

METHODS

Cardiac Magnetic Resonance Imaging Protocol

Each animal was placed in a clinical 1.5-T MRI scanner (Philips Medical Systems, Best, The Netherlands) in a supine position. Multiple anatomic and functional cine images of the heart were obtained by using the retrospectively gated breath-hold balanced turbo filed echocardiographic method with parallel imaging. High-resolution cine loops of the horizontal long axis, left ventricular (LV) outflow tract, and short-axis stacks 8 mm apart were obtained during multiple breath-hold sequential runs.

The following left atrial (LA) volumes were determined: the minimal LA volume (LA_{\min}) at end atrial systole (same as end-ventricular diastole); at end-ventricular systole, the maximal volume (LA_{\max}); the mid-diastolic relative LA minimal volume ($LA_{\text{rel min}}$) corresponding to LV diastasis onset and the end of rapid passive LA emptying; the relative maximal LA volume ($LA_{\text{rel max}}$) immediately before atrial systole, corresponding to end LV diastasis (end diastolic atrial volume). The LV end-diastolic volume and end-systolic volume were used to calculate LV stroke volume (LV_{SV}) and LV ejection fraction (LV_{EF}). All volumes were scaled to account for the changes in the body weight of the pigs over time. The scaled volume = volume at 6 weeks \times (baseline body surface area [BSA]/BSA at 6 weeks). Where the BSA (m^2) = $0.097 \times$ body weight (kg)^{0.633}. LA reservoir volume (LA_{RV}) was defined as the difference between LA volume at end LV systole and the LA volume at the end of early, rapid LV filling, given by $LA_{\max} - LA_{\text{rel min}}$. LA booster pump volume (LA_{BPV}) was defined as end-diastolic atrial volume minus atrial volume at end atrial systole, given by $LA_{\text{rel max}} - LA_{\min}$. LA conduit volume (LA_{CV}) is defined as the difference between LV_{SV} and the volume that enters the LA through the pulmonary veins during early rapid filling of the LV (Doppler E-wave), while the atrium itself is decreasing in volume because of ascent of the mitral annulus. It was calculated as $LA_{CV} = LV_{SV} - (LA_{BPV} + LA_{RV})$. Where LA_{BPV} is defined as LA booster pump volume, and LA_{RV} is defined as LA reservoir volume.

The following parameters were calculated by using equations based on volume ratios during various time points of the LA volume curve:

$$\text{Cyclical LA volume change (LA}_{CC}) = LA_{\max} - LA_{\min}$$

$$\text{LA percentage total emptying (LA}_{PTE}) = (LA_{\max} - LA_{\min}) / LA_{\max} \times 100;$$

$$\text{LA expansion index (LA}_{EI}) = (LA_{\max} - LA_{\min}) / LA_{\min} \times 100;$$

$$\text{LA active ejection fraction (LA}_{EF}) = (LA_{\text{rel max}} - LA_{\min}) / LA_{\max} \times 100;$$

$$\text{LA passive emptying percentage of total emptying (LA}_{PE}) = (LA_{\max} - LA_{\text{rel max}}) / (LA_{\max} - LA_{\min}) \times 100;$$

$$\text{LA passive emptying index (LA}_{PEI}) = (LA_{\max} - LA_{\text{rel max}}) / LA_{\max} \times 100;$$

$$\text{LA active emptying percentage of total emptying (LA}_{AE}) = (LA_{\text{rel max}} - LA_{\min}) / (LA_{\max} - LA_{\min}) \times 100;$$

$$\text{LA active emptying index (LA}_{AEI}) = (LA_{\text{rel max}} - LA_{\min}) / LA_{\text{rel max}} \times 100.$$

LA reservoir function parameters included LA_{CC} , LA_{EI} , and LA_{PTE} ; LA conduit function parameters included LA_{PE} and LA_{PEI} ; and LA_{EF} , LA_{AE} , and LA_{AEI} represented LA booster pump function.

Regional LA function was characterized by quantifying the segmental LA wall motion with cardiac magnetic resonance imaging (MRI) as previously described. The LA wall was divided into 4 segments: anterior, posterior, medial, and lateral segments. The percentage shortening of 4 LA wall segments was quantified by measuring the difference in distance between the superior dome of the LA, which remains stationary during the cardiac cycle, and the corresponding position on the mitral annulus during atrial systole and atrial diastole. The horizontal long-axis cine MRI was used to visualize and quantify the medial and lateral LA wall segmental motion; the LV outflow tract cine MRI was used to quantify the anterior and posterior LA wall segmental motion.

Pressure-Volume Catheter Protocol

The LA and LV PV relationships were acquired simultaneously throughout the study. Baseline data were recorded during steady-state conditions. For each data acquisition run, an electrocardiogram, heart rate, aortic pressure, superior and inferior vena caval flows, LA and LV pressures, and LA and LV conductance signals were acquired at 200 Hz and processed with custom-designed software. The respirator was held at end expiration during data collection (10-15 seconds) to minimize the effects of intrathoracic pressure variation. After steady-state data were obtained (lasting 3-5 heart beats), the inferior vena cava was slowly and progressively occluded to decrease preload and thereby generate atrial PV loops over a wide physiologic range of filling pressures. Data acquisition runs were repeated in triplicate; all runs containing premature ventricular contractions were excluded from analysis. Two to 4 minutes were allowed between runs for hemodynamic stabilization. The system (Lycom 5 DF; Millar Inc, Houston, Tex) was calibrated by determining the resistivity of blood using a calibration chamber. The alpha (conductance gain factor) was used to calculate the absolute volume by correlating the conductance derived volume with flow derived from LA and RA volume using flow meters on the superior vena cava and inferior vena cava. The parallel conductance (G_c) was calculated by injecting hypertonic saline (3 mL, 10%) into the superior vena cava. Atrial (or ventricular) end-systolic pressure ($APA-ES$) and volume ($A-VolA-ES$) points were determined for each cardiac cycle during preload reduction. By means of a least-squares linear regression, a straight line was fit to the following equation: $APA-ES = (EA-ES) \cdot (A-VolA-ES - V_0)$, where $EA-ES$ (mm Hg/mL) and V_0 (mL) are the slope (atrial chamber elastance) and volume-axis intercept, respectively. Static atrial (ventricular) stiffness was defined as the slope of the LA or LV end-diastolic pressure-volume relationship. Atrial end-diastolic pressure ($APA-ED$) and volume ($A-VolA-ED$) points were determined at the time of maximum atrial and minimum ventricular volume for each cardiac cycle during preload reduction. By means of least-squares linear regression, a straight line was fit to the following equation: $APA-ED = A \text{ Stiffness} \cdot (A-VolA-ED - VA-ED)$, where atrial (A) or ventricular (V) stiffness (mL/mm Hg) and $VA-ED$ (mL) are the slopes and atrial diastolic equilibrium volume, respectively.

000 The impact of 6 weeks of atrial fibrillation on left atrial and ventricular structure and function

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The impact of prolonged episodes of AF on atrial and ventricular function has been incompletely characterized. In a porcine model of AF, the LA demonstrated significant structural remodeling and decreased contractility, suggesting that early intervention in patients with persistent AF could mitigate against adverse atrial and ventricular remodeling.