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Right atrial volume and phasic function in pulmonary hypertension

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ABSTRACT

Background: Few studies have focused on right atrial (RA) structure and function in pulmonary hypertension (PH). We sought to evaluate RA volume and phasic function using cardiac magnetic resonance (CMR), and to examine their clinical relevance in PH.
Methods: We prospectively studied 50 PH patients and 21 control subjects. RA volume and indices of phasic function (reservoir volume, ejection fraction [EF], and conduit volume) were evaluated by CMR.
Results: Maximum RA volume index was significantly higher in PH patients (56 [44–70] ml/m^2) than in controls (40 [30–48] ml/m^2) ($p<0.001$). Reservoir volume index was significantly lower in PH than in controls ($p<0.001$), but conduit volume index was higher in PH than in controls ($p=0.008$). RA EF was similar when comparing the two groups ($p=0.925$). Interestingly, RA EF was increased in PH patients with WHO functional class III patients as compared with controls ($p<0.001$) but was reduced in advanced PH patients with WHO functional class IV ($p<0.01$). Maximum RA volume and RA EF significantly correlated with pulmonary hemodynamic indices, atrial and brain natriuretic hormone levels, and CMR-derived right ventricular indices. By contrast, RA reservoir volume correlated with cardiac index and 6-minute walk distance.
Conclusions: PH is associated with increased size, decreased reservoir function, and increased conduit function of the right atrium. RA systolic function indicated by RA EF increases in patients with mild to moderate PH but decreases in patients with advanced PH. Varying associations between RA indices and conventional PH indices suggest their unique role in the management of PH.

1. Introduction

Pulmonary hypertension (PH) is defined by a resting mean pulmonary artery pressure (PAP) ≥25 mm Hg [1]. An increase in PAP causes right ventricular (RV) and right atrial (RA) pressure-overload, leading to right heart failure and premature death. An increase in RA pressure is associated with poor prognosis in patients with PH [2] and thus, accurate evaluation of RA structure and function is potentially critical in the management of PH.

To date, limited attention has been paid to the right atrium in PH. This is partly because of technical difficulties in assessing RA morphology. However, recent advances in cardiac magnetic resonance (CMR) have enabled precise and reproducible assessment of the volume of the right atrium. For example, Jarvinen et al. validated the accuracy of CMR in the measurement of human RA dimension using cadaveric atrial casts [3]. They also assessed phasic function of the right atrium using CMR [4]. Previous studies of the right atrium have been conducted mostly in healthy subjects or in patients with congenital heart disease [5,6] and not in PH patients. Thus, details regarding the impact of PH on RA morphology remain incompletely investigated.

The atria provide three functions during the cardiac cycle—namely, reservoir, conduit, and contractile functions [3,4,7,8]. Coordination of these phasic functions plays an important role for the maintenance of overall cardiac function [9]. In the case of the left atrium, its phasic functions are reportedly impaired in various cardiovascular diseases [10–12]. However, only a small number of studies have addressed the impact of PH on the phasic functions of the right atrium [13,14].

The present study sought to evaluate the volume and phasic function of the right atrium in PH patients using CMR. This study also addressed the possible clinical relevance of measuring RA size and function by comparing RA parameters with established clinical indices of PH.

2. Methods

In this single-center, case–control, prospective, observational study, subjects who met the entry criteria [mean PAP of ≥25 mm Hg and pulmonary capillary wedge pressure (PCWP) of ≤15 mm Hg] were consecutively enrolled between December 2009 and

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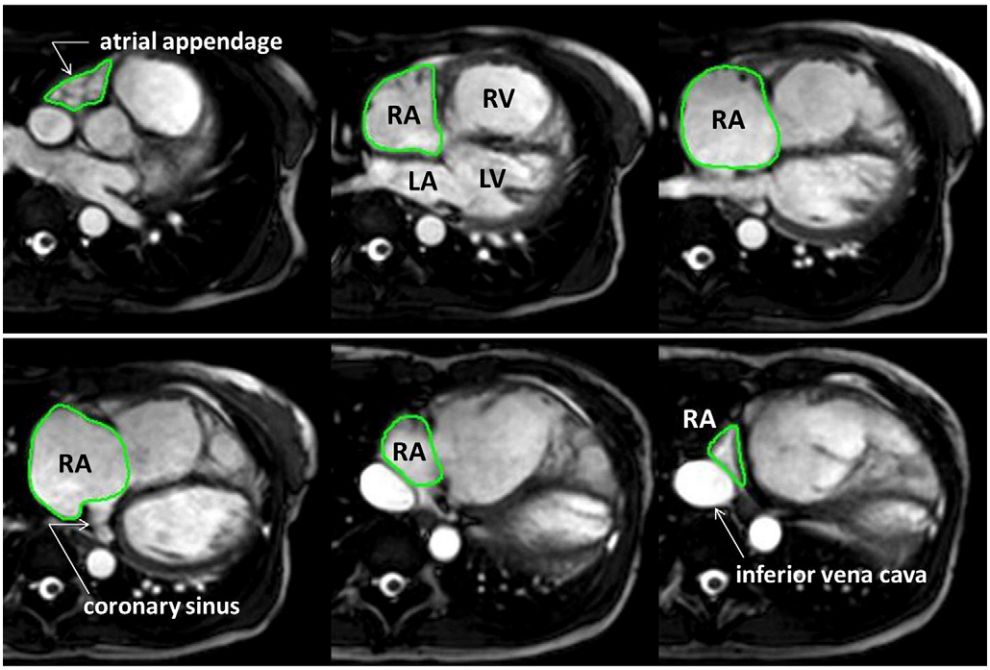

Fig. 1. Representative CMR images for the measurement of right atrial volume. Representative axial CMR images taken at the end diastole are shown. Endocardial contours of RA were manually traced using commercially available software (Extended MR Work Space: ver. 2.6.3, Philips Medical Systems, Amsterdam, The Netherlands). The tracing was performed at 20 phases in a cardiac cycle, and the right atrial volume at each phase was calculated using the same software. Note that the right atrial appendage was included in the right atrial cavity (left top panel), and the coronary sinus (left bottom panel) and the inferior vena cava (right bottom panel) were excluded from the right atrial cavity. CMR, cardiac magnetic resonance; RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle.

September 2011. Exclusion criteria consisted of any myocardial, valvular, or systemic diseases that might exclusively affect cardiac morphology and function, unstable PH condition that required treatment modifications, and inability to obtain or analyze electrocardiogram (ECG)-gated CMR images. Patients with atrial fibrillation/flutter were excluded based on the last criterion. Age- and gender-matched subjects who did not have cardiac and/or respiratory diseases were recruited as control subjects.

Patients with PH underwent right heart catheterization (RHC), CMR, a 6-minute walk test, and measurement of serum atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) levels within a 1-week interval during which they were clinically stable. RHC measurements included PAP, PCWP, RV end-diastolic pressure (EDP), RA pressure, and cardiac output (CO). CO was measured by the thermodilution method, and the mean of three or more measurements was used as representative data.

All subjects gave informed written consent to participate, and the study protocol was approved by the ethics committee of the Hokkaido University Graduate School of Medicine. The present study complied with the Declaration of Helsinki.

2.1. CMR imaging

CMR studies were performed using a 1.5-Tesla Philips Achieva magnetic resonance imaging system (Philips Medical Systems, Best, The Netherlands) with a cardiac five-channel coil, equipped with Master gradients (maximum gradient amplitude, 33 mT/m; maximum slew rate, 100 mT/m/m). Imaging was performed with breath-holding in expiration, using a vector-cardiographic method for ECG-gating. PH patients receiving domiciliary oxygen therapy underwent CMR while being administered the same amount of oxygen that they typically used at rest. From the coronal localizing images, an orthogonal stack of axial slices was planned to cover the heart from a level just below the diaphragm to the bronchial bifurcation, covering the heart in diastole. A total of about 12 axial slices were acquired using a steady-state free precession pulse sequence (repetition time = 2.8 ms, echo time = 1.4 ms, flip angle = 60, acquisition matrix = 192×256, field of view = 380 mm, slice thickness = 10 mm, 0 mm inter-slice gap, 20 phases/cardiac cycle). A slice thickness of 10 mm was greater than the recommended thickness [15], but we adopted it to minimize the number of image acquisitions of the enlarged heart and to reduce the frequency and duration of breath-holding. Breath-holding time for each image acquisition was 10–15 s, which varied depending on the heart rate.

CMR images were evaluated using commercially available software (Extended MR Work Space: ver. 2.6.3, Philips Medical Systems, Amsterdam, The Netherlands). RA and left atrial (LA) volumes were measured using cine axial images obtained from coronal and sagittal scout images to cover the whole heart (Fig. 1). Time–volume curves of the right and left atria were constructed by plotting each instantaneous atrial volume against the R wave at which acquisition was performed. The volume cycle was reconstructed from 20 consecutive atrial volumes. The section was planimetered with a mouse-derived cursor, and simultaneous volumes were totaled given the total cavity volume at every time phase from the contiguous axial view. The inlets of the superior and inferior vena cava and the coronary sinus were excluded from the RA volume. The pulmonary vein inlets were excluded from the LA volume. The volumes of the right and left atrial appendages were included in atrial chamber volumes.

The atrial volume cycle and measurements are shown schematically in Fig. 2. As has been documented in previous reports [3,4], the atrial maximum and minimum volumes were determined from this volume–time curve. The atrial reservoir volume was defined as the difference between the atrial maximum volume and the smallest atrial volume in mid-diastole. The atrial stroke volume was defined as the decrease in atrial volume at end-diastole. If the atrial volume–time curve was continuously down-sloping during diastole, the reservoir volume was considered to be the volume decrease before the final 200 ms of the cardiac cycle, and the atrial stroke volume was defined as the volume reduction over the remaining cardiac cycle. The atrial ejection fraction (EF) was the ratio of atrial stroke volume to the volume at the onset of atrial systole. The atrial conduit volume was calculated as the difference between the RV stroke volume and the sum of RA reservoir and stroke volumes.

RV and left ventricular (LV) volumes were similarly measured using cine axial and short axis images obtained from coronal and sagittal scout images, and manual tracing

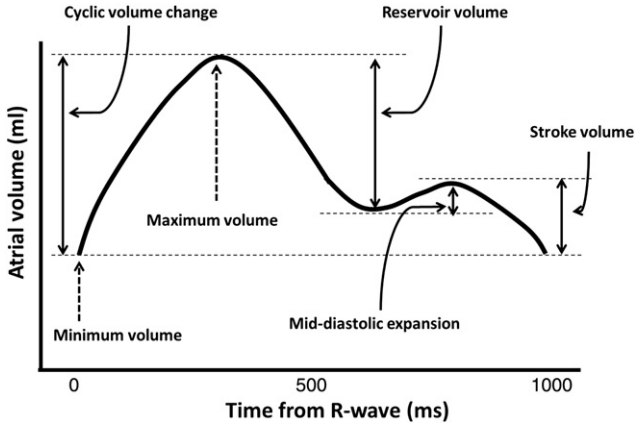

Fig. 2. Schematic time–volume curve of atrium. Schematic time–volume curve and volumetric measurements are shown. See text for details of each measurement.