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Left Ventricular Twist Mechanics in a Canine Model of Reversible Congestive Heart Failure: A Pilot Study

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Summary

Left Ventricular (LV) twist dynamics play important roles in LV systolic and diastolic function. This preliminary study investigated LV twist dynamics in a canine model of reversible congestive heart failure (CHF). Pacing systems were implanted in adult dogs, and continuous chronic right ventricular pacing (230–250 bpm) was applied until CHF induction. Pacing was then stopped to allow the heart to recover. Echocardiography and LV catheterization were performed at baseline, during CHF while pacing was temporarily switched off, and during recovery. Left ventricular twist was computed as the difference between apical and basal rotations measured by two-dimensional speckle tracking. Torsion was further calculated as the LV twist divided by LV long axis. Untwisting rate was computed as the peak diastolic time derivative of twist. In 6 dogs that completed the study, we found that CHF developed after 2–4 weeks of pacing with LV end-diastolic volume, end-systolic volume, end-diastolic pressure, and time constant of relaxation during isovolumic relaxation period (τ) all increasing significantly compared to baseline, and recovering to normal levels 2–4 weeks after pacing was stopped. Left ventricular twist, torsion, and untwisting rate decreased significantly with CHF compared to baseline, and improved during recovery from CHF. In conclusion, LV twist dynamics reflect pacing-induced CHF and its reversal as assessed by echocardiographic speckle tracking.

Keywords

Echocardiography; Speckle tracking; Ventricular twist

Introduction

The cardiac muscle is composed of reciprocal helices.¹ Contraction of these helices results in counterclockwise rotation at the apex and clockwise rotation at the base when viewed from the apex. Left ventricular (LV) twist is defined as apical rotation around the long axis with respect

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to the base. During systole, LV twist facilitates ejection of blood into the arterial system and stores potential energy.² By the end of systole, LV relaxation reduces myocardial tension and initiates recoil of the reciprocal helices (untwisting), releasing the potential energy stored during systole. The reduction in myocardial tension and release of potential energy by untwisting causes LV pressure drop and provides suction force for filling.³ Therefore, twist mechanics play an important role in LV systolic and diastolic function.

Although it has been shown that LV twist and untwisting rate are reduced in patients with systolic dysfunction and in tachycardia-induced heart failure,^{4,5} no data are available on the reversibility of twist and untwisting rate with improvement or complete recovery from heart failure. We therefore performed a pilot study to investigate properties of LV twist and untwisting rate both during CHF and after reversal of CHF in a canine model of pacing-induced heart failure.

Methods

Animal preparation

The study protocol was approved by the animal care and use committees of the Institute of Biosciences and Technology, Texas A&M University, and of the Methodist Hospital Research Institute. The study adhered to the PHS guidelines for the care and use of laboratory animals. Thirteen adult male mongrel dogs were studied (weight, 35–40 kg). In each procedure, the dog was sedated by intramuscular injection of xylazine (0.75–1.5 mg/kg) and atropine (0.02–0.06 mg/kg). Anesthesia was induced by intravenous injection of propofol (5 mg/kg), and maintained with isoflurane inhalation (2%) till the end of each session.

Heart failure model

A pacing system (Promote, Model 3107, St. Jude Medical, CRMD) was implanted in each dog, with the lead-electrodes inserted via the left jugular vein and the pulse generator placed subcutaneously in the left pectoral region. The right ventricle (RV) was paced at a rate of 230–250 bpm continuously for 2 to 4 weeks. Congestive heart failure was confirmed by the presence of associated symptoms and signs, elevated LV diastolic pressure, and depressed ejection fraction (EF). Heart failure symptoms included anorexia, lethargy, ascites, tachypnea, and muscle wasting. After heart failure was confirmed, pacing was stopped to allow the dogs to recover for 4 weeks. Transthoracic echocardiography and LV catheterization were performed at baseline, during CHF while pacing was temporarily switched off, and during recovery after pacing was stopped.

LV catheterization

At each catheterization, a high-fidelity manometric pressure catheter (SPC-350, Millar instruments) was inserted into the LV via the right femoral artery, and pressure was recorded simultaneously with echocardiography. The following variables were measured and calculated from LV pressure: end-systolic pressure (LVESP), end-diastolic pressure (LVEDP), $+dP/dt$, $-dP/dt$, and time constant of relaxation during isovolumic relaxation period (τ). τ was calculated assuming a zero asymptote as described by Weiss et al.⁶

Echocardiography

Transthoracic echocardiography was performed using a color Doppler imaging system with a 1.7–3.4 MHz probe (Vivid 7, GE Healthcare) while the dog was in the left lateral position. Conventional images were obtained for analysis of LV dimensions, end-diastolic volume (LVEDV), end-systolic volume (LVESV), and EF. Two-dimensional (2D) loops of apical 4-chamber, 2-chamber, and long-axis views were obtained at a frame rate of 80–100 frames per

second. In addition, 2D cross-sectional loops were acquired at the apical, middle, and basal LV levels. The apical short-axis view was obtained by moving the probe from the most distal to the apex at the level of minimum LV cavity. The basal short-axis was confirmed by the presence of mitral valve opening during diastole in the middle of the LV cavity. Myocardial deformation and rotation were calculated using 2D speckle tracking (EchoPac, GE Healthcare). Global LV longitudinal myocardial deformation (GS_L), i.e., strain, was calculated from each of 3 apical views by considering the total LV myocardium as a single segment, and the average value was used for final analysis.⁷ Similarly, global LV circumferential strain (GS_C) was calculated from each of 3 short-axis views, and the average value was used for final analysis. The indices GS_L and GS_C were reflective of LV systolic function.^{8,9} Apical and basal rotations were determined from the respective 2D short axis images. Data of apical and basal rotations were exported into MATLAB software (Version 7.0, The MathWorks). Left ventricular twist was computed as the difference between apical and basal rotations, while considering counterclockwise rotation as a positive value and clockwise as negative (Fig. 1). Left ventricular torsion was calculated as LV twist divided by LV end-diastolic long axis to exclude the effect of LV size. Left ventricular untwisting rate was computed as the peak diastolic time derivative of twist.

Statistical analysis

The distribution of the sample was tested using Wilk-Shapiro analysis. Data at different stages of the animal model were compared using one-way repeated ANOVA and post hoc (Holm-Sidak) analysis. A P value <0.05 was considered statistically significant. Continuous data are presented as means $\pm$ SD.

Results

Animals

Complete data sets were available at all 3 stages of the study from 6 dogs, and were analyzed and compared by repeated measure ANOVA. Data from the other dogs were lost during follow up due to premature death, experimental complications, implanted pacing system failure, or poor image quality.

Changes in echocardiographic and hemodynamic variables

As summarized in Table 1, LVEDV and LVESV increased while EF decreased significantly in all dogs during CHF. All of these variables returned to baseline levels following cessation of pacing and recovery from CHF. Global longitudinal and circumferential deformation also decreased during CHF and improved during the recovery period. Similarly, LV twist, torsion, and untwisting rate diminished significantly during CHF compared to baseline (both $P < 0.05$). Twist and torsion increased to baseline level during recovery. Untwisting rate showed a trend of improvement, but the difference did not reach statistical significance. Both $+dP/dt$ and $-dP/dt$ decreased while LVEDP and tau increased significantly during CHF, and all these hemodynamic variables returned to baseline levels during recovery.

Discussion

We performed a pilot study to investigate LV dynamics in a canine model of pacing-induced heart failure. We demonstrated that LV twist, torsion, and untwisting rate were impaired during CHF, and improved upon recovery from heart failure.

Quantification of LV function is usually cumbersome. The most frequent measure of LV systolic function is EF. Measurement of EF as recommended by the American Society of Echocardiography requires accurate manual tracing of the LV endocardium, which can be

difficult. A simple way to quantify LV global systolic function is of clinical significance. Left ventricular twist, as evaluated by 2D speckle tracking technique, may represent a simple noninvasive parameter reflecting LV systolic function.¹⁰ Although different studies have shown that LV twist decreases in patients with systolic dysfunction, twist may vary in different individuals. Left ventricular global longitudinal and circumferential strains decreased during CHF and returned to normal level after recovery. The improvement in LV global strain represents recovery of LV global function. In parallel to changes in LV global strains, LV twist and torsion decreased during CHF and returned to normal upon recovery, suggesting that LV twist is a good indicator of LV systolic function. Our results are in agreement with previous reports demonstrating reduction in LV twist in patients with dilated cardiomyopathy and in tachycardia-induced heart failure.^{4,5} More importantly, our findings indicate that LV twist, or torsion, can be a sensitive parameter for monitoring heart function while managing heart failure.

It has been reported that untwisting rate may be a sensitive parameter reflecting LV relaxation. In an acute animal study, Dong et al found that untwisting rate assessed by magnetic resonance imaging significantly correlated with tau, and was independent of preload and afterload.¹¹ Progression of heart failure is a chronic process that involves significant structural remodeling.^{12,13} Our chronic heart failure model demonstrated that untwisting rate decreased during CHF in parallel with tau. In theory, a weak contraction results in reduced twist and reduced storage of potential energy during systole.^{14,15} Consequently, the release of a large amount of potential energy may be compromised. The combination of active detachment of actin-myosin cross-bridges initiated by Ca^{2+} uptake and passive release of potential energy leads to untwisting. We previously demonstrated that LV untwisting rate is not only determined by LV relaxation, but also by systolic function, which determines the amount of potential energy as well.¹⁶ In the present reversible heart failure model, we did not observe complete recovery of untwisting rate at the end of study. Whether this indicates incomplete recovery of heart failure requires further investigation.

Study limitations

This report describes a pilot study and has limitations. One of the limitations is that we did not study the animals in conscious condition. Constant movement and rapid respiration would have made it difficult to obtain stable images for analysis of LV twist mechanics. Anesthesia might have impacted LV function. However, we used the same dose of anesthetics in every study, and thus the effect of anesthetics on LV twist mechanics at each stage of the study should be similar in each dog. Due to death of a number of animals during CHF and recovery periods, complete data sets were available in only 6 animals. As a result, the small sample size may not be sufficient to reach statistical significance in some comparisons. However, even in this small sample, we still observed significant change in LV twist and torsion. Finally, untwisting rate did not fully recover at the end. We did not perform histological examination on the myocardial tissue. Therefore, it is uncertain whether compromised untwisting rate indeed reflects an incomplete recovery from heart failure.

Conclusions

Left ventricular twist dynamics, as assessed by echocardiographic speckle tracking, reflect pacing-induced CHF and its reversal. Our preliminary findings suggest that LV twist or torsion may be used to monitor LV function during treatment of heart failure.

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Figure 1.

Illustration of measurements of apical and basal rotations. **(A):** Apical rotation depicting a predominant systolic counterclockwise (positive) rotation. **(B):** Basal rotation depicting a predominant clockwise (negative) rotation. MV, mitral valve.

Table 1

Echocardiographic and hemodynamic variables

Variable	Baseline	CHF	Recovery	P Value
LVEDV (ml)	70±19	98±15 ^{*†}	76±18	0.004
LVESV (ml)	38±13	70±14 ^{*†}	43±18	0.001
EF (%)	47±5	29±6 ^{*†}	45±11	0.001
GS _l (%)	-10±4	-8±2 ^{*†}	-11±4	0.05
GS _c (%)	-11±4	-6±2 ^{*†}	-9±5	0.02
LV twist (°)	6±3	3±2 ^{*†}	7±3	0.04
LV torsion (°/m)	90±50	40±30 ^{*†}	100±40	0.02
Untwisting rate (°/s)	101±31	54±16 [*]	72±36	0.02
LVESP (mmHg)	98±10	92±13	93±5	0.21
LVEDP (mmHg)	8.1±2.7	24.8±8.5 ^{*†}	6.8±1.2	<0.001
+dP/dt (mmHg/s)	599±164	449±79 ^{*†}	777±322	0.02
-dP/dt (mmHg/s)	3133±478	2208±346 ^{*†}	2834±399	0.002
Tau (ms)	32±7	47±8 ^{*†}	29±5	0.003

Values shown are from 6 dogs completing all stages of the study.

* Significantly different from value at baseline.

† Significantly different from value during recovery.

LV, left ventricle/ventricular; LVEDV, LV end-diastolic volume; LVESV, LV end-systolic volume, EF, ejection fraction; GS_l, global LV longitudinal strain; GS_c, global LV circumferential strain; LVESP, LV end-systolic pressure; LVEDP, LV end-diastolic pressure; +dP/dt, maximum of first derivative of LV pressure; -dP/dt, minimum of first derivative of LV pressure; Tau, time constant of relaxation.