

## ORIGINAL ARTICLE

# Evaluation of pulmonary arterial pressure in patients with connective tissue disease-associated pulmonary arterial hypertension by myocardial perfusion imaging

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## Funding information

Nature Science Foundation of Hubei Province, Grant/Award Number: 2018CFB353; Wuhan health and family planning commission young and middle-aged medical backbone talent fund, Grant/Award Number: 2018[116]

## Abstract

**Background:** Pulmonary arterial hypertension (PAH) is a complex and severe complication of connective tissue disease (CTD). We aimed to evaluate the application value of myocardial perfusion imaging (MPI) in evaluating CTD-associated PAH (CTD-PAH).

**Methods:** We retrospectively included 88 patients who were diagnosed with CTD between January 2018 and December 2020 at our hospital. Fifty-eight patients had PAH and were included into the CTD-PAH group. Thirty patients without PAH were included in the control group. All patients received routine physical examination, biochemical tests and cardiac function evaluation, right heart catheterization (RHC), and <sup>99m</sup>Tc-MIBI MPI. PAH patients were divided into the mild, moderate, and severe PAH group according to their mean pulmonary artery pressures by RHC. Pearson correlation analysis was used to calculate the correlation between the right ventricle target/background (T/B) and right ventricle stroke volume (RV-SV), total pulmonary resistance (TPR), pulmonary vascular resistance (PVR), mean pulmonary arterial pressure (mPAP), 6-minute walk distance (6-MWD), and N-terminal B-type natriuretic peptide (NT-proBNP). The ROC curves of T/B and pulmonary artery pressure classification were plotted and the sensitivity and specificity of T/B in diagnosing PAH of different severities were analyzed.

**Results:** The analysis of correlation revealed that T/B correlated negatively with 6-MWD and positively with NT-proBNP and exhibited good positive correlation with mPAP, TPR, and PVR by RHC and negative correlation with RV-SV. T/B was of the most diagnostic value for severe PAH, and its correlation with severe PAH was stronger than that with mild PAH and moderate PAH.

**Conclusions:** Target/background is a noninvasive method that can simultaneously evaluate pulmonary arterial pressure and myocardial perfusion of CTD-CHD patients and is particularly of relatively high value for severe PAH patients.

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Clinical trial registration number: ChiCTR20000316

Zengyan Wang and Jiao Li contributed equally to this work.

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**KEYWORDS**

connective tissue disease, diagnosis, myocardial perfusion imaging, pulmonary hypertension, therapeutic efficacy

## 1 | INTRODUCTION

Connective tissue disease (CTD) is an autoimmune disease that is mainly characterized clinically by involvement of multiple systems (Klemm et al., 2019). Pulmonary arterial hypertension (PAH) is a complex and severe complication of CTD and has high mortality (Ojima et al., 2019). CTD-PAH accounts for one-fourth of all PAH cases and has a worse prognosis than other types of PAH, posing a serious threat to human health (Condliffe & Howard, 2015). CTD includes systemic sclerosis (SSc), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), mixed connective tissue disease (MCTD), idiopathic inflammatory myopathies (IIM), and primary Sjogren's syndrome (Pss) (Lin et al., 2020). In Chinese population, CTD-PAH is mainly associated with SLE in Chinese population while CTD-PAH is more commonly associated with SSc in Caucasians (Calderone et al., 2016). The main pathological manifestations of PAH are hypertrophy of the media in the small pulmonary arteries, fibrosis of the intima, proliferation of elastic fibers, plexiform and aneurysmal dilatation, and fibronecrosis of muscularized arterioles (Pietra et al., 2004).

Pulmonary arterial hypertension is defined as a mean pulmonary arterial pressure (mPAP) > 25 mm Hg in the resting state or >30 mm Hg in the active state, while the corresponding pulmonary capillary wedge pressure is less than 15 mm Hg (Hachulla et al., 2005). For several decades, right heart catheterization (RHC) has become the gold standard for diagnosing PAH and evaluating right ventricular function (Schewel et al., 2020). Although the right heart catheter can directly measure the hemodynamics of the right ventricle, RHC is an invasive procedure and is unable to assess myocardial perfusion of the hypertrophic right ventricle. Single-photon positron emission tomography (SPECT) myocardial perfusion imaging (MPI) has been extensively used to assess myocardial perfusion of the left ventricle but has been used less frequently for studying perfusion of the right ventricle. Under normal conditions, the right ventricle rarely takes up radionuclides and cannot be clearly visualized. The after load of the right ventricle is increased in PAH patients, and radionuclide uptake is increased in right ventricle hypertrophy, and MPI has certain feasibility in right ventricle myocardial perfusion in PAH (Liu et al., 2017). Currently, there have been few studies on the relationship between right ventricle myocardial perfusion and hemodynamic parameters of the right heart, and there are also fewer quantitative indicators. Fang W et al. evaluated 24 cases of idiopathic PAH (IPAH) and 43 cases of congenital heart disease-associated PAH (CHD-PAH) using the SPECT parameter myocardial  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) uptake and the results showed that right ventricle FDG uptake (RV/LV ratio) correlated with pulmonary vascular resistance (PVR) in both IPAH and CHD-PAH patients (Fang et al., 2012). The current study utilized Image J to calculate MPI parameter (right

ventricle target/background ratio, T/B) and analyzed its correlation with biochemical parameters, functional parameters, and hemodynamic parameters that were used for evaluating cardiac function. The objective of the current study was to explore whether quantitative MPI parameters could be used to evaluate the severity of right heart damage in CTD-PAH patients and assess pulmonary arterial resistance and pressure.

## 2 | MATERIALS AND METHODS

### 2.1 | Patient selection

All patients provided informed consent. For patients aged <18 years, written informed consent was provided by the parents or legal guardians of the patients. Eight-eight patients who were diagnosed with CTD between January 2018 and December 2020 were included. Fifty-eight cases had PAH and categorized into the CTD-PAH group and 30 patients without PAH were assigned to the control group. The exclusion criteria were (1) age less than 18 years or more than 65 years; (2) other types of PAH; (3) other concomitant severe diseases such as diabetes, hypertension, and chronic pulmonary diseases; (4) patients with unstable diseases such as acute myocardial infarction and aortic dissection; (5) cardiac arrhythmia such as atrial fibrillation, conduction block, or post pacemaker implantation; and (6) NYHA cardiac function class IV. Indication for the resting gated MPI was as follows: 51 patients for fatigue (58%), 15 patients for dyspnea (17%), 20 patients for palpitation (23%), five patients for syncope (6%), 16 patients for chest pain or tightness (18%), and 21 patients for shortness of breath (24%). Some patients have more than one symptom.

Fifty-eight CTD-PAH patients were enrolled, including 51 women. The mean age at diagnosis was  $54.7 \pm 12.2$  years. The mean course of CTD at the time of PAH diagnosis was  $6.6 \pm 1.7$  years. The baseline data of the enrolled patients are shown in Table 1. All patients received RHC examination and  $^{99\text{m}}\text{Tc}$ -MIBI MPI.

### 2.2 | Evaluation and classification of PAH

Pulmonary arterial hypertension was categorized into three groups according to the mean pulmonary arterial pressure (mPAP): the mild PAH group ( $25 \text{ mmHg} < \text{mPAP} \leq 36 \text{ mmHg}$ ), the moderate PAH group ( $36 \text{ mmHg} < \text{MPAP} \leq 45 \text{ mmHg}$ ), and the severe PAH group ( $\text{mPAP} > 45 \text{ mmHg}$ ). The mild PAH group had 20 patients. The mPAP was  $30.2 \pm 3.5 \text{ mmHg}$ . The moderate PAH group had 18 patients. The mPAP was  $41.1 \pm 2.0 \text{ mmHg}$ . The severe PAH group had 20 patients. The mPAP was  $50.2 \pm 3.0 \text{ mmHg}$ .

TABLE 1 Patient baseline data

		CTD-PAH group (n = 58)	Control group (n = 30)	t value or $\chi^2$ value	p value
General information	Female	51	27	0.084	0.772
	Age (year)	54.7 ± 12.2	51.3 ± 14.5	1.161	0.249
	Height (cm)	162.5 ± 12.5	163.5 ± 11.2	-0.343	0.733
	Weight (kg)	56.6 ± 9.7	54.3 ± 10.7	0.928	0.357
	BMI (kg/m <sup>2</sup> )	20.5 ± 2.4	20.6 ± 2.8	-0.158	0.874
	HR (bpm)	80.8 ± 11.9	83.7 ± 12.8	-0.965	0.338
	SPO <sub>2</sub> (%)	95.9 ± 4.2	99.5 ± 0.8	5.176	0.000
Cardiac function index	NT-proBNP (ng/ml)	601.4 ± 184.9	129.7 ± 31.2	13.796	0.000
	6-MWD (m)	357.8 ± 65.7	429.0 ± 53.6	-4.806	0.000
Hemodynamic parameters	RV-SV (ml)	51.2 ± 6.5	66.5 ± 6.3	-10.575	0.000
	TPR (dyne.s/cm <sup>5</sup> )	1095.4 ± 370.4	226.4 ± 57.8	12.736	0.000
	PVR	883.0 ± 338.5	197.6 ± 49.7	10.999	0.000
	PCWP (mmHg)	6.5 ± 0.7	6.3 ± 1.0	0.969	0.336
	mPAP (mmHg)	40.8 ± 8.4	15.7 ± 2.1	16.067	0.000
	sPAP (mmHg)	74.00 ± 4.5	22.8 ± 4.7	45.966	0.000
	dPAP (mmHg)	30.2 ± 8.5	9.5 ± 1.3	13.230	0.000
	mBP (mmHg)	86.71 ± 13.67	84.13 ± 14.2	2.58 ± 6.79	0.075
	sBP (mmHg)	118.2 ± 8.9	122.4 ± 10.1	-1.815	0.074
	dBp (mmHg)	70.6 ± 5.8	73.0 ± 6.3	-1.645	0.105
MPI index	MPI T/B	1.72 ± 0.23	—	—	—

Note:  $p < 0.05$  indicates statistical significance.

Abbreviations: 6-MWD, 6-minute walk distance; BMI, body mass index; dBp, diastolic blood pressure; dPAP, diastolic pulmonary arterial pressure; HR, heart rate; mBP, mean blood pressure; mPAP, mean pulmonary arterial pressure; MPI T/B, MPI target/background ratio; NT-proBNP, N-terminal B-type natriuretic peptide; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RV-SV, right ventricle stroke volume; sBP, systolic blood pressure; sPAP, systolic pulmonary arterial pressure; SPO<sub>2</sub>, oxygen saturation; TPR, total pulmonary resistance.

## 2.3 | RHC examination

All patients received local anesthesia or basic anesthesia *via* percutaneous puncture of the femoral artery and vein. RHC examination was undertaken using the Siemens angiography system (AXIOM Artis dTA, Germany) for measurement of hemodynamic parameters including mPAP, the systolic PAP (sPAP), the diastolic PAP (dPAP), mean blood arterial pressure (mBP), systemic systolic blood pressure (sBP), and systemic diastolic blood pressure (dBp). Other hemodynamic parameters were calculated using Fick method, including right ventricle stroke volume (RV-SV), total pulmonary resistance (TPR), TPR index (TPRI), pulmonary vascular resistance (PVR), PVR index (PVRI), cardiac output (CO), and cardiac index (CI).

## 2.4 | MPI and semiquantitative analysis

All patients underwent <sup>99m</sup>Tc-MIBI rest gated MPI using SPECT with a dual-head detector (Symbia T6; Siemens) with a low-energy high-resolution sensitivity collimator, energy peak 140 keV, window width 20%, matrix 64×64, and elliptical orbit 180°. One frame was acquired per 6° arc and for 30 s per one body position for a total

of 30 frames. <sup>99m</sup>Tc-MIBI (740–925 MBq, 20–25 mCi) was administered intravenously, and after 30–60 min, 250 mL milk or fatty foods were taken to promote excretion of radioactive drugs from the liver. After 90 min, <sup>99m</sup>Tc-MIBI myocardial perfusion tomography was undertaken. Reconstruction was carried out using nonattenuation-corrected filtered back projection (FBP) to generate the short-axis, horizontal long-axis, and vertical long-axis views. All scanning data were randomly assigned to two cardiovascular radiologists with 20 years of clinical experience who were blind to the clinical data of the patients. A circular region of interest (ROI) was selected in the appropriate anatomic section of the right ventricle. Image J was used to determine mean voxel intensity of the target (right ventricle) and background (lung tissues adjacent to the right ventricle) and the target-to-background ratio (T/B) was calculated.

## 2.5 | Statistical analysis

SPSS16.0 was used for statistical analysis. Numerical parameters before and after treatment were compared using paired sample t test. Correlation between T/B and other parameters was calculated using Person correlation method. The intraclass correlation coefficient

TABLE 2 Differences in various parameters in different CTD-PAH subgroups

	N (%)	RV-SV (ml)	TPR (dyne.s/cm <sup>2</sup> )	PVR (dyne.s/cm <sup>2</sup> )	mPAP (mmHg)	6-MWD (m)	NT-proBNP (ng/ml)	T/B
Underlying disease								
SLE	32 (55.2)	52.3 ± 6.2	1030.8 ± 371.1	822.5 ± 335.0	39.8 ± 7.9	347.2 ± 53.3	2126.6 ± 689.0	1.68 ± 0.19
SSc	18 (31.0)	50.0 ± 4.5	1131.0 ± 404.5	902.1 ± 363.5	40.7 ± 10.0	353.1 ± 69.9	2434.7 ± 820.7	1.77 ± 0.26
MCTD	8 (13.8)	49.4 ± 9.4	1273.4 ± 226.5	1082.0 ± 228.1	45.0 ± 6.3	338.4 ± 82.0	2430.5 ± 898.5	1.71 ± 0.25
Gender								
Female	51 (87.9)	50.9 ± 5.5	1077.4 ± 369.6	864.4 ± 339.3	40.2 ± 8.3	353.0 ± 74.9	2307.7 ± 810.3	1.87 ± 0.24
Male	7 (12.0)	53.4 ± 10.5	1226.3 ± 377.1	1018.7 ± 323.5	45.6 ± 8.4	352.1 ± 75.0	2381.6 ± 756.4	1.70 ± 0.22
mPAP classification								
Mild	20 (34.5)	56.0 ± 4.6	637.3 ± 192.6	476.5 ± 140.2	30.2 ± 3.5	390.8 ± 55.6	1644.4 ± 449.2	1.47 ± 0.10
Moderate	18 (31.0)	52.0 ± 6.1*	1187.9 ± 156.6**	936.9 ± 140.0**	41.1 ± 2.0**	350.2 ± 81.7	2047.7 ± 673.0*	1.71 ± 0.14**
Severe	20 (34.5)	46.2 ± 4.3***##	1426.4 ± 196.5***##	1209.2 ± 185.3***##	50.2 ± 3.0***##	324.9 ± 76.7**	3135.3 ± 525.6***##	1.96 ± 0.14***##
Total cohort	58 (100)	51.2 ± 6.5	1095.4 ± 370.4	883.0 ± 338.5	40.8 ± 8.4	352.9 ± 74.3	2316.6 ± 797.9	1.72 ± 0.23

Note: \* means there was a statistical difference compared with mild group ( $p < 0.05$ ); \*\* means there was a significant statistical difference compared with mild group ( $p < 0.01$ ). # means there was a statistical difference compared with moderate group ( $p < 0.05$ ); ## means there was a significant statistical difference compared with moderate group ( $p < 0.01$ ).

(ICC) and Bland Altman plot were used to evaluate the consistency between the two blinded readers. ROC curves for T/B and PAH groups were drawn.  $p < 0.05$  was considered statistically significant.

### 3 | RESULTS

#### 3.1 | Patient baseline data of the two groups

There was no statistical difference in gender, age, body height, body weight, BMI, HR, PCWP, mBP, sBP, and dBP between the two groups. The CTD-PAH group had significantly lower SPO<sub>2</sub>, 6-MWD, and RV-SV than the control group. The CTD-PAH group had significantly higher NT-proBNP, TPR, PVR, mPAP, sPAP, and dPAP than the control group (Table 1). The right ventricle was visualized in the CTD-PAH group by <sup>99m</sup>Tc-MIBI, and the mean T/B was  $1.72 \pm 0.23$ . The right ventricle was not visualized by <sup>99m</sup>Tc-MIBI in the control group <sup>99m</sup>Tc-MIBI.

#### 3.2 | CTD-PAH subgroups, hemodynamic parameters among the groups, and differences among cardiac function parameters

The patients were grouped by etiologies. There was no statistical difference in RV-SV, TPR, PVR, mPAP, 6-MWD, NT-proBNP, and T/B among the SLE group, SSc group, and MCTD group. There was no statistical difference in the above parameters in patients of different sexes. There was no statistical difference in age among the mild PAH group, the moderate PAH group, and the severe PAH group. There was statistical difference in RV-SV, TPR, PVR, mPAP, 6-MWD, NT-proBNP, and T/B among the mild PAH group, the moderate PAH group, and the severe PAH group (Table 2).

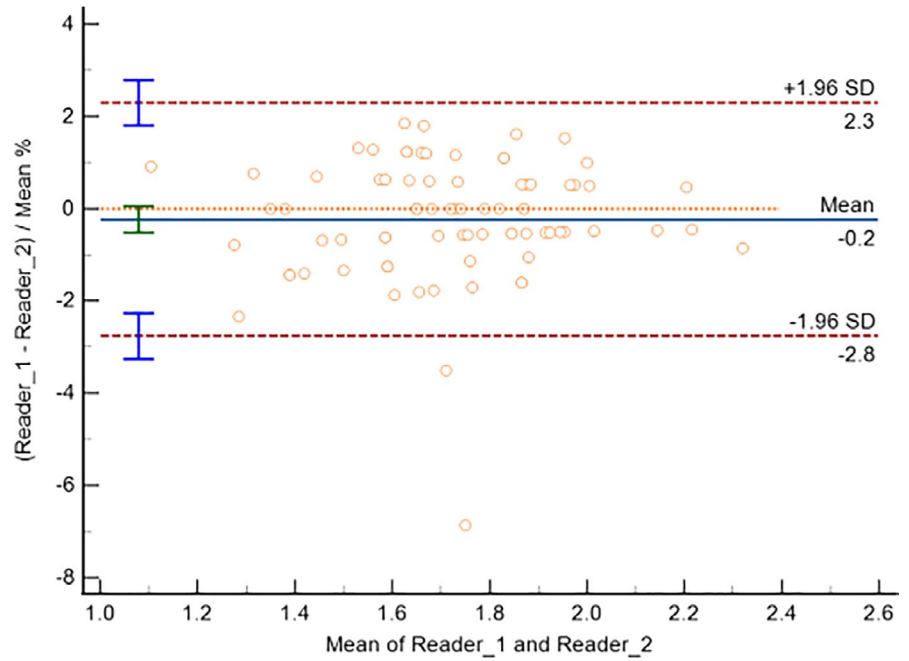
#### 3.3 | <sup>99m</sup>Tc-MIBI imaging and the correlation between T/B and hemodynamic parameters and cardiac function parameters.

All patients underwent <sup>99m</sup>Tc-MIBI SPECT scan. The Bland Altman plot indicated good agreement between the two readers. Reader 2 obtained on average slightly higher mean T/B values than reader 1. However, differences were not statistically significant ( $p > 0.05$ ) (Figure 1). The ICC value was 0.995 ( $p < 0.001$ ), indicating an excellent correlation of T/B between two readers. The perfusion of the right ventricle increased in the CTD-PAH group, and the <sup>99m</sup>Tc-MIBI images of patients of different severities of PAH are shown in Figure 2.

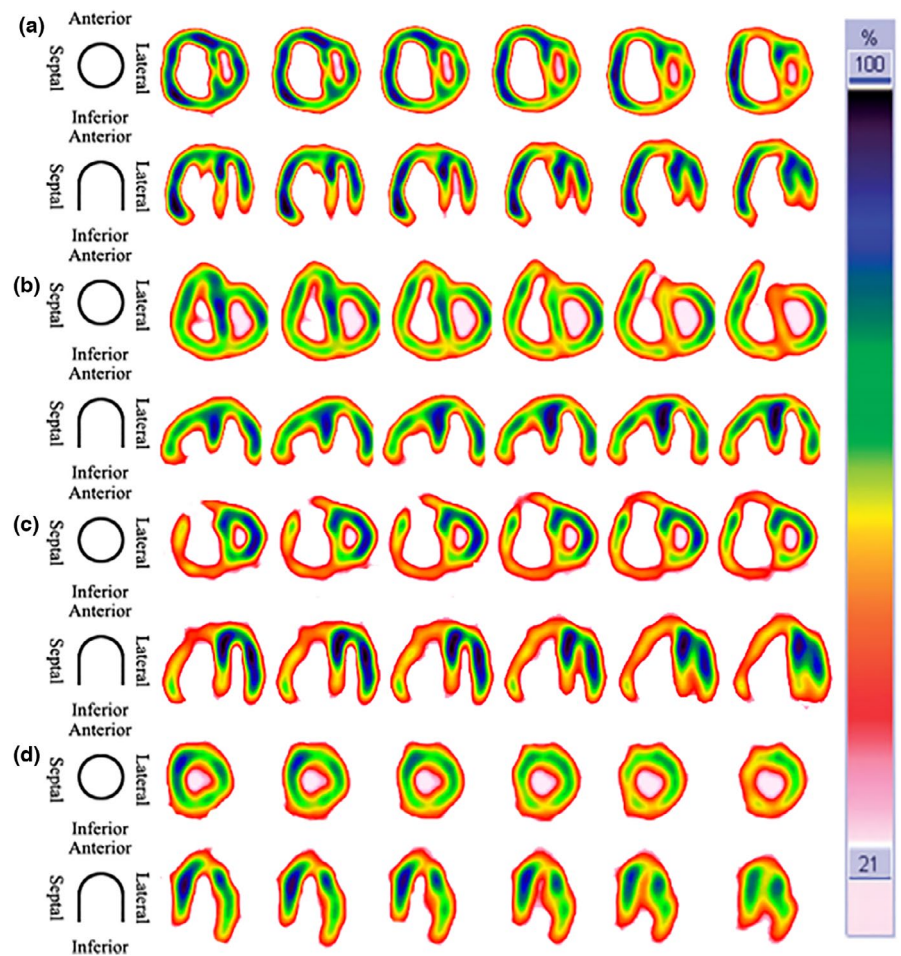
The analysis of correlation between T/B and other parameters is shown in Table 3.

T/B negatively correlated with RV-SV and 6-MWD, and positively correlated with TPR, PVR, mPAP, and NT-proBNP in the mild PAH group, the moderate PAH group, and the severe PAH group.

**FIGURE 1** Bland Altman plots to evaluate the consistency between the two blinded readers



**FIGURE 2** <sup>99m</sup>Tc-MIBI images of patients of different PAH subgroups: (a) the severe PAH group. (b) The moderate PAH group. (c) The mild PAH group. (d) The control group



Moreover, T/B showed the highest correlation with mPAP in the severe PAH group, followed by that in the moderate PAH group. The correlation between T/B and mPAP mild PAH group was lower than that in the moderate PAH group and severe PAH group. When all PAH patients were statistically analyzed, T/B negatively correlated

with RV-SV and 6-MWD, and positively correlated with TPR, PVR, mPAP, and NT-proBNP.

To further evaluate the diagnostic value of T/B for PAP in CTD-PAH patients, we analyzed the ROC curves of T/B for diagnosing patients of different severities of PAH (Figure 3). The results showed

TABLE 3 The analysis of correlation between T/B and other parameters

		RV-SV (ml)	TPR (dyne.s/cm <sup>5</sup> )	PVR	mPAP (mmHg)	6-MWD (m)	NT-proBNP (ng/ml)
Mild	Pearson	-0.383	0.617	0.618	0.616	-0.074	0.534
	<i>p</i> value	0.105	0.005	0.005	0.005	0.763	0.018
Moderate	Pearson	-0.228	0.835	0.795	0.610	-0.280	0.462
	<i>p</i> value	0.348	0.000	0.000	0.006	0.245	0.046
Severe	Pearson	-0.351	0.457	0.467	0.835	-0.284	0.676
	<i>p</i> value	0.129	0.043	0.038	0.000	0.225	0.001
Total	Pearson	-0.529	0.871	0.874	0.884	-0.414	0.797
	<i>p</i> value	0.000	0.000	0.000	0.000	0.001	0.000

Note:  $p < 0.05$  means there is statistical difference.  $p < 0.01$  means there is significant statistical difference.

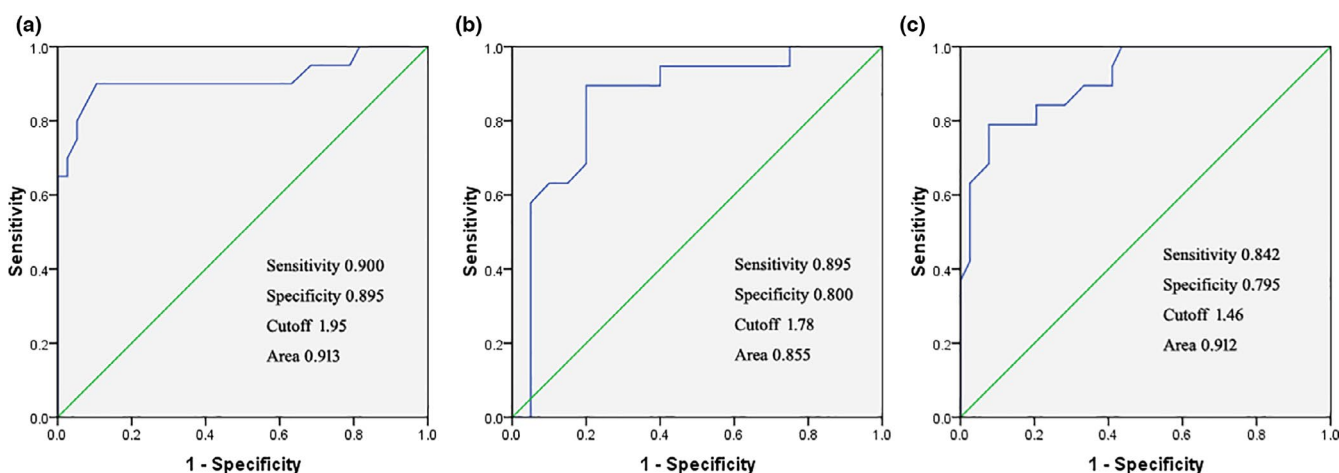


FIGURE 3 The ROC curve of T/B and mPAP in patients with different severities of PAH. (a) The severe PAH group. (b) The moderate PAH group. (c) The mild PAH group

that the area under the curve of T/B for diagnosing severe PAH was 0.913. Using a cutoff of 1.95, the sensitivity was 0.900 and the specificity was 0.895 (95% CI 0.807~0.977). The area under the curve of T/B for diagnosing moderate PAH was 0.855. Using a cutoff of 1.78, the sensitivity was 0.895 and the specificity was 0.800 (95% CI 0.807~0.977). Furthermore, the area under the curve of T/B for diagnosing mild PAH was 0.912. Using a cutoff of 1.46, the sensitivity was 0.842 and the specificity was 0.795 (95% CI 0.927~1.005).

## 4 | DISCUSSION

PAH is a common disease characterized by increased PAP and PVR, and prolonged PAH could lead to systolic dysfunction of the right ventricle, right ventricle hypertrophy, and right ventricle dilation, thus causing right heart failure (Lücke et al., 2019). Congenital heart disease (CHD) and CTD are two main causes of PAH. PAH is a common complication of CTD, called CTD-PAH. Almost all types of CTD could cause PAH, including SLE, SSc, Sjogren's syndrome, and MCTD. In other countries, SSc is the major cause of PAH; SSc-induced pulmonary injuries mainly include pulmonary fibrosis and PAH. Meanwhile, in our country, SLE is the major cause of CTD-PAH,

accounting for approximately 50% SLE-PAH (Wang et al., 2020). The pathologies of CTD-induced PAH probably include endothelial dysfunction, Raynaud phenomenon, inflammatory injury, and formation of autoantibodies (Zanatta et al., 2019). Often due to difficulty in early diagnosis and presence of other concurrent organ damages in CTD-PAH patients, the therapeutic efficacy is poor, and the prognosis is unsatisfactory. PAH has become one of the important causes of aggravation and death of CTD patients.

The evaluation methods for the right heart circulatory system of CTD-CHD patients usually include echocardiography, RCH, and pulmonary artery flotation catheter. These methods have their own advantages and disadvantages. Currently, no method is available that is noninvasive, suitable for all CTD-CHD patients, and can simultaneously assess myocardial perfusion and PAP. Hong et al., 2020, evaluated the systolic function of the right ventricle of CTD-PAH patients using two-dimensional speckle tracking echo cardiography for predicting PAH. Pearson correlation analysis revealed that the systolic pressure of the pulmonary artery positively correlated with the longitudinal strain parameters of the free wall of the right ventricle including Sb, Sm, Sa, and Sg, and negatively correlated with TAPSE and right ventricle FAC ( $p < 0.05$  in all). ROC curve analysis showed that Sb, Sm, Sa, Sg,

and FAC all could predict whether CTD patients have combined PAH (Hong et al., 2020). However, echocardiography is not capable of assessing right ventricle perfusion in CTD patients and cannot learn about myocardial oxygenation. Moreover, PAP by echocardiography is not applicable to patients without tricuspid regurgitation. RCH is the gold standard for PAP evaluation, but it is invasive and is not suitable for multiple measurements in a short period. It is also very expensive. Liu et al. studied 23 PAH patients and 23 PAH-free patients by  $^{99m}\text{Tc}$ -MIBI imaging. The right ventricle was not visualized in any of the non-PAH group but was imaged in 5/7 moderate PAH patients and all 16 severe PAH patients (Liu et al., 2018). Nevertheless, the study did not provide a semi-quantitative PAH evaluation method by  $^{99m}\text{Tc}$ -MIBI.

Myocardial perfusion imaging is an imaging technique that utilizes the tracking properties of myocardial perfusion imaging agents in SPECT or PET to obtain myocardial perfusion images under specific conditions to learn about myocardial blood supply and viability so that the goal of diagnosis, differential diagnosis, prognosis, and monitoring of efficacy can be achieved. Because the right ventricle is thinner and has a lower uptake of radioactivity and is susceptible to partial volume effect, under normal conditions, the right ventricle is not visualized by  $^{99m}\text{Tc}$ -MIBI; but in PAH, the right ventricle afterload is increased, leading to right ventricle hypertrophy. Under this condition, partial volume effect has little influence on imaging, myocardial perfusion increases, hypertrophied the cardiac muscles could take up radionuclides, and are visualized. However, the correlation between semi-quantitative MPI and PAH severity still remains not very clear. Currently, attention has been rarely paid to the relationship between MPI and hemodynamic parameters of the right heart in CTD-CHD patients and the question whether MPI can be used to semi-quantitatively assess PAP. In the current study, we measured T/B of  $^{99m}\text{Tc}$ -MIBI in the target region (right ventricle) and background (lung tissues adjacent to the right ventricle) and analyzed the relation between T/B and biochemical parameters, cardiac function indexes, and hemodynamic parameters and the value for diagnosing PAH of different severities.

Our results indicated that T/B exhibited good correlation with mPAP and had a relatively high sensitivity and specificity in diagnosing PAH of different severities. The area under the curve (AUC) in the severe PAH group was larger than that of the mild PAH group and the moderate PAH group. The possible reason is that the range of mPAP in the severe PAH group was higher than that of the mild PAH group and the moderate PAH group, and T/B rose with increase in PAP. We earlier studied the correlation between T/B and PAP of congenital heart disease-associated PAH patients before and post-treatment, and the results showed that T/B and mPAP declined after treatment to reduced PAP. The likely cause is that though PAP is reduced by PAP lowering treatment, the hypertrophy of the right ventricle cannot be reversed, and the right ventricle still take up certain amounts of  $^{99m}\text{Tc}$ -MIBI. The effect of PAP lowering therapy on T/B is smaller than its effect on PAP. T/B is more suitable for evaluating untreated PAP and we plan to compare the value of T/B in the evaluation of PAH before and after treatment of CTD-CHD.

Overall, our study demonstrated that the semi-quantitative value of MPI in CTD-CHD patients had relatively good correlation with right heart function, PAP or total pulmonary pressure, and TPR and a noninvasive detection method that can simultaneously reflect right heart function, pressure, resistance, and myocardial perfusion. This study has important limitations that should be acknowledged. First, this study's small sample size limits the generalization of these outcomes to a larger population. Secondly, myocardial perfusion imaging is a semiquantitative method to evaluate pulmonary artery pressure. Although it is a noninvasive method, its accuracy needs to be improved.

#### ACKNOWLEDGMENTS

This study was supported by Nature Science Foundation of Hubei Province (No. 2018CFB353) and Wuhan health and family planning commission young and middle-aged medical backbone talent fund (No. 2018[116]).

#### CONFLICTS OF INTEREST

The authors declare there is no conflicts of interest regarding the publication of this paper.

#### DISCLOSURES

There are no relationships with industry.

#### AUTHORS' CONTRIBUTIONS

Zengyan Wang, Jiao Li, and Xiaoke Shang conceived the study, designed the study, and collected the data. All authors analyzed the data and were involved in writing of the manuscript.

#### ETHICS APPROVAL

The study was approved by the ethics committee of the No.1 Hospital of Wuhan city.

#### DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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**How to cite this article:** Wang, Z., Li, J., Wang, X., Liu, M., Liao, M., Zhang, C., & Shang, X. (2022). Evaluation of pulmonary arterial pressure in patients with connective tissue disease-associated pulmonary arterial hypertension by myocardial perfusion imaging. *Annals of Noninvasive Electrocardiology*, 27, e12927. <https://doi.org/10.1111/anec.12927>