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Detection of mechanical complications related to the potential risk of sudden cardiac death in patients with pulmonary arterial hypertension by computed tomography

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ABSTRACT

Background: We explored the value of cardiac computed tomography (CT) for the detection and prediction of mechanical complications related to the risk of sudden cardiac death (SCD) in pulmonary arterial hypertension (PAH) patients.
Methods: PAH patients ($n = 60$, mean age 47 ± 15, 31.7% male) with pulmonary artery (PA) enlargement (≥40 mm) by echocardiography were studied with cardiac CT. Complications explored were the presence of left main coronary artery (LM) compression, airway compression, PA dissection and PA thrombosis in relation to diameters of main PA (MPA) which were measured in (1) axial plane (MPA_{Ax}) and (2) LM oblique view (MPA_{LMobq}).
Results: Mechanical complications were found in 21 patients (35.0%): LM compression in 20 patients; airway compression in 3 patients; and PA thrombosis in 4 patients. Patients with complications had more dilated MPA_{LMobq} than patients without complication (59.4 ± 13.0 mm vs. 42.4 ± 7.0 mm, $p < 0.001$). The area under the receiver operating characteristic curve for MPA_{LMobq} was 0.889 (95% confidence interval: 0.795 to 0.983, $p < 0.001$) with the highest discriminating sensitivity and specificity being 90.5% and 69.2%, respectively at MPA_{LMobq} of 45 mm. MPA_{Ax} failed to predict the presence of mechanical complications ($p > 0.05$).
Conclusion: MPA_{LMobq} ≥ 45 mm was significantly associated with the presence of mechanical complications of PAH. Evaluation with CT should be considered in PAH patients with dilated MPA.

1. Introduction

In patients with pulmonary arterial hypertension (PAH), sudden cardiac death (SCD) is a common cause of mortality [1,2]. "Mechanical complications" of PAH including pulmonary artery (PA) dissection [3,4] and compression of intrathoracic structures [5–8], which are usually related to progressive dilatation of the PA [9], have been suggested as a major cause of SCD [10].

However, the PA diameter at which such mechanical complications are likely to occur and warrant additional surveillance is yet to be clarified, and the utility of cardiac CT in detecting such mechanical complications has not been evaluated. Thus, currently cardiac CT is only recommended in patients with symptoms suggestive of such complications and not routinely used in regular follow up [9].

Therefore, we sought to investigate the presence of mechanical complications that may cause SCD in PAH patients with dilated PA using cardiac CT.

2. Methods

2.1. Population and study protocol

The study subjects were identified through a prospective registry of the pulmonary hypertension center at Severance Cardiovascular Hospital. Group I PAH patients according to European guidelines [9,11] who had been followed up at our institution were screened with transthoracic echocardiography (TTE), and patients with enlarged PA ≥40 mm [5] were consecutively enrolled in a prospective manner from November 2014 to December 2016. The appropriate institutional review committee approved the study and written informed consent was obtained from each patient. The study protocol conforms to the

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ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Clinical data including the etiology of PAH, presence of symptoms, history of PAH-specific medication, parameters of most recent right heart catheterization (RHC), and conventional risk factors for coronary artery disease were collected at the time of the index TTE.

2.2. Cardiac CT examination

Images were obtained with a second-generation dual-source CT scanner (Somatom Definition Flash; Siemens Health Care, Forchheim, Germany). A bolus of 10 mL of iopamidol (Pamiray, 370 mg/mL of iodine; Dongkook Pharma, Seoul, Korea) was first injected, followed by 20 mL of saline at a rate of 5 mL/s. Image reconstruction was performed with a medium kernel (b36f), with the reconstruction section thickness of 0.75 mm and a 0.5-mm increment. Cardiac structure and coronary arteries were evaluated with multiplanar reformation, curved multiplanar reformation, and volume rendering technique.

2.3. Image analysis

De-identified datasets were transferred to a workstation (Vitrea 6.5.3, Vital Images Inc., Minnetonka, Minnesota, USA) and were analyzed by two experienced physicians. Readings independently performed, and a joint reading was performed to reach a consensus in the case of a disagreement.

The presence of four mechanical complications known to be associated with SCD were interrogated with cardiac CT: (1) extrinsic LMCA compression [6,12]; (2) airway compression [13]; (3) PA dissection [14]; and (4) PA thrombosis [10]. Patients were stratified into two groups – patients with or without a complication according to the presence of any of the aforementioned four complications.

Invasive coronary angiography (CAG) was selectively performed when extensive LMCA compression (≥50%) was suspected by cardiac CT, or if a patient complained of angina.

2.4. Measurement of MPA and aortic diameter by cardiac CT

To identify the most effective predictors for mechanical complications, the main pulmonary artery (MPA) diameter and aortic (A) diameter were determined using two different methods: (1) Axial plane (Ax) – The diameter of MPA (MPA_{Ax}) was determined at its widest dimension at the level of bifurcation, perpendicular to its long axis, from inner wall to inner wall, on an image whereby the MPA ran in the axial plane [15–17]. The aortic diameter (A_{Ax}) was measured at the same level [15–17]. (Fig. 1A) (2) LMCA-oblique (LMobq) view: To visualize the structural relation between the LMCA and PA tree, we reconstructed an LMCA-oblique view using curved multiplanar reformation which displays the origin of LMCA from the coronary sinus, the short-axis of the MPA, and the long-axis of the aorta at the same plane. (Fig. 1B) The measurement of MPA and A diameter (MPA_{LMobq} and A_{LMobq}) were determined.

2.5. Transthoracic echocardiography

Echocardiographic studies were performed using commercially available equipment (Vivid S6, GE Medical Systems, Milan, Italy). Standard M-mode, 2-dimensional and Doppler images were obtained according to the American Society of Echocardiography Guidelines [18].

2.6. Statistical methods

Categorical variables are presented as numbers (with proportions), and continuous variables are expressed as mean ± standard deviation (SD). Differences between categorical variables were analyzed by the Chi square test or Fisher exact test, as appropriate. Correlations between PA diameters and other variables were assessed by use of the Spearman R method. Linear regression was used to examine the relationship between CT image metrics and other hemodynamic parameters. Univariable and multivariate logistic regression were performed to estimate predictors of complications. Receiver operating characteristic (ROC) analysis assessed the usefulness of cardiac CT parameters in predicting the presence of complications. A two-sided *P*-value of <0.05 was considered significant, with confidence intervals (CI) of 95%. Statistical analyses were performed using SPSS version 23 software (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Baseline characteristics

Among 322 patients who had been followed up for PAH, dilated PA ≥ 40 mm were identified in 60 patients (18.6% of total cohort population, mean age 47 ± 15 years, 19 [31.7%] male). Overall, the mechanical complications of PAH were identified in 21 patients with dilated MPA (35.0%). The comparisons of baseline clinical, hemodynamic, and echocardiographic characteristics between patients with and without mechanical complications are reported in Table 1. When comparing the underlying etiology of PAH, congenital heart disease-associated PAH, especially PAH associated with unrepaired congenital heart disease, were more prevalent in patients with mechanical complications. However, the prevalence of Eisenmenger's syndrome was not different ($p > 0.999$).

Symptomatic status was not different between groups - only two patients complained typical angina and 7 patients (11.7%) reported atypical angina. Notably, among 19 patients with identified complications, only 5 patients (23.8%) complained of typical or atypical angina.

Those with mechanical complications had higher mean PA pressure (PAP) by RHC, higher right ventricular systolic pressure by TTE, and larger MPA by TTE (all $p < 0.05$). Other echocardiographic parameters and laboratory results showed no significant differences between groups (all $p > 0.05$).

3.2. Prevalence of mechanical complications of PAH and clinical outcomes

Among 21 patients (35.0%) with mechanical complications of PAH, extrinsic LMCA compression by MPA (Fig. 2) was detected in 20 patients (33.3%), airway compression was found in 3 patients (5.0%), and PA thrombosis was found in 4 patients (6.7%). PA dissection was not identified. Six patients had more than two mechanical complications – 3 patients with both LMCA compression and PA thrombosis, and

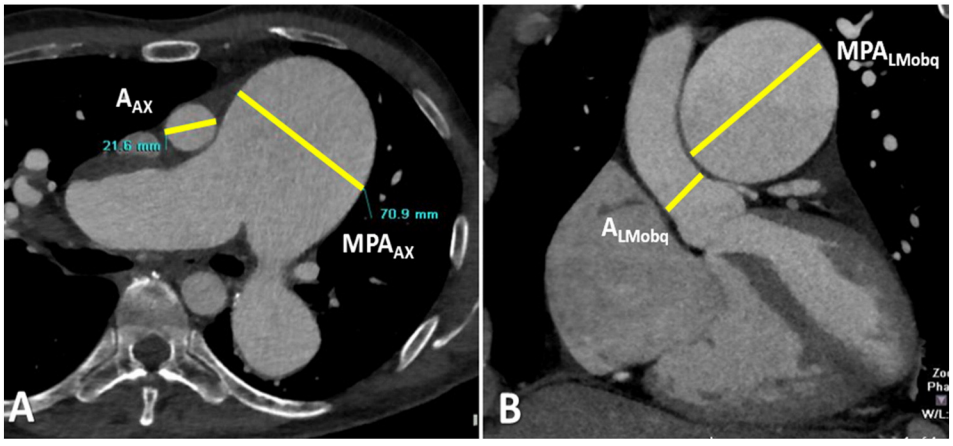

Fig. 1. Measurement of MPA and aortic diameter in cardiac computed tomography using two different methods (A) Measurement in axial plane (Ax, A_{AX} and MPA_{Ax}), and (B) LMCA-oblique (LMobq) view (A_{LMobq} and MPA_{LMobq}). A, aorta; Ax, axial plane; LMCA, left main coronary artery; LMobq, left main coronary artery-oblique view; MPA, main pulmonary artery.

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