



# Estimation of Right Ventricular Dysfunction by the Ratio of Tricuspid Annular Plane Systolic Excursion to Pulmonary Artery Systolic Pressure in Chronic Obstructive Pulmonary Disease Patients: A cross-sectional study

Sanjaya Kumar Shrestha<sup>1</sup>, Anmol Prasad Shrestha<sup>2</sup>, Tunam Khadka<sup>1</sup>

<sup>1</sup>Department of Cardiology, Kathmandu Medical College and Teaching Hospital, Kathmandu, Nepal,

<sup>2</sup>Department of Community Medicine, Kathmandu Medical College and Teaching Hospital, Kathmandu, Nepal

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## Corresponding

Sanjaya Kumar Shrestha  
Associate Professor, Department of  
Medicine (Cardiology),  
Kathmandu Medical College,  
Sinamangal, Kathmandu, Nepal.  
Email: sanjayakumar70@gmail.com

## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is recognized as the third leading cause of death worldwide after cardiovascular diseases and cancers,<sup>1</sup> and was the second highest cause of death among non-communicable diseases in Nepal.<sup>2-3</sup>

## Abstract

**Introduction:** A significant morbidity and mortality in chronic obstructive pulmonary disease (COPD) patients is due to right ventricular (RV) dysfunction and failure. We aimed to assess the severity of RV dysfunction with the relatively new but well validated echocardiographic index of tricuspid annular plane systolic excursion (TAPSE) to pulmonary artery systolic pressure (PASP) that measures the extent of shortening of cardiac fibers during RV contraction against a given afterload, the index of cardiac length-force relationship.

**Methods:** This cross-sectional study was conducted on COPD patients admitted to Kathmandu Medical College hospital, between October to November 2022 after approval from the Institutional Review Committee (Reference: KMC/18102022/07). The convenience sampling method was used and clinico-demographic details of the patients were recorded. Echocardiographic evaluation of the RV function was done by measuring the TAPSE/PASP ratio, as the non-invasive index of RV to pulmonary artery coupling.

**Results:** The median  $\pm$  interquartile range of TAPSE, PASP, TAPSE/PASP ratio, and RV diameter of the patients were  $19 \pm 6$  mm,  $47 \pm 19$  mmHg,  $0.39 \pm 0.19$  mm/mmHg, and  $3.8 \pm 0.7$  cm respectively. 23% of the patients had a TAPSE/PASP ratio of  $\leq 0.3$  mm/mmHg, denoting severe RV dysfunction. TAPSE/PASP ratio had a significant negative correlation with RV diameter ( $\rho = -0.26$ ;  $p = 0.018$ ); modified Medical Research Council dyspnea grade at admission ( $\rho = -0.35$ ;  $p = 0.001$ ); and domiciliary oxygen use ( $\rho = -0.26$ ;  $p = 0.017$ ).

**Conclusion:** The TAPSE/PASP ratio is a meaningful diagnostic parameter for the severity of COPD patients with pulmonary hypertension, and could be a good prognostic indicator.

**Keywords:** COPD; Echocardiography; Pulmonary Artery Systolic Pressure; Right ventricle dysfunction; Tricuspid Annular Plane Systolic Excursion

A significant morbidity and mortality in COPD patients are due to right ventricular (RV) dysfunction and failure, the result of pulmonary hypertension (PH).<sup>4-6</sup> PH is known to be associated with a reduced life expectancy.<sup>7-10</sup> We sought to find out RV dysfunction severity in COPD patients with a novel but a well-validated method of estimating RV dysfunction by echocardiography,

the ratio of tricuspid annular plane systolic excursion (TAPSE) to pulmonary artery systolic pressure (PASP), which measures the extent of shortening of cardiac fibers during RV contraction against a given after-load, and has been shown to be a strong predictor of outcome in PH on a background of interstitial lung disease and COPD.<sup>11-15</sup>

## Methods

**Patients.** This was a hospital-based descriptive cross-sectional study from October 2022 to November 2022. The sample size was calculated as eighty-three, based on the findings from a previous study done at a teaching hospital in Nepal.<sup>6</sup>

$$\begin{aligned} n &= Z^2 \times p \times q / e^2 \\ &= 1.96^2 \times 0.68 \times 0.32 / 0.1^2 \\ &= 83 \end{aligned}$$

where,

n = minimum required sample size

Z = 1.96 at a 95% Confidence Interval (CI)

p = prevalence of RVD among COPD patients from the previous study<sup>6</sup> = 68%

q = 1-p = 32%

e = margin of error, 10%

Eighty-three consecutive patients admitted to the medical ward of Kathmandu Medical College (KMC) with the diagnosis of COPD were enrolled in the study for the echocardiographic evaluation of RV function. Inclusion criteria were any patient admitted to the medical ward with the diagnosis of COPD with LV ejection fraction (EF)  $\geq$  50%. Exclusion criteria were patients with poor echo windows and patients whose tricuspid regurgitation could not be visualized, patients with systolic left ventricular failure (EF < 50%), and patients in atrial fibrillation. The study was approved by the KMC Institutional Review Committee, and written informed consent was obtained from all subjects before enrollment.

**Clinical characteristics.** The following data were collected: age, sex, occupation, number of years of exposure to fire-wood smoke and cigarette smoking status in terms of pack years, modified medical research council dyspnea scale (mMRC) at presentation to the hospital, and use of domiciliary oxygen.

**Echocardiography, TAPSE, and PASP measurement.** Echocardiographic imaging was performed using a General Electric Vivid E95 machine with a 5.2-MHz transducer. The standard two-dimensional, color Doppler and spectral Doppler examinations were

performed on the both left and the right chambers and valves of the heart. Tricuspid annular plane systolic excursion (TAPSE) and pulmonary artery systolic pressure (PASP) was measured and their ratio was calculated. Specifically, TAPSE/PASP ratio was taken as a non-invasive index of RV to PA coupling. To obtain TAPSE, the apical four-chamber view was used, and an M-mode cursor was placed across the lateral tricuspid annulus in real-time. TAPSE was measured as the peak excursion of the tricuspid annulus (millimeters) from the end of diastole to end systole, with values representing TAPSE being averaged over three beats.

RV systolic pressure was determined from the tricuspid regurgitation (TR) jet velocity using the simplified Bernoulli equation, and combining this value with an estimate of the right atrial pressure by the diameter and collapsibility of the inferior vena cava that was added to the calculated gradient to yield PASP.<sup>16</sup> Because subjects had no significant RV outflow tract or pulmonic valve obstruction, RV systolic pressure was considered equal to PASP. TR was evaluated in the apical four-chamber view. RV basal diameter of  $\geq$ 31 mm in females and  $\geq$ 35 mm in males were taken as RV dilatation based on a study on RV dimensions of the Asian population.<sup>17</sup> Based on the PASP measured, patients were categorized into mild PH (26-49 mmHg), moderate PH (50-74 mmHg), and severe PH ( $\geq$  75 mmHg).

Based on previous studies, TAPSE < 17mm has been taken as the cut-off for RV dysfunction and PASP > 25mmHg at rest as a raised pulmonary artery pressure. According to these values we have taken a TAPSE/PASP ratio of less than 0.61mm/mmHg (16mm divided by 26mmHg) as a cut-off value of RV dysfunction. TAPSE/PASP ratio has been shown to be a strong predictor of outcome in PH,<sup>11, 13, 14</sup> and  $\leq$  0.30 mm/mmHg for severe RV dysfunction.<sup>12</sup>

**Statistical analysis.** We used Statistical Package for Social Sciences (SPSS v23, Chicago, IL) to perform all the data entry and analyses. Continuous data were reported as mean  $\pm$  standard deviation (SD) and median  $\pm$  interquartile range (IQR) as appropriate, whereas categorical data were reported as frequency and percentage. We ran Spearman's rank-order correlation and computed Spearman's correlation coefficient ( $\rho$ ) to determine the correlation between TAPSE/PASP ratio and other continuous clinical and echocardiographic variables. We used independent samples Mann-Whitney U Test and the Kruskal-Wallis one-way ANOVA test to analyze the distribution of the TAPSE/PASP ratio among the sub-groups of different predictor variables (socio-demographic, exposure, and clinical). A p-value of  $\leq$  0.05 was considered statistically significant for all tests.

## Results

In our study, the median  $\pm$  interquartile range (IQR) of the TAPSE/PASP ratio was  $0.39 \pm 0.19$  mm/mmHg, with a range of 0.13 to 0.79 [Figure 1]. Based on a TAPSE/PASP ratio of  $\leq 0.61$ , 71 patients (85.50%) had RV dysfunction, compared to the 23 patients (27.70%) based on the conventional TAPSE  $< 17$ mm alone. 19 patients (22.9%) had severe RV dysfunction with TAPSE/PASP ratio  $< 0.30$ .

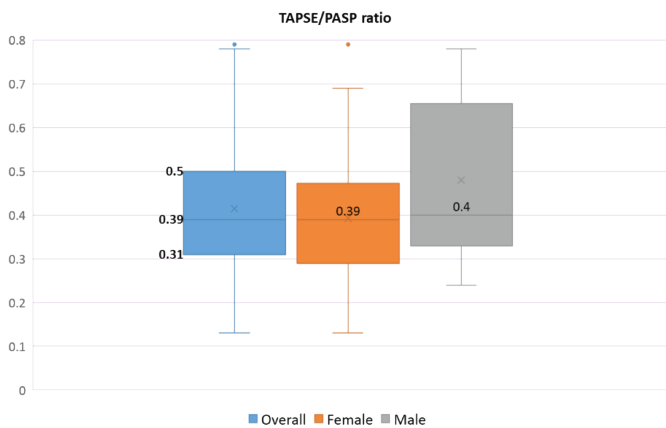


Fig 1: Box and Whisker plot showing the TAPSE/PASP ratio in males, females, and overall

The median  $\pm$  interquartile range (IQR) of TAPSE, PASP, and RV diameter were  $19 \pm 6$  mm,  $47 \pm 19$  mmHg, and  $3.8 \pm 0.7$  cm respectively. All the patients had dilated right ventricles. All 83 patients had pulmonary hypertension (PH), among whom 43 (52%) had mild, 35 (42%) had moderate, and 5 (6%) had severe PH.

Among the 83 COPD patients admitted at KMC, the mean  $\pm$  standard deviation (SD) of their age was  $71 \pm 9.2$  years with a female preponderance of nearly 75%. The majority, 59 patients (71.08%) were homemakers by profession [Table 1].

Table 1. Socio-demographic profile of the patients

S.N.	Variables	Frequency	Percentage	
1	Gender	Male	21	25.3
		Female	62	74.7
		<b>Total</b>	<b>83</b>	<b>100%</b>
2	Occupation	Home-maker	59	71.1
		Farmer	17	20.5
		Industry worker	2	2.4
		Office worker	5	6
		<b>Total</b>	<b>83</b>	<b>100%</b>

72 patients (86.74%) were exposed to firewood smoke with a mean  $\pm$  SD duration of  $45 \pm 16.2$  years. 70 patients (84.33%) were smokers with 45 (64.28%) of them moderate to heavy smokers ( $> 20$  pack years).

Regarding the grading of the COPD patients based on the modified Medical Research Council Dyspnea (mMRC) scale, 35 patients (42%) were in mMRC grade 3, and 29 (35%) were in grade 2 at the time of presentation to the hospital. 38 patients (46%) were under regular domiciliary oxygen use, with a mean  $\pm$  SD of  $3.6 \pm 2.7$  years of oxygen use [Figure 2].

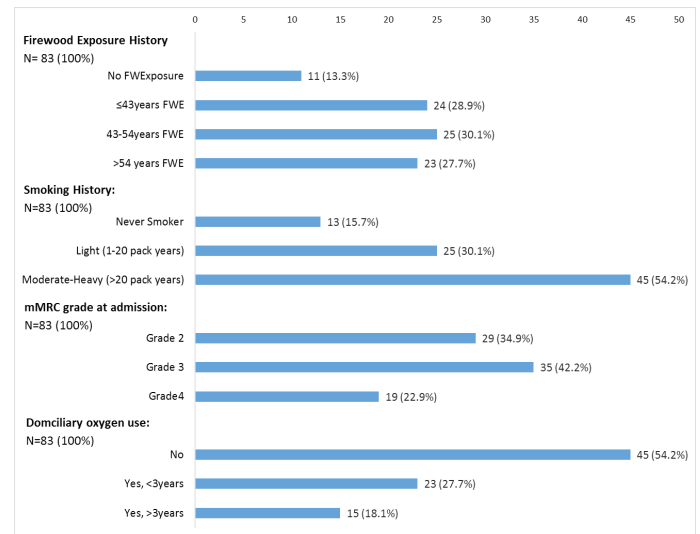


Figure 2. Bar diagram showing the distribution of patients based on firewood exposure history, cigarette smoking, modified Medical Research Council (mMRC) scale at the time of admission, and domiciliary oxygen use

In Spearman's rank-order correlation, we found weak but statistically significant negative correlations of TAPSE/PASP ratio with Right Ventricle (RV) diameter ( $\rho = -0.26$ ;  $p = 0.018$ ); mMRC grade at admission ( $\rho = -0.35$ ;  $p = 0.001$ ); and domiciliary oxygen use ( $\rho = -0.26$ ;  $p = 0.017$ ) [Table 2].

On computing the non-parametric tests of significance, we found a significant association of TAPSE/PASP ratio with the mMRC grade at admission ( $p = 0.005$ ) and domiciliary oxygen use ( $p = 0.024$ ) [Table 3].

**Table 2.** Correlation of TAPSE/PASP ratio with different continuous variables

SN	Independent Variables	Spearman's rank correlation coefficient ( $\rho$ )	p-value	Pearson's correlation coefficient (r)	p-value
1	RV diameter	-0.259*	0.018	-0.300*	0.006
2	mMRC grade at admission	-0.354**	0.001	-0.346**	0.001
3	Domiciliary oxygen	-0.261*	0.017	-0.190	0.86
4	Firewood Exposure duration (years)	-0.131	0.239	-0.168	0.129
5	Smoking pack years	-0.119	0.284	-0.090	0.419

\* Significant at the 0.05 level (2-tailed)

\*\* Significant at the 0.001 level (2-tailed)

**Table 3.** Association of TAPSE/PASP ratio with different predictor variables

SN	Independent Variable Categories	frequency (n)	TAPSE/PASP ratio		Test applied
			Mean $\pm$ SD	p-value	
1	Age				Mann-Whitney U test
	<71 years	44	0.40, 0.15	0.77	
	>71 years	39	0.42, 0.14		
2	Gender			0.38	Mann-Whitney U test
	Male	21	0.48, 0.17		
	Female	62	0.39, 0.13		
3	Firewood Exposure categories (tertiles)			0.11	Kruskal-Wallis test
	No firewood exposure	11	0.446, 0.17		
	$\leq$ 43years firewood exposure	24	0.46, 0.14		
	43-54 yrs firewood exposure	25	0.37, 0.15		
	>54years firewood exposure	23	0.39, 0.12		
4	Smoking categories			0.33	Kruskal-Wallis test
	Never smoker (0 pack years)	13	0.41, 0.14		
	Light smoker (<20 pack years)	25	0.43, 0.12		
	Mod-Heavy smoker (>20 pack years)	45	0.40, 0.16		
5	mMRC grade			0.005*	Kruskal-Wallis test
	2	29	0.41, 0.15		
	3	35	0.39, 0.14		
	4	19	0.34, 0.10		
6	Domiciliary Oxygen use categories			0.024*	Kruskal-Wallis test
	None		0.45, 0.16		
	<3 years		0.38, 0.12		
	>3 years		0.34, 0.10		

\* Significant at the 0.05 level (2-tailed)

## Discussion

Based on findings from previous studies, which showed that a TAPSE/PASP ratio of  $\leq 0.3$  mm/mmHg as a strong predictor of poor outcome in PH on a background of either COPD or interstitial lung disease,<sup>13</sup> nineteen patients (22.9%) fell into this category of severe RV dysfunction. In our study, a TAPSE/PASP ratio of  $\leq 0.3$  mm/mmHg had significant associations with domiciliary oxygen use and mMRC grade of dyspnea. We also found weak but significant negative correlations of TAPSE/PASP ratio with RV diameter ( $\rho = -0.26$ ,  $p = 0.018$ ), mMRC grade at admission ( $\rho = -0.35$ ,  $p = 0.001$ ), and domiciliary oxygen use ( $\rho = -0.26$ ,  $p = 0.017$ ).

The findings of this study provide new insights into RV function evaluation in COPD or pulmonale patients with both pathophysiological and clinical implications. In our study, the COPD patients who required hospitalization, the median  $\pm$  interquartile range of the TAPSE/PASP ratio was  $0.39 \pm 0.19$  mm/mmHg, which was slightly higher than the value of  $\leq 0.3$  given by previous studies as a strong predictor of outcome in PH on a background of either interstitial lung disease or COPD.<sup>13</sup> The need for hospitalization of COPD patients in itself is an indicator of the severity of COPD. The information obtained may be valuable in both the assessment of the treatment and prognostication of COPD or pulmonale patients. In a meta-analysis of TAPSE in COVID-19 patients, it was found that each one-millimeter decrease in TAPSE was associated with an increase in mortality of approximately 20%.<sup>18</sup> However, TAPSE, being a measurement of contraction of RV myocardial fibers, is dependent on the preload (Starling's law in physiology states that the greater the myocardial fibers are stretched the greater the force of contraction up to a certain limit). The index of RV function as the ratio of TAPSE/PASP, which measures non-invasively, the extent of RV contraction (TAPSE) against a given RV afterload (PASP) may be a better indicator of RV function than TAPSE or PASP alone.

As COPD progresses PH increases which results in progressively increased afterload on the RV. The RV adapts to increased afterload by increasing contractility,<sup>19, 20</sup> until a point is reached when the contractility starts to decline as the RV dysfunction increases. Traditionally, PASP has been taken as one of the non-invasive echocardiographic indicators to evaluate the severity of COPD patients. However, the drawback in this measurement is that as the RV dysfunction increases, the strength of RV contractility decreases, and because PASP is an indirect measurement of RV afterload, measured by the pressure gradient across the tricuspid valve, it tends to decrease as the RV contractility decreases, giving

falsely lower values of PASP. Therefore, we need an echocardiographic indicator that truly represents the severity of RV dysfunction. Correcting RV contractility (estimated by TAPSE) by an indirect measure of afterload (PASP) provides a more relevant assessment of RV function.

## Conclusion

TAPSE/PASP ratio as the index of RV dysfunction is a more reliable, non-invasive indicator of RV dysfunction than either TAPSE or PASP taken alone. It measures the extent of RV contraction (TAPSE) against a given RV afterload (PASP). Because hospitalization of COPD patients in itself is an indicator of severity, the median value of 0.39 in our study, may be taken as the cut-off point of severity of COPD patients requiring hospitalization, in our population. We recommend that TAPSE/PASP ratio should be routinely calculated and reported in the echocardiographic evaluation of COPD patients.

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