Acute Effects of Pacing at Different Ventricular Sites on Left Ventricular Rotational Mechanics in a Porcine Model

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Objective: **The purpose of this study was to examine the acute effects of pacing at different ventricular sites on hemodynamics and left ventricular (LV) rotational mechanics using speckle-tracking echocardiography (STE) in a porcine model.**

Design: **A prospective laboratory investigation.**

Setting: **University research laboratory.**

Participants: **Yorkshire pigs.**

Interventions: **In 9 pigs, after midline sternotomy, epicardial pacing was performed from the right ventricular outflow tract (RVOT), right ventricular apex (RVA), and LV free wall.**

Measurements and Main Results: **Two-dimensional STE and conductance catheter-derived LV pressure–volume measurements were made to determine the impact of pacing from various sites on LV rotational parameters (twist/untwist) and hemodynamics. RVOT pacing caused the least decrease in end-systolic pressure from baseline (–9.5%), when compared with RVA (–19.1%) and LV (–23.4%). Systolic and diastolic parameters (Emax, Tau) also were different among RVOT (4.7 ± 0.8 mmHg/mL, 32 ± 4 ms), RVA (3.9 ± 0.7 mmHg/mL, 37 ± 6 ms), and LV sites (3.6 ± 0.8 mmHg/mL, 42 ± 7 ms). Similar to the effects of pacing on hemodynamics, RVOT pacing better preserved LV twist (11.1 ± 1.8 *v* 8.6 ± 1.7, 5.9 ± 0.7 °) and untwisting rate (64.6 ± 8.5 *v* 56.2 ± 5.3, 48.2 ± 8.5 °/s) when compared with RV apical pacing and LV pacing. Furthermore, prolongation of conduction from LV lateral to anteroseptal at LV base (26.5 ± 3.8 *v* 13.8 ± 3.3 ms, $p < 0.05$) and LV midpapillary muscle level (35.6 ± 5.6 *v* 14.1 ± 2.4 ms, $p < 0.05$) was observed with LV pacing compared with RVOT pacing.**

Conclusions: **The present data showed that the LV twist/untwist and cardiac systolic and diastolic function were least affected by RVOT pacing. This finding may be explained by the proximity of this location to the native ventricular conduction system.**

KEY WORDS: ventricular tachycardia, pacing site, LV twist, synchrony

VENTRICULAR PACING commonly is used to improve hemodynamics in patients with heart failure and to treat bradycardia and heart block observed after cardiac surgery. Few earlier reports have demonstrated that the site chosen for ventricular pacing correlates with differing degrees of hemodynamic compromise,[1,2] although the effects of pacing from different sites on left ventricular (LV) mechanical contraction and relaxation are not fully understood.

LV mechanical contraction is initiated at the LV apex that rotates counterclockwise, followed sequentially by contraction of the LV base that rotates clockwise as the electrical impulses travel apico-basally. This twisting motion of the LV is in part due to the specific helical arrangement of the myofibers with a right-hand orientation from the base toward the apex in the endocardial layers and a left-hand orientation in the epicardial layers.[3] Although factors contributing to the effectiveness of LV mechanics are complex, it is recognized that LV twist closely correlates with ventricular systolic function.[4–6] LV twist is calculated as the differences in rotation between the apical and the basal short-axis planes. Conversely, untwisting rate of the ventricle, measured in degrees per second, is related closely to diastolic function.[7–9]

Two-dimensional speckle-tracking echocardiography (STE) has emerged as an excellent, noninvasive method to understand complex cardiac mechanics. Through tracking of unique myocardial signals called "speckle" during a cardiac cycle, STE provides angle-independent information on motion and deformation of LV.[10] Several recent studies have demonstrated that STE-derived LV twist/untwist closely correlates with overall ventricular systolic and diastolic function.[4–6]

While electrical pacing commonly is used, suboptimal positioning of ventricular pacing can cause dyssynchrony, affecting LV performance. To date, the effects of pacing at different ventricular sites on LV twist and untwist remain unclear. In this study, STE was used in a porcine model to compare changes in LV rotational mechanics with changes in hemodynamics derived from intraventricular pressure–volume loop analysis during epicardial ventricular pacing at various sites: Right ventricular outflow tract (RVOT), right ventricular apex (RVA), and LV free wall. It was hypothesized that ventricular pacing from different regions would cause different LV rotational response and that RVOT pacing, because of its proximity to the His-Purkinje conduction system, would best preserve the LV mechanical function.

METHODS

Animal Preparation

The study was approved by the Chancellor's Animal Research Committee at University of California, Los Angeles, and animals were treated in compliance with the National Institutes of Health guidelines for the care and use of laboratory animals. Nine Yorkshire pigs weighing 40 to 45 kg were anesthetized intramuscularly with ketamine (15-25 mg/kg) and xylazine (2 mg/kg) and mechanically ventilated via endotracheal intubation. Anesthesia was maintained by inhaled isoflurane (1%-2%) and intermittent intravenous boluses of fentanyl (5-10 μg/kg). The electrocardiogram was monitored from limb leads. The femoral artery and vein were cannulated for blood pressure measurement and drug infusion. The animals underwent median

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sternotomy followed by creation of a pericardial cradle to expose the heart. Epicardial pacing wires were sewn to the RVA, RVOT and LV free wall. A snare was placed around the inferior vena cava for preload manipulation.

Hemodynamics: PV Loop Measurements

A 5F pigtail 12-pole multielectrode combination conductance-pressure catheter (Millar Instruments, Inc., Houston, TX) was placed in the LV via the right carotid artery and connected to a conductance processor (MPVS Ultra, Houston, TX) for continuous measurement of LV pressure and volume. Proper electrode position was confirmed by ensuring that volume waveforms were obtained from each individual pair of electrodes on the catheter. LV volume was calculated by injecting hypertonic saline (0.2 g NaCl/mL, 2 mL) into the right atrium to obtain a constant offset volume (Vc). The authors measured Vc before and at the end of each experiment and confirmed that Vc remained stable. The conductance catheter method of measuring LV volume is described in detail in their previous studies[6,11] and elsewhere.[12]

Hemodynamic indices were obtained from steady-state pressure-volume (PV) loops during end-expiration. PV relationship was derived during serial preload reduction by inferior vena cava occlusion, as previously reported.[6,13] LV systolic function was assessed by ejection fraction, end-systolic pressure, maximum rate of pressure change (dP/dt_{max}), and Emax, the slope of the end-systolic PV relationship.[14] Diastolic function was assessed by LV end-diastolic pressure, and the minimum rate of LV pressure change (dP/dt_{min}).

Echocardiography: STE Recording and Analysis

Open-chest epicardial echocardiography was performed using a GE Vivid 7 Dimension system (GE Vingmed Ultrasound, Horten, Norway). A 10-MHz, phased-array transducer (GE 10S) was used for echocardiographic imaging. Sector widths were adjusted manually to optimize speckle quality and maintain frame rates of greater than 70 frames per second. Near-field dropout was eliminated by fixing a 5×3 cm section of preharvested pig liver to the echo probe with parafilm. Echocardiographic and hemodynamic data were acquired sequentially during each manipulation, while assuring similar hemodynamics between the two. Three cardiac cycles were recorded for subsequent offline analysis. Two-dimensional short-axis echocardiograms were taken at the basal level, defined as the tips of mitral valve leaflets and apical level, defined as the level proximal to complete end-systolic lumen obliteration. Counterclockwise rotation was defined as a positive angle and clockwise rotation as a negative angle when viewed from the apex towards the base. The accuracy of the image tracking software was verified manually. LV twist is calculated as the differences in rotation between the apical and the basal short-axis planes. Because LV untwisting predominantly occurs during isovolumic relaxation, its assessment reflects the process of LV relaxation. The degree of LV untwisting rate is calculated as $(twist_{es} - twist_{mvo}/twist_{es}) \times 100$/isovolumetric relaxation time, where $twist_{es}$ is twist in degrees at end-systole, $twist_{mvo}$ is twist at mitral valve opening, and isovolumetric relaxation time is the time of isovolumic relaxation in seconds.[15]

Electrophysiology: Depolarization Delay Measurements

A multipolar electrophysiology recording catheter (20 electrodes, 2-mm spacing, St. Jude Medical) was attached to the Prucka Cardiolab electrophysiology system (GE Healthcare, Waukesha, WI) for measuring propagation of the depolarization wavefront. The catheter was lightly sutured on the epicardium at the basal and papillary muscle levels and spanned the lateral wall to the left anterior descending artery, corresponding to the position of the septum on the epicardium.[16] Epicardial unipolar electrograms were obtained from the multipolar catheter and the time interval from peak negative dV/dt from lateral to anteroseptal regions was measured as previously described.[16]

Experimental Protocol

After surgery, the animals were stabilized for a 30-minute period before baseline measurements. Epicardial echocardiographic images and LV PV loops were acquired for offline analysis at baseline and during pacing at RVOT, RVA, and LV free wall sites. The order of pacing at different sites was alternated among animals. Ventricular pacing was maintained for at least 30 seconds before measurements were made. Pacing rate was chosen to be 10 bpm above basal heart rate in order to reduce competition. All hemodynamic variables were allowed to stabilize before the next pacing was initiated. At least 3 cardiac cycles were analyzed per pacing mode. All animals were euthanized at the end of the study with pentobarbital (100 mg/kg) and potassium chloride solution, intravenously.

Statistical Analysis

Analysis was performed using Sigma Stat (Version 3.1), and all data were presented as mean ± SD. The hemodynamic and echocardiographic measurements were compared in the various experimental stages by use of repeated analysis of variance followed by the post-hoc Bonferroni correction. Statistical differences were considered significant at p value less than 0.05.

Two independent observers processed echocardiography images in all animals. Each observer analyzed the same image 2 times. Intraobserver variability was determined by having one observer repeat the measures 1 month after the initial analysis. Interobserver and intraobserver variability were 0.85 and 0.8, respectively.

RESULTS

Figure 1 shows representative PV loops at baseline and during ventricular pacing at RVOT, RVA, and LV. Pacing rate was kept 10 to 15 beats above baseline to prevent competition with intrinsic rate and ranged from 80 to 100 beats per minute. The hemodynamic results are summarized in Table 1. Ventricular pacing at different regions had significantly different hemodynamic effects. RVOT pacing preserved hemodynamics compared with baseline, while RVA pacing significantly decreased end-systolic pressure (19%),