Right ventricular dysfunction in patients with non-severe idiopathic pulmonary fibrosis: a cross-sectional prospective single-center study

Sandra de Barros Cobra (✉ sandrab.cobra@gmail.com)

University of Brasilia <https://orcid.org/0000-0003-0837-339X>

Marcelo Palmeira Rodrigues

University of Brasilia

Felipe Xavier de Melo

University of Brasilia

Nathali Mireise Costa Ferreira

University of Brasilia

Viviane Vieira Passini Soares

University of Brasilia

Verônica Moreira Amado

University of Brasilia

César Augusto Melo e Silva

University of Brasilia

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Abstract

Background Pulmonary hypertension worsens the prognosis of idiopathic pulmonary fibrosis (IPF) and is associated with chronic respiratory failure in advanced disease. However, little is known about the occurrence of pulmonary hypertension and subsequent right ventricular dysfunction in non-advanced IPF patients without hypoxemia at rest. We evaluated right ventricular dysfunction in non-advanced IPF patients and examined the association of right ventricular dysfunction with mean pulmonary artery pressure (mPAP) at rest and during exercise.

Methods This cross-sectional study included patients with blood oxygen saturation levels $\geq 92\%$ at rest, Gender-Age-Physiology Index score ≤ 5 , modified Medical Research Council dyspnea scale score ≤ 3 , and no history of oxygen therapy. Patients underwent transthoracic echocardiography at rest and during cardiopulmonary exercise. Ventricular function was analyzed by measuring conventional parameters and right ventricular global longitudinal strain using two-dimensional speckle-tracking echocardiography. Means were compared using t-test for independent samples.

Results Abnormal speckle-tracking echocardiography findings were identified in 10/27 patients (37%), indicating right ventricular dysfunction (mean mPAP: 21.6 ± 5.5 mmHg at rest, 42.2 ± 14.1 mmHg during maximal exercise). Significant differences in mPAP were observed between patients with right ventricular dysfunction and those without dysfunction (at rest: 26.0 ± 4.8 vs. 19.1 ± 4.2 mmHg, $p = 0.001$; during exercise: 51.3 ± 6.4 vs. 36.9 ± 14.7 mmHg, $p = 0.002$). Right ventricular dysfunction was detected in 37% of non-advanced IPF patients and was associated with increased mPAP at rest and during exercise. Early recognition was only possible using speckle-tracking echocardiography.

Conclusions Right ventricular dysfunction was detected in 37% of non-advanced IPF patients and was associated with increased mPAP at rest and during exercise. Special attention should be given to these patients; as right ventricular dysfunction is suggestive of worse prognosis. These patients could benefit from new specific drugs or even oxygen therapy for transitory hypoxia.

Background

Idiopathic pulmonary fibrosis (IPF) has a higher prevalence with increasing age. IPF generally manifests from age 60 to 70 years and usually has a progressive course, leading to mortality. The mean survival for IPF varies from 2.5 to 3.5 years after diagnosis [1, 2]. One of the main predictors of mortality in IPF patients is World Health Organization group III pulmonary hypertension (PH), which is associated with a greater reduction in life expectancy [1, 3].

The prevalence of PH in IPF patients varies and depends on IPF severity. In early stages of IPF, PH affects <10% of patients [4]. However, as the disease progresses, its prevalence can range from 32% to 85% [2, 3, 5].

PH remains poorly investigated among patients in the early stages of IPF because cardiac catheterization—the gold standard for definitive diagnosis of changes in pulmonary circulation and its repercussions in the right chamber [6]—is not usually performed for clinical follow-up. Furthermore, the clinical signs and symptoms are insufficient for a diagnosis of PH in such patients [7, 8].

Although accurate assessment of PH relies on invasive methods, changes suggestive of this complication can be non-invasively assessed. The use of transthoracic echocardiography (TTE) allows for conventional analysis of right ventricular (RV) performance. Functional analysis of this chamber has traditionally been performed by measuring tricuspid annular plane systolic excursion (TAPSE), Doppler tissue imaging S' wave, and RV systolic function based on the fractional area change (FAC) [9]. However, TTE can be inaccurate because the complex RV anatomy can present diverse anatomical characteristics when subjected to different loading conditions [10].

Nevertheless, RV systolic function assessment with TTE can be more accurate using speckle-tracking echocardiography (STE). This technique can non-invasively and accurately measure subtle myocardial dysfunctions resulting from systolic abnormalities [11], allowing alterations to be perceived even with minor changes in acute post-loading [12].

Currently, information on the early stages of RV dysfunction and its progression to IPF is limited. D'Andrea et al. [13] detected changes in RV contractile function using the STE technique. Nevertheless, this study did not mention the criteria used to define early IPF stages and included patients with severe hypoxemia. In their sample, the mean peripheral oxyhemoglobin saturation (SpO_2) at rest was 83%. It is well known that PH gradually emerges with the development of chronic hypoxia. For this reason, it is important to study patients at rest before severe hypoxemia develops in order to elicit any potential influence of other mechanisms, including those that could be treated with available drugs. Moreover, Han et al. [14] evaluated IPF patients treated with sildenafil and showed the benefit of this drug in a subgroup of IPF patients with RV dysfunction. Based on these data, we may suggest that early recognition of ventricular dysfunction is particularly important.

Exercise-induced PH is widely known to precede resting PH [15]. For this reason, in this study, the authors found it relevant to combine the evaluation of RV dysfunction with non-invasive pulmonary artery pressure measures during exercise and cardiopulmonary testing (CPT), which measures the values of oxygen extraction (VO_2) and the ratio of expired volume/ CO_2 output (VE/VCO_2).

Compared with patients in very advanced IPF stages, patients with mild or moderate IPF may have variable pressure loads because of their broad spectrum of daily life activities. Different daily activity profiles may influence the pressure load due to transient hypoxemia, which is notably variable in IPF patients over a 24-h period [16] or due to differential pressure changes during exercise. In addition, the presence of tissue mediators [17] may contribute to premature PH in IPF patients. To provide additional information on this issue, this study examined the occurrence of RV dysfunction in non-advanced IPF patients without severe hypoxemia at rest.

Methods

This cross-sectional study included 123 consecutive IPF patients. The American Thoracic Society (ATS) and European Respiratory Society criteria were used for diagnosis [18]. These patients were diagnosed and underwent treatment for interstitial lung diseases at the referral center of a university tertiary care institution.

We included patients meeting the following criteria: SpO₂ at rest and in ambient air $\geq 92\%$; no history of oxygen therapy; Gender-Age-Physiology Index score ≤ 5 , which corresponds to mild or moderate disease [19]; and modified Medical Research Council (mMRC) dyspnea scale score ≤ 3 [20]. We excluded patients presenting with left cardiomyopathy, locomotor disease, another severe comorbidity (e.g., stroke, lung cancer, pulmonary thromboembolism), emphysema, or other pulmonary diseases related to IPF. All patients signed an informed consent form. The study was approved by the Ethics Committee of the University of Brasília.

Of the 123 patients evaluated, 38 were selected for baseline TTE acquired according to the protocol recommended by the American Society of Echocardiography [9]. Detailed diastolic function measurements were recorded. Five patients were excluded due to the presence of the following comorbidities: endocardial alterations caused by coronary disease ($n = 2$); dynamic left ventricular (LV) outflow tract obstruction (OTO; $n = 1$); and dilated cardiomyopathy with LV dysfunction, left atrial enlargement, and signs of increased LV filling pressure ($n = 2$). In addition to the five patients excluded following TTE, six refused to participate in the study. Thus, 27 patients completed the study and underwent CPT (**Fig. 1**).

Transthoracic Doppler echocardiography at rest

The examination was performed at rest using Vivid I equipment (GE Healthcare, Milwaukee, WI, USA) with a 2.5–3.5 MHz variable frequency transducer. Doppler analysis was performed in real time, and measurements were obtained from a mean of 3 to 5 beats. Conventional echocardiographic examination was performed to evaluate RV function based on the FAC% (abnormal, $<35\%$), TAPSE (abnormal, <17 mm), and tricuspid annulus (S') (abnormal, <9.5 cm/s) measured by TD [10]. The STE of the RV was considered normal when values were less than -20% [9].

The modified Bernoulli equation was applied to calculate the systolic pulmonary artery pressure (sPAP) from tricuspid regurgitation. A non-invasive estimate of the mean pulmonary artery pressure (mPAP) was calculated using the following formula: $0.61 \times \text{sPAP} + 2$ mmHg [21]. sPAP was assumed to be equal to the RV systolic pressure in the absence of RV OTO or pulmonary stenosis [22]. SPAP values <37 mmHg were considered normal [23].

After measuring the pressure gradient between the RV and right atrium, the estimated right atrial pressure, based on the inferior vena cava inspiratory collapsibility index, was added to the parameter [9, 24]. Images were obtained to optimize the best RV visualization position (i.e., apical four-chamber view, the same for RV diameter measurement), grayscale for STE analysis (50–90 frames/s), and sector depth for better resolution.

Two-dimensional echocardiography using the STE technique to evaluate RV function

Images were analyzed offline with Echo PAC software version 201; (GE Vingmed, Horten, Norway), and the STE technique was used to measure two-dimensional strain [25].

The endocardial region of the RV free wall was manually outlined at the end of the systole and automatically adjusted to include the entire myocardium. Systole in the cardiac cycle was defined using the event-timing feature of the software, which allowed the beginning and end of the RV systole to be delimited.

RV global longitudinal strain (GLS) was evaluated at the basal, medial, and apical portions of the free wall (**Fig. 2**), and the final result was expressed as the mean value of the three segments. GLS is defined as the percentage of myocardial thickening versus the original fiber length and is conventionally represented as a negative value [25].

Cycle ergometer CPT associated with dynamic TTE measurements

Using a cycle ergometer (CG-04; Inbramed®, Porto Alegre, RS, Brazil), all patients underwent an incremental ramp protocol with progressively increasing load. After 1-min rest to allow patients to adapt to the cycle ergometer, CPT was started at 60 rotations/min without load (0 W). Subsequently, the load was steadily increased at 5–30 W/min. Thus, the calculated value of the maximum predicted $\dot{V}O_2$ (O_2 consumed) and patient age, dyspnea level during exercise, and exercise capacity were used to provide an incremental period of 8–12 min, according to ATS recommendations [26]. Expiratory gas measurements were recorded from all patients at each breath for the analysis of ventilatory and cardiovascular variables (Quark PFT; COSMED, Rome, Italy).

The $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, and final expiratory O_2 and CO_2 pressures were recorded as means over 15 s. Continuous heart rate monitoring and electrocardiography were performed, and pulse oximetry (iPod®; Nonin Medical Inc., Plymouth, MN, USA) measurements were continuously recorded. Systolic and diastolic blood pressures were measured using the auscultatory method at each load increase. The anaerobic threshold was non-invasively estimated using the gas exchange method. The slope of $\dot{V}O_2$ versus $\dot{V}CO_2$ graph was analyzed on equal scales (V-slope technique) and confirmed using the

ventilatory technique, which assessed the behavior of ventilatory equivalents ($V'E/V'CO_2$ and $V'E/V'O_2$) and their respective final expiratory pressures. Dyspnea and muscle fatigue sensations were also evaluated throughout the CPT using the Borg effort perception scale [27].

Echocardiographic images were acquired during CPT in the region of the ventricular apex along the left midclavicular line, which allowed for better tricuspid regurgitation image acquisition. During the test period, images were saved each minute for offline analysis to estimate the sPAP value throughout the test. During the recovery period, tricuspid regurgitation spectral traces were recorded to obtain measurements for 3 min after exercise.

Statistical analysis

Normally distributed continuous variables are expressed as mean $\pm$ standard deviation or as range. Categorical variables are expressed as percentages. Means were compared using t-test for independent samples. Results were considered statistically significant when $p < 0.05$. Data were analyzed using SPSS for Mac OS X[®] (version 25.0.0; SPSS Inc., Chicago, IL, USA).

Results

Of the 27 patients who underwent CPT, 16 were men (59.3%). The mean age was 71.5 ± 8.5 years. Eighteen patients (66.7%) took antifibrotic medication; of these patients, 14 (51.8%) and four (14.8%) took pirfenidone and nintedanib, respectively. During patient enrolment, nine (33.3%) patients were not undergoing antifibrotic therapy. Dyspnea was classified as mMRC grade 0 in two (7.4%), grade 1 in 12 (44.4%), grade 2 in eight (29.6%), and grade 3 in five (18.5%) patients. Lung function was assessed by mean forced vital capacity as a percentage of the predicted value for the whole sample and by mean D_LCO as a percentage of the predicted value, which were 67.3 ± 14 and $51.3 \pm 17\%$, respectively. Data are presented in **Table 1**.

Table 1 Demographic data and functional characteristics of the patient sample

Variables	Mean $\pm$ SD	Range
Age (years)	71.4 $\pm$ 8.5	55–87
FVC%	67.6 $\pm$ 14.3	44–100
FEV1%	74.1 $\pm$ 11.7	53–97
FEV1/FVC index	85.6 $\pm$ 5.9	73–95
TLC	71.2 $\pm$ 12.7	45–91
D _L CO%	51.3 $\pm$ 17.5	30–93
SpO ₂ % (at rest)	94.1 $\pm$ 1.6	92–98

SD, standard deviation; FVC%, forced vital capacity as a percentage of the predicted value; FEV1%, forced expiratory volume in 1 s as a percentage of the predicted value; TLC, total lung capacity; D_LCO%, carbon monoxide diffusing capacity of the lung; SpO₂%, peripheral oxyhemoglobin saturation

Echocardiographic data analysis revealed that 17 (63%) patients had normal GLS values, whereas 10 (37%) patients had abnormal GLS values at rest. STE analysis showed no significant differences in RV dysfunction related to sex or age. Of male patients with normal GLS, 64% had RV dysfunction, whereas 50% of male patients with abnormal GLS had RV dysfunction ($p = 0.45$). The mean age of patients without RV dysfunction (normal GLS) was 70 ± 8 years, whereas that of patients with RV dysfunction was 73 ± 9 years ($p = 0.41$). There were no significant differences in spirometry variables between the groups with and without RV dysfunction. Furthermore, no significant differences in SpO₂ values at rest (93.8 ± 1.5 vs. $94.4 \pm 1.6\%$; $p = 0.35$) and D_LCO (47 ± 14 vs. $53 \pm 19\%$; $p = 0.42$) were observed between patients with and without RV dysfunction.

The sPAP estimated by echocardiography was ≥ 37 mmHg in six patients and < 37 mmHg in 21 patients. Data for the mPAP, sPAP, RV function parameters measured by two-dimensional echocardiography, and TD and its relationships with RV function at rest measured by GLS are summarized in **Table 2**.

Table 2 Baseline echocardiographic parameters and their relationships with RV function using the speckle-tracking strain technique

Variable	<i>n</i>	Mean $\pm$ SD	Interval	Normal GLS%	<i>n</i>	Abnormal GLS%	<i>n</i>	<i>p</i>
mPAP (estimated, mmHg)	27	21.6 $\pm$ 5.5	10.4–38.6	19.1 $\pm$ 4.2	17	26.0 $\pm$ 4.8	10	0.001
sPAP (at rest, mmHg)	27	33.1 $\pm$ 9.5	14.0–62.0	28.8 $\pm$ 7.6	17	40.3 $\pm$ 8.3	10	0.001
GLS% (at rest)	27	-21.8 $\pm$ 4.0	-29.0–14.5	-24.0 $\pm$ 3.1	17	-17.9 $\pm$ 1.7	10	
TD RV S' (m/s)	27	0.12 $\pm$ 0.02	0.08–0.17	0.12 $\pm$ 0.02	17	0.12 $\pm$ 0.02	10	0.581
RV FAC (%)	27	49.6 $\pm$ 10.2	35.0–70.0	49.9 $\pm$ 9.4	17	50.1 $\pm$ 12.0	10	0.872
RV TAPSE (cm)	27	2.0 $\pm$ 0.3	1.4–2.8	2.0 $\pm$ 0.2	17	2.0 $\pm$ 0.3	10	0.932

SD, standard deviation; GLS, global longitudinal strain; mPAP, mean pulmonary artery pressure; sPAP, systolic pulmonary artery pressure; RV FAC, right ventricular fractional area change; RV TAPSE, right ventricular tricuspid annular plane systolic excursion toward the RV apex; TDRVS'; tissue Doppler RV peak systolic velocity

Of these variables, only mPAP and sPAP showed significantly higher values in patients with abnormal GLS. This difference persisted after only analyzing patients with normal sPAP at rest (sPAP <37 mmHg). Of these patients, five had abnormal GLS and 16 had normal GLS. The mean mPAP values in patients with and without RV dysfunction were 23.0 ± 0.4 and 18.8 ± 4.1 mmHg ($p = 0.001$), respectively.

During exercise, mPAP differences between patients with and without RV dysfunction became more apparent (**Figs. 3 and 4**). All patients with RV dysfunction showed significantly higher mPAP values during exercise. At peak effort, a mean mPAP value of 51.3 ± 6.4 mmHg was reached in patients with RV dysfunction compared with that of 36.9

± 14.7 mmHg reached in patients without RV dysfunction ($p = 0.002$) (**Table 3**). During exercise, mPAP differences between patients with and without RV dysfunction were also apparent when only analyzing patients with normal sPAP at rest (**Fig. 4**).

No significant differences in CPT variables were observed between patients with and without RV dysfunction (**Table 3**). Sixteen (59.3%) patients had VO_2 below the lower limit ($<83\%$ of the predicted value). Of these patients, seven (43.8%) patients had RV dysfunction. Of the 11 patients with normal VO_2 , only three (27.3%) had RV dysfunction ($p = 0.38$).

Table 3 CPT data related to RV function

	Normal GLS%	<i>N</i>	Abnormal GLS%	<i>n</i>	<i>p</i>
SpO ₂ (initial, %)	94.4 $\pm$ 1.6	17	93.8 $\pm$ 1.5	10	0.353
SpO ₂ (final, %)	87.0 $\pm$ 5.2	12	79.0 $\pm$ 10.7	4	0.060
Borg dyspnea (peak)	5.9 $\pm$ 2.4	17	5.6 $\pm$ 2.0	9	0.773
Borg legs (peak)	5.5 $\pm$ 2.8	17	5.1 $\pm$ 2.9	9	0.690
mPAP (estimated at peak, mmHg)	36.9 $\pm$ 14.7	17	51.3 $\pm$ 6.4	10	0.002
sPAP (estimated at peak, mmHg)	57.2 $\pm$ 24.1	17	81.0 $\pm$ 10.6	10	0.002
VE/VCO ₂ (lactate)	40.0 $\pm$ 6.8	17	44.0 $\pm$ 7.6	10	0.175
VE/VCO ₂ (slope)	36.3 $\pm$ 6.7	17	38.2 $\pm$ 7.7	10	0.527
PETCO ₂ (lactate)	33.7 $\pm$ 4.5	17	31.7 $\pm$ 4.2	10	0.267
VO ₂ (peak, mL/bpm)	9.4 $\pm$ 2.2	17	8.1 $\pm$ 2.3	10	0.163
VE/MVV	56.9 $\pm$ 17.3	17	59.7 $\pm$ 9.3	10	0.648

GLS, global longitudinal strain; SpO₂, peripheral oxyhemoglobin saturation; mPAP, mean pulmonary artery pressure; sPAP, systolic pulmonary artery pressure; VE/VCO₂, volume expired per minute/CO₂ ventilation;

PETCO₂, CO₂ partial pressure at the end of expiration; VO₂, values of oxygen extraction; VE/MVV, volume expired per minute/maximum voluntary ventilation. Data are shown as mean ± standard deviation

Discussion

To our knowledge, this is the first study to examine the presence of RV dysfunction in non-advanced IPF patients without severe hypoxemia, excluding those with SpO₂ <92% at rest. Considering that vasoconstriction due to alveolar hypoxia is one of the most important mechanisms of PH, the presence of RV dysfunction in 37% of our sample was an unexpected finding, suggesting that RV changes begin early in the course of IPF, perhaps independently of chronic hypoxia.

Nevertheless, we may not rule out hypoxia as the main cause of PH and RV dysfunction in IPF patients. The presence of subclinical hypoxia may be related to RV impairment in the early stages of IPF. In these stages, vasoconstriction due to alveolar hypoxia may only occur in some areas of the lung, leading to increased localized pulmonary vascular resistance. Although increases in pulmonary resistance caused by a small area with a low ventilation-to-perfusion ratio could imply enlarged pressure load, it would be insufficient in determining clinically relevant hypoxemia. Alternatively, periods of hypoxia associated with daily activities or during sleep could be related to transient increases in mPAP. Such pressure variations could result in subtle changes in RV contractile function, which are only detectable by GLS, whereas other conventional parameters measured by TTE would remain within normal ranges.

Rodrigues et al. [16] observed that patients with partial pressures of arterial oxygen (PaO₂) >70 mmHg at rest may experience severe hypoxemia (SpO₂ <90%) for a mean of >4 h per day, which would support the periodic occurrence of PH during the day. In agreement with this explanation, a marked increase in mPAP during exercise, which was frequently associated with a concomitant decline in SpO₂, was observed in the present study. A previous study reported that mPAP values >40 mmHg were commonly observed during exercise in advanced IPF patients [28].

In addition to vasoconstriction, mechanisms independent of hypoxia may be involved in PH and RV dysfunction, such as fibrosis-induced vascular bed loss or obliteration [29]. Moreover, the presence of mediators of the fibrogenic process may be directly involved in PH development [30].

Values of conventional echocardiography parameters routinely used to evaluate RV function are comparable in groups with and without GLS-detected RV dysfunction. These parameters lack the sensitivity required to predict RV contractile function changes. Therefore, GLS calculation is currently the best method to analyze myocardial strain in various clinical situations, allowing for early diagnosis of ventricular dysfunction as also observed by others [31].

RV dysfunction was present in patients with normal sPAP at rest as well as in those with mPAP below the values defining PH. Although mPAP levels at rest were within the normal range, our data revealed significantly higher values for patients with RV dysfunction at rest or during exercise. According to a

systematic review [32], the mPAP cut-off value of 25 mmHg used to define PH exceeds the upper limit of normality for cardiac catheterization. In addition, Kimura et al. [33] reported that an mPAP cut-off value of approximately 17 mmHg would significantly discriminate the survival of patients with less advanced IPF stages. Therefore, our findings support the idea that the normal value range used to define the presence or absence of PH is not adequate for this patient group.

In addition, establishing an mPAP cut-off point during maximal exercise can be difficult. Kovacs et al. [32] showed that age is likely an important factor for establishing the normal range. Moreover, there is currently no adequate definition for exercise-induced PH [23].

The RV dysfunction group showed no significant differences in $\dot{V}O_2$ or other CPT parameters, but RV dysfunction was subclinical, which suggests that the cardiovascular deficits of these patients were less important than their ventilatory, gas exchange, and muscle function impairments. However, this interpretation contrasts with the findings of Hansen et al. [34]. These divergent results may be due to our small sample size and reduced statistical power.

This study has some limitations. First, the measurement of RV function by two-dimensional STE only allowed RV analysis in the orthogonal plane. Second, we used TTE as a noninvasive approach to evaluate pressure instead of direct catheterization; however, cardiac catheterization is not commonly indicated for non-advanced IPF patients. Finally, our study lacked data on SpO_2 during sleep.

There are also issues concerning the interpretation of our findings. First, the detection of RV dysfunction in patients with normal mPAP at rest could potentially be an early prognostic marker in IPF patients and could therefore serve as an additional marker for early lung transplant referral. Second, as RV dysfunction and PH in these patients are not exclusively caused by hypoxia, to what extent they coexist with other factors and whether they could be affected by treatments such as antifibrotic agents and pulmonary vasodilators are unclear.

Conclusion

RV dysfunction was detected in 37% of non-advanced IPF patients without severe hypoxemia at rest. Moreover, RV dysfunction was associated with increased mPAP measured by TTE at rest and during exercise. Early recognition was only possible using GLS, which makes this technique an important tool for evaluating IPF patients. Special attention should be given to patients with RV dysfunction, as they may have worse prognosis and could benefit from new specific drugs or even oxygen therapy for transitory hypoxia in the future.

List Of Abbreviations

ATS: American Thoracic Society

CPT: Cardiopulmonary testing

FAC: Fractional area change

GLS: Global longitudinal strain

IPF: Idiopathic pulmonary fibrosis

LV: Left ventricular

mMRC: Modified Medical Research Council

mPAP: Mean pulmonary artery pressure

OTO: Outflow tract obstruction

PH: Pulmonary hypertension

sPAP: Systolic pulmonary artery pressure

RV: Right ventricular

SpO₂: Peripheral oxyhemoglobin saturation

STE: Speckle-tracking echocardiography

TAPSE: Tricuspid annular plane systolic excursion

TTE: Transthoracic echocardiography

VO₂: Values of oxygen extraction

VE/VCO₂: Ratio of expired volume/CO₂ output

VE: Volume expired per minute

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the University of Brasília. All patients signed an informed consent form.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used/or analyzed during the present study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SBC analyzed and interpreted patient data and was a major contributor in writing the manuscript. MPR reviewed all data and made substantial contributions to the conception and design of the work. FXM acquired and analyzed data from CPT. Both NMCF and VVPS selected all patients. VMA reviewed the work. CAMS acquired and analyzed the data and revised the work. All authors read and approved the final manuscript.

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Figures

Figure 1

Patient selection flowchart.

Figure 2

Speckle tracking of a patient with idiopathic pulmonary fibrosis at rest.

Figure 3

Estimated mPAP during exercise between patients with and without RV dysfunction in the entire cohort. mPAP, mean pulmonary artery pressure; RV, right ventricular

Figure 4

Estimated mPAP during exercise between patients with and without RV dysfunction in normal sPAP subgroup. The normal sPAP subgroup consisted of patients with normal sPAP at rest. mPAP, mean pulmonary artery pressure; RV, right ventricular; sPAP, systolic pulmonary artery pressure