

Evaluation of the effects of right ventricular pressure load on left ventricular myocardial mechanics in patients with chronic obstructive pulmonary disease by ultrasound speckle tracking imaging

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Abstract. – **OBJECTIVE:** This paper aims to evaluate the effects of right ventricular pressure load on left ventricular myocardial mechanics in patients with chronic obstructive pulmonary disease (COPD) by ultrasound speckle tracking imaging.

PATIENTS AND METHODS: 119 patients with COPD and pulmonary hypertension (PH) were selected from December 2016 to March 2018 in Xuzhou Municipal Hospital Affiliated to Xuzhou Medical University. 42 healthy subjects were selected as control group. According to the pulmonary arterial systolic pressure (PASP), 41 patients were classified into mild group, 47 in moderate group, and 31 cases in severe group. Echocardiography and STI were used to measure the indexes.

RESULTS: Compared with those in control group, E1 and E/e of moderate group and severe group increased significantly ($p < 0.001$). Compared with those in control group, parameters in moderate and severe groups significantly decreased ($p < 0.001$), including early diastolic mitral annular velocity/late peak blood flow velocity (E/A), left ventricular end diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), PASP and left ventricular end-diastolic diameter (LVEDD), stroke volume (SV), left ventricular end-systolic diameter (LVESD), cardiac output (CO), peak rotation angle and peak time of in the basal and apical segments. Compared with those in control group, parameters in moderate group significantly decreased ($p < 0.001$), including left ventricular strain parameters segmental systolic peak longitudinal strain (LS), circumferential strain (CS), and radial strain (RS). Compared with those in control group, parameters in mild group significantly decreased ($p < 0.001$), including peak rotation angle of basal segment and apical segment of the left ventricle. Compared with those in moderate group, peak rotation angle and peak time of the whole basal segment and apical segment of severe group gradually decreased ($p < 0.001$).

CONCLUSIONS: Left ventricular whole peak rotation angle can be used to sensitively evaluate the change of left ventricular myocardial mechanics function in PH patients, and can reflect changes of left ventricular myocardial mechanics function in patients with COPD when mild PH occurs.

Key Words

Ultrasonic speckle tracking imaging, Chronic obstructive pulmonary disease, Right ventricular pressure load, Left ventricular myocardial mechanics, Left ventricular rotation angle.

Introduction

Chronic obstructive pulmonary disease (COPD) is a common irreversible chronic respiratory disease in the human body. It is mainly caused by a severe lung inflated left and right ventricular structure changes, resulting in left and right ventricular dysfunction^{1,2}. COPD patients are in a state of hypoxia and acidosis for a long time, leading to increased pulmonary vascular resistance, thus resulting in pulmonary hypertension (PH)³. PH is the main cause of increased right ventricular pressure load. Early onset of PH is occult with no obvious clinical features, so most patients were diagnosed in advanced stages⁴. Clinically, intervention method for PH is limited. Early intervention has a close relationship with prognosis of patients. With the development of disease, the 5-year survival rate of severe PH patients is below 50%. End-stage patients often die of right heart failure⁵. Due to the increase in right ventricular load pressure coupled with risk-inducing factors, such as respiratory infections, ventilatory disturbances,

and pulmonary embolism recurrence, some patients' right ventricular diastolic pressure rises sharply, and the right ventricular output suddenly decreases, which causes pulmonary edema, and eventually they die from acute left heart failure^{6,7}.

Studies have shown that PH mainly affects right ventricular function, and right ventricular pressure overload causes right ventricular remodeling⁸. Left and right ventricles belong to heart outer cyst, which is formed by the spiral structure of heart muscle and they share the ventricular septum, so the functions and structures of the right and left ventricle will influence each other⁹. When pulmonary arterial pressure increases, the right ventricular cavity gradually expands, and the increased load causes pressure on right ventricular septum and makes a shift to the left ventricle, resulting in a decrease in left ventricular pressure, leading to pathological changes, limited filling, and eventually resulting in impaired function¹⁰. At present, investigations on PH patients mainly focus on right ventricular function, while studies on left ventricular function are relatively rare¹¹. Ultrasound speckle tracking imaging (STI) technology overcomes the problem of angular dependence of conventional echocardiography. STI is an effective detection method for quantitative assessment of myocardial function, and it has been gradually applied to the study of PH. However, most researches focus on left ventricular strain and bottom rotation function in patients with moderate to severe PH rather than mild PH, and effects of PH on left ventricular myocardial function have not been elucidated¹².

In this work, 119 patients with COPD and PH were treated with STI technology to observe the changes in multiple parameters of the whole body and heart muscle, and influence of increased right ventricular pressure load on left ventricular myocardial mechanics was analyzed. This report provided guidance for the early intervention of patients with COPD and PH.

Patients and Methods

Patients

We selected 119 patients with COPD and PH patients from December 2016 to March 2018 in Xuzhou Municipal Hospital Affiliated to Xuzhou Medical University as subjects. Those patients included 66 males and 53 females, and age ranged from 24 to 71 years, with a mean age of (51.26±10.95) years. At the same time, 42 healthy

subjects were selected as the control group. Control group included 26 males and 16 females, and age ranged from 22 to 67 years, with a mean age of (48.87±12.04) years.

Inclusion and Exclusion Criteria

Inclusion criteria: met diagnostic criteria for PH (2009) established by European Respiratory Association (ERC) and European Society of Cardiology (ESC)¹³; echocardiographic examination of left ventricular ejection fraction (LVEF) > 50%, pulmonary arterial systolic pressure (PASP) > 40 mmHg; patients with complete clinical data; FEV₁/FVC < 70%. This study has been approved by the Ethics Committee of Xuzhou Municipal Hospital Affiliated to Xuzhou Medical University. All participants signed the informed consent. **Exclusion criteria:** Patients with heart-lung-system related diseases such as diabetes mellitus, hypertension, interstitial lung disease, congenital heart disease, coronary heart disease, cardiomyopathy and valvular disease; patients with right ventricular outflow tract obstruction or non-sinus rhythm; patients with moderate or greater tricuspid regurgitation; patients with severe liver or renal or hematopoietic dysfunction; patients with previous family history of mental illness and psychosis.

Methods

Philips iE Elite color Doppler ultrasound diagnostic instrument (Philips, Ultrasound, Bothell, WA, USA) with S5-1 probe (frequency range: 1.0 - 5.0MHz) was used and data were analyzed using Qlab 7.0 quantitative analysis software. Ultrasound Doppler Echocardiography: patients were fixed in left oblique position and parameters were measured, including early diastolic mitral annular velocity (E), late peak blood flow velocity (A), early mitral annular diastolic motion velocity (e), left ventricular end diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), LVEF and left ventricular end-diastolic diameter (LVEDD). Stroke volume (SV), left ventricular end-systolic diameter (LVESD), cardiac output (CO) were calculated. Left ventricular end-systolic volume index (EI) was measured at left ventricular chordae and papillary muscle levels. Velocity of tricuspid regurgitation was measured. PASP and right ventricular systolic pressure (RVSP) were assessed referring to Pak's effort equation, $PASP = RVSP$, $RVSP = 4V^2 + RAP$, V denotes the maximum regurgitation velocity of the tricuspid valve. Right atrial pressure was esti-

mated based on the degree of collapse of inferior vena cava during inspiration. Complete collapse of the right atrial pressure was 5 mmHg, partial collapse was 10 mmHg, and no collapse was 15 mmHg. According to the evaluation of PASP, 119 patients with COPD and PH were divided into mild group, moderate group, and severe group. Mild: 40 to 49 mmHg; moderate: 50 to 70 mmHg; severe: >70 mmHg. STI examination: free breath, and following samples were collected: apical left ventricular long axis two-chamber and three-chamber view and four-chamber views, as well as three each of apical left ventricular papillary muscle, apical level and basal cardiac cycles. Qlab 7.0 workstation was used for analysis to identify end-diastolic endocardium and adventitia, and to automatically track the wall motion in each segment of the region of interest. Peak longitudinal strain value (LS), circumferential strain value (CS) and radial strain value (RS) were measured during segmental systole. Left ventricular systolic longitudinal strain value (GLS), circumferential strain value (GCS) and radial strain (GRS) values were calculated. Images of short axis of the left ventricle, and apex level dynamic images were used to measure overall peak rotation angle and peak time.

Statistical Analysis

Statistical analysis was performed using SPSS 17.0 [Yiyun (Shanghai) Information Technology Co., Ltd.]. Measurement data were expressed as mean±standard deviation ($\bar{x}\pm s$). Chi-square test was used to analyze count data. Comparisons among multiple groups were performed using one-way analysis of variance and the post-hoc test was Dunnett test. $p<0.05$ indicated a difference with statistical significance.

Results

Baseline Data of Mild, Moderate, Severe, and Control Groups

According to the pulmonary arterial systolic pressure (PASP), 41 patients were classified into mild group, 47 in moderate group, and 31 cases in severe group. With the increase of PASP value, heart rate of mild, moderate and severe patients showed an increasing trend ($p<0.001$) (Figure 1). There was no significant difference in clinical baseline data including gender, age, hemoglobin, total bilirubin, serum creatinine, arterial oxygen partial pressure, arterial carbon

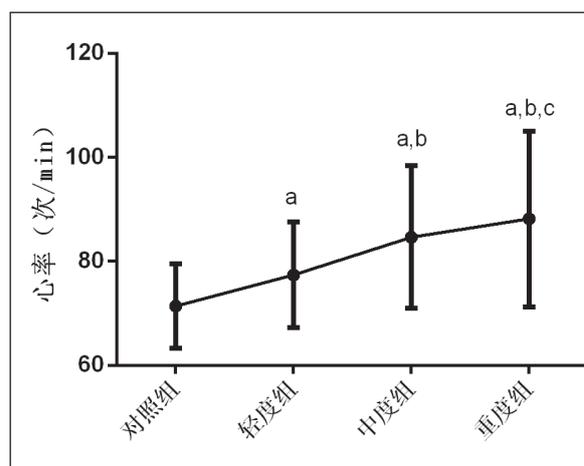


Figure 1. Heart rate of mild, moderate and severe patients.

dioxide partial pressure, blood oxygen saturation, systolic blood pressure, and diastolic blood pressure among mild, moderate, severe, and control groups ($p>0.05$) (Table I).

Left Ventricular Echocardiographic Parameters in Mild, Moderate, Severe, and Control Groups

With the increase of PASP, left ventricular pressure increased gradually. Compared with those in control group, EI and E/e in moderate group and severe group increased significantly ($p<0.001$). Compared with those in the moderate group, PASP, EI and E/e in severe group increased significantly ($p<0.001$). Compared with those in control group, E/A, LVEDV, LVESV, LVEDD, LVESD, SV, and CO significantly decreased in moderate and severe groups ($p<0.001$). Compared with those in moderate group, these indicators significantly decreased in severe group ($p<0.001$). There was no significant change in LVEF in the mild, moderate, severe, and control groups ($p>0.05$) (Table II).

Left Ventricular Strain Parameters in Mild, Moderate, Severe, and Control Groups

With the increase of PASP, left ventricular strain parameters LS, CS, and RS gradually decreased ($p<0.001$). Compared with those in control group, left ventricular strain parameters LS, CS and RS in moderate group significantly decreased ($p<0.001$). Compared with those in the moderate group, those parameters significantly decreased in severe group ($p<0.001$) (Table III).

Table I. Baseline data of mild, moderate, severe, and control groups [n(%)] ($\bar{x}\pm s$).

Indexes	Mild (n=41)	Moderate (n=47)	Severe (n=31)	Control (n=42)	F/X ²	p
Gender [n (%)]					1.093	0.779
Male	22 (53.66)	28 (59.57)	16 (51.61)	26 (61.90)		
Female	19 (46.34)	19 (40.43)	15 (48.39)	16 (38.10)		
Age (years)	49.15±11.24	51.62±10.87	50.47±11.83	48.87±12.04	0.540	0.655
Hemoglobin (g/L)	158.3±24.9	155.7±29.4	153.2±30.4	161.8±25.7	0.670	0.571
Total bilirubin (umol/L)	22.7±14.8	21.4±11.7	19.8±13.5	21.7±10.3	0.812	0.317
Blood creatinine (umol/L)	66.1±12.8	64.7±10.2	67.3±13.8	63.7±13.1	0.596	0.618
Arterial oxygen partial pressure (mmHg)	67.8±13.8	65.9±15.6	64.3±14.7	63.7±13.5	0.647	0.585
Arterial carbon dioxide partial pressure (mmHg)	35.7±5.1	34.8±5.2	35.6±5.7	34.1±6.1	0.734	0.532
Blood oxygen saturation (%)	91.2±7.2	92.7±6.1	91.3±6.8	92.4±6.3	0.546	0.651
Heart rate (times/min)	77.38±10.13 ^a	84.64±13.74 ^{a,b}	88.16±16.93 ^{a,b,c}	71.37±8.16	14.070	<0.001
Systolic pressure (mmHg)	114.68±12.28	116.52±13.67	115.68±14.35	113.34±12.87	0.459	0.711
Diastolic pressure (mmHg)	74.21±7.26	75.17±8.14	75.24±8.43	74.42±8.46	0.165	0.919

Notes: compared with control group, ^a $p<0.001$; compared with mild group, ^b $p<0.001$; compared with moderate group, ^c $p<0.001$.

Table II. Left ventricular echocardiographic parameters in mild, moderate, severe and control groups ($\bar{x}\pm s$).

Indexes	Mild (n=41)	Moderate (n=47)	Severe (n=31)	Control (n=42)	F	p
EI	1.07±0.10	1.24±0.37 ^a	1.51±0.41 ^{a,b}	0.95±0.08	27.270	<0.001
E/A	1.43±0.52	1.22±0.29 ^a	1.01±0.23 ^{a,b}	1.51±0.47	11.240	<0.001
E/e	6.51±2.01	8.41±6.64 ^a	10.57±6.87 ^{a,b}	6.42±2.04	5.592	<0.001
LVEDV (ml)	73.24±11.64	62.37±9.24 ^a	51.28±9.11 ^{a,b}	73.94±12.68	34.460	<0.001
LVESV (ml)	24.93±5.16	19.84±4.51 ^a	12.46±4.63 ^{a,b}	25.37±5.14	52.730	<0.001
LVEF (%)	64.49±5.47	63.17±5.28	63.95±4.93	64.73±5.63	0.743	0.527
LVEDD (mm)	46.98±5.01	39.27±4.22 ^a	31.71±4.05 ^{a,b}	47.31±4.58	96.110	<0.001
SV (ml)	47.24±9.17	37.43±9.01 ^a	28.46±7.52 ^{a,b}	47.82±11.15	33.990	<0.001
LVEDSD (mm)	28.11±4.38	24.16±4.11 ^a	19.82±3.99 ^{a,b}	28.37±4.26	32.330	<0.001
CO (L/min)	3.59±1.04	3.15±0.68 ^a	2.17±0.57 ^{a,b}	3.61±1.22	17.910	<0.001

Notes: compared with control group, ^a $p<0.001$; compared with moderate group, ^b $p<0.001$

Table III. Left ventricular strain parameters in mild, moderate, severe and control groups ($\bar{x}\pm s$).

Indexes	Mild (n=41)	Moderate (n=47)	Severe (n=31)	Control (n=42)	F	p
LS						
GLS	-18.93±6.21	-14.25±4.15 ^a	-11.87±3.09 ^{a,b}	-19.25±6.37	17.770	<0.001
LAT	-18.11±7.35	-15.27±4.78 ^a	-12.37±3.22 ^{a,b}	-18.45±7.52	7.677	<0.001
IVS	-19.20±6.81	-14.47±4.47 ^a	-11.58±3.69 ^{a,b}	-19.43±7.63	15.060	<0.001
CS						
GCS	-18.89±2.59	-16.37±2.35 ^a	-13.87±2.13 ^{a,b}	-19.21±2.63	36.780	<0.001
LAT	-19.94±3.81	-16.54±3.51 ^a	-13.71±2.84 ^{a,b}	-20.13±3.94	26.060	<0.001
IVS	-20.79±4.25	-16.74±3.79 ^a	-12.55±3.38 ^{a,b}	-21.14±4.13	37.260	<0.001
RS						
GRS	25.87±5.46	21.79±4.11 ^a	16.57±3.16 ^{a,b}	26.46±5.47	32.800	<0.001
LAT	23.86±6.01	19.25±5.64 ^a	16.56±4.79 ^{a,b}	24.13±5.98	15.470	<0.001
IVS	24.33±7.29	20.58±4.87 ^a	17.09±2.43 ^{a,b}	24.76±7.46	12.760	<0.001

Notes: compared with control group, ^a $p<0.001$; compared with moderate group, ^b $p<0.001$

Left Ventricular Rotation Parameters in Mild, Moderate, Severe, and Control Groups

With the increase of PASP, total peak rotation angle and peak time of the left ventricular base-mid and apical segment gradually decreased. Compared with those in control group, peak rotation angle of basal segment and apical segment of the left ventricle in mild group significantly decreased ($p<0.001$), and peak rotation angle and peak time of in the basal and apical segments significantly decreased in moderate and severe groups ($p<0.001$). Compared with those in moderate group, peak rotation angle and peak time of the whole basal segment and apical segment of severe group gradually decreased ($p<0.001$) (Table IV).

Discussion

COPD as one of the most common human diseases worldwide has high incidence, modality, and mortality rate¹⁴. COPD causes unexpired pressure and hyperinflation in the lungs of human body, which in turn increases intrathoracic pressure and eventually leads to the appearance of PH, and circulatory failure is one of the manifestations of end-stage COPD and PH¹⁵. The onset of COPD is occult with no specific clinical manifestation. Most patients are diagnosed in advanced stages and circulatory failure may happen^{16,17}. The sensitivity of conventional echocardiography in the diagnosis of COPD with early changes in left ventricular function is low. Our study provided guidance for the early diagnosis of clinical COPD and PH using STI technology.

Scholars have shown that PH mainly affects right ventricular function of lungs. With the increase of right ventricular pressure load, right ventricle gradually undergoes eccentric remodeling changes, resulting in pathological changes in

the right ventricle, leading to reduced function and being spherical in shape¹⁸. Left and right ventricles are in the same system. When right ventricular pressure load rises, blood flow in right ventricle gradually decreases, while the left atrium's return flow will decrease, and left atrium and left ventricular compliance filling will also decrease, and then function of the left ventricle will be affected¹⁹. As the right ventricular pressure load rises, process of blood flow in coronary artery and venous veins back to the right atrium will be affected, resulting in cardiac coronary artery and venous ischemia, which will eventually lead to weakened left ventricular blood supply and affect left ventricular function²⁰. Results of this paper showed that left ventricular echocardiographic parameters LVEDV, LVESV, LVEDD, LVESD, SV, CO in COPD and PH patients showed a decreasing trend with the increase of PASP, indicating that the left ventricular cavity of the patient gradually decreases with the increase of PASP. EI and E/e showed an increasing trend and E/A showed a decreasing trend, which indicates that the left ventricular diastolic function was impaired. Dongming et al²¹ used echocardiography to detect left ventricular and right ventricular function in PH patients and they found that function of myocardial contraction in right ventricle was weakened, and left ventricular myocardial systolic function also decreased. In the early period of left ventricular contractile dysfunction, heart can maintain normal LVEF through the body's compensatory defense mechanism, and changed stress and strain value of ventricular wall obtained by STI can be used to quantify overall strain and torsion angle of the heart²². Results of this report showed that with the increase of PASP, no significant changes in LVEF were observed in the mild, moderate, severe, and control groups, and the left ventricular strain parameters LS, CS, and RS gradually de-

Table IV. Left ventricular rotation parameters in mild group, moderate group, severe group and control groups ($\bar{x}\pm s$).

Indexes	Mild (n=41)	Moderate (n=47)	Severe (n=31)	Control (n=42)	F	p
Basal segment						
Overall peak rotation angle (°)	-5.09±4.31 ^a	-3.83±3.16 ^{a,b}	-2.99±2.54 ^{a,b,c}	-6.89±4.53	7.781	<0.001
Peak time (ms)	0.31±0.06	0.39±0.08 ^a	0.43±0.10 ^{a,b}	0.28±0.05	33.900	<0.001
Apical segment						
Overall peak rotation angle (°)	7.21±4.24 ^a	6.07±3.97 ^{a,b}	4.57±3.08 ^{a,b,c}	9.16±4.58	8.471	<0.001
Peak time (ms)	0.19±0.05	0.15±0.04 ^a	0.11±0.02 ^{a,b}	0.20±0.06	28.490	<0.001

Notes: compared with control group, ^a $p<0.001$; compared with mild group, ^b $p<0.001$; compared with moderate group, ^c $p<0.001$.

creased. Compared with those in control group, left ventricular strain parameters LS, CS, and RS significantly decreased in moderate group. Compared with those in the moderate group, left ventricular strain parameters LS, CS, and RS significantly decreased in severe group, which is consistent with previous studies.

STI technology is a new approach to study overall function and cardiac locality²³. Zhou et al²⁴ has confirmed that the left ventricular myocardium is formed by inferior right helix of intimal myocardium, left helix of the adventitia and mid toroidal myocardium, and pressure load is one of the main factors affecting rotation. Results of this work show that with the increase of PASP, rotation ability of basal segment and the apical segment of the left ventricular decreased gradually. Compared with those in control group, peak rotation angle and peak time of basal segment and apical segment in moderate and severe groups significantly decreased. Compared with those in moderate group, peak rotation angle and peak time of basal segment and apical segment in severe group significantly decreased.

Our data support that the decrease in left ventricular rotation is caused by increased pressure load in PH patients. Previous researches only focus on moderate-severe PH patients; those of mild PH mainly rely on animal models. Results of our study showed that compared with the control group, peak rotation angle of left ventricular basement segment and apical segment significantly decreased in mild group, indicating that the left ventricular total peak rotation angle applied to evaluate the change of left ventricular cardiac mechanics function in PH patients has better sensitivity and can provide guidance for the treatment and prognosis of patients with COPD and PH.

The investigation was conducted in strict accordance with the exclusion and inclusion criteria. There was no significant difference in clinical baseline data including gender, age, hemoglobin, total bilirubin, serum creatinine, arterial oxygen partial pressure, arterial carbon dioxide partial pressure, blood oxygen saturation, systolic blood pressure, and diastolic blood pressure among mild, moderate, severe, and control groups. Therefore, our data are reliable. However, COPD often affects the structure and function of the left ventricle, leading to difficulties in the process of echocardiography examination. Therefore, in our works studies, we will further detect lung hyperinflation and left ventricular structure and function to confirm the conclusions of this study.

Conclusions

We showed that with the increase in PASP, right ventricular pressure load gradually increased, therefore, left ventricular myocardial mechanical properties were impaired, and left ventricular strain gradually decreased with the increased right ventricular pressure load. Left ventricular whole peak rotation angle can be used to sensitively evaluate the change of left ventricular myocardial mechanics function in PH patients, and can reflect changes of left ventricular myocardial mechanics function in patients with COPD when mild PH occurs.

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Conflict of Interest

The authors declare that they have no competing interests.

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