Original Article
CMRI study of cardiac structure and function in the patients with pulmonary heart disease in high altitude areas

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Abstract: Objective: This present study aims to evaluate the cardiac structure and function of patients with pulmonary heart disease and healthy controls in residing in high-altitude regions. Methods: Cardiac structure and function indexes, as well as right ventricular myocardial mass (RVMM), were determined in patients with pulmonary heart disease (pulmonary heart disease group, n=18) and healthy controls (control group, n=20) by Skyra 3.0T magnetic resonance imaging. Results: Cardiac structure indexes were higher in the pulmonary heart disease group than in the control group, and some indexes were significant different between the pulmonary heart disease group and control group (P<0.05). Furthermore, right ventricular end-diastolic volume (RVEDV), right ventricular end-systolic volume (RVESV) and RVMM were higher in the pulmonary heart disease group than in the control group. In addition, right ventricular stroke volume (RVSV) and right ventricular ejection fraction (RVEF) were lower in pulmonary heart disease group than in the control group. Differences in RVSV, RVEF and RVMM between the pulmonary heart disease group and control group were statistically significant (P<0.05). Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) were higher in the pulmonary heart disease group than in the control group, and left ventricular stroke volume (LVSV) and left ventricular ejection fraction (LVEF) were lower in the pulmonary heart disease group than in the control group. Differences in LVSV and LVEF between the pulmonary heart disease group and control group were statistically significant (P<0.05). Conclusion: Cardiac magnetic resonance imaging (CMRI) can accurately evaluate cardiac structure and function in patients with pulmonary heart disease, and provide an image basis for the clinical assessment of cardiac structure and function, especially in the aspect of right ventricular cardiac function.

Keywords: High altitude, pulmonary heart disease, cardiac magnetic resonance imaging

Introduction

Chronic pulmonary heart disease (CPHD) is a kind of heart disease caused by chronic lesions in lung tissues, thoraxes and pulmonary arteries. These lesions lead to increased pulmonary vascular resistance (PVR) and pulmonary artery hypertension (PAH). Subsequently, these would cause right ventricular hypertrophy (RVH); and ultimately, the possibility of patient death due to cardiac failure [1]. According to investigations in epidemiology, the morbidity rate of pulmonary heart diseases is comparatively high in China, with an average prevalence rate of 0.41-0.47%. Furthermore, most patients were above 40 years old; and it was found that its prevalence rate increases with age [2]. As reported

by Tian Zhongxin et al., the incidence of pulmonary heart diseases is higher in high altitude regions than that in plain areas [3].

Xining is located at a high altitude area, with an elevation of 2,260 meters. Oxygen content in this area ranges from 209.6 to 234.8 g/m³, and pressure ranges from 77.273 to 77.406 Kpa. Due to environmental factors such as low pressure, hypoxia, windiness, cold weather, large diurnal temperature difference and dry weather, residents in this area are more susceptible to respiratory tract infections (RTIs) or pulmonary diseases. Furthermore, these residents would suffer from CPHD as time passes. CPHD examination methods have continuously become more diverse such as X-ray, electrocardio-

gram (ECG), ultrasonic cardiogram and cardiac magnetic resonance imaging (CMRI). However, each of these methods has its own limitations. For example: in X-ray examinations, the measured values obtained from single images are accurate. Although electrocardiogram (ECG) examination is simple, fast and economic, it cannot measure and evaluate cardiac structures and functions. Ultrasonic cardiogram can dynamically observe cardiac anatomic structures and movements in real time, but image quality can easily be influenced by the operator's technique or gas within the lungs of patients; in particular, when heart structure changes occur, it would be hard to acquire accurate cardiac function values using the hypothetic calculation method of geometrical morphology [4]. However, there have been certain achievements regarding the evaluation of the cardiac structure and function of healthy individuals using CMRI. Moreover, structures and functions of the left and right ventricles can be assessed in an accurate and non-invasive way. Therefore, clinical treatment and the evaluation of therapeutic effects on patients with CPHD residing in high-altitude regions are of great importance [5, 6].

Data and methods

Study objects

A total of 18 patients, who were clinically diagnosed with CPHD in Qinghai Provincial People's Hospital from March 2013 to March 2015, were selected for this study. These patients were assigned as the pulmonary heart disease group. Patients in this group comprised of 12 male and six female patients, and patient age ranged between 50 and 75 years old (average age, approximately 63.67 ± 4.61). General information of patients including name, gender, age, stature, weight, chief complaint, and past medical history were recorded.

Patients who satisfy the following conditions were included in the pulmonary heart disease group (inclusion criteria): (1) age within 50-75 years old; (2) individuals who were born and live in high-altitude areas, or moved to a high-altitude area for more than ten years; (3) clinical symptoms accord to the diagnosis of pulmonary heart disease (with reference to the *National Diagnostic Criteria for Pulmonary Heart Disease in 1977* and the *Diagnostic Criteria using Ultrasonic Cardiogram Revised in*

the Third Professional Conference on Pulmonary Heart Disease 1980) [7].

Patients who satisfy the following conditions were excluded from the pulmonary heart disease group (exclusion criteria): (1) CPHD patients accompanied by coronary heart disease, valvular heart disease, congenital heart disease (CHO), or some other reasons that may lead to pathological changes of the right ventricle and affect the measured results; (2) individuals who have contraindications to magnetic resonance, or are unable to cooperate with the examination.

Control group: Twenty healthy gender- and age-matched individuals were selected for this study. These individuals have no smoking history or cardiopulmonary disorders. Individuals in this group comprised of 13 males and seven females, and age of these individuals ranged between 50 and 75 years old, with an average age of 62.73 ± 5.35.

This study was approved by the Ethics Committee of Qinghai Provincial People's Hospital, and all participants provided a signed informed consent prior to heart MRI examinations.

Research method

According to inclusion criteria, a total of 38 individuals, including both pulmonary heart disease patients and healthy individuals, underwent magnetic resonance imaging (MRI) examinations.

MRI examination equipment

A magnetic resonance imaging apparatus (Skyra 3.0T, Siemens, Germany) was used, as well as a phased-array heart-dedicated surface coil pair with electrocardio-gating and respiratory-gating techniques.

Examination and Imaging position

Patients were instructed to hold their breath and lie on their back on the examination bed with tranquillization. The horizontal axis center of the coil was aimed at the sternum midpoint for scanning.

(1) Basic imaging position: perpendicular to the transverse view, coronary view and sagittal view of the body axis. (2) Specific imaging posi-

Table 1. Cardiac structure measurement of the control group and pulmonary heart disease group ($\bar{x}$ ±s)

Parameters	Control group (n=20)	Pulmonary heart disease group (n=18)	T value	P value
Miniature chamber septum thickness (mm)	9.43±1.31	12.00±2.88	3.614	0.001
Main pulmonary artery diameter (MPAD) (mm)	22.78±1.06	34.28±6.13	8.269	<0.001
Right ventricular outflow width diameter (mm)	29.88±3.10	38.96±4.97	6.837	<0.001
Right ventricular transaction diameter (RVT) (mm)	37.03±4.80	41.52±10.83	1.679	0.102
Right ventricular long diameter (mm)	78.86±9.81	81.07±11.94	0.625	0.536
Right atrial transverse diameter (RATD) (mm)	43.77±5.22	53.90±12.66	3.286	0.002
Right atrium long diameter (mm)	48.74±6.96	61.93±13.98	3.738	0.001
Left atrial diameter (mm)	35.11±4.49	37.86±8.22	1.297	0.203
Left ventricular end diastolic (LVEDD) (mm)	49.77±5.58	55.11±12.96	1.68	0.102
The inner diameter of aortic sinus (mm)	30.14±2.33	36.58±5.44	4.829	<0.001

Table 2. Right ventricular function and right myocardium volume measurements of control group and pulmonary heart disease group ($\bar{x}$ ±s)

Parameters	Control group (n=20)	Pulmonary heart disease group (n=18)	T value	P value
RVEDV (ml)	75.28±17.21	76.24±29.62	0.124	0.902
RVESV (ml)	47.90±10.74	56.34±25.66	1.348	0.186
RVSV (ml)	27.23±12.87	19.34±9.88	-2.101	0.043
RVEF (%)	35.45±10.46	27.28±9.70	-2.486	0.018
RVMM (g)	25.10±11.54	32.77±9.58	2.215	0.033

Table 3. Left ventricular function measurement of control group and pulmonary heart disease ($\bar{x}$ ±s)

Parameters	Control group (n=20)	Pulmonary heart disease group (n=18)	T value	P value
LVEDV (ml)	78.96±13.04	90.89±50.40	1.022	0.313
LVESV (ml)	36.12±10.16	54.85±46.99	1.74	0.09
LVSV (ml)	42.65±7.23	36.05±9.77	-2.38	0.023
LVEF (%)	55.15±8.42	46.48±15.44	-2.179	0.036

for the heart only. Using this software, both left ventricular function and right ventricular functions with complicated shapes and structures could be measured.

Results processing

Atrial chamber septum thickness, main pulmonary artery diameter (MPAD), right ventricular outflow width diameter, right ventricular transaction diameter (RVTD), right ventricular long diameter, right atrial transverse diameter (RATD), right atrium long diameter, left atrial diameter, left ventricular end-diastolic diameter (LVEDD), and inner diameter of the aortic sinus of subjects in the pulmonary heart disease group and control group were measured using both the black blood sequence and bright blood sequence. Each measurement was independently performed three times by three experienced radiologists, and average values were obtained.

Left and right ventricular functions were analyzed using cardiac-specific software (Argus). Left and right ventricular end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), cardiac output (CO) and ejection fraction (EF), as well as right ventricular myocardial mass (RVMM), were obtained.

tions of the heart: two-chamber, four-chamber, vacuum chamber, and true four chambers.

Checking sequences and methods

Checking sequence of cardiac morphology: (1) Black blood sequence: half-fourier acquisition single-shot turbo spin-echo (HASTE). (2) Bright blood sequence: true fast imaging with steady state precession (True FISP).

Cardiac short axis images from the heart to the apex with a thickness of 6-8 mm and a total of 10 layers were collected. Cardiac function was analyzed using Argus post-processing software

Statistical methods

Statistical analysis was conducted using SPSS 17.0 statistical software. Measurement data

were presented as mean ± standard deviation (x ± SD). Independent sample *t*-test was used for comparisons between two groups. *P*<0.05 was considered statistically significant.

Results

Table 1 lists the cardiac structure measurement results for the pulmonary heart disease group and control group. Atrial chamber septum thickness, main pulmonary artery diameter, right ventricular outflow width diameter, RVTD, right ventricular long diameter, RATD, right atrium long diameter, left atrial diameter, LVEDD and inner diameter of the aortic sinus are higher in the pulmonary heart disease group than in the control group. Differences in atrial chamber septum thickness, MPAD, right ventricular outflow width diameter, RATD, right atrium long diameter, and the inner diameter of the aortic sinus between the pulmonary heart disease group and control group were statistically significant (*P*<0.05). However, differences in RVTD, right ventricular long diameter, left atrial diameter and LVEDD between the pulmonary heart disease group and control group were not statistically significant (*P*>0.05).

Table 2 lists the right ventricular function and right ventricular myocardial mass measurement results for the pulmonary heart disease group and control group. Right ventricular end-diastolic volume (RVEDV), right ventricular end-systolic volume (RVESV) and RVMM in the pulmonary heart disease group were higher than in the control group. Furthermore, RVSV and RVEF were lower in the pulmonary heart disease group than in the control group. Differences in RVSV, RVEF and RVMM between the pulmonary heart disease group and control group were statistically significant (*P*<0.05); while differences in RVEDV and RVESV between the pulmonary heart disease group and control group were not statistically significant (*P*>0.05).

Table 3 lists the left ventricular function measurements for the pulmonary heart disease group and control group. LVEDV and LVESV were higher in the pulmonary heart disease group than in the control group; and LVSV and LVEF were lower in the pulmonary heart disease group than in the control group. Differences in LVSV and LVEF between the pulmonary heart disease group and control group were statistically significant (*P*<0.05), while differences in LVEDV and LVESV between the pul-

monary heart disease group and control group were not statistically significant (*P*>0.05).

Discussion

On the account of this special geographical environment, people who reside in high attitude areas have a high risk of contracting secondary pulmonary heart diseases. The evaluation of the right ventricular structure and function has important implications for the prognosis of this disease [8-10]. CMRI is an alternative non-invasive examination technique, which is more accurate in diagnosing the right ventricle lesions [11-13]. As reported in previous studies, the cardiac morphology index measured by MRI surpasses the ultrasound method [14, 15]. Zhou Lu *et al.* [16] studied the effect of CMRI on the evaluation of the structure and function of the left and right ventricles. They concluded that CMRI combined with standard planer positioning can provide an accurately evaluation of the structure and function of the left and right ventricles. In particular, CMRI exhibits remarkable advantages in evaluating the structure and function of the right ventricle; and thus, this method can be used for the diagnosis and treatment of heart disease surveillance. Furthermore, Zhang Zhuoli *et al.* [17] have established the right ventricular volume and ejection fraction in healthy Chinese individuals using fast cine MR imaging in breath-hold technique, and concluded that fast cine MR imaging in breath-hold technique can accurately measure right ventricular volume and ejection fraction. Therefore, fast cine MR imaging in breath-hold technique is regarded as a routine examination technique in the evaluation of heart disease patients. According to a large number of experimental and clinical studies, CMRI is the most accurate way to measure heart function; and is known as the 'gold standard' [18]. Compared with other cardiac screening methods, CMRI has the following advantages: (1) no ionizing radiation and no need to use radionuclides and iodinated contrast agents; (2) images are not bound by position restrictions and the limitations of radionuclide decay and ultrasonic sound attenuation; (3) high resolution of time and space for both qualitative and quantitative analyses, and can conveniently provide cardiac function and structure parameters; (4) highly repeatable data and small variations of measurements, which ensure the reliability of the test results; (5) high resolution

rate and high specificity of soft tissues, which are conductive to the diagnosis.

Contrastive analysis of cardiac structure between the pulmonary heart disease group and control group

Cardiac structure indicators were higher in the pulmonary heart disease group than in the control group, but the difference in right ventricular diameter, right ventricular long diameter, left atrial diameter and LVEDD between these two groups were not statistically significant. The reason may be due to the fact that the right ventricular structure in pulmonary heart disease patients may suffer from clear pathological changes, which is connected with hypoxic pulmonary hypertension caused by secondary pulmonary heart diseases. High pressure environments can cause strong contractions on the right ventricle against subsequent loads (i.e. pulmonary hypertension). Myocardial contractility becomes insufficient due to increasing pulmonary artery pressure. Hence, cardiac cells improve myocardial contractility through proliferation, in order to maintain normal ejection levels [19]. Due to the small amount of the right atrial myocardia, proliferation could not compensate for the overload generated by pulmonary hypertension; and this leads to a comprehensive increase in the right atrium, but with minimal impact on the left ventricular structure (left atrial diameter, LVEDD). On the contrary, the aortic root diameter was wider in the pulmonary heart disease group than in the control group. This is probably because the right ventricular decompensation affected the left ventricular output, which led to compensatory left ventricular hypertrophy, followed by increased aortic root diameter. The right ventricular diameter and right ventricular long diameter did not exhibit a significant increase, which may be due to the affect of low pressure and hypoxia at high altitudes and other special environmental characteristics.

Comparative analysis of left and right ventricle functions between the pulmonary heart disease group and control group

Right ventricular stroke volume (RVSV) and right ventricular ejection fraction (RVEF) measurements were significantly lower in the pulmonary heart disease group than in the control group, while RVEDV, RVESV and RVMM measurements were higher in the pulmonary heart disease group than in the control group. The difference in RVEDV and RVESV between these two groups was not statistically significant, while differences in RVSV, RVEF and RVMM between these two groups were not statistically significant. The reason may be due to the increase in pulmonary vascular resistance and resultant pulmonary hypertension. Right ventricular hypertrophy occurs in order to overcome pulmonary vascular resistance, which increases RVMM. As this disease progresses, right ventricular hypertrophy would fail to overcome pulmonary vascular resistance, resulting to right ventricular dysfunction. Thus, RVSV and RVEF decreases. On the other hand it may be attributed to the special geographical environments, such as high altitudes. In these regions, people can easily contract lung diseases, leading to pulmonary hypertension and right heart failure.

LVEDV and LVESV measurements were higher in the pulmonary cardiac disease group than in the control group, while LVSV and LVEF measurements are lower in the pulmonary heart disease group than in the control group. The difference in LVSV and LVEF was statistically significant, but the difference in LVEDV and LVESV was not statistically significant between the two groups. The reason may be due to the fact that the right and left ventricles are intrinsically and necessarily linked through the pulmonary vascular system. Inevitably, right ventricular dysfunction affects left ventricular function, and the right ventricular output reduction leads to the decline in left ventricular preload and left atrial filling. Therefore, the LVSV and LVEF decreases.

The most common cause of CPHD is due to chronic obstructive pulmonary disease (COPD). COPD patients often have hypoxemia, resulting in hypoxic pulmonary vasoconstriction, followed by structural changes in the pulmonary vasculature. This may cause patients to suffer from pulmonary hypertension, which may increase the right ventricular load and lead to right ventricular hypertrophy; and finally evolve into CPHD [20-22]. The study of Gao Yan *et al.* [23] found that patients with mild to moderate COPD have right ventricular hypertrophy, and their RVMM increases. These patients can only rely on this compensation to maintain their own right heart function; hence, ejection fraction value decreases less. However, right ventricu-

lar hypertrophy occurs and progress in patients with severe COPD, and EDV in the right ventricle further decreases. This further reduces the compensation ability of the right ventricle, which finally causes RVEF to decrease; resulting in right ventricular dysfunction [24, 25]. This suggests the possibility of the combination of COPD and pulmonary heart disease. As pulmonary arterial pressure rises and exceeds the compensatory ability of the right ventricle, right cardiac output decreases, right ventricular systolic residual blood volume increases, and end-diastolic pressure increases. This would induce the expansion of the right ventricle and right heart failure, which would then cause the ejection fraction value to further decline; that is, the disease will evolve into lung disease, but the stroke volume would maintain at normal levels to compensate for the reduction in RVEF [26].

Research results have shown that CMRI can also be used as a means of determining the severity of pulmonary heart disease and efficacy assessments. Through comparative CMRI and echocardiography studies, researchers have found [27] that ESV measured by echocardiography is significantly lower than by CMRI; and with the difference was statistically significant. Furthermore, ejection fraction was significantly higher when measured by echocardiography than by CMRI. Overall evaluation has shown that the systematic measurement of cardiac function by echocardiography is one grade higher than by CMRI, suggesting that CMRI has more diagnostic value to patients with ventricular dysfunction. With technology innovation and software development, the CMRI method would receive more attention in clinic practice.

In conclusion, CMRI can accurately evaluate cardiac structure and function in patients with pulmonary heart disease; providing a reliable imaging basis for the clinical diagnosis and treatment of pulmonary heart disease.

Disclosure of conflict of interest

None.

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