Ventricular restraint therapy for heart failure: The right ventricle is different from the left ventricle

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Objective: Effects of ventricular restraint on the left ventricle are well documented, but effects on the right ventricle are not. We hypothesized that restraint affects the right and left ventricles differently.

Methods: We studied acute effects of restraint on left and right ventricular mechanics in healthy sheep (n = 14) with our previously described technique of adjustable and measurable restraint. Transmural pressure, myocardial oxygen consumption indices, diastolic compliance, and end-systolic elastance were assessed at 4 restraint levels for both ventricles. We then studied long-term effects of restraint for 4 months in an ovine model of ischemic dilated cardiomyopathy (n = 6). Heart failure was induced by coronary artery ligation, and polypropylene mesh was wrapped around the heart to simulate clinical restraint therapy. All subjects were followed up with serial cardiac magnetic resonance imaging to assess left and right ventricular volumes and function.

Results: Restraint decreased left ventricular transmural pressure ($P < .03$) and myocardial oxygen consumption indices ($P < .05$) but not left ventricular diastolic compliance ($P = .52$). Restraint had no effect on right ventricular transmural pressure ($P = .82$) or myocardial oxygen consumption indices ($P = .72$) but reduced right ventricular diastolic compliance ($P < .01$). In long-term studies, restraint led to reverse left ventricular remodeling with decreased left ventricular end-diastolic volume ($P < .006$) but did not affect right ventricular end-diastolic volume ($P = .82$).

Conclusions: Ventricular restraint affects the left and right ventricles differently. Benefits of restraint for right ventricular function are unclear. The left ventricle can tolerate more restraint than the right ventricle. With current devices, the right ventricle may limit overall therapeutic efficacy. (J Thorac Cardiovasc Surg 2010;139:1012-8)

Ventricular restraint is a nontransplant surgical treatment for heart failure in which the entire epicardial surface is wrapped with a prosthetic material.[1,2] The intent is to provide circumferential diastolic support to the failing heart and prevent progressive ventricular remodeling. Although no clinically approved restraint device is currently available for use, numerous animal studies and clinical trials have demonstrated that devices such as the Acorn CorCap Cardiac Support Device (Acorn Cardiovascular, Inc, St Paul, Minn) can induce reverse remodeling of the left ventricle (LV) and lead to improvement in LV volumes, ejection fraction (EF), and sphericity index.[3-14] The precise mechanics through which restraint engenders these changes, however, remains unknown. With our previously described technique in which the amount of applied restraint can be measured and quantified (Figure 1), we demonstrated that ventricular restraint decreases LV transmural myocardial pressure (P_{tm}) and indices of myocardial oxygen consumption (Mvo_2) in a large animal model.[15-16] These results imply that decreased LV wall stress is one mechanism through which restraint promotes reverse remodeling. We also showed that restraint level determines the degree of improvement in P_{tm} and indices of Mvo_2, implying that the amount of restraint applied is critical in determining therapeutic efficacy.

Most published studies analyzing the effects of ventricular restraint have focused on the LV, because LV dysfunction is the primary pathology for which restraint therapy is indicated. Thus restraint has logically targeted improvement in LV function. All current ventricular restraint devices, however, involve the application of epicardial pressure around the entire heart, including the right ventricle (RV). Because the RV is restrained, alterations in right heart mechanics and physiology are possible. To date, however, there have been no definitive studies evaluating the effect of ventricular restraint on the RV.

In this study, we hypothesized that ventricular restraint has different effects on RV function and mechanics than on those of the LV. We tested this hypothesis by performing

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Abbreviations and Acronyms

AMVR = adjustable and measurable ventricular restraint
C_d = diastolic compliance
CVP = central venous pressure
EDP = end-diastolic pressure
EDV = end-diastolic volume
E_{es} = end-systolic elastance
EF = ejection fraction
LV = left ventricle
MAP = mean arterial pressure
M_{VO_2} = myocardial oxygen consumption
P_{max} = maximal pressure tested
P_{tm} = transmural myocardial pressure
RV = right ventricle

both acute and long-term studies of ventricular restraint in a sheep model.

MATERIALS AND METHODS

Study Overview

This study was performed in 2 parts. (1) Acute, terminal studies evaluated the effect of ventricular restraint level on RV and LV P_{tm}, indices of M_{VO_2}, compliance, and hemodynamics. (2) Long-term, 4-month longitudinal studies investigated the effects of simulated clinical restraint on RV and LV remodeling in an ovine model of ischemic dilated cardiomyopathy.

A total of 20 (14 for acute studies, 6 for long-term studies) adult male sheep (weight range 30–40 kg) were used in this study. All animals received humane care in compliance with the Guide for Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html). The protocol was approved by the Institutional Animal Care and Use Committee at Harvard Medical School.

Acute Studies: Effects of Restraint Level on Ventricular Mechanics

Adjustable and measurable ventricular restraint. Because current clinical restraint devices such as the Acorn CorCap Cardiac Support Device do not allow either the measurement or adjustment of wrap tightness, restraint is applied at an arbitrary level of tightness.[6,9,23] To address these limitations, we have previously developed and described adjustable and measurable ventricular restraint (AMVR), in which a fluid-filled epicardial balloon is placed around the entire ventricular surface.[16] The balloon is surgically placed around the heart and secured to the atrioventricular groove.

The AMVR balloon is hemiellipsoidal in shape and composed of medical grade polyurethane sheets (Polyzen, Inc, Apex, NC). Each balloon is composed of two 1-mm thick layers. The outer layer of the balloon is flexible but nonstretchable, whereas the inner layer is redundant. An access line placed between the layers allows measurement of the pressure within the balloon lumen, as well as the addition or withdrawal of fluid. Because the outer layer of the balloon is nonstretchable, fluid introduced into the balloon lumen has only one direction of filling space–inward, toward the heart. This creates a tighter wrap. Conversely, withdrawal of fluid from the balloon lumen creates a looser wrap. The balloon access line is connected to a Statham P10EZ pressure transducer (SpectraMed, Oxford, Calif). By measuring the luminal pressure within the balloon when the heart is largest—end diastole—wrap tightness (or restraint level) may be precisely quantified. To change restraint level, fluid is added or removed from the balloon while balloon luminal pressure is monitored in real time. At end diastole, the fluid within the balloon lumen and access line is static. Cardiac magnetic resonance imaging has confirmed this (unpublished data). Because the fluid is static, the pressure measured by the access line should reflect the entire balloon luminal pressure.

Pressure–volume analysis. Fourteen normal sheep were placed under general anesthesia and underwent AMVR balloon placement by median sternotomy. A 16-gauge intravenous line was placed in the left external jugular vein for access and measurement of central venous pressure (CVP). An electromagnetic aortic flow probe (Carolina Medical Electronics, King, NC) was placed to measure aortic flow. High-fidelity micromanometers (Millar Instruments, Houston, Texas) were placed in the LV, RV, and aorta. An 8F conductance catheter for volume measurement (Webster Laboratories, Baldwin Park, Calif) was placed in the RV or LV.[17-19] All electrocardiographic and hemodynamic signals were sampled at 200 Hz. We arbitrarily defined the maximal pressure tested (P_{max}) in our study as the level at which mean arterial pressure (MAP) fell by 10 mm Hg, indicative of tamponade physiology. In our animal model, P_{max} was 8.0 mm Hg. For each subject, all signals were recorded at 4 sequential restraint levels: 0 (baseline), 3.0 mm Hg ($P_{max}/3$), 5.0 mm Hg ($2P_{max}/3$), and 8.0 mm Hg (P_{max}). All data were collected for 20 beats and with the ventilator off to avoid respiratory variations. The heart rate varied among animals (range 55–115 beats/min) but remained fairly consistent for any given subject at all restraint levels tested. At each restraint level, an inferior vena caval occlusion was performed to determine the RV and LV end-systolic elastance (E_{es}) and diastolic compliance (C_d) values.

Data were analyzed on a microcomputer with the program MATLAB (The Mathworks, Natick, Mass). End diastole was defined as the time point in the cardiac cycle that corresponded to the R wave on the electrocardiogram, which closely represents closure of the mitral valve. Begin ejection was defined as the point at which aortic flow first became nonzero, whereas end systole was defined as the point at which aortic flow became zero after the beginning of ejection. Hemodynamic signals were ensemble averaged across 10 beats. P_{tm} across the heart wall was defined as the ventricular pressure minus the epicardial pressure (as measured by the balloon). The transmural tension–time index was calculated by integrating P_{tm} with respect to time across the cardiac cycle. The end-systolic pressure–volume relationship and the end-diastolic pressure–volume relationship were determined from the caval occlusion data by the procedure of Kono and colleagues.[20] The transmural pressure–volume area was calculated for each restraint level.[20-21]

Long-Term Studies: Effects of Restraint on Ventricular Morphology and Function

Heart failure model. A postinfarction ovine model of heart failure, previously described by Moainie and associates,[22] was utilized. This model includes many of the features of human ischemic dilated cardiomyopathy and LV remodeling, such as increased LV end-diastolic volume (EDV) and end-systolic volume, increased sphericity index, reduced LV EF, and decreased systolic wall thickening. A left anterior thoracotomy was performed through the 4th intercostal space in 6 sheep. The first 2 diagonal branches of the left anterior descending coronary artery were identified and ligated with 4-0 polypropylene sutures. The thoracotomy was closed in layers, and the animal was allowed to recover. Cardiac magnetic resonance imaging was performed 8 weeks after infarction to document heart failure. By this time, heart failure developed in all animals, with LV EF less than 40% and a 100% increase in LV EDV from baseline. There was hypokinesis of the anterior to anterolateral wall, consistent with infarction of the area supplied by the ligated coronary arteries.

Simulated clinical ventricular restraint. To simulate clinical restraint therapy, a polypropylene mesh (Ethicon, Inc, Somerville, NJ) was