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Right atrial function in patients with pulmonary hypertension: A study with two-dimensional speckle-tracking echocardiography

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ABSTRACT

Background: The role of right atrial (RA) dysfunction in patients with pulmonary hypertension (PH), as evaluated by two-dimensional speckle-tracking echocardiography (2D-STE) remains to be determined.

Methods: Sixty consecutive PH patients and 30 healthy volunteers were included. RA function was evaluated by 2D-STE, and the following parameters were recorded: an average longitudinal strain (LS) curve that included LSpos during RA filling and LSneg representing RA active contraction (their summation is LStot), the phasic RA volumes, total RA emptying fraction, and the ratio of RA passive and active emptying to total emptying. The associations between these indices and the results of invasive pulmonary hemodynamics, cardiac structure and function, and NT-terminal pro brain natriuretic peptide (NT-proBNP) level were evaluated.

Results: LStot, total RA emptying fraction, LSpos, passive RA emptying fraction were significantly lower, while the contribution of active RA empting fraction/total RA emptying fraction was higher in PH patients than in controls. Among PH patients, LStot was negatively correlated with greater RA size, RA pressure, and pulmonary vascular resistance, but not pulmonary artery pressure, while LStot was also negatively associated with right ventricular enlargement and higher NT-proBNP. In receiver–operator characteristic analysis, RA LStot was of optimal accuracy for prediction of WHO-function class ≥III in PH patients.

Conclusions: PH was associated with impaired reservoir and conduit function, but enhanced active contract function of RA, while RA LStot confers an optimal predictive effect of poor WHO-function class in PH patients.

1. Introduction

Pulmonary hypertension (PH) is a pathophysiological disorder complicating many cases of cardiopulmonary disease and characterized by elevated pulmonary vascular resistance (PVR) secondary to pulmonary vascular remodeling [1]. As a result, right heart failure has become the principal cause of mortality in patients with PH [2]. Generally, PH is defined as an increase in the mean pulmonary arterial pressure (PAPm) ≥ 25 mm Hg at rest as assessed by right heart catheterization (RHC) [3]. The symptoms of PH are non-specific and mainly related to progressive right ventricular (RV) dysfunction. Moreover, elevated right atrial pressure (RAP) is most common in patients with volume overload and may suggest ventricular dysfunction or overall fluid overload [4], and RV function is a key determinant of exercise capacity and outcome in patients with PH. In addition, elevated RAP reflects RV overload in PH and is an established risk factor for poor survival in the long-term prognostic [5,6]. Thus, RAP has important implications for the management of patients with PH. It has been proposed that enlargement of RA size is another prognostic factor for adverse outcome in PH patients despite many other cardiovascular conditions, such as heart failure with reduced ejection fraction and RV dysfunction [7]. However, few studies have evaluated the prevalence and correlations of RA dysfunction in PH [8].

Physiologically, RA has been proven to play an integral role in cardiac performance by modulating right ventricular function with its reservoir, conduit, and contractile functions [9]. With the development of novel imaging tools, the role of RA in PH may become evident with non-invasive studies in patients. Real time three-dimensional (3D) iRotate imaging technique calculation of atrial volume enables the assessment of atrial phasic volume changes and intensive description of atrial function over its size. In addition to RA chamber function, RA myocardial mechanics are needed to detect subclinical dysfunction and differentiate among several pathophysiological situations [10]. Previous studies showed that 2D-STE is feasible for the evaluation of RA myocardial mechanics [11], which represent a new parameter for evaluating RA

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function. Based on the above facts, in this study, we aimed to evaluate the role of RA function in patients with PH via a 2D-STE method.

2. Methods

2.1. Study population

The study population of 70 patients with PH was recruited from April 2015 to February 2016. Inclusion criteria for both studies were PAPm ≥ 25 mm Hg and pulmonary capillary wedge pressure (PCWP) ≤ 15 mm Hg at rest as assessed by RHC. Exclusion criteria consisted of any myocardial, valvular, or systemic diseases that might affect cardiac morphology and function; unstable PH condition that required treatment modifications; or inability to obtain or analyze electrocardiogram. Patients with pulmonary atrial hypertension due to congenital heart disease were excluded. Patients with atrial fibrillation/flutter were also excluded.

Sixty patients had data sets available for 2D-STE and 3D iRotate imaging technique. Patients with atrial fibrillation ($n = 1$), congenital heart disease ($n = 3$), or poor image quality ($n = 6$) were excluded. Ultimately, 60 patients were included in the study. Among the 60 patients, 50% were diagnosed with pulmonary artery hypertension, and 40% were classified as chronic thromboembolism pulmonary hypertension, whereas 10% were diagnosed with takayasu arteritis-associated pulmonary hypertension. Age- and gender-matched subjects who did not have cardiac and/or respiratory disease were recruited as controls.

This study was approved by the local ethics committee before performance, and written informed consent was obtained from all patients.

2.2. Image acquisition

All of the patients underwent standard transthoracic echocardiography using a commercially available Philips EPIQ 7C machine equipped with an X5-1 probe. Two-dimensional echocardiography studies included an apical 4-chamber view optimized for RA. Three consecutive heart cycles were recorded during breath-holding with stable electrocardiogram tracing, in order to minimize respiratory movements and obtain images suitable for RA size quantitation and 2D-STE analysis. All patients were examined in the left lateral decubitus position using a greyscale second-harmonic two-dimensional imaging technique, with adjustment of image contrast, frequency, depth, and sector size for adequate frame rate and optimal RA border visualization.

2.3. Standard echocardiography methods

All patients underwent echocardiography following the same protocol. RV functional measures including tricuspid annular plane systolic excursion (TAPSE), RV index of myocardial performance (RIMP), RV fractional area change (RVFAC), and Doppler-derived tricuspid lateral annular peak systolic velocity (TA S′) were measured in accordance with the American Society of Echocardiography guidelines [12]. Right heart size was quantified as the RV diastolic area and RA area at the end of systole. Right heart overload was assessed by the RV end diastolic area (RVEDA), RV/LV basal diameter, and eccentricity index (EI). The severity of tricuspid regurgitation (TR) was assessed by measuring the jet area of the TR and categorized as none, mild (TR area < 5 cm^2), moderate (TR area between 5 and 10 cm^2), and severe (TR area > 10 cm^2). The left ventricular ejection fraction was also assessed according to the recommendations of the American Society of Echocardiography [12].

2.4. Image analysis

2.4.1. Deformation: 2D-STE analysis

2D-STE analysis was performed on grayscale images from the apical 4-chamber view, with the frame rate optimized to 50 to 90 frames/s (median, 74 frames/s; range, 57–81 frames/s), and images were stored digitally. Next, the 2D-STE data set was transferred to an advanced data quality quantification system (QLAB version 10.3.1; Philips Healthcare, Andover, MA) for offline analysis. Strain analysis was performed in all studies with adequate image quality. For RA deformation, the endocardial borders were tracked automatically when lateral, and septal tricuspid annular points and a third point in the roof of RA were manually positioned in the apical 4-chamber view. Then the software automatically generated a 15-mm wide region of interest, and these data were manually adjusted. Tracking quality was confirmed visually, and segments that failed to be tracked by the software were adjusted manually as needed. Segments that could not be tracked properly after manual adjustment were rejected. Regional longitudinal strain values from the 18-segment model were averaged to obtain global longitudinal strain (GLS) and then automatically generated an average GLS curve. In our study, we timed our strain analysis to the P-wave on the ECG (atrial contraction); therefore, active RA contraction is shown as an early 'negative' strain (myocardial shortening, LSneg), which is followed by a large positive wave describing RA myocardial lengthening during passive conduit function (LSpos). Overall RA reservoir function is represented by 'total' strain (LStot), the summary of all strain components when the RA fills from the minimum volume to the maximum volume [13].

2.4.2. RA volume: real time 3D iRotate imaging analysis

RA volume was analyzed using a real time 3D iRotate imaging technique, which required the apical 4-chamber and 2-chamber to be analyzed at the same time in one cardiac cycle. The sample line went through the tip of the tricuspid valve. The endo cardiac border was traced in the apical 4-chamber and 2-chamber views at the same frame, paying attention to exclude the area between the tricuspid leaflets and annulus to obtain the RA area. Next, tracing was then performed by tracking the endocardial borders manually on the RA in the 4-chamber view and in the 2-chamber view at the same time during the cardiac cycle using the ejection fraction & volume module. Then the RA maximum volume was automatically calculated by the software using the area-length method at the time of tricuspid valve opening. Using the same procedure, we also measured the RA minimum volume as the smallest RA cavity during the cardiac cycle, just before tricuspid valve closure, and RA pre-emptying volume as the RA volume corresponding at a P-wave peak on the electrocardiogram tracing [14]. From RA volumes, RA total emptying fraction was defined as (RA maximal volume − RA minimal volume) / RA maximal volume. RA passive emptying fraction was defined as (RA maximal volume − RA pre-emptying volume) / RA maximal volume. RA active emptying fraction was defined as (RA pre-emptying volume − RA minimal volume) / RA pre-emptying volume. To assess the contribution of each RA emptying phase to the total RV filling, we also calculated the ratio of RA passive and active emptying fraction to the total RA emptying fraction [13].

2.5. Right heart catheterization

Patients with PH were recommended to receive RHC if they were with the following clinical situations [1]: (1) RHC is a class I and level of evidence C recommendation to the suspected PH patients; (2) RHC was performed to confirm the diagnosis of pulmonary artery hypertension or chronic thromboembolism pulmonary hypertension; (3) RHC was performed to evaluate of the severity of hemodynamics impairment and using vasoreactivity test to evaluate the pulmonary circulation in selected patients; or (4) RHC was also performed to assess the treatment efficacy of drugs and support decisions on correction in patients with congenital cardiac shunts. In our study, all PH patients underwent RHC on the same day after echocardiographic examination. The RHC was conducted from internal jugular or femoral vein access with local anesthesia. The hemodynamic measurements obtained from RHC reports included PAPm, RAP, PCWP, PVR and so