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● *Original Contribution*

MOTION ANALYSIS OF RIGHT VENTRICULAR DYSFUNCTION UNDER MILD OR MODERATE PRESSURE OVERLOAD CAUSED BY ACUTE PULMONARY EMBOLISM

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Abstract—Acute pulmonary embolism (APE) is the third most common cause of death in the United States. Appearing as a sudden blockage in a major pulmonary artery, APE may cause mild, moderate or severe right ventricular (RV) overload. Although severe RV overload produces diagnostically obvious RV mechanical failure, little progress has been made in gaining a clinical and biophysical understanding of moderate and mild acute RV overload and its impact on RV functionality. In the research described here, we conducted a pilot study in pigs using echocardiography and observed the following abnormalities in RV functionality under acute mild or moderate RV overload: (i) occurrence of paradoxical septal motion with "waving" dynamics; (ii) decrease in local curvature of the septum ($p < 0.01$); (iii) lower positive correlation between movement of the RV free wall and movement of the septum ($p < 0.05$); (iv) slower rate of RV fractional area change ($p < 0.05$); and (v) decrease in movement stability, particularly in the middle of the septum ($p < 0.05$). (E-mail: Nima.Tajbakhsh@asu.edu)

Key Words: **Acute pulmonary embolism, Mild or moderate right ventricular pressure overload, Biomarker, Paradoxical septal motion, Rate of right ventricular transverse fractional area change, Active contours, Motion analysis.**

INTRODUCTION

Acute pulmonary embolism (APE) is the third most common cause of death in the United States, with at least 600,000 cases occurring annually (Galson 2008), resulting from the migration of emboli to the lungs and obstruction of pulmonary blood vessels. APE often presents with clinically vague symptoms such as chest pain and shortness of breath. Therefore, diagnostic differentiation of APE from other possible causes is difficult. In fact, the lack of clinically specific symptoms leads to frequent APE misdiagnosis (Alonso-Martinez et al. 2010). However, APE misdiagnosis and its corresponding high level of mortality can be reduced if proper clinical tests and signs are developed.

Right ventricular (RV) pressure overload is found in 50% of patients with APE (Grifoni et al. 2000, Ribeiro et al. 1997) and affects RV mechanical function. Therefore, imaging markers capable of detecting RV dysfunction during pressure overload could aid in the diagnosis of APE. In particular, clinical echocardiographic studies (Jardin et al. 1997, Mansencal et al. 2003) report RV dilation, hypokinesis and paradoxical motion of the inter-ventricular septum as the signs of RV mechanical dysfunction caused by APE. McConnell et al. (1996) suggested a RV echocardiographic functional sign that was originally reported to have a specificity of 94% and sensitivity of 77%, although its diagnostic utility has been questioned (Casazza et al. 2005; Lopez-Candales et al. 2010b). However, these clinical echocardiography studies report fully developed mechanical RV abnormalities as a result of mostly severe RV pressure overload, whereas the functional impact of acute mild or moderate RV pressure overload has been addressed only in a few research studies (Cho et al. 2009; Groth et al. 2010).

In the current animal pilot study, we propose new bioinformatics parameters for analysis of RV mechanical

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function based on echocardiographic images obtained at baseline and after induction of acute mild or moderate RV pressure overload.

METHODS

Figure 1 provides an overview of our study. The experiments began with animal preparation. The next stage was image acquisition using echocardiography, during which microspheres were intravenously injected to induce elevated RV pressure loading.

Animal preparation and modeling of acute pulmonary embolization

The study was approved by the Institutional Animal Care and Use Committee of the Mayo Clinic. Five adult pigs were used. We used pigs because the cardiopulmonary system of these animals closely resembles that of humans. The animals were anesthetized with 2% isoflurane and mechanically ventilated. Blood pressure was measured in the right and left ventricles with Millar catheters (Millar Instruments, Houston, TX, USA), introduced into the heart through the internal jugular vein and carotid artery, respectively. Medial sternotomy was performed to open the chest of the animal and gain access to the heart. Pericardium was left intact and baseline RV and LV pressures were recorded.

Acute pulmonary embolism was simulated based on a previously described animal model (Bottiger et al. 1996; Dias-Junior et al. 2005). Briefly, a femoral vein was cannulated and stepwise intravenous injections of 300-μm microspheres (Sephadex G50, Pharmacia Fine Chemicals, Uppsala, Sweden) were administered in 1- to 5-mL increments to induce APE and sudden RV systolic pressure elevation to mild or moderate levels. Capitalizing on our previous work (Cho et al. 2009), we used a gradation of loading severity based on systolic RV pressure: mild ($\geq$35 and $<$50 mm Hg), moderate ($\geq$50 and $<$60 mm Hg) and severe ($\geq$60 mm Hg).

Echocardiography scans

Echocardiographic images were obtained in an open-chest setting. This setting does not limit the

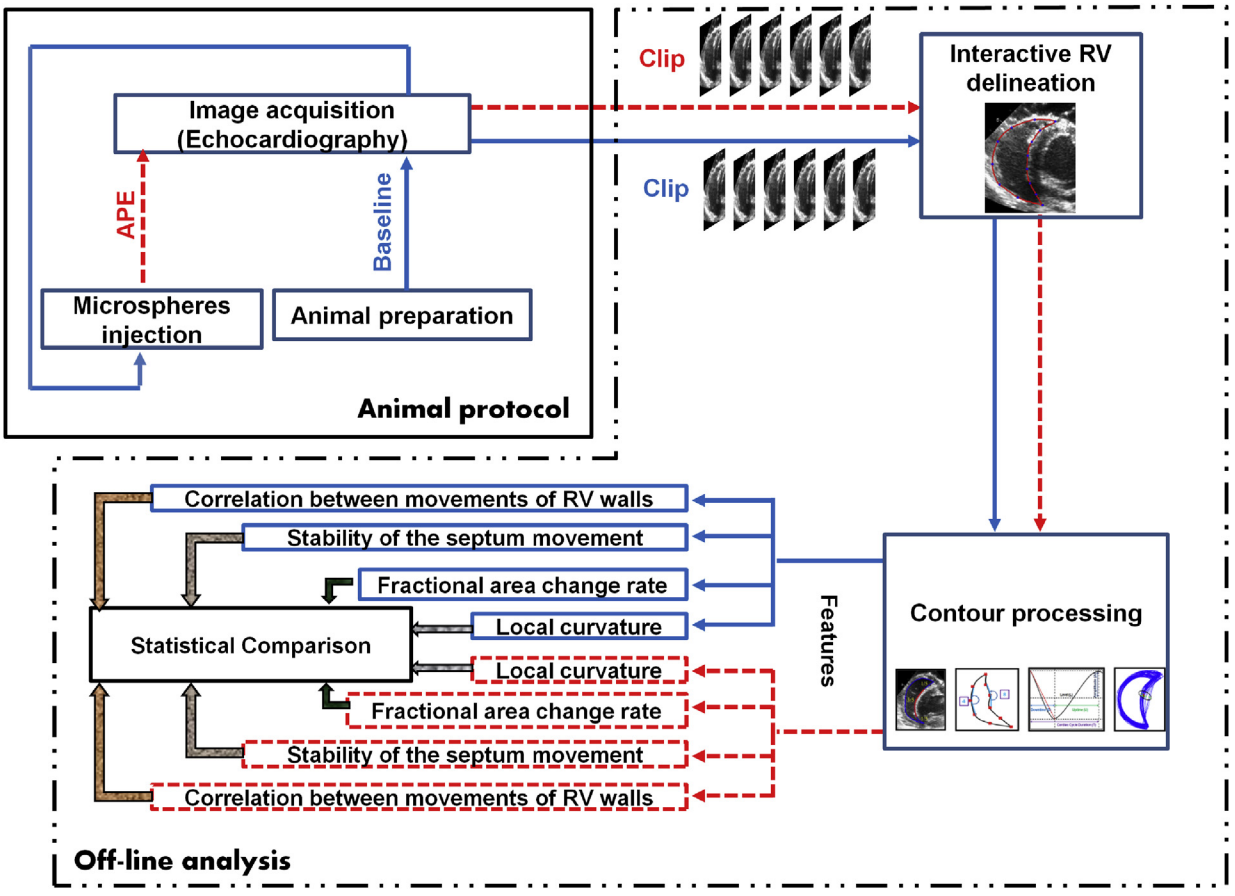

Fig. 1. Overview of the study. Microsphere administration simulates acute pulmonary embolism (APE) in animals by elevating right ventricular (RV) pressure overload to the mild or moderate level. The image acquisition yields two clips; one captured before and the other after administration of microspheres. The RV boundaries of each clip are then extracted and processed; four features representing RV functionality are computed and statistically evaluated.