Original Article

Correlation Between Echocardiographic and Hemodynamic Measurements in Right Atrium and Right Ventricle Assessments of Patients with Pulmonary Hypertension

Correlação entre Medidas Ecocardiográficas e Hemodinâmicas na Avaliação do Átrio Direito e Ventrículo Direito em Pacientes com Hipertensão Pulmonar

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Abstract

Introduction: Pulmonary hypertension (PH), a serious clinical condition, can lead to right ventricular systolic dysfunction (RVSD) with prognostic implications. Patients with suspected PH should undergo transthoracic echocardiography (TTE) for diagnosis and evaluation as the main screening and follow-up exam.

Objective: To verify the associations of and agreement between measurements of mean pressure in the right atrium (RA) and RVSD with TTE

Method: Individuals diagnosed with PH were included. All patients underwent TTE and RCC. The following were evaluated by TTE: right atrial area (RAA), mean right atrial pressure through the diameter and collapsibility of the inferior vena cava (RMAPTTE), RA strain (RAS), tricuspid annular plane systolic excursion, fractional area change, RV free wall strain, and tricuspid s' wave. Mean RA pressure (RMAPRCC) and cardiac index (CI) were evaluated through the RCC.

Results: Of the 16 patients, 13 were female. The mean patient age was 44.4 (±14.9) years. An association was found between RMAPRCC and AAD, RMAPTTE, and RAS (r=0.845, r=0.621, and r=-0.523, respectively; p<0.05). There was an association between the mortality risk categories measured by the RAA and RMAPRCC measures (X2=10.42; p=0.003), with moderate agreement (k=0.44; p=0.012). RVSDJ was present in 10 patients. There was an association between RVSD (present or absent) and CI (r=0.522; p=0.04) with moderate agreement (k=0.43; p=0.037).

Conclusion: The TTE and RCC measurements showed an association in the assessment of mean right atrial pressure, especially between RAA and RMAPRCC. An association with RVSD and moderate agreement between methods were also noted.

Keywords: Hypertension, Pulmonary, Echocardiography, Ventricular Dysfunction, Right, Catheterization.

Resumo

Introdução: *Hipertensão Pulmonar (HP), uma condição clínica grave, pode levar à disfunção sistólica do ventrículo direto (DSVD), com implicações prognósticas. Pacientes com suspeita de HP devem ser submetidos ao ecocardiograma transtorácico (ECOTT) para diagnóstico e avaliação, colocando-o como o principal exame de triagem e acompanhamento.*

Objetivo: *Verificar a associação e a concordância das medidas referentes à pressão média no átrio direito (AD) e à disfunção sistólica do ventrículo direto (DSVD) ao (ECOTT) e ao cateterismo de câmaras direitas (CCD) em pacientes com (HP).*

Métodos: *Foram incluídos indivíduos com diagnóstico de (HP). Todos os pacientes foram submetidos ao ECOTT e CCD. Avaliou-se pelo ECOTT: área do átrio direito (AAD), pressão média do átrio direito (AD) através por meio do diâmetro e da colapsabilidade da veia cava inferior ($PMAD_{ECOTT}$), strain AD (SAD), TAPSE (excursão sistólica do plano anular tricúspide), MAF (mudança da área fracional), SPLVD (strain da parede livre do VD) e onda s´ tricuspídea. Pelo CCD avaliaram-se pressão média do ($PMAD_{CCD}$) e índice cardíaco (IC).*

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Resultados: *Dos 16 pacientes, 13 eram do sexo feminino. A idade média foi de 44,4 anos (±14,9). Constataram-se associação entre pressão média do átrio direito PMADCCD com área do átrio direito, PMADECOTT pressão média do átrio direito e SAD strain do átrio direito (r=0,845, r=0,621 e r=-0,523, respectivamente; p< 0,05). Verificou-se associação entre as categorias de risco de mortalidade, mensuradas pelas medidas AAD da área do átrio direito e pressão média do átrio direito PMADCCD (X2=10,42; p=0,003), com concordância moderada (k=0,44; p=0,012). DSVD A disfunção sistólica do ventrículo direto estava presente em dez pacientes. Houve associação entre disfunção sistólica do ventrículo direto DSVD (presente ou ausente) e índice cardíaco IC (r=0,522; p=0,04), com concordância moderada (k=0,43; p=0,037).*

Conclusão: *As medidas do ecocardiograma transtorácico (ECOTT) e cateterismo de câmara direita (CCD) demostraram associação na avaliação da pressão média do átrio direito com melhor associação entre área do átrio direito AAD e pressão média do átrio direito ($PMAD_{CCD}$). Houve associação com concordância moderada quanto à disfunção sistólica do ventrículo direto (DSVD) entre métodos.*

Palavras-chave: *Hipertensão pulmonar, Ecocardiografia, Disfunção Ventricular Direita, Cateterismo.*

Introduction

Pulmonary hypertension (PH) is a potentially severe clinical condition characterized by hemodynamic changes resulting from several pathophysiological mechanisms that can lead to progressive right ventricular (RV) failure and even death.[1]

The early detection and accurate disease severity classification are essential for diagnosing PH and ensuring that patients receive the best treatment.[2]

All patients with suspected PH should undergo transthoracic echocardiography (TTE) to diagnose and evaluate PH repercussions as the main screening test.[3,4] RV systolic pressure and right atrial (RA) mean pressure are estimated by TTE. Additionally, right chamber characteristics are evaluated, especially regarding PH-related structural and functional disorders.[2,3,5] TTE measurements have prognostic importance in PH patients. Those referring to RV systolic function assessment, which can be determined by quantifying the tricuspid annular plane systolic excursion (TAPSE), RV fractional area changes (FAC), tricuspid annular systolic velocity (tricuspid s□), and RV free wall strain (RVFWS) stand out.[6] Adequate RA assessments are highly relevant in the context of PH, as mean RA pressure and its dimensional increase are prognostic factors for patients with PH,[7–9] but the reliability and accuracy of noninvasive assessments are limited. RA strain (RAS) analysis also has prognostic importance for patients with PH.[6]

PH treatment is linked to an adequate diagnosis, which starts after clinical suspicion and echocardiogram compatible with the disease, followed by the PH group identification. After concluding the diagnosis of pulmonary arterial hypertension (group 1), a differential diagnosis is made between several causes with a subsequent risk stratification (1-year mortality). This stratification considers clinical, imaging, and hemodynamic parameters, including RA area (RAA) and mean pressure obtained by right chamber catheterization (RCC). This assessment is recommended every 3–6 months to achieve/maintain a low-risk profile with treatment associated with good exercise capacity, good quality of life, good RV function, and a low risk of mortality.[4]

Most patients with PH are referred for RCC to confirm the diagnosis and assess its severity, prognosis, and response to specific therapies during the disease course. This test is considered the gold standard for these assessments.[10] Although safe, RCC is invasive and its generalized use is not recommended, as its acquisition and interpretation require special attention and expertise.[11,12]

Thus, this study aimed to verify the accuracy and precision of mean pressure parameters in RA and RV dysfunction on TTE versus the corresponding measurements obtained by RCC in patients with PH.

Methods

The study was developed in accordance with the Regulatory Guidelines and Norms for Human Research (resolution 466/2012 of the National Health Council and Declaration of Helsinki) and approved by the local institutional ethics committee. All participants signed an informed consent form.

Participants

This study population consisted of patients referred for RCC for PH assessment in 2019–2021. The inclusion criteria were age over 14 years, being of either sex, and diagnosis of PH in groups 1 (pulmonary arterial hypertension, including idiopathic disease) and 4 (chronic thromboembolic pulmonary hypertension) according to clinical PH classification.[13] The exclusion criteria were significant arrhythmia, severe heart failure, inadequate TTE echocardiographic window, and incomplete invasive measurements.

Instruments and procedures

The patients initially attended pre-scheduled appointments at cardiology outpatient clinics for inclusion criteria screening. The included patients were evaluated for demographic data collection (age, sex, body mass index [BMI]) and clinical and physical examination findings (functional class, group, medication use) after signing the informed consent form. Subsequently, all patients underwent TEE in the echocardiography laboratory and, after 3–4 h, underwent RCC in the hemodynamics laboratory.

Transthoracic echocardiography

All patients underwent TEE performed by a single experienced echocardiographer using a Philips CX 50 device

with a 2.5–3.5 MHz multifrequency transducer. Cardiac chamber echocardiographic measurements were performed according to the transthoracic echocardiographic examination guidelines of the American Society of Echocardiography[14] and the consensus document of the European Society of Cardiovascular Imaging and the American Society of Echocardiography for left atrial, RV, and RA deformity imaging on echocardiography.[15]

The following hemodynamic measurements were obtained and/or calculated by TTE: RV systolic pressure (RVSP; in mmHg) calculated by the formula 4 × peak tricuspid regurgitation velocity^2 + estimated mean RA pressure ($MRAP_{TTE}$); and mean pulmonary artery pressure (MPAP; in mmHg) calculated by the formula 0.6 × pulmonary artery systolic pressure (PASP).

The RAA (in cm^2) was measured in the four-chamber apical plane at the end of ventricular systole (frame before tricuspid valve opening). The RAS and RVFWS were analyzed through optimized images obtained in the apical four-chamber plane focused on the RV, with a frame rate > 50 Hz with the QRS as the reference point. QLAB 13 (Philips) software version 13.0 (2019) was used for these analyses. The RVFWS was calculated as the mean peak systolic deformity of each of the three long free wall segments expressed as an absolute value. The mean RAS of each atrial wall segment (reservoir function) was calculated through the positive peak wave at the end of ventricular systole.

The parameters used to analyze RV systolic function obtained in the apical four-chamber plane were TAPSE obtained by positioning the unidimensional mode cursor (M) in the basal region of the lateral tricuspid annulus (VN > 16 mm); FAC obtained in two-dimensional mode by tracing the RV endocardial borders and area in systole and diastole and using the formula: FAC=100 (RV area in diastole – RV area in systole)/RV area in diastole (VN>34%); tricuspid s-wave velocity with the positioning of the tissue Doppler volume sample in the basal region of the lateral tricuspid ring (VN>9.4 cm/s), and RVFWS previously described (absolute VN>19%). When one of the four parameters was changed on echocardiography, the diagnosis of RV systolic dysfunction (RVSD) was confirmed.

$MRAP_{TEE}$ evaluated through the inferior vena cava was estimated by images acquired in the subcostal window. The diameter was measured 1–2 cm distant from the junction of the inferior vena cava (IVC), with the RA and the diameter evaluated at the end of expiration. An IVC diameter < 2.1 cm that collapsed > 50% with inspiration received a MRAP value of 3 mmHg, while an IVC diameter > 2.1 cm that collapsed to < 50% received a value of 15 mmHg. In scenarios in which the IVC diameter and collapse did not fit this parameter, an intermediate value of 8 mmHg was used.[4]

Right chamber catheterization

RCC was performed according to the American Heart Association guidelines[4] using a Philips FD10 fluoroscopy device and a TEB SP12 polygraph machine. A JR catheter was introduced through the right cubital or right femoral vein and advanced under radioscopic guidance through the superior vena cava, RA, and tricuspid valve to the pulmonary artery (PA).

Systolic pressure, diastolic pressure, and MPAP were measured in this position in addition to pulmonary capillary pressure, cardiac output (CO), and cardiac index (CI). CO was calculated using the indirect Fick method.

As for RCC, the following measurements were extracted from the pulmonary systolic pressure (systolic PP, in mmHg) and mean systolic pressure (mean PP, in mmHg). RA pressure (RAP; in mmHg) and CI (in L/min/m^2) were also measured to identify patients with ventricular dysfunction (<2.8 L/min/m^2) and no dysfunction (>2.8 L/min/m^2).

Statistical analysis

SPSS software version 25.0 was used for all statistical analyses.

Initially, normality and homogeneity were verified using the Shapiro-Wilk and Levene tests, respectively.

Categorical variables are presented as absolute (n) and relative (%) frequency, while parametric continuous variables are presented as mean and standard deviation (SD) or median and interquartile range.

Linear regression and the Pearson chi-square test were performed for continuous and categorical variables, respectively, to verify the association between the TTE and RCC measurements. The magnitudes of the correlations were analyzed based on Munro's classification: low (0.26–0.49), moderate (0.50–0.69), high (0.70–0.89), and very high (0.90–1.00).[16] A significance level of 5% was used here.

Bland-Altman and intraclass correlation coefficient (ICC–k) analyses were performed after identifying the associations. The Bland-Altman analysis brings two important pieces of information: (1) the bias, which consists of the difference between the measurements and whether this is constant between the range of measurements; and (2) the limit of agreement, which represents the range of possible errors. Therefore, the bias informs the accuracy and the limit of agreement (precision).[17] A significance level of 5% was considered for all analyses.

Results

Participants

The study included 19 participants referred for RCC, with three being excluded due to the unavailability of TEE or RCC data.

Of the 16 participants, 13 (81.3%) were women. Patient ages were 14–69 years, and only three participants were older than 60 years (18.8%). Patient BMI was 13.9–42.30 kg/m^2, with most participants being within the normal range (n=10 [62.5%]). Regarding New York Heart Association functional classification, 37.5% of the patients were class III and 31.2% were class II. Group 1 was predominant (n=13 [81.2%]) with the most common etiology being congenital heart disease (n=7 [53.8%]), followed by idiopathic (n=4 [30.8%]).

Another finding was that half of the patients took specific medications for PH treatment, with 4 (25%) taking

two medications, including riociguat, bosentan, sildenafil, and ambrisentan.

RV systolic pressure was estimated using the peak velocity of tricuspid regurgitation in all patients.

Table 1 presents the participants' demographic, clinical, and physical examination data.

Table 2 presents the echocardiographic measurements of the participants' cardiac chambers and ventricular function.

Table 3 presents the TEE and RCC hemodynamic measurement values.

Right atrium

In the linear regression analysis, a positive strong association was found between $MRAP_{RCC}$ and RAA; a positive moderate association between $MRAP_{RCC}$ and $MRAP_{TEE}$; and a negative moderate association between RAP and RAS (Table 4 and Figure 1). However, no agreement was observed between measurements (Figure 2).

An association was found between risk categories (1-year mortality from PH) measured by $MRAP_{RCC}$ and $MRAP_{TTE}$ (X^2=10.42; p=0.003), with moderate agreement (k=0.44; p=0.012;). (Table 5)

Table 1 - Patients' demographic, clinical, and physical examination data (N=16).

Data	Values
Sex	
Women	13 (81.2)
Men	3 (18.8)
Age, years	44.4 (14.9)
BMI, kg/m2	26.5 (7.5)
BMI category	
Low weight	1 (6.2)
Normal weight	10 (62.6)
Overweight	1 (6.2)
Grade I obesity	1 (6.2)
Grade II obesity	1 (6.2)
Grade III obesity	2 (12.5)
NYHA functional classification	
I	3 (18.8)
II	5 (31.2)
III	6 (37.5)
IV	2 (12.5)
PH group	
1	13 (81.2)
Congenic cardiopathy	7 (53.8)
Idiopathic	4 (30.8)
Rheumatologic disease	2 (15.4)
4	3 (18.8)
Chronic PTE	3 (18.8)
Medication use	
Yes	8 (50.0)
No	8 (50.0)

BMI, body mass index; NYHA, New York Heart Association; PH, pulmonary hypertension; PTE, pulmonary thromboembolism. Data on age and BMI are presented as mean and SD; data on sex, BMI category, functional class, etiology, and medication use are presented as absolute (n) and relative (%) values.

Ventricular dysfunction and cardiac index

RVSD was present in 10 participants (62.5%). A moderate association was observed between ventricular dysfunction categories (present and absent) measured by TTE and RCC (r=0.522; p=0.04), with moderate agreement (k=0.43; p=0.037; Table 6). However, no associations were observed between categories (with and without dysfunction) identified through the CI variable (RCC) for each of the echocardiographic criteria analyzed alone (TAPSE, tricuspid annulus s', FAC, RAS, and RVFWS;). (Table 7)

Discussion

The study verified the association between TEE and RCC RA and RV morphofunctional assessment values in a group of participants with PH.

Table 2 – Echocardiographic measurements.

Variable	Values
LA, mm	35.19 (±3.67)
RVOT, mm	35.13 (±7.56)
Basal RV, mm	48.13 (±11.18)
Medium RV, mm	36.81 (±10.34)
Longitudinal RV, mm	78.25 (±8.09)
RV thickness, mm	6.08 (±1.94)
RAA, cm²	23.71 (±9.34)
RVDD, mm	45.38 (±7.03)
RVSD, mm	29.31 (±5.06)
LVEF, %	64.50 (4.50)
TAPSE, mm	1919 (±5.83)
Tricuspid s', cm/s	10.61 (±2.79)
FAC, %	34.56 (±15.03)
RVFWS, %	19.68 (±8.50)
RAS, %	24.57 (±11.27)

Data are presented as mean ± standard deviation except for LVEF and RVFWS, which are presented as median (interquartile range). FAC, fractional area change; LA, left atrium; LVDD, left ventricular diastolic diameter; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic diameter; RAA, right atrial area; RAS, right atrial strain; RV, right ventricle; RVOT, RV outflow tract; RVFWS, right ventricle free wall strain; TAPSE, tricuspid annular plane systolic excursion; tricuspid s', tricuspid annulus s' wave.

Table 3 - Hemodynamic TEE and RCC measurements.

Measurement	TTE
RVSP, mmHg	59.44 (24.10)
Mean PAP, mmHg	44.21 (20.37)
Measurement	**RCC**
SPAP, mmHg	68.50 (28.71)
MPAP	37.37 (15.37)
MRAPRCC, mmHg	12.69 (8.14)
CI, L/min/m²	3.43 (1.57)

Data are presented as mean (standard deviation). CI, cardiac index; MPAP, mean pulmonary artery pressure; MRAPRCC, mean right atrial pressure by right chamber catheterization; PAP, pulmonary arterial pressure; RCC, right chamber catheterization; RVSP, right ventricular systolic pressure; SPAP, systolic pulmonary artery pressure; TTE, transthoracic echocardiography.

The mean RAP measured by RCC ($MRAP_{RCC}$) was associated with RA measurements taken on TEE (RAA, $MRAP_{TTE}$, and RAS). These data corroborate the study findings of Yuko Fukuda et al. including a moderate correlation with the sum of the three RAS components (reservoir, content, and pump) and $MRAP_{RCC}$ (r=0.56, p=0.005). The sum of RAS also demonstrated prognostic value in that study.[9] However, in our study, despite the association, no agreement was noted between measurements, probably due to the sample size.

RAA is accurately assessed through two-dimensional planimetry only in the apical four-chamber plane, which has implications since RA performance is a three-dimensional phenomenon. However, when RA measurements were evaluated in our study, the RA showed a strong association with $MRAP_{RCC}$. Greater software availability in the future that can examine cardiac resonance will provide relevant information about this framework in the context of PH.[9]

$MRAP_{TTE}$ is performed through the respiratory variability of the IVC, which has limited accuracy due to being relatively subjective. In addition, a certain degree of an RA pressure increase may be required before IVC dilation. As this measurement is used to calculate pulmonary pressures (PASP and MPAP), an inappropriate sum of values may occur. This influence depends on PH level, being less important in more severe than borderline cases.[18] Venkateshvaran et al. showed that RA pressure estimated by TEE was falsely increased in more than 1/3 of cases, which led to overestimated RVSP and MPAP values.[20] Thus, the use of the absolute tricuspid

Tabela 4 – Associação entre $PMAD_{CCD}$ e AAD, $PMAD_{ECOTT}$ e SAD.

Variable	R value	P value
RAA	0.845	<0.001
RAP	0.621	0.010
RAS	-0.523	0.038

MRAPRCC, mean right atrial pressure by right chamber catheterization; RAA, right atrial area; MRAPTTE, mean right atrial pressure on transthoracic echocardiography; RAP, right atrial pressure; RAS, right atrial strain.

Table 5 – Association between categories determined by RAA and $MRAP_{RCC}$.

$MRAP_{RCC}$ risk category	RAA risk category		
	Low	Moderate	High
Low	3 (18.75)	2 (12.50)	0 (0.00)
Moderate	1 (6.25)	3 (18.75)	1 (6.25)
High	0 (0.00)	2 (12.50)	4 (25.0)

Data are presented as absolute and relative frequency. MRAPRCC, mean right atrial pressure by right chamber catheterization; RAA, right atrial area.

Table 6 – Association between ventricular dysfunction categories by TEE and RCC measurements.

RCC: presence of CI	TTE: presence of CI	
	Absent	Present
Absent	6 (37.5)	5 (31.2)
Present	0 (0.00)	5 (31.2)

Data are presented as absolute and relative frequency. CI, cardiac index; RCC, right chamber catheterization; TTE, transthoracic echocardiography.

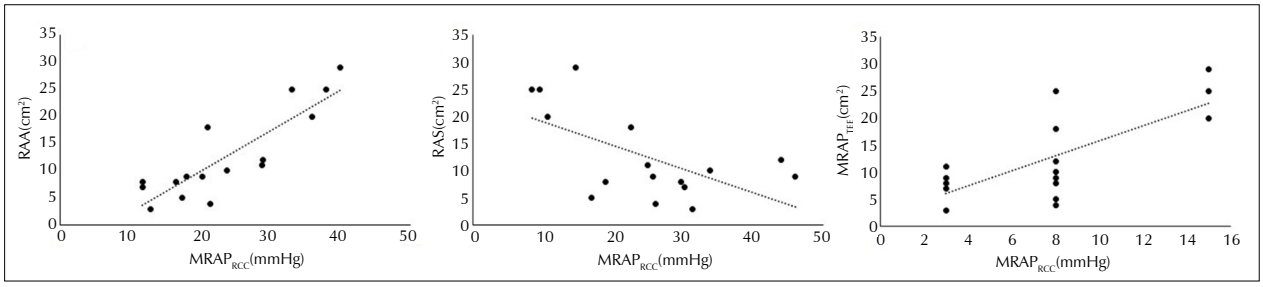

Figure 1 – *Association between MRAPRCC, RAA, MRAPTEE, and RAS.*

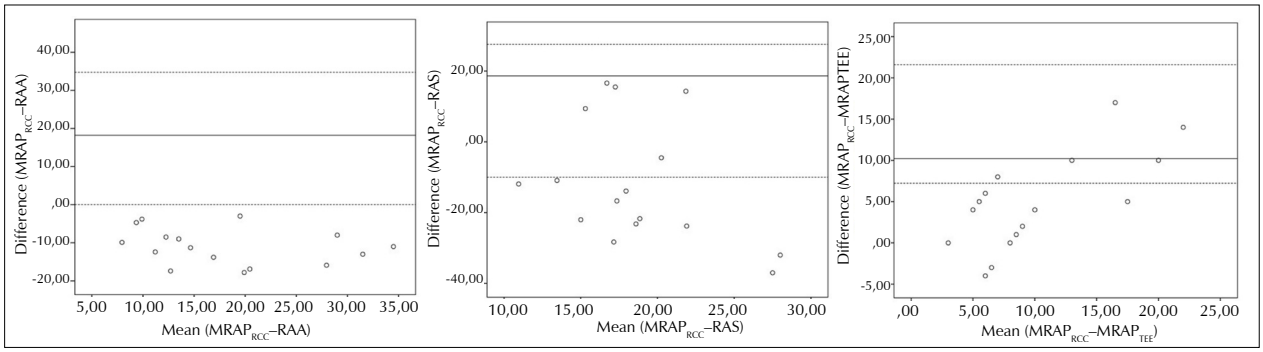

Figure 2 – *Bland-Altman plots of MRAPRCC, RAA, MRAPTEE, and RAS values.*

Table 7- Association between ventricular dysfunction variables by TTE and RCC.

Variable	Presence of dysfunction	CI: Presence of dysfunction		p value
		No	Yes	
TAPSE	No	9 (56.2)	2 (12.5)	0.107
	Yes	2 (12.5)	3 (18.8)	
Tricuspid s'	No	9 (56.2)	2 (12.5)	0.107
	Yes	2 (12.5)	3 (18.8)	
FAC	No	7 (43.8)	1 (6.2)	0.120
	Yes	4 (25.0)	4 (25.0)	
RAS	No	7 (43.8)	1 (6.2)	0.120
	Yes	4 (25.0)	4 (25.0)	
RVFWS	No	5 (31.2)	1 (6.2)	0.363
	Yes	6 (37.5)	4 (25.0)	

Data presented as absolute and relative frequency. CI, cardiac index. Other abbreviations are as shown in Table 2.

regurgitation velocity is recommended in PH assessment as recommended by international guidelines.[4,19]

PH can be classified as carrying a low, intermediate, or high risk of clinical worsening or death. Patients judged at low, intermediate, or high risk have an estimated 1-year mortality of <5%, 5–10%, and >10%, respectively.[4] $MRAP_{RCC}$ and TEE RAA are used to determine PH prognostic scores.[4] This study showed a strong association with moderate agreement between these measurements at each risk level, showing good accuracy.

Due to its anatomical complexity, the RV is the most difficult cardiac chamber to analyze functionally. Cardiac resonance, the gold standard for RV morphofunctional analysis, has no technical limitations in image acquisition, but its lower availability, greater complexity, and higher cost make it unfeasible as a method of choice. On the other hand, TEE has low cost and high feasibility, making it the most attractive method for the initial assessment of global RV function and leaving cardiac resonance for selected cases.[21,22]

RV systolic function can be identified by reduced CI values on RCC and RVSD measurements on TEE. We found an association between LVSD measurements on TEE and CI on RCC with moderate agreement. In this study, CO was calculated using the indirect Fick method, which is less accurate than the direct Fick method and thermodilution with the Swang Ganz, which may explain this result. In addition, RV measurements by TEE change early, before an effective CO change on RCC occurs, which could corroborate this finding.[17,23]

No associations were observed between categories (with and without dysfunction) assessed through the CI variable (RCC) for each of the echocardiographic criteria analyzed alone. This result is probably due to the small number of patients in our sample.

Study limitations

This study has limitations such as its small sample size. However, we consider this a pilot study from which we will expand our sample to obtain more robust results. Cardiac resonance imaging is not available in our service to correlate echocardiographic measurements with the gold standard method, but the tests were performed by an experienced echocardiographer and patients with inadequate windows were excluded. Another limitation was the lack of echocardiographic intra- and interobserver variation assessments, but the tests were performed by an examiner with extensive experience testing patients with PH. Use of the indirect Fick method to perform the RCC hemodynamic measurements may be another limiting factor, but since the high cost of the Swan Ganz catheter limits its routine use, the thermodilution method was not used in this study.

Conclusions

TEE and RCC measurements showed an association in the assessment of MRAP, especially between RAA and $MRAP_{RCC}$. An association with RVSD and moderate agreement between methods were also noted.

Authors' contributions

Each author contributed individually and significantly to the development of this article. Jardim FV, Zacarias L, Masson JB, Zeredo AT: Writing and Performing Surgeries; Azeredo AT, Rassi D, Rassi S: Data Analysis and Writing; Azeredo AT, Graner D, Rassi S, Figueiredo A, Costa S, Sampaio D: Review of the Article and Intellectual Concept of the Article.

Conflict of interest

The author declares that he has no conflict of interest

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