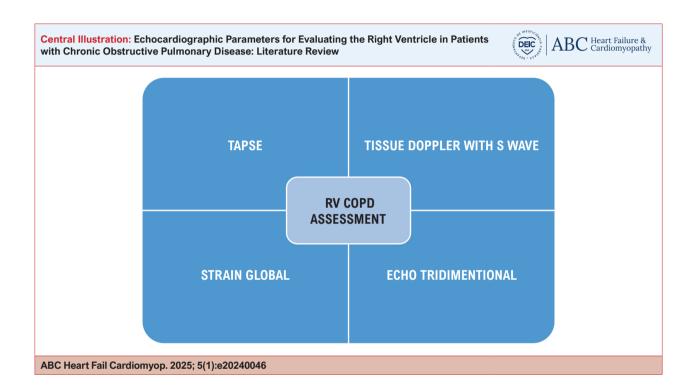




# Echocardiographic Parameters for Evaluating the Right Ventricle in Patients with Chronic Obstructive Pulmonary Disease: Literature Review

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#### **Abstract**

Chronic obstructive pulmonary disease (COPD) is a lung disease that often has an indolent course and systemic repercussions. Its main cause is constant and prolonged exposure to cigarette smoke or other gases. Such particles lead to reduced airflow and consequent lung hyperinflation with varying degrees of airway obstruction, also causing skeletal muscle dysfunction, respiratory failure, and

#### Keywords

Right Ventricular Dysfunction; Chronic Obstructive Pulmonary Disease; Doppler Echocardiography; Global Longitudinal Strain

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decreased peripheral blood flow. COPD patients with concomitant cardiovascular disease (CVD) have a worse prognosis than simply the prognosis of each disease alone. However, it is difficult to establish what the risk is for a given group of patients due to the complex network of etiological and pathophysiological interactions underlying both diseases. Quantitative and qualitative echocardiographic assessment of right ventricular function is becoming of increasing interest in cardiac diseases that affect the right ventricle (RV), such as congenital heart disease and pulmonary hypertension (PH). However, it is still challenging due to the complex anatomy of the RV. The objective is to revisit the echocardiographic parameters that functionally assess the RV in patients with COPD, even if they do not present clinical signs of ventricular dysfunction.

#### Introduction

Since the first description of pulmonary circulation in the 16th century, knowledge of the complex interaction between the heart and lungs has improved considerably. Hypoxemia plays a classic role in the development of complications

such as pulmonary hypertension and right ventricular (RV) dysfunction in patients with chronic obstructive pulmonary disease (COPD). However, more recent findings have revealed the presence of vascular structural and functional alterations of the RV, even in patients with mild COPD without hypoxemia or pulmonary hypertension. Compared with the left ventricle, the anatomy of the RV is unique and complex, which makes its assessment more difficult during routine examinations.<sup>1</sup>

COPD is a chronic lung disease with an often indolent course and systemic repercussions. Its main cause is constant and prolonged exposure to cigarette smoke or other harmful gases that lead to reduced airflow with lung hyperinflation due to varying degrees of airway obstruction, causing skeletal muscle dysfunction, respiratory failure, and decreased peripheral blood flow.<sup>1</sup>

COPD patients with concomitant cardiovascular disease (CVD) have a worse prognosis than simply the prognosis of each disease alone. However, it is difficult to establish a risk ratio for a given patient due to the complex network of etiological and pathophysiological interactions underlying both diseases.<sup>2</sup>

COPD is a heterogeneous and multifactorial clinical condition with an estimated global prevalence of 11.7%. Exacerbations are the leading cause of hospitalization for COPD, and different variables are associated with a significantly high number of readmissions in these patients.<sup>3,4</sup>

COPD exacerbations comprise an acute event in the natural course of the disease, with a change in baseline dyspnea, cough, and/or sputum color with a real need to change regular medication. COPD exacerbations represent a key factor in the increased morbidity, healthcare costs, and mortality in COPD and have received increasing attention in recent years. Most of these patients experience at least one exacerbation per year, and a considerable proportion (approximately 17%) experience three or more episodes per year. COPD exacerbations are classified as severe for those patients who require hospitalization, according to the GOLD classification.<sup>1,2</sup> These events, when more severe, mostly result in hospitalization and have a negative impact on quality of life, lung function, and functional capacity. Previous studies indicate that comorbidities associated with the primary respiratory disease may also worsen during hospitalization. It is known that COPD patients who experience exacerbations more frequently have lower quality of life and significantly higher mortality when compared to other COPD patients, in addition to an increased risk of cardiovascular disease.3

Quantitative echocardiographic assessment of right ventricular function is becoming of increasing interest in cardiac diseases affecting the right ventricle, such as congenital heart disease, pulmonary hypertension (PH), and COPD, but remains challenging due to the complex anatomy of the RV.<sup>4</sup>

Two-dimensional (2D) echocardiographic methods of RV performance analysis employ geometric models that do not accurately represent the RV shape. Real-time three-dimensional (3D) echocardiography allows us to measure RV end-diastolic volume and ejection fraction independently of its shape. Tissue Doppler and strain echocardiography are new means of assessing myocardial wall motion and deformation,

and it has been suggested that the use of strain-derived indices could be proposed as an adjunctive tool in the overall assessment of right ventricular function. Three-dimensional echocardiography provides a rapid and comprehensive quantitative assessment of ventricular myocardial dynamics and has been applied to the study of the right ventricle, mainly in patients with pulmonary hypertension. However, the hemodynamic value of these new echocardiographic parameters in the clinical setting of RV dysfunction has not been clearly established.<sup>4,5</sup>

The guidelines provided by the American Society of Echocardiography (ASE) indicate that the RV is often neglected, as it is a predominantly quantitative examination, due to its difficulty in assessing volumes and its geometric complexity. Regarding the use of echocardiography with the strain method, the ASE points out that among the advantages of using this method is the ability to provide an estimate of the regional and global function of the observed chamber; however, few studies have been carried out to evaluate the method in the RV truly.<sup>5,6</sup>

#### Objective

The objective is to revisit the echocardiographic parameters that functionally assess the RV in patients with COPD, even if they do not present clinical signs of ventricular dysfunction.

#### Method

This study was conducted through an integrative literature review in order to establish greater knowledge about RV echocardiographic parameters in patients with COPD. A qualitative integrative review was performed by searching for articles in the electronic databases LILACS, Scielo, Cochrane Library, and PubMed, using MeSH descriptors: "Chronic Obstructive Pulmonary Disease", "Right Ventricle", "Echocardiogram" and "Systolic Function".

Independent researchers analyzed the articles. The data included the definition of subjects, methodology, sample size, measurement of variables, analysis method, and underlying concepts used. This protocol should include the databases that will be used, the inclusion and exclusion criteria, and the descriptors used, in addition to indicating how the studies will be selected and the models to extract data and assess quality.

### Two-dimensional evaluation of the right ventricle

According to current guidelines for cardiac chamber quantification, echocardiographers must utilize multiple acoustic windows to visualize the RV accurately. Furthermore, there is a great need to measure multiple parameters (Central Figure) since there is no single index of contractility that perfectly describes RV performance.<sup>5,7</sup>

In daily clinical practice, the most common indices that can be used to assess RV systolic function are tricuspid annular plane systolic excursion (TAPSE), tricuspid lateral annular systolic velocity derived from tissue Doppler imaging (S' wave), RV myocardial performance index (RVPI), and fractional area change (FAC).<sup>8</sup>

TAPSE is a measure of RV longitudinal function. TAPSE <16 mm indicates RV systolic dysfunction. This measurement is made from the lateral tricuspid annulus (Figure 1). Although TAPSE expresses a measure of longitudinal function, it has been shown to correlate well with techniques for estimating global RV systolic function, such as radionuclide-derived ejection fraction.<sup>7,8</sup>

Right ventricular systolic function may be significantly impaired despite normal TAPSE in some cases of severe pulmonary arterial hypertension. On the other hand, RV performance may be preserved despite reduced TAPSE, as is frequently observed after cardiovascular surgery.<sup>7,8</sup>

Furthermore, this parameter is relatively load and angle-dependent; there may be some variations in the values depending on the rotation of the cardiac axis. However, TAPSE is the most frequently used index for assessing RV performance since it is easily obtained and demonstrates diagnostic and prognostic values in many stages of cardiovascular and pulmonary diseases.<sup>8,9</sup>

In patients with advanced heart failure and significant LV dysfunction, a TAPSE  $\leq$  14 mm predicted all-cause mortality in multivariate analysis.<sup>8.10</sup>

Furthermore, a study by Alhamshari et al.<sup>11</sup> reported that TAPSE could be a reliable tool for assessing RV function in obese patients admitted with acute myocardial infarction. They concluded that obese individuals had higher TAPSE at the time of acute myocardial infarction than non-obese patients. Furthermore, the authors reported that obese patients with better RV performance developed acute heart failure less frequently than the others.<sup>12</sup> McLaughlin et al.<sup>13</sup> demonstrated that children with dilated cardiomyopathy were more likely to develop RV systolic dysfunction as

measured by TAPSE, which was also associated with a worse prognosis.<sup>13</sup>

There is an interesting finding by Ozpelit et al. in their study of elderly individuals diagnosed with pulmonary arterial hypertension and COPD. The authors found that the indices that influence prognosis in elderly patients were different from those in younger patients (e.g., TAPSE was an independent predictor of death only in the elderly group).<sup>14</sup>

The use of FAC as a reference method for RV systolic function is due to its proven efficacy as a parameter independent of age, LV ejection fraction, and heart failure, among others. The results obtained reinforce that FAC is a highly accurate method in the Chagas population, confirming the findings of Asmer et al.<sup>15</sup> It is also important to highlight the similar accuracy of FAC in comparison with TAPSE, a widely established method for assessing RV systolic function whose execution also uses M-mode as a tool.<sup>15,16</sup>

Two-dimensional FAC <35% indicates RV systolic dysfunction. It is important to ensure that the entire right ventricle is included in the section, including the apex and lateral wall in both systole and diastole. Care should be taken to exclude trabeculations during planimetry of the RV area.<sup>12</sup>

The S' wave is easy to measure, reliable, and reproducible. An S' velocity <10 cm/s indicates RV systolic dysfunction. This measurement correlates well with other measures of global RV systolic function. It is important to keep the basal segment and annulus aligned with the Doppler cursor to avoid errors.<sup>17</sup> As with TAPSE, the S' wave reflects the function of the longitudinal fibers, which play an important role in RV contraction.

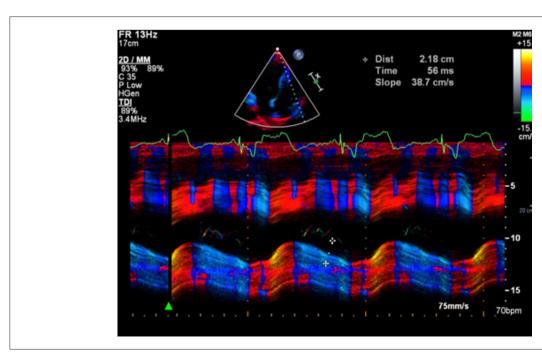


Figure 1 - TAPSE.

The S' wave is usually obtained by the approach apical 4-camera view, placing a tissue Doppler cursor at the lateral tricuspid annulus or mid-basal segment of the RV free wall. Care must be taken to achieve parallel alignment of the Doppler beam with the direction of RV longitudinal excursion. In addition, it is essential to measure the highest velocity of the ejection wave and not the anterior isovolumetric contraction wave, which is the most common error.<sup>17</sup>

The advantages and disadvantages of the S' wave (Figure 2) are comparable to those observed during TAPSE. It is simple to obtain and has prognostic data, but on the other hand, it is angle-dependent, influenced by the overall motion of the heart, and does not always correspond to the global systolic function of the RV.<sup>18</sup>

Wang et al. reported that tissue Doppler-derived S' had a stronger correlation with RV ejection fraction measured by cardiovascular magnetic resonance (MRI) than other indices (TAPSE, FAC, myocardial acceleration during isovolumetric contraction) and the best parameter to detect RV dysfunction with EF  $\leq$  20% was S' < 8.79 cm/s. 19

The lower reference value for the S wave of pulsed tissue Doppler is 9.5 cm/s. Color tissue Doppler can also measure the S wave, but it is not prevalent. In this case, the cutoff value is low (6 cm/s) since the encoded data represent average velocities.<sup>20</sup>

RV-MPI (right ventricular myocardial performance index) is a calculation based on tissue Doppler velocities or RV pulse wave velocities (isovolumetric relaxation time – isovolumetric contraction time/RV ejection time). These variables are measured during flow and do not require full RV visualization. RV-MPI is limited in patients with irregular

heart rates and when right atrial (RA) pressure is elevated, as this affects isovolumic relaxation time. An abnormal RV-MPI is >0.43 if measured by pulsed-wave Doppler or >0.54 if measured by tissue Doppler.<sup>21</sup>

Studies to validate the quantification of Pulmonary Insufficiency (PI) by two-dimensional echocardiography tend to overestimate the value compared to magnetic resonance imaging. The greatest effectiveness for quantification by 2D is determined by the joint analysis of several indexes established in the literature.<sup>21</sup>

Studies to validate the quantification of PI by echocardiography (2D) show a tendency to overestimate the value when compared to MRI. The greatest efficacy for quantification by 2D is determined by the joint analysis of several indexes established in the literature. Mercer-Rosa et al. showed a moderate correlation between the relationship of the time-velocity integral of pulmonary flow in diastole and systole and the regurgitant fraction by MRI, establishing a cutoff value to stratify the important degree, suggesting the incorporation of this index with the other parameters for greater efficacy. 17,21

Regarding the assessment of right ventricular dimensions, the literature shows poor agreement between linear measurements assessed by 2D and MRI, with 2D tending to underestimate. (Table 1) However, given the complex geometry of the RV that prevents visualization in a single plane, it is clear that linear measurement alone compromises the assessment. The inclusion of planimetry of the end-diastolic area, associated with two-dimensional measurements in the apical four-chamber and parasternal short-axis planes for assessment of the outflow tract, contributes to accuracy. In studies conducted by both

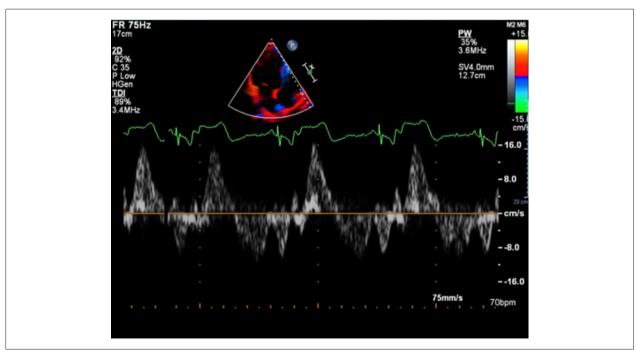


Figure 2 - S wave.

Table 1 – Parameters assessed for right ventricle systolic function by two-dimensional echocardiography

Parameter	Normal Value	Limitations
		Dependent angle
Tissue Doppler S wave	Greater than 9.5 cm/s	It does not represent a complete assessment of right ventricular function, especially in transplant patients.
TAPSE	Greater than 17 mm	Dependent angle
Fractional Area Change (FAC)	Greater than 35%	Neglects the contribution of RV outflow tract for assessment of general systolic function
Myocardial performance index (IPM)	Greater than 0.43 (pulsed Doppler)	Not reliable when right atrial pressure is elevated

TAPSE: tricuspid annular plane systolic excursion; RV: right ventricle.

authors, Shiran et al. and Alghamdi et al., in adults with pulmonary hypertension with COPD and children with congenital heart disease, it was possible to estimate volumes by measuring the diastolic area indexed in the two-dimensional plane with good correlation.<sup>22,23</sup>

A new parameter to assess RV systolic function, which is simple to acquire, was recently analyzed, called right ventricular outflow tract systolic excursion (RVOT\_SE). This method proved to be accurate for assessing RV systolic function when compared with fractional area variation (FAC) and tricuspid annular plane systolic excursion (TAPSE), in addition to confirming a worse prognosis for those patients with values below the cutoff line for RV dysfunction. Since this entity has its own characteristics, including segmental RV alterations, it is essential to prove the applicability of RVOT\_SE in further studies.<sup>23</sup>

As demonstrated, several indices are routinely used, such as fractional change in area (FAC), tricuspid annular systolic excursion (TAPSE), tricuspid annular peak systolic velocity, and the myocardial performance index. Each of them has advantages and limitations, variable feasibility and reproducibility, and questionable diagnostic and prognostic efficacy.<sup>24</sup> It is believed that, at present, none of them, in isolation, is a good indicator of RV systolic function in patients with COPD. Since the vector of longitudinal contraction is the most important due to the orientation of the predominant longitudinal muscle fibers from the tricuspid annulus to the apex, preference will be given to indices that explore movement in the longitudinal axis in the assessment of regional or global RV longitudinal function.<sup>25</sup>

Current guidelines from the American Society of Echocardiography (ASE) indicate performing several quantitative methods using two-dimensional echocardiography to assess the RV adequately.

#### Evaluation of the right ventricle by the strain method

Initially, the evaluation of 2D strain using the speckletracking method with already available software was limited to the analysis of left ventricular myocardial deformation, with the RV evaluation performed by these same programs generating inaccurate results.<sup>26</sup> However, through technological advances and artificial intelligence, it is now possible to perform, in a fully automated manner, the analysis of right ventricular longitudinal strain from two-dimensional (2D) and three-dimensional (3D) projections.<sup>27</sup>

The assessment of peak systolic longitudinal strain has enabled greater accuracy in the functional analysis of the RV, with the peculiarity of enabling early detection of dysfunction that precedes the reduction of the conventional ejection fraction. The incorporation of strain into other conventional parameters of functional assessment has contributed to accuracy, representing an advance in the challenge of echocardiography for assessing the RV. (Table2) The word "speckle" refers to the granular appearance of the image generated by an optical coherence imaging system, such as laser, optical coherence tomography, or ultrasonography.<sup>28</sup>

The strain offers an approach to assessing contractile capacity that rectifies displacement inaccuracies, resulting in reduced sensitivity to the orientation of the acquired imaging plane. The operational suitability of the two-dimensional strain method is conditioned by the intrinsic quality of the images obtained, with the correct identification of the endocardial border emerging as the determining factor.<sup>7</sup> The assessment of myocardial deformation using the speckle tracking technique (STE-2D) is influenced by cardiac translational motion, Doppler angle, and pre- and post-load states. Right ventricular systolic contraction is predominantly mediated by the deformation of longitudinally oriented myocardial fibers, representing approximately 75% of the total, while the impact of the deformation of radial fibers is remarkably limited. This circumstance reinforces the recent contribution of right ventricular longitudinal strain as a relevant tool in the assessment of right ventricular systolic function and directing the analysis, especially to the endocardial and epicardial borders.29

Furthermore, it is important to highlight the assessment of three-dimensional strain of the right ventricle, an approach of significant utility, since it provides comprehensive information not only on the longitudinal function but also on the circumferential and radial functions of this cardiac cavity. However, it is worth highlighting that the main limitations of advanced techniques for assessing RV function are the presence of a limited acoustic thoracic window, inadequate temporal resolution, and arrhythmias, as well as, in the case of deformation indices, the variability of the software of different brands of equipment. In addition, this methodology presents

Table 2 – Most frequent echocardiographic findings in chronic obstructive pulmonary diseasepatients with right ventricle dysfunction

#### Decreased TAPSE in patients with severe pulmonary hypertension

TAPSE as an independent predictor of mortality in elderly patients with pulmonary hypertension

Assessment of right ventricular function by various methods in patients with COPD

Use of global longitudinal strain to detect early RV dysfunction

RV: right ventricle; COPD: Chronic obstructive pulmonary disease.

a solid agreement with the results obtained through MRI, recognized as the reference standard.<sup>30</sup>

This technique has been used to detect subclinical RV dysfunction, with the global longitudinal strain (GLS) parameter (Figure 3) as the strongest predictor in patients with COPD. Therefore, in patients with COPD, it is possible to select those who require careful monitoring and early intervention to prevent the development of RV dysfunction and cardiovascular complications based on the analysis of these echocardiographic parameters, which could thus lead to an improvement in the patient's life expectancy. Its use has also been consolidated for both diagnosis and prognosis, especially in patients with heart failure, pulmonary hypertension, ischemic heart disease, restrictive heart disease, and valvular heart disease, supporting RV strain as a highly relevant tool for clinical practice.<sup>31</sup>

Furthermore, the incorporation of advanced computational solutions driven by artificial intelligence not only improves procedural efficiency but also mitigates disparities between observers.<sup>32</sup>

# Evaluation of the right ventricle by three-dimensional echocardiogram

Three-dimensional echocardiography, used primarily in experimental settings, is now widely available in hospitals. Its method of operation is described as "an emitted ultrasound pulse that propagates in a straight line, interacting with the different acoustic interfaces of the thoracic cavity until it reaches the heart."33

Three-dimensional (3D) echocardiography has contributed to volumetric and functional assessment, allowing the analysis of all segments without contraindications, but requires specific equipment that is not available in all echocardiography

laboratories. There is a significant correlation between 3D and MRI and a certain tendency for 3D to underestimate volumes when there is marked dilation.<sup>34,35</sup>

New techniques, such as 3D ejection fraction (EF) and RV longitudinal strain (RVLS)/strain ratio, allow us to overcome some imperfections of traditional indices, but unfortunately, they are not always available.

Botelho et al. compared RV anatomy and systolic function assessed by traditional methods and advanced echocardiographic parameters in 20 patients, mainly men, with stable, moderate to severe COPD, with 20 control patients. Patients with COPD had significantly higher pulmonary artery systolic pressure and RV-free wall thickness than controls. In contrast, they showed lower TAPSE, lower volume by 3D echocardiography, and lower strain values than controls. Only one (5%) patient with COPD showed no RV-related echocardiographic abnormalities. In conclusion, their results indicated subclinical RV dysfunction in patients with stable COPD.<sup>24</sup>

#### **Conclusions**

Assessment of right ventricular systolic and diastolic performance using echocardiographic parameters is a powerful prognostic indicator in patients with COPD since RV dysfunction is related to reduced exercise capacity and an unfavorable prognosis and is essential for stratifying cardiovascular risk in these patients. Two-dimensional methods need to be performed concomitantly and using several slices. Therefore, it is worth emphasizing that the clinical attitude for decision-making in the evaluation of the RV in patients with COPD depends on an integrated approach between clinical data and different echocardiographic methods, thus seeking

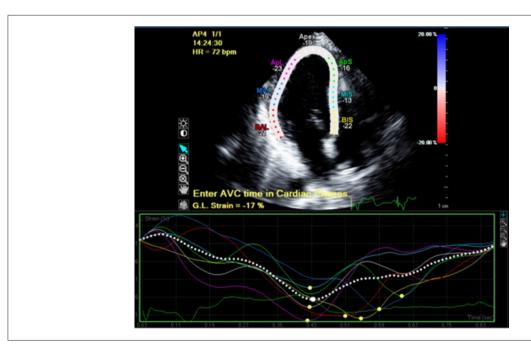


Figure 3 - Strain VD

the best perspective for the patient. The use of strain and three-dimensional echocardiography has been gaining more and more ground for the adequate evaluation of RV function in this population.

Further studies with a larger number of individuals with mild to severe COPD and with exacerbation of the disease need to be carried out to validate new echocardiographic methods using strain and 3D echocardiography.

#### **Author Contributions**

Conception and design of the research: Bispo ICA, Brambila VM; Acquisition of data: Brambila VM, Chagas GC, Pereira MLRG, Melo MAM; Analysis and interpretation of the data and Critical revision of the manuscript for content: Bispo IGA; Writing of the manuscript: Bispo IGA, Brambila VM, Chagas GC, Pereira MLRG, Melo MAM.

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This article does not contain any studies with human participants or animals performed by any of the authors.

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