

Keywords: Cardiac Disease; Echocardiograms; Increased Left Atrial

Introduction

Increased left atrial (LA) volume is a risk marker for atrial fibrillation, stroke, and heart failure, and it has been correlated with increased cardiovascular mortality [1–7]. International guidelines and clinical practice recommend that LA volume be indexed to body surface (B.S.A.) [8,9]. However, in obese individuals there is a tendency to underestimate these values, often placing individuals with an enlarged left atrium as normal, after indexing by a high B.S.A.. This is an important problem, because obesity is associated with atrial fibrillation [10] and it appears to be mediated by left atrial dilatation [11]. The prevalence of obesity is increasing, it is likely that prevalence of obesity-related AF will increase as well. B.S.A. is an isometric measure, which assumes that LA size has a linear relationship to body size. However, organ size (i.e., heart size) and body size do not grow proportionally; in other words, their relationship is nonlinear [12]. Many parameters can be indexed for height, especially in obese individuals. Alternative forms of scaling, including allometric size variable such as height raised to an exponent, may help address this issue [12,13]. The normal values and how the left atrial volume indexed for height behaves in obese and overweight individuals under normal conditions of cardiovascular health is not well explained in the literature, especially in a Brazilian population. The current work aims to clarify these questions.

Methods

This is a pilot, observational, descriptive, retrospective study. Echocardiographic data, age, sex, weight, height and body surface were obtained from the data file of the echocardiography service of Hospital Ana Nery, from 2018-2021. Patients with normal echocardiograms, in sinus rhythm, with no history or evident cardiovascular disease (mild systemic arterial hypertension and non-insulin dependent diabetes without target organs involvement), were included independent of any other factor. In all patients, in addition to LA volume, LA and LV dimensions, wall thickness, left ventricular mass, LV ejection fraction, and aortic root diameter were also recorded. Left atrial volumes were obtained by the Simpson's biplane method of disks using apical four chamber and two chamber views at ventricular end-systole. The data of each patient were reviewed to verify there was no missing data and to be sure that the exam was normal, with special attention to LV diastolic dysfunction parameters, such as the E' waves of the medial and lateral mitral annulus. Exclusion criteria: any parameter of abnormality such as LA maximum diameter at the parasternal long axis > 40mm, indexed LA

volume > 34ml/m², left ventricular wall relative thickness > 0.42, increased left ventricular indexed mass, ejection fraction less than 55%, any change suggesting LV diastolic dysfunction such as reduced medial (< 7cm/s) or lateral (<10cm/s) and mitral regurgitation more than minimal. A total of 645 charts reported as normal echocardiograms were reviewed, and 545 patients were included in the study. The protocol of the study was approved by the Research Ethics Committee of the Hospital Ana Nery (HAN/SESAB), Salvador-BA, which waived the need to obtain written informed consent.

The LA volume were than indexed for B.S.A., height, height² and height^{2.7} in four groups of patients:

- Group I, low weight (B.M.I. < 20 kg/m²)
- Group II, normal weight (B.M.I. ≥ 20 kg/m² and < 25 kg/m²),
- Group III, overweight (B.M.I. ≥ 25 kg/m² and < 30 kg/m²),
- Group IV, obese (B.M.I. ≥ 30 kg/m²).

Data Analysis

Quantitative data are described as mean ± standard deviation and IC 95%. Categorical data are described as an absolute number and percentage. The means, standard deviations (SD) and 95% confidence intervals (CI) of the quantitative variables were obtained for the total of patients and for the subgroups. To comparisons, we considered normal indexed left atrial volume for height, height² and height^{2.7} the interval from 2 SD below and 2 SD above the mean of the normal weight group (B.M.I. ≥ 20 kg/m² and < 25 kg/m²). Student's t test was used to compare means between two independent groups, and the ANOVA test of variance for comparisons between the three groups according to B.M.I. (normal, overweight, and obese) with the Bonferroni test for post hoc analysis between pairs of groups. The chi-square test was used to compare categorical variables. Receiver operating characteristic (ROC) curve analysis was used to identify the indexation method that best predicted increased LA. Statistical analysis were performed with IBM SPSS statistics version 21. Statistical significance was considered as P < 0.05 two-tailed.

Results

A total of 545 patients, mean age 50.5 ± 13.4 y., 335 females (61,5%) and 210 males (38.5%) were analyzed. The anthropometric measurements are detailed in table I. There were 145 normal weight (26.6%), 215 overweight (39.4%), 154 obese (28.3%) and 31 low weight (5.7%) patients. Obesity was more commonly seen in females (75%) just as

there was a trend towards more overweight in women (59%). The LA diameter and volume progressively increased from low-weight (Low-wt), normal, overweight (Over-wt) and obese groups (table II and figure 1). When indexed by BSA the LA volume did not differ between groups. Otherwise, when indexing by height, height² and height^{2.7}, we observed a progressive and statistically significant increase in the volume of the left atrium (figure 1). The normal values of LA volume according to height, height^{2.7} and height² (allometric measurements) were obtained by the mean ± 2 standart deviations (SD) in the normal weight group. For height the normal values varied from 17.0 to 35.0 ml/m (mean ± SD 26.0 ±4.5). For height² the normal values of LA volume varied from 10.4 to 21.6 (mean ± SD 16.0 ± 2.8). For height^{2.7} the normal values varied from 7.0 to 15.8 ml/m^{2.7} (mean ± SD 11.4 ± 2.2). The normal LA volume for height^{2.7} differed between male and female (11.4±2.4 and 12.8±2.6, p<0.001). Table III describes the normal values and the maximum limit of normality for indexing the left atrium by height, height²

and height^{2.7}. Sixteen of 215 (7.4%) of overweight patients and 32 of 154 (20.8%) obese patients were reclassified from normal to dilated left atrium when indexed by height, 19 of 215 (8.8%) and 35 of 154 (22.7%), respectively, when indexed by height², and 18 of 215 (8.4%) and 33 of 154 (21.4%), respectively, when indexed by height^{2.7} according to gender (figure 2). In the normal weight group, only one patient was reclassified as enlarged LA when indexed by height² or by height^{2.7} and 3 patients were reclassified when indexed by height. No low-weight patients were reclassified as enlarged LA when indexed by height, using any one of the three methods. The results of ROC analyses for the best cutoff values to identify LA enlargement in obese or overweight patients are shown in Figure 3 and Table IV. LA was considered enlarged if at least two of the three indexation methods by height were above normal values. LA volume indexation by height² had the highest area under curve (AUC 1.0, 95% CI 0.999-1.0) followed by LAvol/ht^{2.7} (AUC 0.989, 95% CI 0.98-0.997), LAvol/h (AUC 0.972, 95% CI 0.957-

Table I: Anthropometric data on the total number of patients and in the normal weight, underweight, overweight, and obese groups.

	Total	Min	Max	Low-wt	Normal	Over-wt	Obese	P
Age	50.5 (13.4)	17	83	45.4 (17.5)	51.6 (14.4)	51.1 (12.7)	49.8 (12.2)	0.096
Weight (Kg)	73.4 (15.7)	27	139	49 (8.2)	62 (7.7)	73.4 (8.8)	89.1 (14.3)	<0.001
Height (cm)	163.1 (9.4)	135	192	164.5 (9.1)	163.5 (9.2)	163.6 (9.6)	161.8 (9.3)	0.214
B.S.A. (m ²)	1.79 (0.21)	1.1	2.5	1.52 (0.17)	1.67 (0.15)	1.80 (0.16)	1.93 (0.19)	<0.001
m ^{2.7}	3.78 (0.59)	2.25	5.82	3.9 (0.57)	3.8 (0.59)	3.8 (0.61)	3.7 (0.57)	0.224
m ²	2.67 (0.31)	1.82	3.69	2.71 (0.30)	2.68 (0.31)	2.68 (0.32)	2.63 (0.30)	0.220
B.M.I. Kg/m ²)	27.6 (5.3)	11.2	53.4	18.0 (1.8)	23.1 (1.3)	27.4 (1.3)	33.95 (3.9)	<0.001

Table II: Left atrium sizing and indexing by body surface area between normal weight, low weight, overweight and obese patients.

	Total	Low-wt	Normal	Over-wt	Obese	P
LA diam (mm)	34.2 (3.7)	30.4 (4.8)*	33.0 (3.6)	34.9 (3.2)*	35.3 (3.3)*	<0.001
LAvol (ml)	45.5 (9.3)	37.4 (9.6) ^a	42.6 (7.9)	46.6 (8.6)*	48.3 (9.8)*	<0.001
LAvol/B.S.A.	25.5 (4.5)	24.6 (5.2)	25.6 (4.3)	26.0 (4.4)	25.1 (4.8)	0.173
LAvol/ht	27.9 (5.4)	22.7 (5.3)*	26.0 (4.5)	28.5 (4.8)*	29.9 (5.7)*x	<0.001
LAvol/h ^{2.7}	12.2 (2.6)	9.8 (2.2)*	11.4 (2.2)	12.4 (2.3)*	13.3 (2.8)*+	<0.001
LAvol/ht ²	17.1 (3.4)	13.8 (3.1)*	16.0 (2.8)	17.4 (3.0)*	18.5 (3.6)*+	<0.001

* P<0.01 comparing to normal weight; ^a P<0.02 versus normal weight; + P<0.01 obese versus overweight; x P=0.055 obese versus overweight

Table III: Normal values and the maximum normal for left atrium indexing by height, height² and height^{2.7}.

	Normal	Maximum normal
LAvol/B.S.A.	25.6 ± 4.3	34.2
LAvol/ht (ml/m)	26.0 ±4.5	35.0
LAvol/ht ² (ml/ m ²)	16 ± 2.8	21.6
LAvol/ht ^{2.7} (ml/ m ^{2.7})	11.4 ± 2.2	15.8
male	11.4 ± 2.4	16.2
female	12.8 ± 2.6	18.0

Citation: Edmundo J. Nassri Camara, Flávia R. do Prado Valladares, Ng Kin Key, Paloma Fonseca Santana, Jun Ramos Kawaoka, Thais Harada Campos, Marcus Ribeiro de O. Santana, Alex Costa Cunha, Danilo Sousa Sampaio, Gustavo Pinheiro Santana, Luis Gustavo S. Brito, Narjara de O. Cardoso Dourado, Saulo Jende Nascimento, Alice Povoas A. L. Lira, Nailly N. do Nascimento, Romeu Pacheco F. dos Santos, Sérgio Rodrigo F. Rocha, Thaise Gordiano Machado. Indexing of Left Atrial Volume by Body Surface Area and Height in a Brazilian Population without Previous Heart Disease and with a Normal Heart on Echocardiography. Behavior in Obese and Overweight Patients. *Cardiology and Cardiovascular Medicine*. 7 (2023): 25-31.

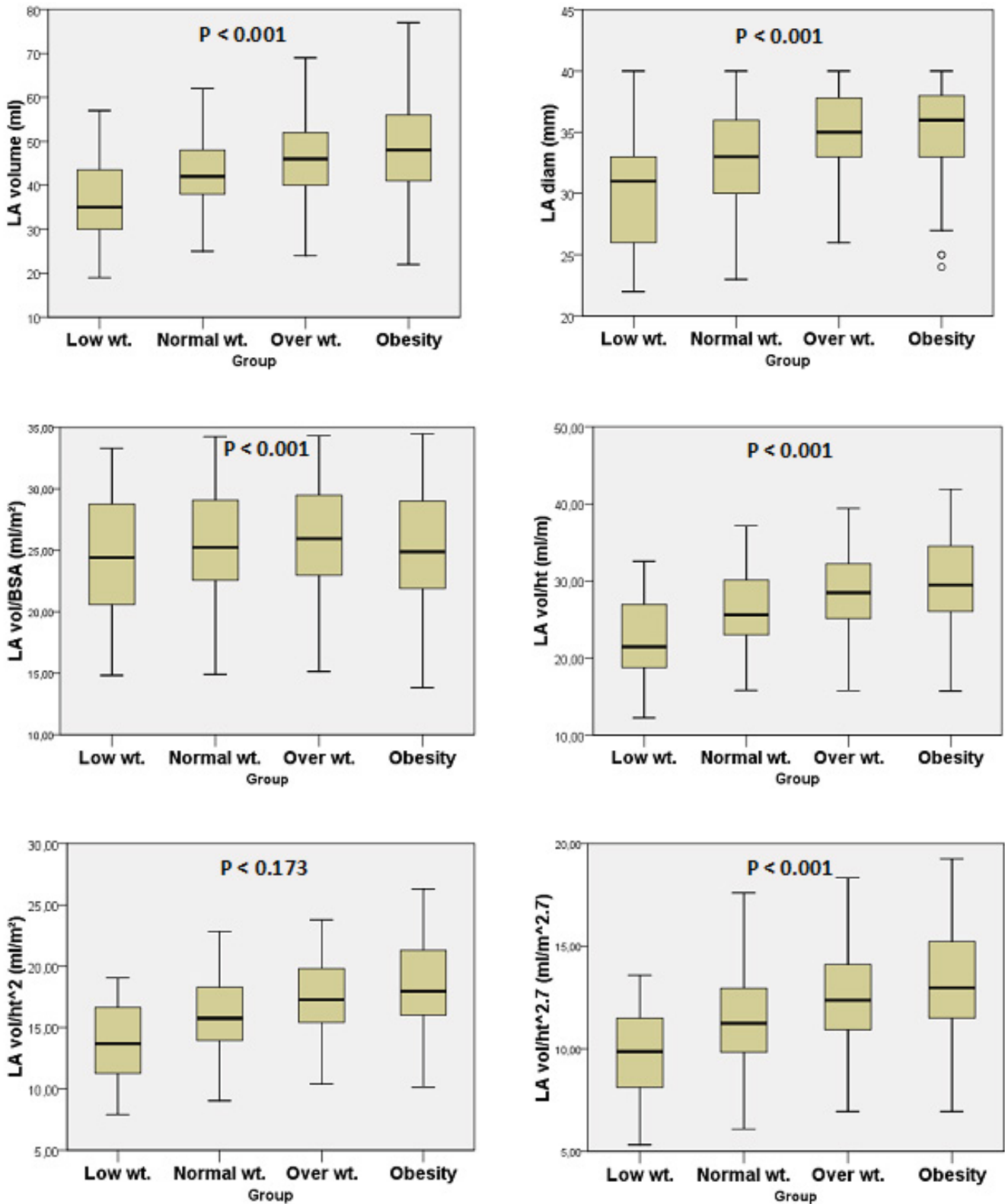


Figure 1: Left atrial volume indexed by B.S.A. and by height (using three different methods). Mean ± SD.

Citation: Edmundo J. Nassri Camara, Flávia R. do Prado Valladares, Ng Kin Key, Paloma Fonseca Santana, Jun Ramos Kawaoka, Thais Harada Campos, Marcus Ribeiro de O. Santana, Alex Costa Cunha, Danilo Sousa Sampaio, Gustavo Pinheiro Santana, Luis Gustavo S. Brito, Narjara de O. Cardoso Dourado, Saulo Jende Nascimento, Alice Povoá A. L. Lira, Nailly N. do Nascimento, Romeu Pacheco F. dos Santos, Sérgio Rodrigo F. Rocha, Thaise Gordiano Machado. Indexing of Left Atrial Volume by Body Surface Area and Height in a Brazilian Population without Previous Heart Disease and with a Normal Heart on Echocardiography. Behavior in Obese and Overweight Patients. Cardiology and Cardiovascular Medicine. 7 (2023): 25-31.

Proportion of left atrial enlargement according to the indexing method

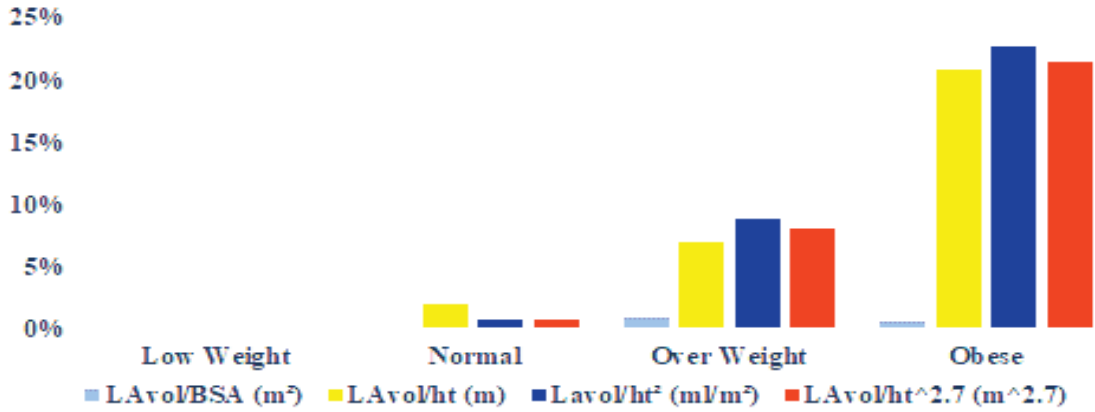


Figure 2: Proportion of left atrial enlargement according to the indexing method.

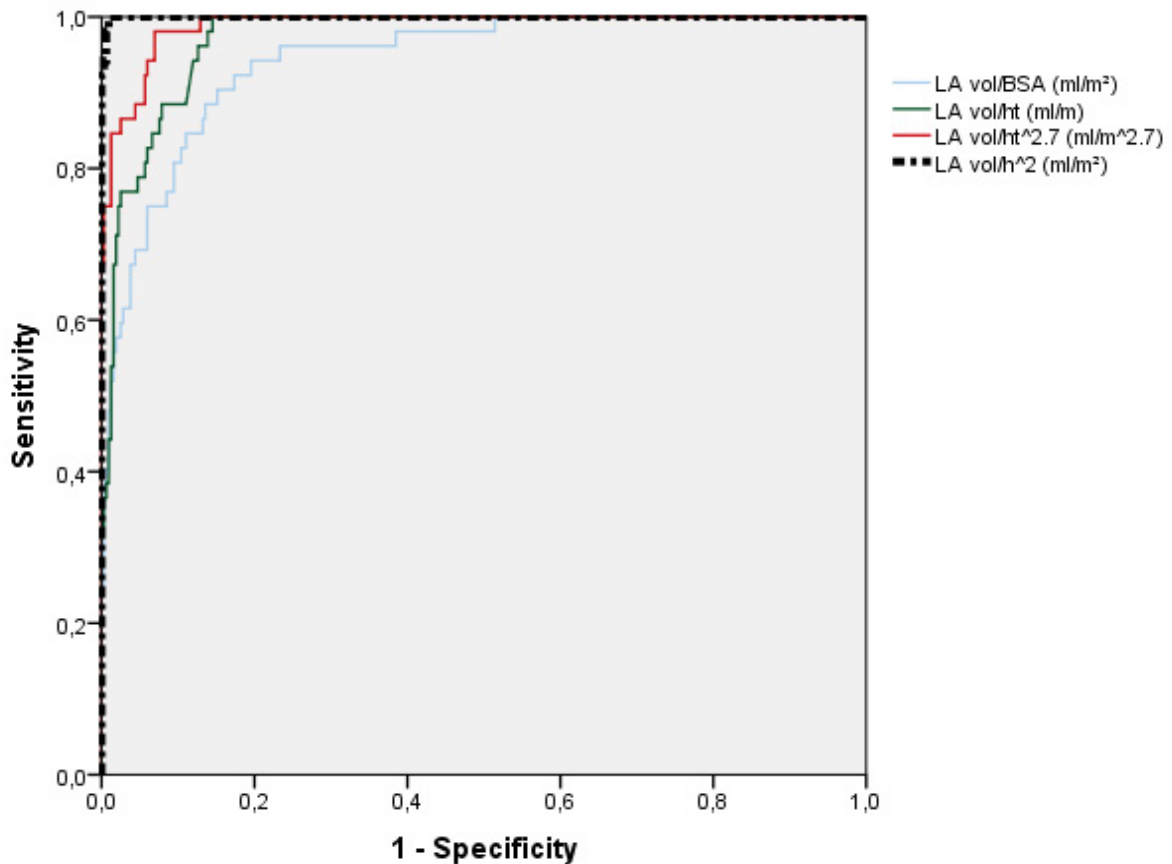


Figure 3: Receiver operating characteristic (ROC) curve analysis for prediction of enlarged LA in obese or overweight patients. Enlarged LA was defined as at least two abnormal of the three methods of volume indexation by height. BSA, body surface area; ht, height; m^{2.7}, meters raised to exponent 2.7; m², meters squared.

Citation: Edmundo J. Nassri Camara, Flávia R. do Prado Valladares, Ng Kin Key, Paloma Fonseca Santana, Jun Ramos Kawaoka, Thais Harada Campos, Marcus Ribeiro de O. Santana, Alex Costa Cunha, Danilo Sousa Sampaio, Gustavo Pinheiro Santana, Luis Gustavo S. Brito, Narjara de O. Cardoso Dourado, Saulo Jende Nascimento, Alice Povoá A. L. Lira, Nailly N. do Nascimento, Romeu Pacheco F. dos Santos, Sérgio Rodrigo F. Rocha, Thaise Gordiano Machado. Indexing of Left Atrial Volume by Body Surface Area and Height in a Brazilian Population without Previous Heart Disease and with a Normal Heart on Echocardiography. Behavior in Obese and Overweight Patients. Cardiology and Cardiovascular Medicine. 7 (2023): 25-31.

Table IV: Results of ROC analyses to identify LA enlargement* in obese or overweight patients.

Variables	AUC	95% CI	Optimal cutoff value	Sensitivity	Specificity
	LAvol/BSA (ml/m ²)	,943		0.914-0.973	29.2
LAvol/ht (ml/m)	,972	0.957-0.987	34.4	84.60%	93.40%
LAvol/ht ^{2.7} (ml/m ^{2.7})	,989	0.980-0.997	15	98.10%	93.10%
LAvol/ht ² (ml/ht ²)	1,000	0.999-1.000	21.5	100%	99.10%

*LA enlargement was defined if at least two of the three indexation methods by height were above normal values.

0.987) and LAvol/BSA (AUC 0.943, 95% CI 0.914-0.973). Operational cutoff values with corresponding predictive characteristics for obese or overweight patients are presented in Table IV. Interestingly, we found 29.2 ml/m² the best cutoff value if we use LAvol/BSA to the diagnosis of LA enlargement in obese or overweight patients.

References

1. Kizer JR, Bella JN, Palmieri V, et al. Left atrial diameter as an independent predictor of first clinical cardiovascular events in middle-aged and elderly adults: The Strong Heart Study (SHS). *Am Heart J* 151 (2006): 412-418.
2. Armstrong AC, Liu K, Lewis CE, et al. Left atrial dimension and traditional cardiovascular risk factors predict 20-year clinical cardiovascular events in young healthy adults: the CARDIA study (2014).
3. Bombelli M, Facchetti R, Cuspidi C, et al. Prognostic Significance of Left Atrial Enlargement in a General Population Results of the PAMELA Study *Epidemiology/Population*. (2014).
4. Gardin JM, McClelland R, Kitzman D, et al. M-Mode echocardiographic predictors of six- to seven-year incidence of coronary heart disease, stroke, congestive heart failure, and mortality in an elderly cohort (The Cardiovascular Health Study). *Am J Cardiol* 87 (2001): 1051-1057.
5. Laukkanen JA, Kurl S, Eränen J, et al. Left Atrium Size and the Risk of Cardiovascular Death in Middle-Aged Men. *Arch Intern Med*. 165 (2005):1788-1793.
6. Baumgartner H, Hung J, Bermejo J, et al. Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr* 30 (2017): 372-392.
7. Fernandes LP, Barreto ATF, Neto MG, et al. Prognostic power of conventional echocardiography in individuals without history of cardiovascular diseases: A systematic review and meta-analysis. *Clinics* 76 (2021): 1-12.
8. Lang RM, Badano LP, Victor MA, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 28 (2015): 1-39.e14.
9. Singh M, Sethi A, Mishra AK, et al. Echocardiographic Imaging Challenges in Obesity: Guideline Recommendations and Limitations of Adjusting to Body Size (2020).
10. Zia I, Johnson L, Memarian E, et al. Anthropometric measures and the risk of developing atrial fibrillation: a Swedish Cohort Study. *BMC Cardiovasc Disord* 21 (2021): 1-10.
11. Wang TJ, Parise H, Levy D, et al. Obesity and the Risk of New-Onset Atrial Fibrillation. *JAMA* 292 (2004): 2471-2477.
12. Jeyaprakash P, Moussad A, Pathan S, et al. A Systematic Review of Scaling Left Atrial Size: Are Alternative Indexation Methods Required for an Increasingly Obese Population? *J Am Soc Echocardiogr* 34 (2021): 1067-1076.e3.
13. Davis EF, Crousillat DR, He W, et al. Indexing Left Atrial Volumes. *JACC Cardiovasc Imaging* 15 (2022).
14. Abed HS, Samuel CS, Lau DH, et al. Obesity results in progressive atrial structural and electrical remodeling: Implications for atrial fibrillation. *Hear Rhythm* 112 (2012).
15. Laurent S, Lip GY, McManus R, et al. ESC/ESH Guidelines for the management of arterial hypertension (2018).

Citation: Edmundo J. Nassri Camara, Flávia R. do Prado Valladares, Ng Kin Key, Paloma Fonseca Santana, Jun Ramos Kawaoka, Thais Harada Campos, Marcus Ribeiro de O. Santana, Alex Costa Cunha, Danilo Sousa Sampaio, Gustavo Pinheiro Santana, Luis Gustavo S. Brito, Narjara de O. Cardoso Dourado, Saulo Jende Nascimento, Alice Povoá A. L. Lira, Nailly N. do Nascimento, Romeu Pacheco F. dos Santos, Sérgio Rodrigo F. Rocha, Thaise Gordiano Machado. Indexing of Left Atrial Volume by Body Surface Area and Height in a Brazilian Population without Previous Heart Disease and with a Normal Heart on Echocardiography. *Behavior in Obese and Overweight Patients. Cardiology and Cardiovascular Medicine*. 7 (2023): 25-31.

Supplementary Table I: Normal values and the maximum normal (mean + 2 SD) for left atrium indexing by height, height² and height^{2.7} and by sex.

	N	Normal	Maximum normal	P
LAvol/B.S.A.		25.6 ± 4.3	34.2	
male	69	25.4 ± 4.4	34.2	0.73
female	76	25.7 ± 4.3	34.3	
LAvol/ht (ml/m)		26.0 ± 4.5	35.0	
male	69	26.4 ± 4.6	35.6	0.32
female	76	25.7 ± 4.4	34.5	
LAvol/ht ² (ml/ m ²)		16 ± 2.8	21.6	
male	69	15.6 ± 2.9	21.4	0.175
female	76	16.3 ± 2.8	21.9	
LAvol/ht ^{2.7} (ml/ m ^{2.7})		11.4 ± 2.2	15.8	
male	69	11.4 ± 2.4	16.2	0.005
female	76	12.8 ± 2.6	18.0	

Citation: Edmundo J. Nassri Camara, Flávia R. do Prado Valladares, Ng Kin Key, Paloma Fonseca Santana, Jun Ramos Kawaoka, Thais Harada Campos, Marcus Ribeiro de O. Santana, Alex Costa Cunha, Danilo Sousa Sampaio, Gustavo Pinheiro Santana, Luis Gustavo S. Brito, Narjara de O. Cardoso Dourado, Saulo Jende Nascimento, Alice Povoá A. L. Lira, Nailly N. do Nascimento, Romeu Pacheco F. dos Santos, Sérgio Rodrigo F. Rocha, Thaise Gordiano Machado. Indexing of Left Atrial Volume by Body Surface Area and Height in a Brazilian Population without Previous Heart Disease and with a Normal Heart on Echocardiography. Behavior in Obese and Overweight Patients. *Cardiology and Cardiovascular Medicine*. 7 (2023): 25-31.