Int J Clin Exp Med 2016;9(12):23386-23396
www.ijcem.com /ISSN:1940-5901/IJCEM0032177

Original Article

Characteristics of pulmonary arterial flow derived from phase contrast magnetic resonance imaging in patients with pulmonary arterial hypertension: correlations with right ventricular function and hemodynamics

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Received May 14, 2016; Accepted August 9, 2016; Epub December 15, 2016; Published December 30, 2016

Abstract: Background: The phage contrast cardiac magnetic resonance (CMR) can encode the flow character, which enables flow velocity and volume to be assessed. We designed this prospective study to validate that pulmonary artery (PA) net forward flow measured by phase contrast CMR could be a useful parameter to assess right ventricle stoke volume noninvasively in pulmonary arterial hypertension (PAH) patients. Methods: PAH patients were observed prospectively. Right heart catheterization (RHC), echocardiogram and CMR were performed within one week. Correlations between parameters derived from phase contrast CMR, and right ventricular function and hemodynamics derived from RHC and echocardiogram were analyzed. Results: Thirty PAH patients were enrolled. Average pulmonary arterial (PA) velocity (r=0.455, P=0.011; r=-0.575, P=0.001), PA forward flow volume (PA_FFV_PC, r=0.465, P=0.010; r=-0.532, P=0.003), PA net forward flow volume (PA_net FFV_PC, r=0.492, P=0.006; r=-0.592, P=0.001) all had significant positive correlations with TAPSE and negative correlations with PVR. At the same time, PA_FFV_PC (r=-0.392, P=0.036) and PA_net FFV_PC (r=-0.420, P=0.023) also had significant negative correlations with N-terminal pro brain natriuretic peptide. PA_FFV_PC (r=0.732, P<0.001), PA_net FFV_PC (r=0.764, P<0.001), aortic forward flow volume (Ao_FFV_PC, r=0.737, P<0.001), aortic net forward flow volume (Ao_net FFV_PC, r=0.733, P<0.001) all had significant positive correlations with RV stroke volume (RVSV_RHC) which also must be measured invasively. Bland-Altman analysis showed that PA_net FFV_PC and Ao_net FFV_PC had good consistency with RVSV_RHC. Conclusions: PA flow characteristics can reflect right heart function of PAH patients, and PA_net FFV_PC also had a good consistency with RVSV_RHC.

Keywords: Phase contrast imaging, magnetic resonance, pulmonary arterial hypertension, pulmonary arterial flow characteristics, correlation

Introduction

Pulmonary arterial hypertension (PAH) is a condition with mean pulmonary arterial pressure (mPAP) ≥25 mmHg, pulmonary capillary wedge pressure (PCWP) ≤15 mmHg and pulmonary vascular resistance (PVR) >3 Wood units (WU) in the absence of other causes of precapillary pulmonary hypertension [1]. Comprehensive evaluation of this disease needs to consider both pulmonary circulation hemodynamics and right ventricular function. Methods, which are simple, reproducible, accurate and easy-to-use, are necessary to assess conditions of PAH patients.

Cardiac magnetic resonance (CMR) with high spatial resolution can accurately and reproducibly assess right ventricular structure and function [2, 3]. Volume and mass of ventricles can be derived from short axis images [4]. However, evaluation of right ventricular (RV) volume and RV stroke volume from short axis images in patients with PAH patients is very difficult because of RV complex anatomy, more trabeculation and tricuspid regurgitation [5]. While,

blood flow characteristics of pulmonary arteries (PA) can be encoded by phase contrast CMR, which enables PA flow velocity to be assessed [6]. Using blood velocity and the cross-sectional area of chosen vessels, volumetric flow can be calculated, and at the same time cardiac stroke volume can also be measured by this sequence.

Previous studies have investigated the value of CMR phase-contrast patterns in the main pulmonary artery for functional assessment in patients without pulmonary hypertension (PH) or PH patients with mixed etiologies [7]. Some retrospective studies [8-11] have demonstrated that parameters derived from phase contrast CMR had significant values in the diagnosis and assessment of PH. In this study, we explored correlations between hemodynamics, right ventricular (RV) function measured by right heart catheterization, and pulmonary arterial flow characteristics measured by phase contrast CMR in prospectively enrolled PAH patients. We aimed to figure out whether PA net forward flow could be a useful parameter to assess right ventricle stoke volume noninvasively.

Methods

Patients selection

Patients, who were diagnosed with PAH for the first time were recruited prospectively in this study between October 2010 and December 2012. The diagnosis of PAH was based on 2009 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) guidelines for pulmonary hypertension [12], defined by a mean pulmonary arterial pressure ≥25 mmHg and a pulmonary capillary wedge pressure ≤15 mmHg at rest as assessed by right heart catheterization (RHC). The etiology of PAH was also determined by 2009 ESC/ERS guidelines [12]. We excluded (1) congenital heart disease associated pulmonary arterial hypertension (CHD-PAH) with system-to-pulmonary shunts; (2) pulmonary hypertension (PH) due to left heart disease; (3) PH due to lung diseases and/or hypoxemia; (4) chronic thromboembolic pulmonary hypertension; (5) PH with unclear and/or multifactorial mechanisms; (6) patients with unstable hemodynamic conditions; (7) patients with contraindications of CMR examination; (8) patients who refused to participate in this study. All patients underwent RHC, echocardiography and CMR within 1 week, and in this interval they did not receive any PAH targeted drugs. As CMR was not a routine exam for PAH in our hospital, written informed consents were obtained from all participants before they received CMR. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of Fuwai Hospital (ethical approve number: No. 402).

Right heart catheterization protocol

Right heart catheterization was performed by an experienced cardiologist, using a Swan-Ganz catheter introduced via femoral or internal jugular vein approach following standard methods. Hemodynamics including mean right atrial pressure (mRAP), systolic, mean and diastolic pulmonary arterial pressure (sPAP, mPAP, dPAP) and PCWP were recorded. Cardiac output (CO) was measured by thermodilution method (the mean value of three-time measurement). PVR was calculated by the following equation: Cardiac index was calculated as CI = CO/body surface area. RV stroke volume (RVSV_RHC) was calculated as RVSV_RHC = CO/heart rate.

Echocardiography protocol

All echocardiography examinations were performed on the Philips iE33 system by an expert echocardiographic physician, and images were analyzed offline after procedure. Tricuspid annular plane systolic excursion (TAPSE) was acquired by M-mode image, with cursor placing through tricuspid lateral annulus, and the displacement of tricuspid annulus from the end-diastole to the end-systole was measured. The S' known as tricuspid annular systolic excursion velocity was measured by Tissue Doppler image (TDI) in the apical 4-chamber view. During this process, whether patients have intracardiac shunt were also detected.

MRI protocol

CMR was performed on a Siemens 1.5 T Sonata scanner (Siemens Medical Solutions, Erlangen, Germany), and simultaneous ECG recording was used to correct phase offset errors. Short-axis cine images including the whole LV and RV from apex to base were acquired by the gradi-

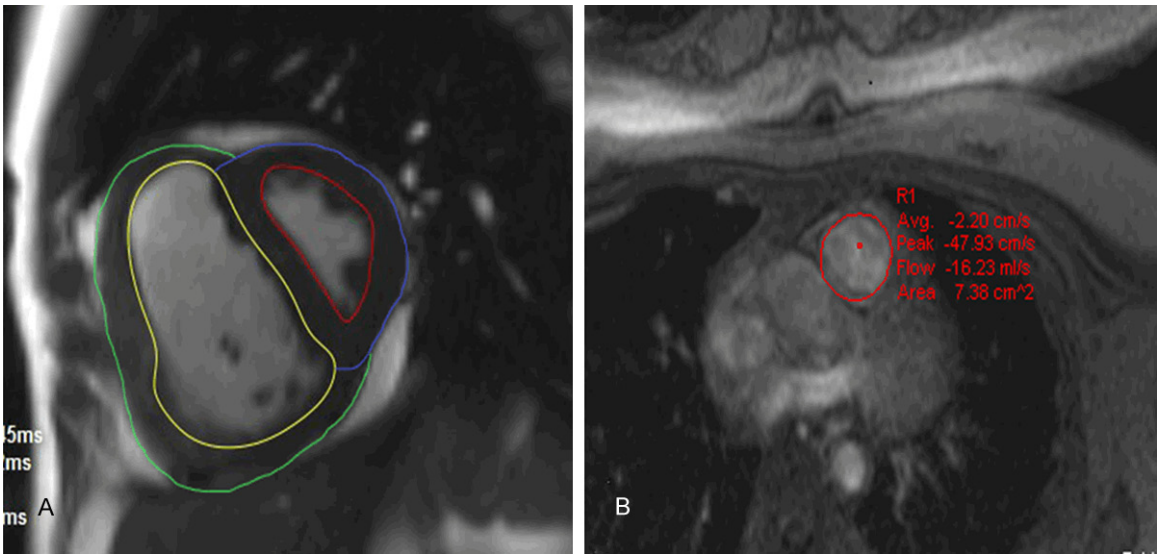


Figure 1. Measurements of ventricle volumes (A) and pulmonary arterial flow characteristics (B) by CMR. The endocardium and epicardium outline ventricles were drawn manually to obtain volumes RV and LV (A. yellow line: endocardium of RV, green line: epicardium of RV, red line: endocardium of LV, blue line: epicardium of RV). The maximal and minimal pulmonary artery cross-sectional areas were also traced manually from the cine images (B). The software then calculated the velocity in each of the voxels included within the contour and integrated the values over area and time to obtain pulmonary arterial flow characteristics.

Table 1. Baseline demographics and clinical characteristics of study patients

Variable	Value
Patient, n	30
Age, years	28.90±10.25
Female, n (%)	23 (76.7)
Subgroups	
IPAH, n (%)	18 (60.0)
CHD-PAH, n (%)	5 (16.7)
CTD-PAH, n (%)	5 (16.7)
HPAH, n (%)	2 (6.6)
WHO-FC	
II, n (%)	15 (50.0)
III, n (%)	15 (50.0)
6MWD, m	394.47±103.07
Systolic blood pressure, mmHg	114.60±15.30
Diastolic blood pressure, mmHg	66.40±10.63
Body mass index, kg/m^2	21.69±1.81
Heart rate, beats/min	81.10±14.21
NT-proBNP, fmol/ml	1300.23±992.46

CHD-PAH: pulmonary arterial hypertension associated with congenital heart disease; CTD-PAH: pulmonary arterial hypertension associated with connective tissue disease; IPAH: idiopathic pulmonary arterial hypertension; HPAH: heritable pulmonary arterial hypertension; NT-proBNP: N-terminal pro-brain natriuretic peptide; 6MWD: six minute walk distance; WHO-FC: world health organization functional class.

ent-echo pulse sequence (True-FISP by Siemens, repetition time/echo time, 34 ms/1.6 ms; flip angle, 60 degrees; field of view, 280×340 mm^2; matrix, 150×256; voxel size, 1.9×1.3 mm; slice thickness, 8 mm). Phase contrast imaging was performed orthogonally to the pulmonary trunk and aorta. Phase contrast imaging parameters were as follows: repetition time, 5.6 milliseconds; echo time, 2.7 milliseconds; slice thickness, 10 mm; field of view, 48×28.8 mm^2; bandwidth, 62.5 kHz; matrix, 256×128; 20 reconstructed cardiac phases; and velocity encoding, 150 cm/s.

The endocardium and epicardium outline of RV and LV were drawn manually using Argus software (Siemens Medical Solutions, Erlangen, Germany) by an experienced radiologist to obtain RV and LV volumes (**Figure 1**). The interventricular septum was considered as part of the LV. The myocardial volume for each slice was calculated by multiplying the area of the RV wall by the slice thickness. The product of the sum total of the myocardial slice volumes for each ventricle and the density of myocardium (1.05 g/cm^3) gave an estimate of RV mass. The maximal and minimal pulmonary artery cross-sectional areas were also traced manually from the cine images. The software then

Table 2. Parameters measured by right heart catheterization, cardiac magnetic resonance and echocardiography

Characteristic	Value
Right Heart Catheterization Measurements	
mRAP, mmHg	7.23±5.72
mPAP, mmHg	61.07±19.52
sPAP, mmHg	92.37±28.28
dPAP, mmHg	42.53±15.53
PCWP, mmHg	8.38±5.08
RVSV, ml	46.69±16.20
RVCI, L/min/m^2	2.35±0.93
PVR, dyn/s/cm^5	1312.40±666.51
CMR measurements	
CMR-morphology	
RVEDV, ml	178.68±65.02
RVESV, ml	132.56±63.91
RVSV, ml	46.13±10.76
RVM, g	89.58+10.76
LVEDV, ml	70.95±13.87
LVESV, ml	31.71±11.39
LVSV, ml	39.24±10.62
LVM, g	53.47+10.62
CMR-RV function	
RV ejection fraction, %	28.11±10.22
RV Cardiac index, L/min/m^2	2.42±0.75
Phase contrast-Pulmonary Artery Flow	
Minimal area, mm^2	9.58±3.60
Maximal area, mm^2	11.71±4.22
Average area, mm^2	10.51±3.72
PA distensibility, %/mmHg	0.55±0.42
PA compliance, mm^2/mmHg	0.05±0.04
PA relative area change, %	23.65±13.37
Average PA velocity, cm/s	56.29±21.01
Peak PA velocity, cm/s	72.33±17.70
Retrograde flow volume, ml	3.29±4.49
Forward flow volume, ml	47.68±14.53
Net forward flow volume, ml	44.39±16.22
Phase contrast-Aortic Artery Flow	
Minimal area, mm^2	6.08±2.16
Maximal area, mm^2	7.99±2.38
Average area, mm^2	6.97±2.19
Average Aortic velocity, cm/s	57.37±18.10
Peak Aortic velocity, cm/s	67.83±17.37
Retrograde flow volume, ml	0.78±0.75
Forward flow volume, ml	46.42±13.61
Net forward flow volume, ml	45.65±13.64
Transthoracic echocardiographic measurements	
TAPSE	15.71±3.09
S`	8.79±1.85
RV ejection fraction, %	31.12±6.77

mRAP: mean right atrial pressure; mPAP: mean pulmonary arterial pressure; PA: pulmonary artery; sPAP: systolic pulmonary arterial pressure; dPAP: diastolic pulmonary arterial pressure; PCWP: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance; RV: right ventricle; RVSV: right ventricle stroke volume; RVSV: right ventricle stroke volume; RVCI: right ventricle cardiac index; RVEDV: right ventricle end diastolic volume; RVESV: right ventricle end systolic volume; LVEDV: left ventricle end diastolic volume; LVESV: left ventricle end systolic volume; LVSV: left ventricle stroke volume; CMR: cardiac magnetic resonance; S`: tricuspid annular plane systolic velocity; TAPSE: tricuspid annular plane systolic excursion.

calculated the velocity in each of the voxels included within the contour and integrated the values over area and time to obtain the following parameters: peak velocity, average velocity, forward flow volume, retrograde flow volume, and net forward flow volume (**Figure 1**). Among them, PA net forward flow volume actually refers to the RV stroke volume measured by phase contrast CMR. PA relative area change (PA RAC) was calculated as [(maximal PA area-minimal PA area)/minimal PA area]. PA distensibility was calculated as [(maximal PA area-minimal PA area)/minimal PA area×100%/(sPAP-dPAP)] and PA compliance was calculated as [(maximal PA area-minimal PA area)/(sPAP-dPAP)].

Statistical analysis

All statistical analyses were performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, Illinois). Continuous variables with Gaussian distribution were presented as means ± standard deviation, and others were presented as absolute numbers and percentages. Pearson's correlation coefficient was used to assess the correlations between echocardiographic and RHC values versus CMR parameters. The agreement of different methods was analyzed by the method of Bland Altman, and Bland Altman plots were performed. Bias was defined as the mean value of the differences between RVSV_RHC and CMR measured parameters. Precision was defined as 1 standard deviation (SD) of the differences and limits of agreement as the bias ±1.96 SDs reported as millilitres. Consistency rate was defined as the percentage of spots which located in the area of 95% Limits of Agreement. A p value <0.05 was considered statistically significant.

Table 3. Correlations between phase-contrast MR imaging parameters, MR volumetry parameters and hemodynamic features and parameters reflecting right ventricular function

	NT-proBNP		mRAP_RHC		TAPSE		PVR		RVSV_RHC	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
PA RAC	0.054	0.781	-0.135	0.478	0.109	0.567	0.006	0.973	0.225	0.232
PA Distensibility	0.037	0.85	-0.009	0.962	0.171	0.366	-0.213	0.259	0.182	0.334
PA Compliance	0.134	0.489	0.286	0.125	0.072	0.707	-0.078	0.682	0.001	0.994
Average PA velocity	-0.355	0.059	-0.279	0.135	0.455	0.011*	-0.575	0.001*	0.719	<0.001*
Peak PA velocity	-0.116	0.549	0.173	0.361	0.078	0.684	-0.045	0.814	0.33	0.075
PA_FFV_PC	-0.392	0.036*	-0.269	0.150	0.465	0.010*	-0.532	0.003*	0.732	<0.001*
PA_net FFV_PC	-0.42	0.023*	-0.340	0.066	0.492	0.006*	-0.592	0.001*	0.764	<0.001*
PA_RFV_PC	0.261	0.172	0.356	0.053	-0.276	0.139	0.421	0.020*	-0.393	0.032*
Ao_FFV_PC	-0.481	0.008*	-0.476	0.008*	0.636	<0.001*	-0.635	<0.001*	0.737	<0.001*
Ao_net FFV_PC	-0.478	0.009*	-0.471	0.009*	0.636	<0.001*	-0.639	<0.001*	0.733	<0.001*
Ao_RFV_PC	-0.031	0.874	-0.053	0.780	-0.029	0.878	0.112	0.555	0.04	0.834
RVSV_volumetry	-0.214	0.265	0.357	0.053	0.247	0.189	-0.275	0.142	0.471	0.009*
LVSV_volumetry	-0.471	0.010*	0.553	0.002*	0.576	0.001*	-0.58	0.001*	0.657	<0.001*
RVEDV_volumetry	0.588	<0.001*	0.640	<0.001*	-0.399	0.029*	0.344	0.062	-0.336	0.070
LVEDV_volumetry	-0.366	0.051	-0.176	0.351	0.449	0.013*	-0.506	0.004*	0.454	0.012*
RVESV_volumetry	0.635	<0.001*	0.648	<0.001*	-0.447	0.013*	0.397	0.030*	-0.421	0.021*
LVESV_volumetry	-0.014	0.943	0.358	0.052	0.009	0.961	-0.076	0.690	-0.060	0.735
RVM_volumetry	0.400	0.031*	0.456	0.011*	-0.129	0.498	0.283	0.129	-0.102	0.591
LVM_volumetry	0.086	0.658	0.211	0.264	0.042	0.827	0.101	0.596	0.064	0.735

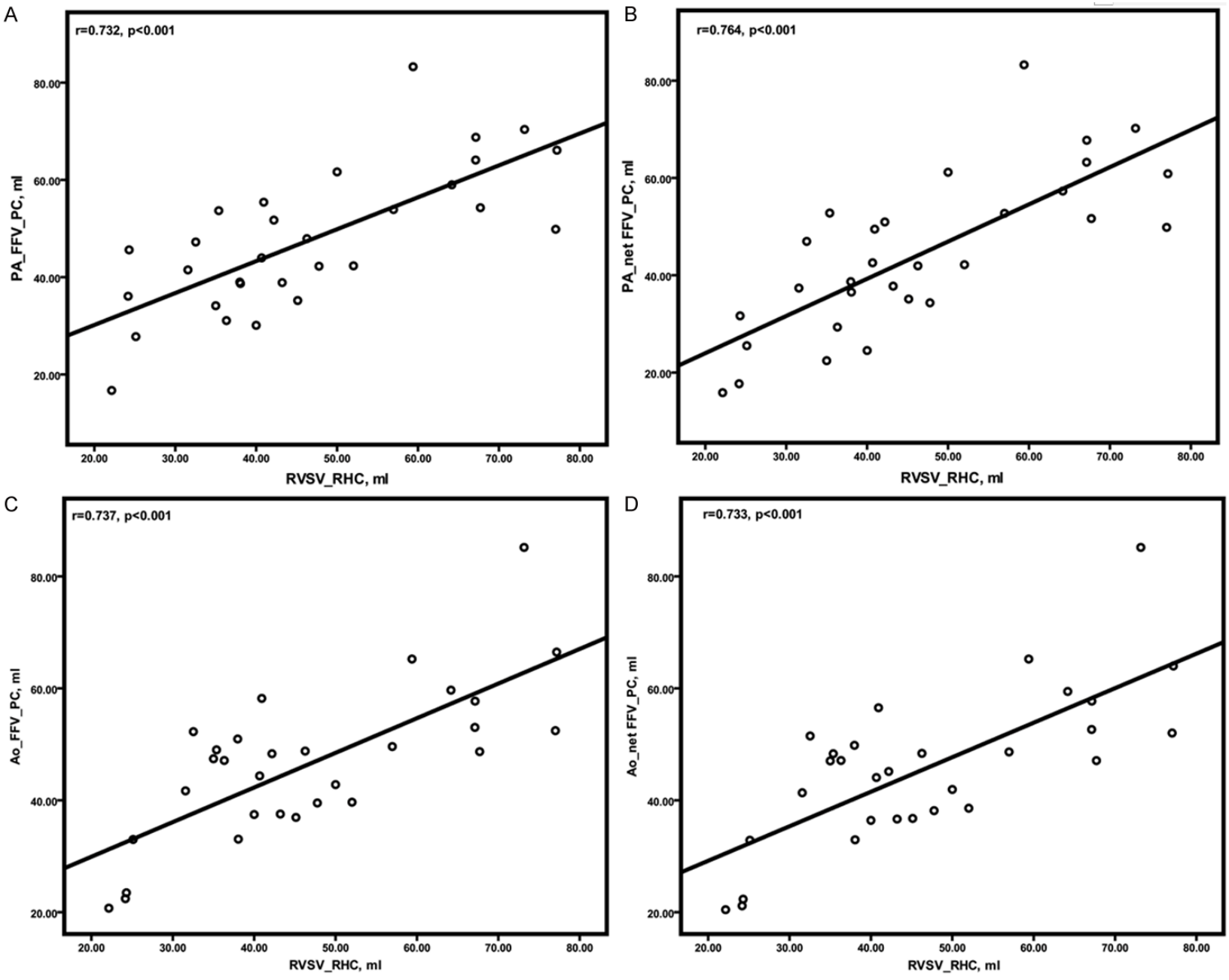
*P<0.05; mRAP_RHC: mean right atrial pressure measured by RHC; RVSV_RHC: right ventricle stroke volume measured by RHC; PA RAC: PA relative area change; PA_FFV_PC: PA forward flow volume measured by phase contrast CMR; Ao_FFV_PC: forward flow volume of aortic artery measured by phase contrast CMR; PA_net FFV_PC: net forward flow volume of PA measured by phase contrast CMR; Ao_net FFV_PC: net forward flow volume of aortic artery measured by phase contrast CMR; PA_RFV_PC: retrograde flow volume of PA measured by phase contrast CMR; Ao_RFV_PC: retrograde flow volume of aortic artery measured by phase contrast CMR; RVSV_volumetry: right ventricle stroke volume measured by CMR volumetry; LVSV_volumetry: left ventricle stroke volume measured by CMR volumetry; RVEDV_volumetry: right ventricle end diastolic volume measured by CMR volumetry; LVEDV_volumetry: left ventricle end diastolic volume measured by CMR volumetry; RVESV_volumetry: right ventricle end systolic volume measured by CMR volumetry; LVESV_volumetry: left ventricle end systolic volume measured by CMR volumetry; RVM_volumetry: mass of right ventricle measured by CMR volumetry; LVM_volumetry: mass of left ventricle measured by CMR volumetry.

Results

A total of 30 patients were finally enrolled in this study. No patients had intracardiac shunt. Their clinical characteristics were noted in **Table 1**. RHC, CMR and echocardiography parameters were listed in **Table 2**.

As shown in **Table 3**, correlation analysis showed that average PA velocity (r=0.455, P=0.011), PA forward flow volume (PA_FFV_PC, r=0.465, P=0.010), PA net forward flow volume (PA_net FFV_PC, r=0.492, P=0.006) all had significant positive correlations with TAPSE, which reflects RV systolic function. At the same time, PA_FFV_PC (r=-0.392, P=0.036) and PA_net FFV_PC (r=-0.420, P=0.023) also had significant negative correlations with N-terminal pro brain natriuretic peptide (NT-proBNP), which indicates the dysfunction of right heart. Correlation analysis also showed that average PA velocity (r=-0.575, P=0.001), PA_FFV_PC (r=-0.532, P=0.003), PA_net FFV_PC (r=-0.592, P=0.001) all had significant negative correlations with PVR, which must be measured invasively. PA_FFV_PC (r=0.732, P<0.001), PA_net FFV_PC (r=0.764, P<0.001), aortic forward flow volume (Ao_FFV_PC, r=0.737, P<0.001), aortic net forward flow volume (Ao_net FFV_PC, r=0.733, P<0.001) all had significant positive correlations with RV stroke volume (RVSV_RHC) which also must be measured invasively (**Figure 2**).

RVSV_volumetry (r=0.471, P=0.009) and LVSV_volumetry (r=0.657, P<0.001) also had significant positive correlations with RVSV_RHC, but LVSV_volumetry had a more close correlation with RVSV_RHC. RV end diastolic volume (RVEDV_volumetry, r=0.588, P<0.001; r=0.640, P<0.001), RV end systolic volume (RVESV_volumetry, r=0.635, P<0.001; r=0.648, P<0.001) and RV mass (RVM_volumetry, r=0.400, P=0.031; r=0.456, P=0.011) all had signifi-


A
r=0.732, p<0.001
PA_FFV_PC, ml
RVSV_RHC, ml
B
r=0.764, p<0.001
PA_net FFV_PC, ml
RVSV_RHC, ml
C
r=0.737, p<0.001
Ao_FFV_PC, ml
RVSV_RHC, ml
D
r=0.733, p<0.001
Ao_net FFV_PC, ml
RVSV_RHC, ml
20.00
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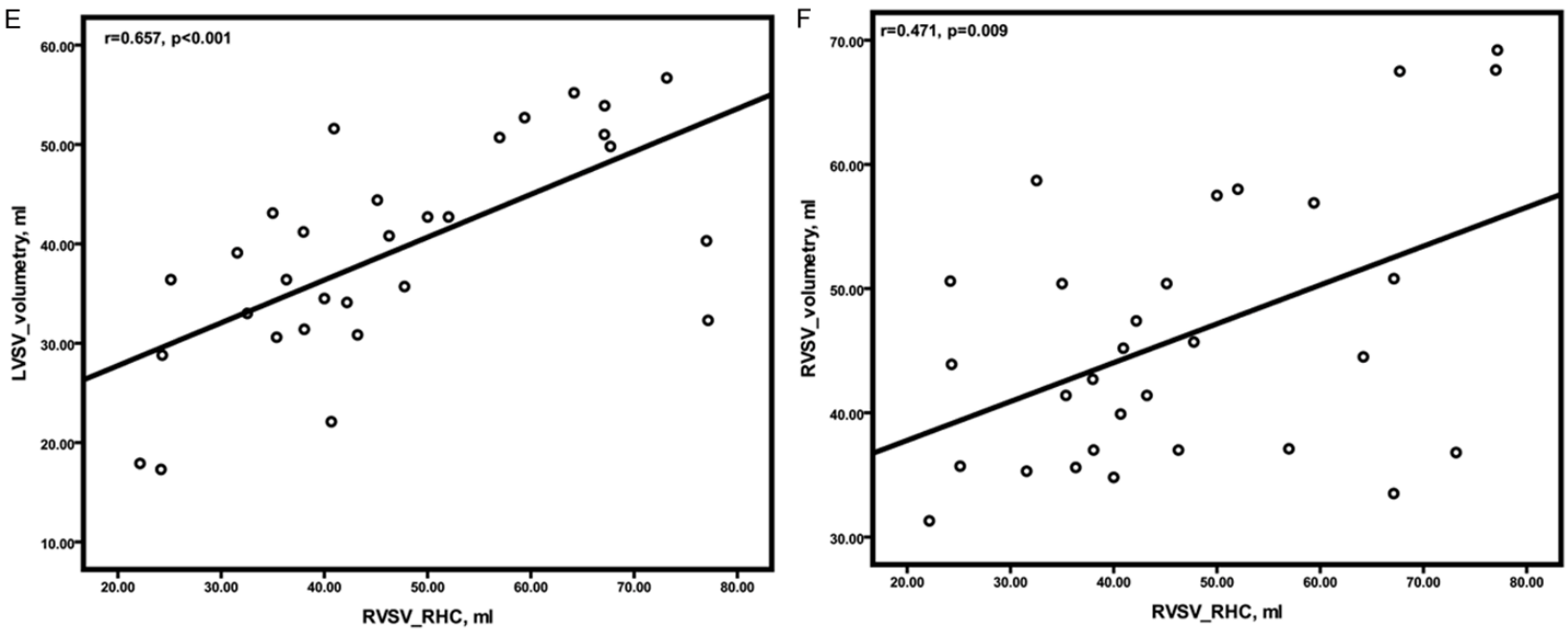

Figure 2. Pearson's correlation analysis between RVSV_RHC and PA_FFV_PC (A), PA_net FFV_PC (B), Ao_FFV_PC (C), Ao_net FFV_PC (D), LVSV_volumetry (E), and RVSV_volumetry (F).

Table 4. Correlations between flow volume characteristics and cardiac morphology parameters measured by cardiac phase-contrast MR imaging

	RVEDV_volumetry		RVESV_volumetry		RVSV_volumetry		LVEDV_volumetry		LVESV_volumetry		LVSV_volumetry	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
PA_FFV_PC	-0.009	0.994	-0.075	0.692	0.394	0.031*	0.643	<0.001*	0.19	0.314	0.636	<0.001*
PA_RFV_PC	0.453	0.012*	0.461	0.010*	0.003	0.987	-0.042	0.824	0.29	0.119	-0.367	0.046*
PA_net FFV_PC	-0.133	0.482	-0.195	0.302	0.352	0.056	0.588	0.001*	0.09	0.637	0.671	<0.001*
Ao_FFV_PC	-0.245	0.193	-0.29	0.12	0.247	0.188	0.605	<0.001*	0.08	0.676	0.704	<0.001*
Ao_RFV_PC	0.059	0.759	-0.003	0.986	0.374	0.042*	-0.191	0.311	-0.052	0.783	-0.194	0.305
Ao_net FFV_PC	-0.247	0.188	-0.289	0.121	0.226	0.231	0.614	<0.001*	0.082	0.665	0.713	<0.001*

*P<0.05.

cant positive correlation with NT-proBNP and mRAP_RHC.

As presented in **Table 4**, RVSV_ volumetry only had a positive correlation with PA_FFV_PC (r=0.394, P=0.031), while LVSV_ volumetry correlated significantly with PA_FFV_PC (r=0.636, P<0.001), PA_net FFV_PC (r=0.671, P<0.001), Ao_FFV_PC (r=0.704, P<0.001) and Ao_net FFV_PC (r=0.713, P<0.001). At the same time, PA_FFV_PC correlated significantly with Ao_FFV_PC (r=0.773, P<0.001), and PA_net FFV_PC also had a significant positive correlation with Ao_net FFV_PC (r=0.802, P<0.001).

Bland-Altman analysis showed that PA_net FFV_PC, Ao_net FFV_PC, RVSV_ volumetry, and LVSV_ volumetry all had good consistency with RVSV_RHC (**Figure 3**), and Ao_net FFV_PC only had a little higher consistency rate compared with others (**Table 5**).

Discussion

In the present study, we validated the value of PA flow characteristics in evaluating RV function of PAH patients, and found PA_net FFV_PC had a good consistency with RVSV_RHC.

Recent studies have demonstrated that CMR could assess the structure and function of PAH with high accuracy and reproducibility using short-axis images [2, 3], which is not easy to be achieved by echocardiography and RHC. However, this CMR sequence is less suitable to evaluate pulmonary circulation hemodynamics [8]. Encoding CMR signal phase with velocity enables pulmonary arterial flow characteristics to be profiled. By multiplying blood velocity with cross-sectional area of the pulmonary artery, the right ventricular stroke volume, which is an important prognostic parameter of PAH, can be obtained [13].

A previous study had investigated the accuracy of phase-contrast CMR to measure stroke volume of RV measured by Fick method [5]. Their results showed that stroke volume measured by PA flow had limited accuracy in PAH patients, while LV volumes and aorta flow were to be preferred for the measurement of SV [5]. However, in our study, SV from both PA and aortic flow had good consistencies with SV measured by thermodilution method in PAH patients, which were quite different from the previous study. Reasons for these differences can be summarized as followings: firstly, in the previous study, four out of 34 patients had right to left shunt, but none of our patients had intracardiac shunt; secondly, their aortic flow characteristics were only acquired from nine patients, while all of our patients had both PA and aortic flow characteristics; thirdly, they applied the direct Fick method as the reference standard, while we applied the thermodilution method. All these above may lead to the differences between the previous study and ours.

In this study, we also found PA_FFV_PC, PA_net FFV_PC, Ao_FFV_PC and Ao_net FFV_PC all had significant negative correlations with NT-pro BNP, and significant positive correlations with TPASE. So they might be useful parameters to evaluate RV function. However above parameters all had significant negative correlations with PVR, which was in accordance with the study of García-Alvarez et al [14]. So these parameters might be affected by RV afterloads. Moreover, we found PA_FFV_PC, PA_net FFV_PC, Ao_FFV_PC and Ao_net FFV_PC all had good correlations with LVSV-volumetry, but they did not correlate well with RVSV_ volumetry. Two main factors contributed to this: the complex anatomy of RV and tricuspid regurgitation in PAH patients [5]. So the application of RVSV_volumetry must be cautious.

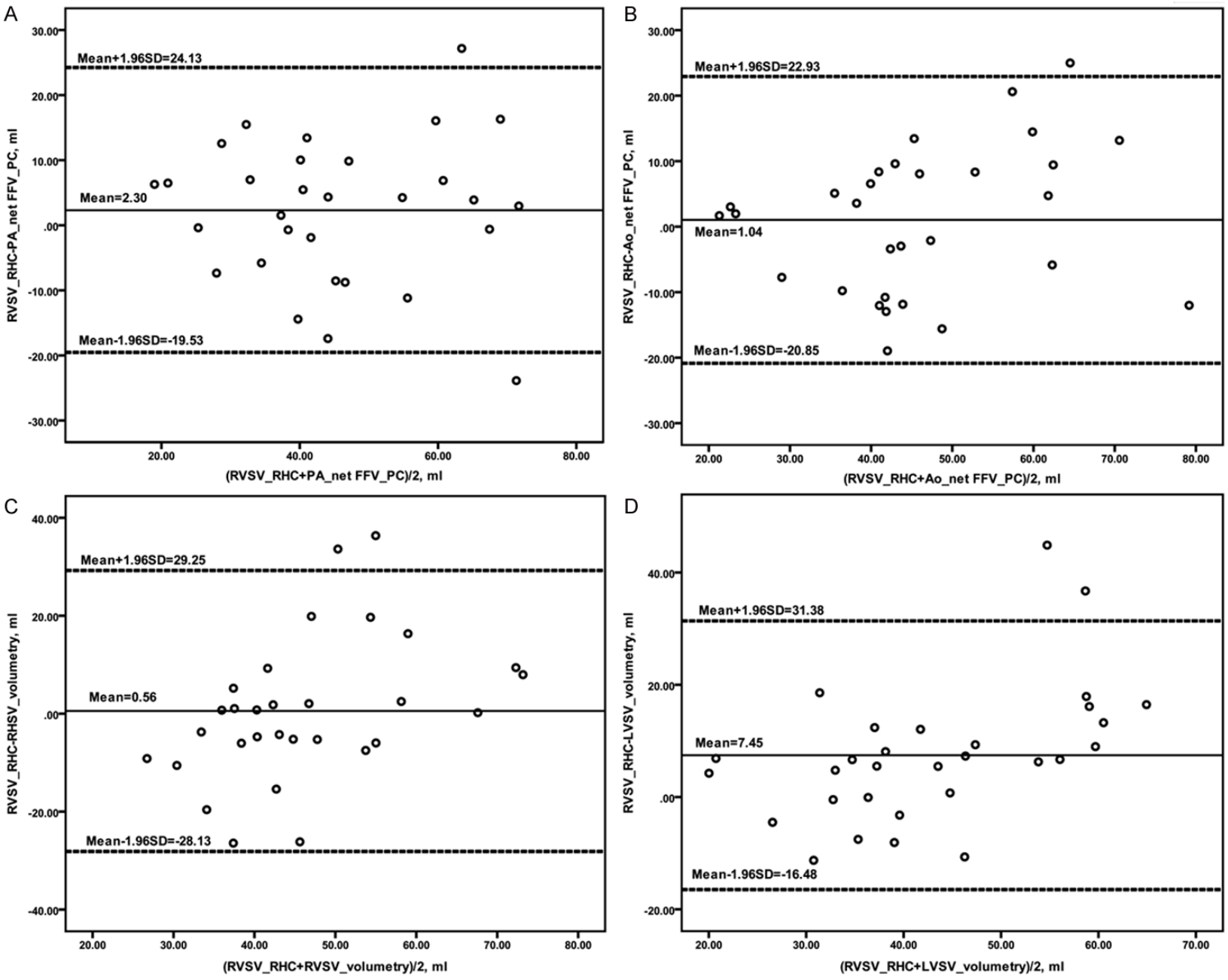
A
Mean+1.96SD=24.13
Mean=2.30
Mean-1.96SD=-19.53
RVSV_RHC-PA_net FFV_PC, ml
(RVSV_RHC+PA_net FFV_PC)/2, ml
B
Mean+1.96SD=22.93
Mean=1.04
Mean-1.96SD=-20.85
RVSV_RHC-Ao_net FFV_PC, ml
(RVSV_RHC+Ao_net FFV_PC)/2, ml
C
Mean+1.96SD=29.25
Mean=0.56
Mean-1.96SD=-28.13
RVSV_RHC-RHSV_volumetry, ml
(RVSV_RHC+RVSV_volumetry)/2, ml
D
Mean+1.96SD=31.38
Mean=7.45
Mean-1.96SD=-16.48
RVSV_RHC-LVSV_volumetry, ml
(RVSV_RHC+LVSV_volumetry)/2, ml

Figure 3. Bland-Altman plots showing variability between cardiac magnetic resonance imaging derived PA_net FFV_PC (A), Ao_net FFV_PC (B), RVSV_volumetry (C), LVSV_volumetry (D) and right heart catheterization derived right ventricular stroke volume. Values are ml. Central line demonstrates bias; outer lines demonstrate upper and lower limits of agreement (±1.96 standard deviations [SD]).

Table 5. Results of Bland-Altman analyses of CMR based measurements for stroke volume

	Bias	Precision	95% Limits of Agreement	Consistency rate (%)
PA_net FFV_PC	2.30	11.14	-19.53 to 24.13	93.33
Ao_net FFV_PC	1.04	11.17	-20.85 to 22.93	96.67
RVSV_volumetry	0.56	14.64	-28.13 to 29.25	93.33
LVSV_volumetry	7.45	12.21	-16.48 to 31.38	93.33

According to the study of Swift et al [10], the relationships between PA relative area change (RAC), compliance and distensibility versus PVR were reflected by inverse linear models, and relationships between PA compliance and distensibility versus mPAP were most closely reflected by exponential relationships. Kang et al, also found a negative relationship between distensibility and PVR [15]. However in our study, no significant correlation was found between PA average velocity, PA RAC, compliance or distensibility versus PVR or mPAP (r= -0.284, P=0.128; r=0.083, P=0.663; r=-0.247, P=0.189; r=-0.289, P=0.121). This difference may partially due to the heterogeneity of patients included, and the not very large study sample size of ours. In addition, pulmonary vascular remodeling in our cohort seemed to be more severe than the population in the study of Swift. Therefore, parameters reflecting the elastic properties of the pulmonary vessel wall may not change much even PVR or mPAP increased, as showed in the study of Swift. So the ability of parameters, which reflect pulmonary vessel elastic properties, to evaluate PAH needs further study, especially in patients with very severe or mild PAH.

Moreover, we found PA_FFV_PC, PA_net FFV_PC, Ao_FFV_PC, Ao_net FFV_PC, and LVSV_volumetry all had significant negative correlations with NT-proBNP, while RVEDV and RVESV all had significant positive correlations with NT-pro BNP. These findings are very reasonable, because NT-proBNP is a generally accepted indicator for heart dysfunction. Enlarged RVEDV reflects the heavy preload of RV which is due to right heart dysfunction. At the same time, PA_FFV_PC, PA_net FFV_PC, Ao_FFV_PC, Ao_net FFV_PC all reflect RV stoke volume, and impaired RV stoke volume may also due to RV dysfunction. So CMR parameters are very useful indicators for RV dysfunction.

The present study had some limitations. Firstly, RHC, CMR and echocardiography were not performed on the same day, which may result in bias in the correlations between the parameters measured by different methods. However, patients did not administrate targeted drugs in the interval of these examinations, and we also excluded patients with instable hemodynamics. So bias of hemodynamics could be controlled to a low level. Secondly, the sample size was small, which did not allow us to investigate the characteristics of pulmonary flow in patients with different causes. Thirdly, the prognostic values of these parameters derived from phase contrast CMR were not investigated. Fourthly, phase contrast CMR measurements may be affected by turbulent flow, which may result in inaccuracies.

Conclusions

PA flow characteristics can reflect right heart function of PAH patients, and PA_net FFV_PC also had a good consistency with RVSV_volumetry. So phase contrast CMR can be used as a noninvasive method to measure right heart stroke volume.

Acknowledgements

This study was supported by a national grant from Chinese Ministry of Science and Technology (Project number: 2011BAI11B15).

Disclosure of conflict of interest

None.

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