in *Circulation*[1] and has also triggered the design of a multicenter trial to provide such values.[2]

Published reference values of the normal sized heart are scarce.[3–11] Most of these articles include small patient numbers and go back to the 1980s and 1990s, when spatial resolution of 2-dimensional (2D) echocardiography was limited and mainly motion (M)-mode imaging was used (Table 1). The majority of these studies were focused on left ventricular (LV) cavity size,[3–5,7–10,12] reference values for atrial and right ventricular dimensions barely exist.[6,11]

Particularly in valvular heart disease, accurate assessment of cardiac cavity enlargement is crucial. Several studies in the past have reported cutoff values of LV dimensions, which indicate the necessity of a surgical intervention in severe aortic[13–20] or mitral[21–26] regurgitation. These cutoff values have entered the current guidelines[27,28] for the management of valvular heart disease. It was consistently shown that besides symptomatic status and ventricular systolic function, LV dimensions are predictive of outcome.[15,16]

However, it has not been assessed whether cutoff values of cardiac cavity dimensions would be of even higher predictive value if they were adjusted for body size, sex, and age.

Furthermore, several of these studies were limited by an under-representation of women, particularly those focused on aortic regurgitation (76%–87% men).[13–19] This fact has been shown to result in under-treatment of women with aortic regurgitation and higher mortality rates.[20]

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Table 1. Publications on Normal Values of Left Ventricular Cavity Dimensions by Echocardiography

Reference	n	No. of Women	No. of Men	Age	LV_{EDD} Women	LV_{EDD} Men	Mode
Henry et al[4]	136	58 (34%)	78 (57%)	20–97	Regression equations and graphs		MM
Devereux et al[5]	133	55 (41%)	78 (59%)	44±12	45±4	50±5	MM
Triulzi et al[6]	72	34 (47%)	38 (53%)	15–76	Regression equations		2D
Hammond et al[7]	162			44±13	50±5		MM
Lauer et al[8]	2922	1666 (57%)	1256 (43%)	30–62	48±3	51±4	MM
Lauer et al[9]	812	524 (65%)	288 (35%)	20–45	46.1±3.0	50.8±3.6	MM
	914	503 (55%)	411 (45%)	20–45	47.5±3.6	51.1±3.7	
George et al[10]	45		45 (100%)	22±2		52.4±3.3	MM

2D indicates 2-dimensional; LV_{EDD}, left ventricular end-diastolic diameter; and MM, motion-mode.

The present prospective study was intended to assess the impact of body size, sex, and age on the normal heart size. We, furthermore, provide a calculation tool that facilitates the application of the results of our statistical analysis in the individual patient.

Methods

Between November 2008 and June 2012, we prospectively included 622 consecutive individuals (52.7% women) who were referred to our outpatient clinic for a standard transthoracic echocardiogram. Age was limited to ≥17 years.

Exclusion criteria comprised a cardiac murmur at auscultation, a history of cardiac disease, such as coronary artery disease, cardiomyopathy, rheumatic disease with cardiac involvement, valvular or congenital heart disease, and hypertension. If more than mild valvular heart disease was present, participants were also excluded from this protocol.

Study participants were weighed on a calibrated scale without shoes, jacket, or coat, and height was determined.

The ethical committee of the Medical University of Vienna approved the study protocol. All patients gave written informed consent.

Echocardiographic Measurements

Study participants underwent a comprehensive echocardiographic examination by board-certified physicians in the echocardiographic laboratory of the Medical University of Vienna using high-end scanners, such as Siemens Acuson Sequoia C512 and GE (General Electric) Vivid 7. All measurements were obtained according to current recommendations for cardiac chamber quantification.[29]

Left Ventricle

LV end-diastolic diameters (LV_{EDD-2D}) were measured by 2D echo from the apical 4-chamber view. LV end-diastolic and end-systolic volumes ($LV_{EDD-vol}$, LV_{ES-vol}) were calculated using the biplane method of discs (modified Simpsons rule) from the apical 4-chamber and apical 2-chamber views. LV end-diastolic and end-systolic diameters (LV_{EDD-MM}, LV_{ESD-MM}) by M-mode were determined from the parasternal short axis view.

Right Ventricle

Right ventricular end-diastolic diameters (RV_{EDD-2D}) and areas (RV_{area}) were measured by 2D echo from the apical 4-chamber view.

Atria

End-systolic longitudinal left and right atrial diameters (LA_{diam}, RA_{diam}) and areas (LA_{area}, RA_{area}) were measured by 2D echo from the apical 4-chamber view.

Atrial volumes (LA_{vol}, RA_{vol}) were determined with the area–length method using the 2D apical 4-chamber and apical 2-chamber views.

LV Wall Thickness

End-diastolic diameters of the interventricular septum were measured by 2D echo from the apical 4-chamber view (IVS_{2D}) and by M-mode from the parasternal short axis view (IVS_{MM}). End-diastolic diameters of the posterior wall (PW_{MM}) were also measured by M-mode from the parasternal short axis view.

Statistical Analysis

To identify influence factors on echocardiographic measurements, multivariable linear regressions with stepwise selection were performed with data of 500 consecutive study participants, accounting for height, weight, sex, and age. Only variables with *P* values <0.01 were left in the linear regression models with stepwise selection. 95% confidence intervals and *P* values of the corresponding test were calculated for the regression coefficients. Model assumptions were checked using residual plots. Baseline characteristics were compared between men and women using unpaired *t* tests. M-Mode values and 2D measurements were compared using paired *t* tests. To evaluate an additional potential impact of BSA and body mass index (BMI) on top of the parameters of height and weight, similar analyses were performed, including these 2 parameters. Analyses were repeated by replacing height and weight by BSA.

In addition, bootstrap samples were drawn 1000×. A linear regression with stepwise selection was performed for each bootstrap sample. A local significance level of 0.01 was applied as a selection criterion to keep overfitting low. Variables, which were included in >70% of the samples, were selected. For each bootstrap sample, a linear regression with the chosen independent variables was performed.

To test the validity of the regression model obtained from the data of the 500 consecutive study participants (test data set), data of another 122 individuals (validation data set) were used.

In this cohort, mean and SD of original measurements and of predicted measurements, using the regression models from the test data set, were calculated. Furthermore, mean bias (mean difference between original and predicted value), mean absolute bias (mean absolute difference between original and predicted value), and root

Table 2. Baseline Characteristics

	All (n=622)	Range	Women (n=328)	Range	Men (n=294)	Range	*P* Value
Age, y	41.8±15.5	17–91	43.8±14.8	17–91	38.3±16.0	17–82	<0.0001
Height, cm	169.6±10.0	143–200	164.2±6.9	143–183	178.6±7.8	156–200	<0.0001
Weight, kg	72.6±18.6	32–240	66.1±14.0	32–128	83.4±20.4	54–240	<0.0001
BMI, kg/m²	25.1±5.6	12.8–74.1	24.6±5.4	12.8–50.0	26.1±5.8	16.1–74.1	0.001
BSA, m²	1.8±0.3	1.2–3.5	1.7±0.2	1.2–2.4	2.0±0.2	1.6–3.5	<0.0001

BMI indicates body mass index; and BSA, body surface area.

mean squared error (square root of the mean squared difference between original and predicted value) were assessed.

Statistical analyses were performed using SAS 9.2 for Windows (SAS statistical software, SAS Institute, Cary, NC).

Results

Table 2 shows the baseline characteristics of the study population. Study participants were aged between 17 and 91 (mean, 42±16) years, 52.7% were women. Height ranged from 143 to 183 cm in women (mean, 164±7 cm) and from 156 to 200 cm in men (mean, 179±8 cm). Body weight ranged from 32 to 128 kg in women (mean, 66±14 kg) and from 54 to 240 kg in men (mean, 83±20 kg).

Average cardiac dimensions as determined in the test cohort (n=500) are given below. Tables 3 and 4 show the results of the multivariable regression analysis.

Left ventricle*

- 2D echo (Table 3)
  - LV_{EDD-2D} 43.2±4.3 mm
  - $LV_{EDD-vol}$ 96.8±28.9 mL
- M-Mode (Table 4)
  - LV_{EDD-MM} 46.4±5.2 mm
  - LV_{ESD-MM} 28.9±4.4 mm

*M-Mode estimates significantly overestimated 2D measurements of the LV_{EDD} by 3.2±4.5 mm (*P*<0.001)

Right ventricle

- 2D echo (Table 3)
  - RV_{EDD-2D} 29.6±3.9 mm
  - RV_{area} 19.4±4.7 cm^2

Left atrium

- 2D echo (Table 3)
  - LA_{diam} 45.4±5.2 mm
  - LA_{area} 15.0±3.5 cm^2
  - LA_{vol} 38.9±14.7 mL

Right atrium

- 2D echo (Table 3)
  - RA_{diam} 45.7±5.1 mm
  - RA_{area} 13.6±3.6 cm^2
  - RA_{vol} 33.7±14.1 mL

LV wall thickness†

- 2D echo (Table 3)
  - IVS_{2D} 9.8±1.2 mm
- M-Mode (Table 4)
  - IVS_{MM} 9.4±1.3 mm
  - PW_{MM} 9.2±1.3 mm

†Septal wall thickness estimates by 2D echo overestimated M-mode measurements by 0.4±1.9 mm on average (*P*<0.001)

BMI and BSA

In a further linear regression analysis with stepwise selection, the influence of BMI and BSA was evaluated in addition to weight, height, sex, and age. BSA influenced all analyzed cardiac cavity dimensions, whereas BMI revealed no statistically significant influence (data not shown). Thus, in a third linear regression analysis, weight and height were replaced by BSA. However, using BSA instead of height and weight did not increase the statistical stability and accuracy of the model as reflected by similar coefficients of determination (data not shown).

Bootstrap Estimates

Bootstrap estimates (n=1000) were performed for all measurements and confirmed the high stability of the regression models. Bootstrap mean values for the corresponding regression coefficients were close to the corresponding regression coefficients of the original model (data not shown).

Validation Data

Table 5 describes the accuracy of measures predicted by the regression model (test data set, n=500) in 122 study participants. Best agreement was found for 2D measurements (root mean squared error, 0.88–3.93) and M-mode measurements (root mean squared error 0.90–3.66). Larger deviations, as expected, were observed for areas (root mean squared error, 2.37–4.42) and volume estimates (root mean squared error, 10.35–18.73).

Calculator

Based on the results of the multivariable regression analysis, we designed a calculator, which estimates cardiac dimensions and accounts for sex, age, height, and weight.

Discussion

Whether the heart of an individual patient is enlarged bears important information in clinical cardiology. Surprisingly, however, the evidence concerning reference values of the normal sized heart is scarce. Most publications in the field were solely focused on the left ventricle[3–5,7–10] (Table 1), not taking the right ventricle or atria into account. Moreover, almost all of these articles go back to the 1980s and 1990s when M-mode was the primary echocardiographic modality. Only Triulzi et al[6,12] and Lauer et al[9] examined the influence of body size on adult LV dimension variability and also described sex-specific differences.

The acquisition of reproducible M-mode measurements of the LV cavity size, however, is challenging. Today, 2D imaging of the LV from the apical 4-chamber view is the mainstay. Nevertheless, to our knowledge, no systematic reference values of the normal sized heart on the basis of 2D measurements exist.

Although the prognostic importance of left atrial area and volume has repeatedly been pointed out, data about the normal size of the left atrial area or volume are very limited.[6,30] Data on the normal sized right ventricle and right atrium are even more limited. Recent guidelines on echocardiographic assessment of the right heart in adults[11] lack information concerning a potential impact of body size, sex, or age.

Because of the lack of published indexing recommendations, clinical cardiologists at present may use the same normal range of cardiac cavity dimensions for everybody, including competitive athletes, and old, frail patients. This fact frequently causes diagnostic ambiguity. The stakes for resolving such diagnostic ambiguity are high as consequences for the individual patient may be considerable. Particularly, in

Table 3. Results of the Multivariable Regression Model, 2D Measurements

Variable	Regression Coefficients	95% Confidence Interval Limits		*P* Value
LV_{EDD-2D}				
Intercept	20.98637	13.82007	28.15268	<0.0001
Weight	0.07404	0.05687	0.09121	<0.0001
Height	0.11429	0.07359	0.15499	<0.0001
Sex	−1.45756	−2.25856	−0.65657	0.0004
Age	−0.04141	−0.06023	−0.02260	<0.0001
$LV_{EDD-vol}$				
Intercept	−39.37731	−91.07454	12.31991	0.1351
Weight	0.42808	0.30268	0.55349	<0.0001
Height	0.73703	0.44358	1.03049	<0.0001
Sex	−9.47838	−15.24652	−3.71023	0.0013
Age	−0.33895	−0.47457	−0.20332	<0.0001
RV_{EDD-2D}				
Intercept	15.94580	9.13081	22.76078	<0.0001
Weight	0.04375	0.02731	0.06020	<0.0001
Height	0.07014	0.02731	0.06020	0.0005
Sex	−2.35620	−3.15617	−1.55622	<0.0001
RV_{area}				
Intercept	−0.97314	−10.35089	8.40461	0.8384
Weight	0.09270	0.06347	0.12193	<0.0001
Height	0.10040	0.04619	0.15460	0.0003
Sex	−2.62433	−3.69133	−1.55733	<0.0001
Age	−0.03906	−0.06443	−0.01369	0.0027
LA_{diam}				
Intercept	34.23014	32.30756	36.15272	<0.0001
Weight	0.11356	0.09181	0.13530	<0.0001
Sex	−1.73000	−2.59145	−0.86855	<0.0001
Age	0.09453	0.07041	0.11866	<0.0001
LA_{area}				
Intercept	−4.07280	−9.31691	1.17130	0.1277
Weight	0.05673	0.04028	0.07317	<0.0001
Height	0.08135	0.04926	0.11344	<0.0001
Age	0.02779	0.00956	0.04602	0.0029
LA_{vol}				
Intercept	−34.73810	−57.37315	−12.10305	0.0027
Weight	0.21533	0.14446	0.28620	<0.0001
Height	0.31554	0.17710	0.45397	<0.0001
Age	0.10538	0.02674	0.18403	0.0087
RA_{diam}				
Intercept	35.52012	33.62341	37.41683	<0.0001
Weight	0.10712	0.08567	0.12857	<0.0001
Sex	−2.03817	−2.88803	−1.18831	<0.0001
Age	0.08743	0.06364	0.11123	<0.0001
RA_{area}				
Intercept	9.15398	7.54409	10.76388	<0.0001
Weight	0.07818	0.05971	0.09665	<0.0001
Sex	−1.85918	−2.55769	−1.16067	<0.0001

(continued)

Table 3. Continued

Variable	Regression Coefficients	95% Confidence Interval Limits		*P* Value
RA_{vol}				
Intercept	18.97912	12.61130	25.34693	<0.0001
Weight	0.27999	0.20694	0.35304	<0.0001
Sex	−8.55635	−11.31925	−5.79344	<0.0001
IVS_{2D}				
Intercept	7.66249	7.19746	8.12753	<0.0001
Weight	0.02031	0.01505	0.02557	<0.0001
Sex	−0.56512	−0.77349	−0.35675	<0.0001
Age	0.02344	0.01761	0.02928	<0.0001

2D indicates 2-dimensional; diam, diameter; EDD, end-diastolic diameter; IVS, interventricular septum; LA, left atrium; LV, left ventricular; RA, right atrium; RV, right ventricle; and vol, volume.

patients with small body dimensions, the diagnosis of cardiac enlargement may not be made because of an erroneous underestimation, leading to delayed treatment and poor prognosis.

Such a causal relationship has been described several years ago.[20] Cutoff values of LV size indicating the need for surgery in aortic regurgitation[27,28] are based on 7 studies published between 1991 and 2006.[13–19] The proportion of female patients in these studies was low with an average of 19.1% (range, 13%–24%). The work of Klodas et al[20] demonstrated an excess late mortality of women with aortic regurgitation after valve surgery when these cutoff values were applied. This observation was explained by delayed surgery in women, who never reached the cutoff values presumably because of smaller hearts at baseline. The European guidelines for the management of valvular heart disease[28] state that the patient's stature should be considered, and that indexing is helpful for decision making. Aortic valve replacement for aortic regurgitation, for instance, is recommended when the LV end-systolic diameter exceeds 25 mm/m^2 BSA. However, this cutoff value again was derived from those studies that comprised <20% women.[13–19]

Current scaling methods mostly normalize cardiovascular structures to BSA by simply using the form $y=x$/BSA, where x is the cardiovascular parameter, and y is the scaled cardiovascular parameter.[1] It is noteworthy that BSA quantifies both muscle and adipose tissues and extravascular fluid volumes. The contribution of adipose tissue and extravascular fluid to BSA, however, may vary widely between men and women and in dependence of age.

The aim of the present prospective study was to collect data of normal sized hearts, analyze them with respect of body size, sex, and age. We, furthermore, provide a calculation tool to estimate reference values for the normal sized heart.

Table 4. Results of the Multivariable Regression Model, M-Mode Measurements

Variable	Regression Coefficients	95% Confidence Interval Limits		*P* Value
LV_{EDD-MM}				
Intercept	15.38196	8.54423	22.21970	<0.0001
Weight	0.07658	0.05280	0.10036	<0.0001
Height	0.15007	0.10616	0.19397	<0.0001
LV_{ESD-MM}				
Intercept	26.76878	24.90119	28.63637	<0.0001
Weight	0.04765	0.02621	0.06909	<0.0001
Sex	−2.11032	−2.93269	−1.28795	<0.0001
IVS_{MM}				
Intercept	7.34011	6.80535	7.87488	<0.0001
Weight	0.01872	0.01266	0.02477	<0.0001
Sex	−0.53678	−0.77686	−0.29671	<0.0001
Age	0.02469	0.01797	0.03141	<0.0001
PW_{MM}				
Intercept	7.49088	6.95555	8.02622	<0.0001
Weight	0.01964	0.01357	0.02570	<0.0001
Sex	−0.57818	−0.81862	−0.33775	<0.0001
Age	0.01489	0.00816	0.02162	<0.0001

EDD indicates end-diastolic diameter; ESD, end-systolic diameter; IVS, interventricular septum; LV, left ventricular; MM, motion-mode; and PW, posterior wall.

Table 5. Prospective Validation of Predicted Dimensions

	Measured (n=122)	Predicted (n=122)	Mean Bias	Mean Absolute Bias	RMSE
$LV_{EDD\text{-}2D}$, mm	41.61±3.83	42.73±2.59	1.12	2.51	3.21
$LV_{EDD\text{-}vol}$, mL	84.66±23.81	94.16±16.31	9.53	15.44	18.73
$RV_{EDD\text{-}2D}$, mm	27.88±3.85	29.24±2.12	1.36	2.70	3.38
RV_{area}, cm^2	15.77±3.92	19.02±3.17	3.25	3.72	4.42
LA_{diam}, mm	43.57±4.40	45.16±2.80	1.16	3.11	3.93
LA_{area}, cm^2	15.21±3.08	14.91±1.58	−0.30	2.22	2.70
LA_{vol}, mL	41.13±13.08	38.46±6.05	−2.67	9.44	11.84
RA_{diam}, mm	44.90±4.09	45.47±2.75	0.57	2.85	3.55
RA_{area}, cm^2	13.80±2.90	13.38±1.87	−0.43	1.86	2.37
RA_{vol}, mL	35.02±12.47	32.75±7.44	−2.27	8.14	10.35
IVS_{2D}, mm	9.46±1.152	9.72±0.62	0.26	0.71	0.88
$LV_{EDD\text{-}MM}$, mm	44.51±4.04	46.19±2.39	1.68	2.89	3.66
IVS_{MM}, mm	9.43±1.14	9.36±0.60	−0.07	0.72	0.90
PW_{MM}, mm	8.96±1.20	9.12±0.56	0.16	0.75	0.91

2D indicates 2-dimensional; diam, diameter; EDD, end-diastolic diameter; IVS, interventricular septum; LA, left atrium; LV, left ventricular; measured, values measured by transthoracic echocardiography; MM, motion-mode; PW, posterior wall and vol, volume; RA, right atrium; RSME, root mean squared error; RV, right ventricle.

Our study revealed considerable differences in cardiac size depending on sex, body size, and age. The average male person in our cohort (1.79 m; 85 kg; 37 years; BMI, 25.9 kg/m²; BSA, 2.03 m²) had a LV end-diastolic diameter (2D) of 46.0±3.8 mm compared with the average female (1.64 m; 66 kg; 43 years; BMI, 24.5 kg/m²; BSA, 1.73 m²) whose LV end-diastolic diameter was significantly smaller (41.4±3.5 mm; $P<0.001$). Furthermore, when we compared a young tall man (1.95 m; 115 kg; 34 years; BMI, 30.2 kg/m²; BSA, 2.50 m²) with an elderly small woman (1.51 m; 48 kg; 83 years; BMI, 21.1 kg/m²; BSA, 1.42 m²), LV end-diastolic diameters were 50.4 mm (95% CI, 44.1–56.7) versus 37.4 mm (95% CI, 31.1–43.7), respectively.

This demonstrates that tall and rather heavy individuals consistently meet accepted thresholds for normal LV end-diastolic diameters.[3–10] However, a small (female) person may experience a significantly dilated left ventricle although the end-diastolic LV diameter is still far below 50 mm, but still may be classified as normal.

The present study clearly shows that besides height and weight, sex and age are significant predictors of cardiac cavity dimensions. Thus, a thorough assessment of an individual's heart should include the consideration of all 4 variables.

Limitations

Our data have been collected in a single center in central Europe, thus the ethnic background of our study population was mainly whites. No Asian or black individuals were studied. Thus, conclusions concerning other ethnic populations are limited.

Conclusions

The present work shows that sex, age, and body size affect the normal heart size. These parameters need to be considered when cutoff values indicating the need for treatment or even surgery are applied.

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Disclosures

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CLINICAL PERSPECTIVE

Therapeutic decisions in cardiology are determined frequently by cardiac chamber size. The present study shows that one size does not fit all. Cardiac chamber size is influenced by body size, sex, and age. These parameters need to be considered when cutoff values indicating the need for treatment or even surgery are applied. To alleviate the assessment of the individual patient, a calculator based on our statistical analysis is provided.

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