ORIGINAL ARTICLE

Echocardiographic Reference Values for Right-Sided Heart Chambers in a Healthy Population

Valores ecocardiográficos de referencia de las cavidades derechas en una población sana

ARACELI B. SEGOVIA[1], GISELA M. KILLINGER[1], LAURA GARATE[1], NINA SALINAS[1], DIEGOMANENTE[1], JUAN M. FILIPUZZI[1], CARLOS A, RODRÍGUEZ CORREA[2]

ABSTRACT

Background: The evaluation of right-sided heart chambers is extremely important for the diagnosis and prognosis of different conditions. However, there is little information in the literature on the reference values of the right-sided heart chamber dimensions and right ventricular function.
Objective: The aim of this study was to establish the reference values of the right-sided heart chambers, to identify the differences associated with sex and anthropometric variables and to evaluate the interobserver and intraobserver variability in determining these values.
Methods: The study included healthy men and women ≥16 years. Strict exclusion criteria were applied. A subgroup of 40 people underwent multiple measurements of the right-sided heart chambers and interobserver and intraobserver variability was estimated.
Results: A total of 438 persons were included; 55.2% (n = 242) were men. Mean age was 34 ± 9 years. There were significant differences in the variables analyzed between men and women that persisted after they were indexed by body surface area. Interobserver concordance (ICC > 0.75) was excellent in 50% of the variables evaluated, fair to good (ICC 0.4 to 0.75) in 47.4% and poor (ICC <0.4) in 2.6%. Intraobserver concordance was excellent in 54.8% of the variables, fair to good in 42.8% and poor in 2.4%.
Conclusion: Reference values for the evaluation of right-sided heart chambers are presented. The differences observed between sexes and related to body surface area emphasize the need for discriminating according to these parameters in daily practice. Interobserver and intraobserver concordance ranged between good and excellent for most of the variables analyzed.

Key words: Ventricular Function, Right – Heart Atria – Heart Ventricles – Echocardiography – Body Surface Area - Sex

RESUMEN

Introducción: La evaluación de las cavidades cardíacas derechas es de gran importancia diagnóstica y pronóstica en diversas patologías. Sin embargo, existen pocos datos bibliográficos acerca de los valores de referencia de sus dimensiones así como de la función del ventrículo derecho.
Objetivo: Nuestro objetivo fue establecer dichos valores, identificar diferencias asociadas al sexo y a variables antropométricas y evaluar la variabilidad inter- e intraobservador en su determinación.
Material y métodos: Se incluyeron prospectivamente personas sanas ≥16 años, de ambos sexos. Se aplicaron estrictos criterios de exclusión. Se realizó la evaluación ecocardiográfica con múltiples mediciones de cavidades derechas y la estimación de la variabilidad inter- e intraobservador en un subgrupo de 40 personas.
Resultados: Se incluyeron 438 personas, el 55,2% (n=242) fueron hombres. La media de edad fue 34±9 años. Las variables analizadas mostraron diferencias significativas entre hombres y mujeres, que persistieron al indexarlas a superficie corporal. La fuerza de concordancia para la variabilidad interobservador fue excelente (CCI >0,75) en el 50% de las variables estudiadas, regular a buena (CCI 0,4 a 0,75) en el 47,4% y pobre (CCI< 0,4) en el 2,6%. La concordancia intraobservador fue excelente en el 54,8% de las variables, regular a buena en el 42,8% de ellas y pobre en el 2,4%.
Conclusión: Presentamos valores de referencia para la evaluación de las cavidades derechas. Las diferencias observadas entre sexos y según la superficie corporal hacen necesaria su discriminación acorde con dichos parámetros en la práctica diaria. La concordancia interobservador e intraobservador fue excelente a buena en la mayoría de las variables estudiadas.

Palabras claves: Función ventricular derecha - Ventrículos derecho - Atrios cardíacos - Ecocardiografía - Superficie corporal - Sexo

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Address for reprints: Araceli B. Segovia. Centro Rossi. Beruti 2853 – (C1425BBG) Ciudad Autónoma de Buenos Aires, Argentina.
E-mail: asegovia@cdrossi.com

[1] Echocardiography Laboratory, Centro Rossi, Autonomous City of Buenos Aires, Argentina.
[2] Chief of the Department of Cardiology, Centro Rossi, Autonomous City of Buenos Aires, Argentina.
Echocardiography Laboratory, Centro Rossi, Autonomous City of Buenos Aires, Argentina.

INTRODUCTION

Right-sided heart chambers have an important prognostic value (1, 2) in several conditions, as congenital heart defects, (3) pulmonary hypertension, (4) heart failure, (5) arrhythmogenic right ventricular (RV) dysplasia, (6) and pulmonary embolism. (7) Therefore, the estimation of right-sided heart chamber dimensions and function is essential for the diagnosis and follow-up of these patients. (8, 9) However, there is no sufficient information in the literature compared to the information available of left-sided heart chambers. (10, 11)

Although magnetic resonance imaging (MRI) is the method of choice for the evaluation of the right heart (12), echocardiography is more commonly used because it is more accessible and cost-effective. The complex anatomy of these chambers and the anterior and retrosternal location of the right ventricle make echocardiography evaluation difficult and produce significant variability in the resulting measurements. For this reason, the aims of the present study were to estimate reference values for right-sided heart chamber dimensions and function by echocardiography in healthy volunteers, and correlate these parameters with sex, age and other anthropometric variables. Interobserver and intraobserver variability were also estimated as a consequence of the complex anatomy and the technical difficulties described.

METHODS

Study population

The cohort was made up of healthy men and women >16 years of age who were prospectively evaluated in our center for preventive health check-up. The patients did not present history of cardiovascular or systemic diseases. Health check-up consisted of complete history taking and physical examination with blood pressure, heart rate, body weight and height assessments. Body surface area (BSA) (13) and body mass index (BMI) were calculated. Laboratory tests, electrocardiogram, 12-lead exercise stress test, chest x-ray and echocardiography were performed in all the cases. Strict exclusion criteria were applied (Table 1).

Echocardiographic evaluation

A Philips Affiniti 50 ultrasound machine (Bothell, WA, USA) was used for color Doppler transthoracic echocardiography. All measurements were made with an S 4-2 transducer, using second harmonic imaging at end expiration to avoid translation motion and respiratory motion artifacts. Dimensions were quantified by two-dimensional echocardiography using inner-edge-to-inner-edge method, following the recommendations of the American Society of Echocardiography. (10, 11) Table 2 shows the specific measurements of the right chambers obtained in the RV inflow tract view, short axis view at the level of the great vessels, apical 4-chamber view and subcostal 4-chamber view. In the apical 4-chamber view, visualization of the lateral RV wall and interventricular septum was prioritized, with correct visualization of the apex to avoid foreshortening.

Interobserver and intraobserver variability

Interobserver and intraobserver variability was analyzed in a subgroup of 40 persons that were randomly selected from the study group. Two different operators performed the evaluation. The variables analyzed were measured by each observer in a blind fashion at two different times, 0 and 1, with an interval of 30 days, applying the same methods used for the total population. Variability was determined by the intraclass correlation coefficient (ICC) (14), and was considered poor if the ICC was >0.4, good if ICC was between 0.4 and 0.75 and excellent when ICC was >0.75.

Statistical analysis

The distribution of the variables analyzed (normal or Gaussian distribution versus non normal o non-Gaussian distribution) was assessed using Kolmogorov Smirnov Z-statistics. The variables with normal and non-Gaussian distribution were presented as mean ± standard deviation, or median and interquartile range, respectively. Continuous variables with normal and non-Gaussian distribution were compared using Student's t test or the Wilcoxon test, respectively. Pearson's correlation coefficient was used to calculate the correlation (r) between the variables. Interobserver and intraobserver variability was determined with the ICC. (14) A p value < 0.05 was considered statistically significant. All the statistical calculations were performed using SPSS® Statistics Base 20 software package.

Table 1. Exclusion criteria

Exclusion criteria
Cardiovascular risk factors: HT, DBT, dyslipidemia, obesity
Cardiovascular events, left ventricular dysfunction
Heart valve disease (except for mild mitral regurgitation, mild tricuspid regurgitation and mild pulmonary regurgitation)
Non-ischemic heart disease
Systemic diseases or conditions producing hemodynamic changes
Pulmonary disease/COPD
HIV/AIDS
Pulmonary hypertension
Use of anorectic drugs
High performance athletes
Chest wall or spinal cord malformations
Inadequate ultrasound window

DBT: Diabetes mellitus; COPD: Chronic obstructive pulmonary disease; HIV/AIDS: Human immunodeficiency virus/Acquired immunodeficiency syndrome; HT: Hypertension.

Table 2. Standardization of echocardiographic right ventricular dimension, right atrial dimension and right ventricular function measurements

View	Variable	Specifications
Right ventricular dimensions		
Parasternal short axis view at the level of the great vessels	RVOT1	At end-diastole, perpendicular to the middle point of aortic valve closure
Parasternal short axis view at the level of the great vessels	RVOT2	At end-diastole, 1 cm proximal to the P annulus
Parasternal short axis view at the level of the great vessels	P annulus	End-systole
Parasternal short axis view at the level of the great vessels	PA	At end-systole, 1 cm proximal to the P annulus
Apical 4-chamber view	T annulus	End-diastole
Apical 4-chamber view	RVD1	At end-diastole, longitudinal diameter from the tricuspid annulus plane to the apex
Apical 4-chamber view	RVD2	At end-diastole, junction of the basal and middle RV chamber
Apical 4-chamber view	RVD3	At end-diastole, junction of the middle and apical RV chamber
Apical 4-chamber view	EDA	At end-diastole, including chamber trabeculations and papillary muscles
Apical 4-chamber view	ESA	At end-systole, including chamber trabeculations and papillary muscles
Subcostal 4-chamber view	RV thickness	With the zoom function, at the level of the tip of the anterior tricuspid leaflet
Right ventricular function		
Apical 4-chamber view	FAC %	Fractional area change between diastole and systole
Apical 4-chamber view	TAPSE	Tricuspid annulus plane systolic excursion
Apical 4-chamber view	Tissue Doppler PSV	Tissue Doppler peak systolic velocity of the lateral tricuspid annulus
Right atrial dimensions		
RV inflow tract	RA volume 1	At the end of ventricular systole (largest volume) excluding the inferior vena cava, the superior vena cava and RA appendage
Apical 4-chamber view	RAD1	At the end of ventricular systole, major dimension
Apical 4-chamber view	RAD2	At the end of ventricular systole, minor dimension
Apical 4-chamber view	RA area	At the end of ventricular systole, by planimetry
Apical 4-chamber view	RA volume 2	At the end of ventricular systole
Subcostal 4-chamber view	RA volume 3	At the end of ventricular systole
Subcostal view	IVC	At 1 cm from the junction with the right atrium

EDA: Right ventricular end-diastolic area; ESA: Right ventricular end-systolic area; FAC: Fractional area change; IVC: Inferior vena cava; P annulus: Pulmonary annulus; PA: Pulmonary artery; RA: Right atrial; RAD: Right atrial dimension; RV: Right ventricular; RVD: Right ventricular diameter; RVOT: Right ventricular outflow tract; PSV: Peak systolic velocity; T annulus: Tricuspid annulus; TAPSE: Tricuspid annulus plane systolic excursion.

RESULTS

From March 2014 to January 2017, 438 healthy subjects who were prospectively evaluated in our center for preventive health check-up were included in the study. Mean age was 34.3±9 years (range: 16 to 64 years) and 242 (55.2%) were men. The demographic data are shown in Table 3. Twenty-four percent of the subjects were current smokers or former smokers, with exclusion of other cardiovascular risk factors.

Table 3 shows the reference values of our healthy population. The most difficult variables to measure were: pulmonary annulus diameter, estimated in 94% of the cases; pulmonary artery (PA) diameter, estimated in 94.7% of the cases and the right atrial (RA) volume obtained in the subcostal view in 93% of the cases and in the RV inflow tract in 97% of the cases. A suboptimal ultrasound window was the main limitation to obtain these data. The other variables were obtained in all (100%) the patients.

In most determinations, the values obtained were significantly higher in men. However, there were no significant differences between men and women in the values of the PA diameter, RV transverse diameter at the junction between the middle and inferior third in the apical 4-chamber view (RVD3), diastolic RV free wall thickness in the subcostal view and the RA volume 3 measured in the RV inflow tract (Figure 1 a-b). The parameters of RV function and systolic pulmonary artery pressure were similar in men and women.

There was a weak correlation between age and most of the variables analyzed. However, the correlation was moderate, though statistically significant, after indexing for weight, height, and BSA, with a small difference favoring the latter. The strongest association was obtained between BSA and RV end-diastolic area (EDA) ($r = 0.52$; $p = 0.0001$), RV end-systolic

Table 3. Reference values in the total population, men and women, and indexed by BSA

Variable	Total	Men	Women	p value	Total/BSA	Men/BSA	Women/BSA	p value
Right ventricular dimensions								
LVOT1 (2) (mm)	27 (24-30)	28 (25-31)	25 (23-28)	0.0001	(1)15 ± 2.3	14.6 ± 2	15.6 ± 2	<0.00001
LVOT2 (1) (mm)	23 ± 3.7	24 ± 3.7	21.7 ± 3	0.0001	(1)12.9 ± 2.1	12.6 ± 2	13 ± 2	<0.00001
P annulus (2) (mm)	21 (18-23)	21 (19-24)	20 (18-22)	0.006	(1)11.5 ± 1.9	11 ± 1.9	12 ± 1.78	<0.00001
PA (2) (mm)	20 (18-22)	20 (18-23)	19 (18-21)	**0.23**	(1)11.2 ± 2	10.6 ± 1.9	11.9 ± 1.9	<0.00001
T annulus (2) (mm)	29 (26-32)	30 (26-33)	27(25-30)	0.0001	(2)16 (14-17.6)	15.7 (13.7-17)	16.7 (15.2-17.9)	**0.09**
RVD1 (1) (mm)	69.5 ± 8	72 ± 8	66 ± 7.6	0.0001	(1)38.7 ± 4.7	37.5 ± 4	40 ± 4.7	<0.00001
RVD2 (2) (mm)	30 (27-34)	32 (29-36)	28.5 (26-31)	0.001	(1)17 ± 2.9	16.9 ± 3	17.5 ± -2.7	0.028
RVD3 (2) (mm)	21 (17-24)	22 (18-26)	19 (16-22.6)	**0.149**	(2)11 (9.8-13.7)	11 (9.6-13.6)	11 (9.9-13.7)	**0.8**
EDA (2) (cm²)	17 (14-20)	18 (16-21)	15 (13-17)	0.0001	(1)9.5 ± 1.8	9.8 ± 1.9	9 ± 1.7	0.001
ESA (2) (cm²)	10 (9-12)	11 (10-13)	9 (7-10)	0.0001	(2)5 (4.6-6.6)	5.7 (4.9-6.8)	5 (4-6)	0.03
RV thickness (2) (mm)	4 (3.7-4.8)	4.2 (3.7-5)	4 (3.6-4.4)	0.063	(1)2 ± 0.4	2.2 ± 0.4	2.4 ± 0.44	<0.00001
RV function								
TAPSE (2) (mm)	24 (22-26)	24 (22-27)	24 (21-26)	**0.06**				
FAC (1) (%)	39.7 ± 6.65	39.2 ± 6.8	40+/-6	**0.22**				
PSV (2) (cm/s)	13.7 (12-15)	14 (12-15)	13 (12-15)	**0.72**				
RA dimensions								
RA volume 1 (2) (ml)	40 (33-49)	42(36-53)	37 (30-45)	0.037	(1)23 ± 6	23±6	22.8 ± 6.6	**0.5**
RA volume 2 (2) (ml)	36.9 (30-45)	41.8(34-49)	31 (26-38)	0.05	(1)21 ± 5	22±5	19.8 ± 5	<0.00001
RA volume 3 (2) (ml)	44.5 (35-55)	47(38-57)	41 (32-53)	**0.1**	(1)25.9 ± 8	25.9±8.5	26 ± 7.9	**0.9**
RAD1 (1) (mm)	43.9 ± 5	45.7± 4.7	41.8 ± 4.9	0.0001	(1)24.5 ± 2.8	23.8±2.6	25.5 ± 2.9	<0.00001
RAD2 (2) (mm)	36 (33-40)	38(35-42)	34 (31-38)	0.0001	(1)20 ± 2.9	19.9±2.7	21 ± 3	<0.00001
RA area (2) (cm²)	14(12-16)	15(13-17)	13 (11-14)	0.0001	(1)7.9 ± 1	8±1	7.9 ± 1	**0.2**
SPAP (1) (mmHg)	23.8 ± 3.5	23.6 ± 3.5	24 ± 3.5	**0.61**				
IVC (2) (mm)	16 (14-18)	16(14-18)	15 (14-17)	0.01				

(1) Expressed as mean ± SD, (2) Expressed as median and interquartile range.
EDA: Right ventricular end-diastolic area; ESA: Right ventricular end-systolic area; FAC: Fractional area change; IVC: Inferior vena cava; P annulus: Pulmonary annulus; PA: Pulmonary artery; RAD: Right atrial dimension; RVD: Right ventricular diameter; RVOT: Right ventricular outflow tract; SPAP: Systolic pulmonary artery pressure; PSV: Peak systolic velocity; T annulus: Tricuspid annulus; TAPSE: Tricuspid annulus plane systolic excursion.

area (ESA) (r = 0.48; p = 0.0001), RV longitudinal diameter (RVD1) (r = 0.41; p = 0.0001), RA major dimension (RAD1) (r = 0.46; p = 0.0001), RA minor dimension (RAD2) (r = 0,4; p = 0.0001), RA area (r = 0.52; p = 0.0001) and RA volume in the apical 4-chamber view (RA volume 2) (r = 0.49; p = 0.0001).

Table 3 shows the values corresponding to the general population and to men and women indexed by BSA, as it is the anthropometric variable with the best correlation. The values indexed by BSA were higher in women, except for EDA, ESA and RA volume 2, which were higher in men. There were no differences between men and women in the BSA-indexed values of the tricuspid annulus, RVD3, RA volume 1, subcostal view of RA volume (RA volume 3) and RA area.

Table 4 shows that the ICC for interobserver and intraobserver variability ranged from good (0.4-0.75) to excellent (>0.75) in most cases. The greatest interobserver variability occurred in the quantification of RV free wall thickness (ICC 0.34) and RVD3 (ICC 0.4) followed by ESA (ICC 0.47) and RA volume 3 (ICC 0.48). The worst intraobserver concordance was seen in the estimation of RV free wall thickness (ICC 0.28).

DISCUSSION

The evaluation of right-sided heart chamber function and dimensions is vital for the diagnosis and prognosis of several conditions; (1-3) however, qualitative assessment lacks accuracy. (15) In our study, we were able to estimate the reference values by echocardiography in healthy subjects using standardized measurements to reduce such variability. The differences found between women and men and the correlation with BSA make it necessary to have indexed values differentiated by sex.

The reference values of RV dimensions and RA volume obtained in the apical 4-chamber view are slightly lower than those reported in the guidelines for cardiac chamber quantification (11) and in the NORRE study (16). However, the guidelines for cardiac chamber quantification only provide total values with no differences by gender and not indexed by BSA, and the determinations of right-sided heart chamber dimensions in the NORRE study presented the greatest variability.

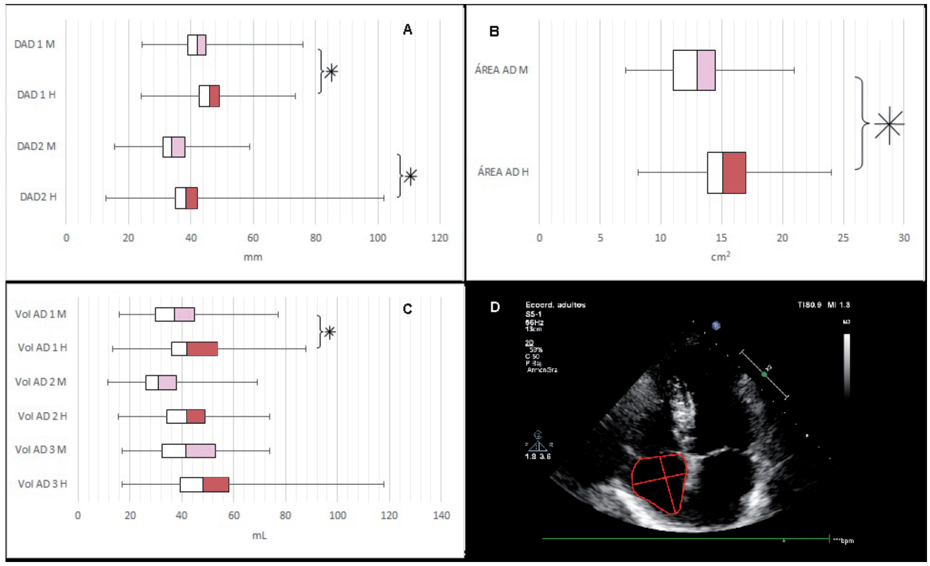

Fig. 1.a. Sex differences in right atrial dimension **A.** Right atrial major and minor dimensions. **B.** Right atrial area in 4-chamber view. **C.** Right atrial volumes 1, 2 and 3. **D.** Example of right atrial measurement from the apical 4-chamber view. (*) p< 0.05.

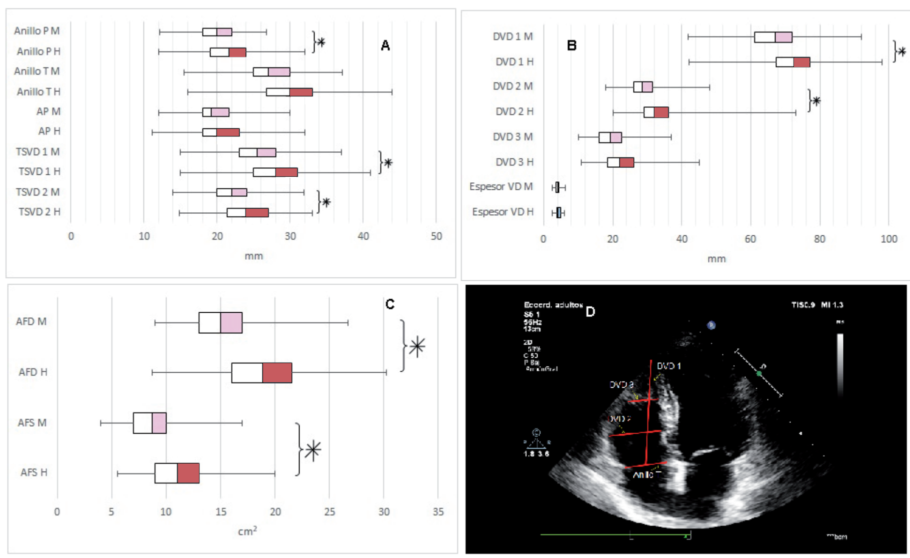

Figure 1.b. Gender differences in right ventricular dimensions and areas. **A.** Diameters obtained in the parasternal short axis view at the level of the great vessels and apical 4-chamber view at the level of the tricuspid annulus **B.** Right ventricular diameters and thickness **C.** Right ventricular end-diastolic area and end-systolic area. **D.** Example of right ventricular measurement from the apical 4-chamber view. (*) p< 0.05.
EDA: End-diastolic area; ESA: End-systolic area; P annulus: Pulmonary annulus; T annulus: Tricuspid annulus; PA: Pulmonary artery; RVD1: Right ventricular diameter 1 (longitudinal); RVD 2: Right ventricular diameter 2 (basal); RVD 3: Right ventricular diameter 3 (mid-apical third); RV thickness: Right ventricular thickness in the subcostal view; RAD: Right atrial dimension; RVD: Right ventricular diameter; RVOT1: Right ventricular outflow tract 1; RVOT2: Right ventricular outflow tract 2; M: Man; F: Woman.

Besides estimating the right heart dimensions mentioned in the current guidelines, (10, 11) we also measured the tricuspid annulus dimension, which provides significant prognostic value in patients undergoing mitral valve surgery or repair (17, 18) the pulmonary annulus diameter and the pulmonary artery diameter which are important to follow-up patients with congenital heart defects. (19) The proximal and distal RV outflow tract dimensions, useful for the diagnosis of arrhythmogenic RV dysplasia, were estimated and indexed by BSA. (6) The availability of indexed parameters in healthy people allows a more specific use of these criteria for the diagnosis of this condition, particularly in special populations such as athletes. (20, 21)

In accordance with our findings, the MESA study (12), which estimated RV mass, volumes, and ejection fraction using MRI in 4,204 volunteers, and the study by D'Oronzio et al. (22) also showed significant sex differences for right-sided heart dimensions. In most of the variables analyzed, the values were higher in men, except for PA, RVD3, RV thickness and RA volume 3, in which no significant differences were observed.

In line with the information provided by Willis et al., (23) we did not find any differences between men and women in the variables of RV function. This finding is opposed to that of the NORRE study (16) and the JAMP study (24), in which RV fractional area change was higher in women.

When the correlation between age and right heart dimensions and function is evaluated, there is a significant trend toward greater RV function parameters and a reduction in RV volumes. (12, 16, 25) Yet, we did not find a significant correlation between age and most of the variables analyzed. This finding is similar to the one reported by Willis et al. (23) and is probably

Table 4. Interobserver and intraobserver variability

Variable	Interobserver variability ICC	Intraobserver variability ICC
RVOT1	0.79	0.94
RVOT2	0.52	0.9
P annulus	0.63	0.6
PA	0.77	0.7
T annulus	0.8	0.76
RVD1	0.9	0.83
RVD2	0.77	0.72
RVD3	**0.4**	0.57
EDA	0.8	0.77
ESA	**0.47**	0.75
RV thickness	**0.34**	**0.28**
TAPSE	0.89	0.72
PSV	0.97	0.82
FAC	0.65	0.63
RA volume 1	0.59	0.7
RA volume 2	0.68	0.86
RA volume 3	**0.48**	0.64
RAD1	0.84	0.79
RAD2	0.9	0.78
RA area	0.67	0.91

EDA: End-diastolic area; ESA: End-systolic area; FAC: Fractional area change; IVC: Inferior vena cava; P annulus: Pulmonary annulus; PA: Pulmonary artery; RAD: Right atrial dimension; RVD: Right ventricular diameter; RVOT: Right ventricular outflow tract; SPAP: Systolic pulmonary artery pressure; PSV: Peak systolic velocity; T annulus: Tricuspid annulus; TAPSE: Tricuspid annulus plane systolic excursion.

due to not having included patients >64 years as a result of the strict exclusion criteria used.

In our study, BSA was the anthropometric parameter that yielded the best correlation with the dimensions obtained. This finding is consistent with the one described in the rest of the international scientific literature (16, 22, 23) and in the local study by Romero et al., (26) emphasizing the importance of indexing these variables by BSA, such as it is done with left-sided heart chambers. The sex differences in the parameters indexed by BSA remain in most variables and are usually greater in women, except for RA volume 3, EDA and ESA, which were greater in men, as Willis et al. have reported. (23) Tricuspid annulus dimension, RVD3, RA volume 1, RA volume 3, RA area and RV function parameters, all indexed by BSA, did not present significant differences between women and men.

In spite of the complex anatomy of the right cardiac chambers and of the great variability in the estimation of their dimensions and function, there is generally no information about the variability detected during these estimations. (22, 24) In accordance with the studies by Foale et al, (27) and Willis et al. (23) all the measurements were made in a prospective and standardized manner, with subsequent evaluation of interobserver and intraobserver variability. Unlike other studies (16), most of the variables analyzed obtained a good to excellent ICC for interobserver and intraobserver variability. Right ventricular free wall thickness was the parameter with the highest interobserver and intraobserver variability. This finding is similar to the aforementioned study (23), although the authors used the M-mode in the parasternal long-axis view while we made the measurements in the subcostal view, using the zoom function to obtain a magnified view of the tricuspid valve opening in diastole. Despite such variability was statistically significant, it does not seem to be clinically relevant due to its low absolute value. The analysis of EDA and RVD3 also showed poor ICC, probably due to the dense trabecular pattern that prevents the correct evaluation of the endocardium and to the smaller end-systolic dimension in the first case, as other authors have previously described. (23-27)

Our study has limitations. We did not evaluate racial differences that had been demonstrated in previous studies. (23, 24) Elderly healthy subjects had little representation due to the strict exclusion criteria used.

CONCLUSIONS

Reference values for the evaluation of right-sided heart chambers were established and the differences between sexes and those related to BSA were demonstrated. We observed good interobserver and intraobserver correlation in most variables, except for those technically difficult to measure by echocardiography.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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