The Left Ventricle Responds to Acute Graded Elevation of Right Ventricular Afterload by Augmentation of Twist Magnitude and Untwist Rate

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Background: The right and left ventricles share the interventricular septum, which mechanically transmits pressure gradients. The aim of this study was to investigate how acute mild or moderate right ventricular (RV) afterload affects left ventricular (LV) function.

Methods: In 14 open-chest pigs (mean weight, 43 ± 4 kg) with preserved pericardium, acute mild (>35 and ≤50 mm Hg) and moderate (>50 and ≤60 mm Hg) RV pressure loading conditions were induced by constriction of the pulmonary artery. Hemodynamic parameters and LV twist and untwist were evaluated under each condition.

Results: From baseline to mild and moderate RV afterload, the mean RV systolic pressure increased from 31.0 ± 4.3 to 41.1 ± 2.7 and 52.7 ± 3.4 mm Hg ($P < .001$), while LV twist magnitudes increased from 15.4 ± 5.1° to 18.5 ± 3.1° and 19.8 ± 5.0° ($P = .004$), respectively. Absolute values of LV untwist rate increased from −116.9 ± 64.9°/sec to −160.0 ± 53.3°/sec and −169.1 ± 47.0°/sec, respectively ($P = .001$). After adjusting for all variables, only the ratio of the early and atrial components of mitral inflow and RV outflow tract acceleration time was significantly associated with the LV twist magnitude and LV untwist rate.

Conclusions: In an acute setting, the left ventricle responds to suddenly elevated RV afterload and decreased RV stroke volume by promptly increasing its twist magnitude and untwist rate. (J Am Soc Echocardiogr 2011;24:922-9.)

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The right ventricle has limited tolerance to an acute increase in afterload and responds with a decrease in stroke volume, which decreases left ventricular (LV) preload.[1] Aside from hemodynamic dependence, the right and left ventricles are also interdependent by sharing the interventricular septum (IVS), which mechanically transmits pressure gradients. In chronic right ventricular (RV) pressure overload, the IVS straightens, LV end-diastolic filling decreases, and eventually, cardiac output becomes impaired.[2] However, whether the left ventricle immediately mechanically responds to a sudden RV pressure overload has not been fully elucidated.

LV twist, whose morphologic basis is in the transmural transition from right-handed subendocardial to left-handed subepicardial helically oriented cardiac myofibers,[3] has been associated with LV preload and myocardial contractility. A close linear relationship has been shown between twist magnitude and LV stroke volume during LV preload or afterload alterations.[4]

Considering the interdependency of the right and left ventricles and changes in LV twist mechanics in altered loading conditions, we hypothesized that the left ventricle would respond to a decrease in RV output caused by an acute elevation in RV afterload by increasing its twist magnitude and untwist rate.

METHODS

Animal Preparation

This study was approved by the Institutional Animal Care and Use Committee. Fourteen pigs (11 males; mean weight, 43 ± 4 kg) were anesthetized with 2% isoflurane and mechanically ventilated with an Ohmeda 7800 ventilator (GE Healthcare, Madison, WI).

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Abbreviations
IVS = Interventricular septum
LV = Left ventricular
RV = Right ventricular
RVOT = Right ventricular outflow tract

Pressures in the aorta, left ventricle, right ventricle, and right atrium were measured with high-fidelity catheters (Millar Instruments, Houston, TX) placed via internal jugular vein and internal carotid artery cannulations. The animal's chest was opened through midsternotomy while maintaining pericardial integrity. An external pneumatic cuff occluder was placed tightly around the pulmonary artery approximately 1 inch above the level of the pulmonary valve. Placement of the occluder required a short pericardial incision, which was then repaired by a suture. Preservation of baseline LV and RV hemodynamic states was verified.

Conventional and Doppler Echocardiography

Epicardial echocardiograms were obtained using a Vivid 7 scanner (GE Healthcare, Milwaukee, WI) and a 3-MHz handheld transducer. Systolic and diastolic LV dimensions, cavity areas, wall thicknesses, and LV ejection fraction were measured. LV volumes in diastole and systole were measured by tracing endocardial borders in the apical two-chamber and four-chamber views using the modified Simpson's method.[5] LV stroke volume was calculated from LV outflow tract diameter and flow velocity-time integral measured by Doppler. RV stroke volume was calculated from pulmonary annular diameter and flow velocity-time integral, both measured during each intervention. Acceleration time of flow within the RV outflow tract (RVOT) was calculated from a starting point of the flow Doppler wave to the point of its peak velocity.[6] The early (E) and atrial (A) components of mitral inflow velocities and the deceleration time of the E velocity were obtained with spectral Doppler. Mitral annular septal and lateral as well as tricuspid lateral velocities were obtained with tissue Doppler.[7] RV measurements included systolic and diastolic dimensions and areas and RV fractional area change expressed as a percentage. Areas were planimetered in the apical four-chamber view.[8] An LV eccentricity index, a measure of septal displacement, was assessed in mid short-axis views at both end-diastole and end-systole as $D2/D1$, where $D2$ is the cross-sectional LV dimension parallel to the septum, and $D1$ is the LV dimension perpendicular to $D2$ and bisecting the septum.[9,10] Tricuspid annular peak systolic excursion was determined by M-mode measurement of the displacement of the lateral tricuspid annulus during systole and diastole in an apical four-chamber view.[11] The RV and LV myocardial performance indices were calculated using a previously derived formula.[12,13]

Speckle-Tracking Echocardiography

Speckle tracking by echocardiography, which is a useful method in the analysis of RV motion[14] and has been validated against sonomicrometry and tagged magnetic resonance imaging,[15,16] was used for LV twist measurements. LV basal and apical short-axis as well as apical four-chamber images were obtained at the end-expiratory period, with frame rates ranging from 80 to 120 frames/sec and transducer frequencies ranging from 1.7 to 2.5 MHz. To standardize the scans among the individual animals, the basal level was defined as one showing the tips of the mitral valve leaflets, whereas the apical level was defined just proximal to the level with LV cavity obliteration at the end-systolic period in a short-axis view.[15-17] By convention, counterclockwise LV rotation (as viewed from the apex) was expressed as a positive value and clockwise LV rotation as a negative value.[18] LV rotation values were averaged from three consecutive heartbeats using EchoPAC version 7.0.0 (GE Healthcare). LV twist magnitude was calculated as the net difference between the basal and apical peak rotation angles during systole.[16] Untwist rate was defined as the net difference between the basal and apical peak rotation rates during diastole.

Study Protocol

Scans and data were collected at baseline (with the pulmonary pneumatic occluder in place) and during the graded interventions including acute mild (>35 and ≤ 50 mm Hg) and moderate (>50 and ≤ 60 mm Hg) RV pressure overload,[19] induced by constricting the main pulmonary artery. After restoring baseline conditions, each intervention lasted about 20 min. Data collection started about 10 min into each intervention, after an equilibration period. We also explored severe RV pressure loading (>60 mm Hg), but only a few animals were able to maintain this condition.

Statistical Analysis

Data are expressed as mean ± SD. Unless stated otherwise, the measurements are peak values obtained during systole. A mixed linear model was used for parametric comparisons, where three loading conditions (i.e., baseline, mild, and moderate) were considered as fixed effects and animals were treated as repeated effects. Comparisons between the graded loading conditions were assessed using paired t tests. Multiple regression analysis with backward elimination was used to determine independent variables predictive of changes in twist magnitude and untwist rate; a more conservative analysis using a mixed linear model was also performed subsequently to confirm the results. P values $< .05$ were considered statistically significant. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).

Interobserver and Intraobserver Reproducibility

Two independent observers processed the twist magnitude analysis by tracking twice. Interclass and intraclass correlation coefficients were used to test reproducibility using the same criteria as for κ statistics (≥ 0.75, excellent; 0.4 to <0.75, good; and <0.4, poor).

RESULTS

Baseline data were obtained from all 14 animals. Data at mild and moderate pressure overload were obtained from 12 and 13 animals, respectively. Artifacts prevented reliable motion tracking in two animals, so that twist data at mild and moderate RV afterload conditions were available from 11 pigs, whereas untwist data at mild and moderate grades could be obtained from 12 animals. We also explored severe RV afterload by inducing systolic RV pressure >60 mm Hg.[20] Only six and five data sets were obtainable for twist and untwist conditions, respectively; the rest of the animals were unable to tolerate the acute severe RV pressure overload.

RV and LV Hemodynamics

Hemodynamic results are shown in Table 1. Both mean RV systolic and diastolic pressures increased with increasing afterload. Mean LV systolic pressure was lower at each intervention compared with