Semi-quantitative assessment of pulmonary arterial hypertension associated with congenital heart disease through myocardial perfusion imaging

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Abstract

Objective: The study aimed to use myocardial perfusion imaging (MPI) as a semi-quantitative method to assess the clinical severity of pulmonary arterial hypertension (PAH) in patients with congenital heart disease (CHD). **Subjects and Methods:** A total of 24 patients with PAH related to CHD (PAH-CHD) who received interventional or medical treatment were included. All patients underwent physical examination, cardiac function evaluation, biochemical test, echocardiography, right heart catheterization (RHC), and MPI with ^{99m}Tc-methoxyisobutyl isonitrile (^{99m}Tc-MIBI) pre and 6 months post treatments. The correlation between MPI target/background (T/B) ratios and other variables were calculated. The receiver operating characteristic (ROC) curves were developed to evaluate the diagnostic value of T/B ratios. **Results:** Most of the cardiac functional parameters, surplus pulse O_2 (SPO_2), biochemical values and right heart catheterization parameters were found significantly elevated after treatment ($P<0.05$). Pre-treatment MPI showed that T/B ratio had strong correlations with SPO_2, Borg scale, cardiac output (CO), cardiac index (CI), right ventricular stroke volume (RV-SV), pulmonary artery pressure (PAP), total pulmonary resistance (TPR), total pulmonary resistance index (TPRI), pulmonary vascular resistance (PVR), and pulmonary vascular resistance index (PVRI). After 6 months treatment, the correlation between T/B ratios and most of these parameters measured were reduced. Receiver operating characteristics curves showed that the diagnostic performance of MPI T/B ratio in moderate/severe PAH patients was significant. The area under the curve (AUC) when measured pre-treatment was 0.929 ($P=0.002$) and reduced to 0.800 ($P=0.046$) at post-treatment. **Conclusion:** Semi-quantitative MPI has high diagnostic value in evaluating the severity level of pulmonary arterial hypertension in patients with congenital heart disease. The diagnostic performance of MPI at pre-treatment was superior to that at post-treatment. More cases need to be included for further study.

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Introduction

Over the past decade, cardiologists have been investigating pulmonary arterial hypertension (PAH) as an important entity in cardiovascular disease [1, 2]. Pulmonary arterial hypertension is defined as an increase in mean pulmonary arterial pressure (mPAP) >25mmHg at rest as assessed by right heart catheterization (RHC), with a normal pulmonary capillary wedge pressure [3]. Among the different complications of congenital heart disease (CHD), PAH is common in this population owing to high pulmonary blood flow and systemic-to-pulmonary shunts, especially in untreated/ undertreated patients [4-6]. The diagnosis carries a high risk of heart failure, infectious endocarditis, and cerebral thrombosis [7], and, if untreated, is associated with a high mortality rate. Specific CHD anomalies involving pulmonary-systemic shunts, such as ventricular septal defect (VSD) and patent ductus arteriosus (PDA), predictably lead to PAH and sometimes result in Eisenmenger syndrome (ES) with a prevalence of 1.1% to 12.3% amongst CHD patients [5, 6]. There is also a risk of developing PAH in atrial septal defect (ASD) [8, 9]. Diagnosing, assessing, and monitoring PAH development and response to treatment is of great importance in the CHD population.

For decades, RHC has remained the gold standard in diagnosing PAH and evaluating right ventricular (RV) function [10, 11]. This invasive procedure measures RV hemodynamics directly. Development of a noninvasive method that assesses both RV performance and PAH severity would be ideal. Myocardial perfusion imaging (MPI) by gated single-photon emission tomography (SPET) has been widely used in simultaneous evaluation of left ventricular (LV) function and myocardial ischemia [12, 13]. However, it still needs to be assessed for evaluating RV performance and PAH severity. Lubiszewska et al. (2000)

[14] assessed RV function and RV impairment in patients with complete transposition of the great arteries (TGA) after the Mustard or Senning operation using ^{99m}Tc methoxyisobutyl isonitrile (^{99m}Tc-MIBI) MPI. The result showed that the extent of myocardial perfusion abnormalities correlated well with impairment of RV and LV function, and myocardial perfusion defects could be a sensitive predictor of systemic ventricular impairment. In patients with TGA, the RV at systemic pressure was hypertrophied and the myocardial mass was greater than the low-pressure LV, so SPET studies easily visualized myocardial uptake in the RV, and did not visualize the LV as completely.

Congenital heart disease patients with PAH (PAH-CHD) suffer from RV pressure overload, which provides the possibility of evaluating RV abnormalities and PAH severity. There have been a limited number of studies evaluating PAH-CHD with semi-quantitative MPI. In this study, the severity of PAH in CHD patients was assessed by MPI before and after treatment, and correlated with biochemical, functional, ultrasonic and hemodynamic parameters. The aim of this study was to prospectively assess the diagnostic value of MPI in evaluating the severity level of PAH in CHD patients, and compare the pre- and post-treatment difference of MPI along with a set of quantifiable diagnostic parameters. To the best of our knowledge, there is no report about the comparison of semi-quantitative MPI with the ventricular hemodynamic parameters obtained by right heart catheterization (RHC), and its application for evaluation of PAH in CAD is rare.

Subjects and Methods

Patients

This study was approved by the Ethics Committee of Wuhan Asia Heart Hospital, and all enrolled patients gave informed consent. For the patients under the age of 18, the patients' parents or legal guardians gave consent. Inclusion criteria for participation in this study included (1) (mPAP) at rest >25 mmHg; (2) the pulmonary capillary wedge pressure ≤15 mmHg, according to well-accepted clinical criteria [3, 15]; (3) age >8 years and <55 years. Exclusion criteria included severe comorbidities such as diabetes, hypertension, chronic pulmonary diseases, etc., and functional class IV according to New York Heart Association (NYHA) Functional Classification.

Twenty-four CHD patients (10 males, 14 females; age 13-35y, mean 25±6.9y) were enrolled in this study. All patients were diagnosed with CHD combined with PAH, including 11 VSD, 7 ASD and 6 PDA cases. Twenty out of 24 patients had been diagnosed at least three years ago but did not accept any treatment because of self-neglect or limited medical condition. The other 4 patients were newly diagnosed. Among the 24 patients, 9 patients with ES received per os treatment with bosentan, sildenafil, or tadalafil; while the other 15 patients were treated with intervention with or without the combination of oral medicines. The following information were collected and compared pre- and 6 month post-treatment: Cardiac function assessments including 6 minute walking distance (6-MWD) and Borg scale of perceived exertion, biochemical test including N-terminal pro-B-type natriuretic peptide (NT-proBNP) and cardiac troponin I (CTnI), echocardiography, right heart catheterization (RHC) and ^{99m}Tc-MIBI myocardial perfusion imaging (MPI).

PAH assessment and classification

Patients were classified into three PAH groups according to the severity of mPAP: mild PAH, 25mmHg<mPAP≤36 mmHg; moderate PAH, 36mmHg<mPAP≤45mmHg; and severe PAH, mPAP>45mmHg. NYHA Functional Classification was as follows [16, 17]: class I (cardiac disease but no symptoms or limitation in ordinary physical activity), class II (mild symptoms) and class III (marked limitation in activity, comfortable only at rest).

Right heart catheterization (RHC)

Right heart catheterization was performed in the catheterization laboratory using conscious sedation and local anesthesia. The usual invasively measured hemodynamic parameters, including mPAP, systolic pulmonary artery pressure (sPAP), diastolic pulmonary artery pressure (dPAP), mean blood pressure (mBP), systolic blood pressure (sBP) and diastolic blood pressure (dBP), were recorded using angiographic system (Axiom Artis dTA, Siemens, Erlangen, Germany). Other hemodynamic parameters, including RVSV, total pulmonary resistance (TPR), total pulmonary resistance index (TPRI), pulmonary vascular resistance (PVR), pulmonary vascular resistance index (PVRI), cardiac output (CO) and cardiac index (CI), were calculated using Fick's method.

MPI and semi-quantification

Resting gated ^{99m}Tc-MIBI SPET was performed before treatment and 6 months following treatment initiation. The heart rate (HR) and blood pressure were monitored and ECG was obtained. Myocardial perfusion index was performed as previously described [18, 19]. Briefly, SPET MPI was performed 60-90min after intravenous injection of ^{99m}Tc-MIBI (740-925MBq) using a dual-detector gamma camera (Symbia T6, Siemens, Erlangen, Germany), equipped with a low-energy, all-purpose collimator, centered on the 140keV photopeak with a 20% symmetrical energy window. Data were acquired in a 64×64 matrix along an elliptical orbit with six intervals over 180°. Reconstruction was performed using a Butterworth filtered back projection algorithm without attenuation correction, and short-axis, horizontal long-axis, and vertical long-axis images were generated. Circle-shaped regions of interest (ROI) at the appropriate anatomical location of the RV covering the area from the subendocardium to the subepicardium in each slice were set. Circular ROI on lung tissue adjacent to RV of each slice were also set. The average pixel intensities of the target RV and background (lung tissue adjacent to RV) were measured using open-source software (Image J, National Institutes of Health, Washington DC, USA). The mean target-to-background (T/B) ratio of each slice was calculated.

Statistical analysis

Comparison of parameters before and after treatment was performed using the Paired-Samples t-test. Correlation of MPI T/B ratio values with other parameters was calculated using Pearson's correlation coefficients. The ROC curves of MPI T/B ratio for detecting moderate/severe PAH patients were developed based on data collected pre- and post-treatment (SPSS version 16.0 software, IBM, Armonk NY, USA). Statistical differences were determined to be significant at $P<0.05$.

Results

Changes in clinical parameters before and after treatment

Table 1 shows the pre- and post-treatment parameters collected from PAH-CHD patients, including biochemical profiles, cardiac function evaluation, hemodynamic parameters and MPI measurement. Significant differences were observed in most of biochemical examinations, cardiac function parameters, and as well as hemodynamic parameters between pre-treatment and post-treatment results. Cardiac biomarkers, se-rum NT-proBNP and CTnI ($P<0.05$) and Borg scale ($P<0.01$), were decreased significantly in post-treatment group, while 6-MWD was increased. Hemodynamic parameters demonstrated similar trend. For examples, RV-SV was increased ($P<0.05$), while TPR, TPRI, PVR, PVRI, mPAP, sPAP and dPAP were decreased ($P<0.01$). Other parameters, including CO and CI, were not significant altered at post-treatment group. However, the semi-quantification of MPI images, represented by MPI T/B ratio, showed no statistical difference between pre-treatment and pre-treatment groups.

The correlation between MPI semi-quantification and clinical parameters

Resting gated ^{99m}Tc-MIBI SPET was performed pre- and post-treatment in all patients. All pixel intensities in the image of the RV were semi-quantified. Increased perfusion in the RV was observed in PAH patients with high severity. As shown in Figure 1, the RV were visualized clearly in the moderate and severe PAH patients (Figure 1A and 1B), but not in the mild PAH patient (Figure 1C). No significant difference in MPI images was observed between pre- and post-treatment patients.

Paired t-test comparison of the MPI T/B ratios showed no statistical significance between pre- and post-treatment groups. However, Pearson correlation analysis showed pre-treatment MPI T/B ratio values have highly correlation with many cardiac function variables and hemodynamic parameters (Pearson correlation coefficient >0.400), including positive correlation with Borg scale, TPR, TPRI, PVR, PVRI, mPAP, sPAP, and dPAP, and negative correlation with CO, CI, RVSV, and SPO2 (Table 2). After treatment, only a few clinical parameters were still correlated with T/B ratio values, including parameters TPR, TPRI, PVR, PVRI, mPAP, sPAP and dPAP (Table 3).

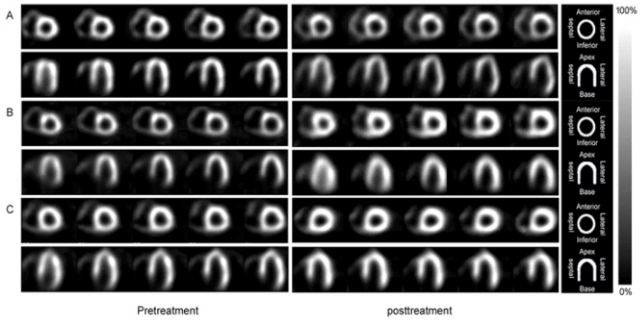

Figure 1. Pre- and post-treatment MPI images from representative patients. Representative images were selected from severe (A), moderate (B) and mild (C) PAH patient groups, respectively. T/B rations of A, B and C were 1.87, 1.64, 1.30 before treatment, and 1.90, 1.66 and 1.25 after treatment, respectively. The upper two panels in each case show the short axis images, while the lower panels show the horizontal long-axis views. The intensity bar on the right was used as the standard of the radial intensity when quantification was applied.

Diagnostic performance of MPI T/B ratio in PAH-CHD

Although MPI T/B ratio could not distinguish post-treatment group from pre-treatment group, we further evaluated if MPI T/B ratio had some diagnostic value in differentiation of the severity of PAH before and after treatment. Table 4 showed, again, that MPI T/B ratios in all groups showed no significant difference between pre- and post-treatment, suggesting that MPI semi-quantification is not sensitive enough in evaluating the treatment outcome of PAH.

To further assess the diagnostic performance of MPI T/B ratio in detecting the severity of PAH, ROC analysis was performed to evaluate its sensitivity and specificity for discriminating moderate/severe PAH from mild PAH. Figure 2A showed the ROC curve for pre-treatment MPI T/B ratio and the area under curve (AUC) of 0.929±0.055 ($P=0.002$), indicating that the pre-treatment MPI T/B ratio had a decent relevance with PAH severity. With the cutoff of 1.855 to diagnose the moderate/severe PAH, the sensitivity was 0.867 and the specificity was 1.000. The ROC result of post-treatment MPI T/B ratio for detecting moderate/severe PAH had a decreased AUC of 0.800±0.108 ($P=0.046$). Using 1.825 as a cutoff, the sensitivity was 0.706 and the specificity was 0.800. These results suggested MPI T/B ratio is a potential variable to indicate and evaluate moderate/severe PAH-CHD patients, and that its correlation with PAH severity at pre-treatment is stronger than at post-treatment.

Discussion

This study investigated the clinical performance of MPI T/B ration in response to routine PAH treatment and its correlation with the clinical severity of PAH. These findings suggested a potential diagnostic value of quantitative MPI test in disguising moderate/severe PAH from mild PAH.

Congenital heart disease is fairly common in newborns, with an incidence of rate around 1 in 100 [20]. Because of the advances in pediatric cardiology and surgery, the survival rate of CHD patients has increased through the decades and

Table 1. *Comparison of heart function parameters after the treatments*

Characteristics		pre-treatment	post-treatment	Paired differences	P value
Demographic information	Height(cm)	157.54±11.06	157.75±10.50	0.21±0.72	0.170
	Weight(kg)	51.83±10.70	51.86±10.81	0.03±0.56	0.773
	BSA(m^2)	1.53±0.21	1.53±0.20	0.002±0.009	0.357
	BMI(kg/m^2)	20.75±2.69	20.70±2.74	0.05±0.31	0.441
	HR(bpm)	81.58±13.47	80.50±11.66	1.08±4.88	0.288
	SPO_2(%)	94.10±5.37	95.87±4.04	1.77±2.49	0.002
Biochemical examination	NT-proBNP (ng/ml)	1332.40± 1967.79	958.96± 1351.94	373.41± 646.70	0.010
	CTnI (ng/ml)	0.014±0.012	0.010±0.009	0.004±0.009	0.031
Cardiac function parameters	6-MWD(m)	444.96±62.29	491.62±38.62	46.67±31.81	0.000
	Borg scale	1.46±1.22	0.73±0.83	0.73±0.66	0.000
Hemodynamic parameters	RV-SV(ml)	59.79±25.63	67.98±32.62	8.19±14.35	0.01
	TPR ($dyne{\cdot}s{\cdot}cm^{-5}$)	1092.0±725.66	817.00±461.74	275.04±429.75	0.005
	TPRI ($dyne{\cdot}s{\cdot}cm^{-5}{\cdot}m^{-2}$)	1657.2±1083.86	1241.0±695.70	416.16±637.40	0.004
	PVR ($dyne{\cdot}s{\cdot}cm^{-5}$)	894.42±616.05	659.38±401.60	235.04±365.53	0.004
	PVRI ($dyne{\cdot}s{\cdot}cm^{-5}{\cdot}m^{-2}$)	1358.30±922.65	1002.1±606.25	356.25±541.47	0.004
	mPAP (mmHg)	52.25±16.80	46.58±15.60	5.67±8.02	0.002
	sPAP (mmHg)	82.13±23.54	74.04±23.56	8.08±10.18	0.001
	dPAP (mmHg)	37.25±15.20	32.75±13.50	4.5±7.33	0.006
	mBP (mmHg)	86.71±13.67	84.13±14.17	2.58±6.79	0.075
	sBP (mmHg)	115.25±18.00	113.04±18.90	2.21±11.62	0.362
	dBP (mmHg)	72.46±12.48	69.75±12.64	2.71±6.50	0.053
	CO (L/min)	4.74±1.34	5.05±1.25	0.31±1.41	0.29
	CI (L/min)	3.16±1.04	3.32±0.78	0.17±1.02	0.432
MPI	MPI T/B ratio	1.85±0.23	1.85±0.21	0.00±0.03	0.948

BSA: body surface area; BMI: body mass index; BMR: basal metabolic rate; HR:heart rate; NT-proBNP: N-terminal pro-B-type natriuretic peptide; CTnI: cardiac troponinI; 6-MWD: six-minute walk distance; RV-SV:right ventricular stroke volume; TPR: total pulmonary resistance; TPRI: total pulmonaryresistance index; PVR: pulmonary vascular resistance; PVRI: pulmonary vascular resistance index; mPAP: mean pulmonary artery pressure; sPAP: systolic pulmonary artery pressure; dPAP:diastolic pulmonary artery pressure; mBP: mean blood pressure; sBP: systolic blood pressure; dBP: diastolic blood pressure; CO: cardiac output; CI:cardiac index; MPI T/B ratio: myocardial perfusion imaging target/background ratio.

Table 2. *Correlation of pre-treatment MPI T/B ratio values with other parameters*

Variables	NT-pro BNP	CTnI	6-MWD	Borg scale	SPO2	TPR	TPRI	PVR	PVRI
Pearson	0.097	0.212	-0.397	0.495*	-0.446*	0.504*	0.534*	0.519*	0.545**
P value	0.667	0.345	0.067	0.019	0.038	0.017	0.010	0.013	0.009
Variables	**CO**	**CI**	**RV-SV**	**mPAP**	**sPAP**	**dPAP**	**mBP**	**sBP**	**dBP**
Pearson	-0.514*	-0.567**	-0.424*	0.599**	0.643**	0.497*	0.207	0.029	0.313
P value	0.014	0.006	0.049	0.003	0.001	0.019	0.356	0.899	0.157

,P<0.05;,P<0.01.*

Table 3. *Correlation of post-treatment MPI T/B ratio values with other parameters*

Variables	NT-pro BNP	CTnI	6-MWD	Borg scale	SPO2	TPR	TPRI	PVR	PVRI
Pearson	0.100	0.336	-0.293	0.326	-0.282	0.506*	0.541**	0.517*	0.546**
P value	0.659	0.126	0.186	0.138	0.203	0.016	0.009	0.014	0.009
Variables	**CO**	**CI**	**RV-SV**	**mPAP**	**sPAP**	**dPAP**	**mBP**	**sBP**	**dBP**
Pearson	-0.249	-0.406	-0.375	0.523*	0.543**	0.438*	0.296	0.322	0.247
P value	0.263	0.061	0.085	0.012	0.009	0.042	0.181	0.144	0.267

,P<0.05;,P<0.01.*

Table 4. *MPI T/B ratio in different groups at pre- and post-treatment*

Variables	NYHA classifications			PAH groups		
	I	II	III	Mild	Moderate	Severe
Pre-treatment	1.60±0.26	1.91±0.14	1.76±0.42	1.29±0.02	1.76±0.06	1.95±0.12
Post-treatment	1.63±0.20	1.90±0.14	1.77±0.42	1.32±0.08	1.76±0.05	1.95±0.12
P value	0.560	0.348	0.225	0.437	0.861	0.379

more patients with CHD now survive into adulthood, leading to a higher incidence of pulmonary artery hypertension related to CHD in adult patients as a result. With increased lung vascularity inducing elevated afterload of the RV, PAH eventually leads to RV hypertrophy [21], with its associated maladaptive contractile dysfunction, RV dilatation, and heart failure [22, 23]. Based on the complicated situations in PAH-CHD, the patients are normally divided into four groups, including (1) ES; (2) left-to-right shunts; (3) PAH with co-incidental CHD and (4) post-operative PAH [24]. Regarding the different causes of CHD, certain types of abnormalities including VSD, PDA or transposition of the great arteries (TGA) have the tendency to progress to PAH earlier than others. So far, the right heart catheter is still the gold standard for assessing pulmonary artery pressure, but it is an invasive method. Ultrasound can provide data on pulmonary arterial pressure in some patients, but is limited to patients with tricuspid regurgitation. Therefore, it will be of great importance to have a relatively easy and non-invasive method for PAH assessment.

Myocardial perfusion imaging has been used to evaluate hypertrophy [16, 17], ischemia [18-20] and fatty acid metabolism [21-23]. The RV free wall is not normally visualized on MPI when the patient is at rest. However, myocardial uptake of perfusion radionuclide by the RV is increased and obvious

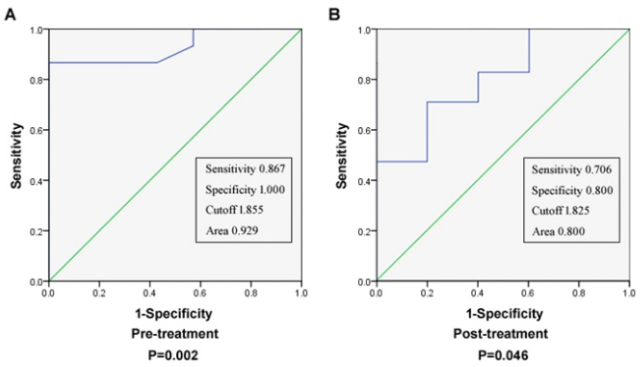

Figure 2. Receiver operating characteristic (ROC) analysis of MPI T/B ratios on PAH patients (moderate+severe groups vs. mild group). The ROC curves were created by plotting the sensitivity (true positive rate, TPR) against 1-specificity (false positive rate, FPR) of the MPI T/B at pre- treatment (A) and post-treatment (B). The best cut-off points, as well as the values of sensitivity and specificity, are indicated.

in patients under pathological conditions that cause pressure or volume overload of the RV. Some researches explored the relationship between the MPI and the hypertrophic RV myocardium of pressure-overload. Rabinovich et al. (2013) [24] performed thallium-201 myocardial imaging of the RV by using the counts ratio in patients with pressure-overloaded RVs in congenital heart defects. RV counts were of equal or even greater intensity as those of the LV. Ono Y (1982) [25], using thallium-201 in patients with complete transposition before or after operation, stated that the degree of thallium-201 uptake was well correlated with systolic pressure of the pulmonary ventricle and myocardial imaging can provide a reliable mean for the qualitative and quantitative assessment of TGA. However, the correlations between MPI results and the severity of PAH are still not very clear. In this study, we examined and analyzed a series of parameters of function and hemodynamics in CHD-PAH patients. Using MPI and RHC, we demonstrated the correlations of these variables with MPI T/B ratios, and proved that the semi-quantified MPI analysis could contribute to the PAH diagnosis in detecting moderate/severe cases.

For years, RHC parameters have been used as the gold standards for PAH diagnosis and assessment [26]. In the present study, we quantified the images from MPI and measured the perfusion of ^{99m}Tc-MIBI in the target region (RV) by comparing to the perfusion of the background. The correlation analysis of MPI T/B ratio with mPAP levels from RHC examination provided strong evidence for MPI being performed as another diagnostic standard (Table 3). After 6 months of treatment, some indexes, including 6-MWD, Borg scale, NT-proBNP, CTnI, RV-SV, TPR, TPRI, PVR, PVRI, mPAP, sPAP, and dPAP had showed obvious improvement. However, MPI T/B ratio did not show significant change in all subgroups (Table 4). One potential reason is that both oral medicine and intervention had limited effect in reversing ventricular remodeling and influencing the RV perfusion. Besides, MPI T/B ratio is a semi-quantitative index which is not as sensitive as some quantitative parameters. Therefore, our data suggests MPI might not be a suitable index to evaluate the therapeutic response.

For the patient who was first diagnosed PAH or had not accept treatment to decrease the pulmonary artery pressure, MPI T/B ratio showed a strong correlation with PAH severity based on the mPAP levels obtained from RHC, especially when predicting severe and moderate PAH (Figure 2B and Figure 2C). When pulmonary artery pressure increases, the RV coronary flow also increases to meet an increase in myocardial oxygen demand. Furthermore PAH leads to RV hypertrophy which contributes to the increased RV tracer uptake in myocardial perfusion studies. After 6 months of treatment, ROC curve analysis showed the correlation between MPI T/B ratios and the PHA grading decreased, but remained statistically significant. Increased RV tracer uptake is often seen in patients with overloaded RV and positive correlations to pulmonary artery pressure (PAP) have been demonstrated. How-ever, few studies compared the correlations between MPI and RHC parameters before and after treatment in CHD-PHA patients. The data showed that the magnitude of increased RV uptake on MPI is a useful noninvasive means of estimating pulmonary artery pressure. Besides, compared with RHC, MPI more closely reflects the perfusion of myocardium. Taken together, all previous report and the present study indicate that a combination of the RHC with MPI is a potential test to evaluate changes in the RV in patients with PAH.

Overall, we examined, semi-quantified, and compared the parameters of MPI, biochemical examination, heart function and hemodynamic parameters in mild and moderate/severe CHD-PAH patients in both pre- and post-treatment conditions. Our results showed a strong correlation of MPI T/B ratio and mPAP levels and PAH severity based on RHC data as well as some cardiac function parameters, providing the diagnostic value of MPI test as an additional noninvasive assessment in the evaluation of severity level of PA-H-CHD patients. Notably, MPI may not be suitable to evaluate the therapeutic outcome in this set of patients. It should be noted that the sample size in this study was small. More cases from multiple centers will be collected in the future for an in-depth research to investigate the diagnostic and prognostic value of MPI test in PAH patients.

Study limitations

There were some limitations in this research. Only one semi-quantitative parameter obtained from MPI, namely T/B ratio, was included in the current study, which provided limited information. Other factors, such as RV size and RV contractility were not addressed. Moreover, this single T/B index could not keep in pace with clinical improvement after therapy for PAH. The reasons are the image of RV is not as clear as that of LV, and thus it is difficult to measure the nonspherical RN size and contractility using MPI. Until now, there are very few studies exploring the functions of RV with MPI in patients with PAH and comparing the changes before and after treatment. The most important reason is no suitable and acceptable quantitative or semi-quantitative methods available. Therefore, we used PV-to-lung count ratio as a semi-quantitative index. Although it is not good and sensitive enough, this index could

reflect the relative state of blood perfusion flow in the RV. We hope to have better way to draw the outline of RV, and expect a better software in order to calculate the functions of RV as those of LV.

The authors of this study declare no conflicts of interest

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