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PRECLINICAL STUDIES

Implantation of an Elastic Ring at Equator of the Left Ventricle Influences Cardiac Mechanics in Experimental Acute Ventricular Dysfunction

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Objectives We hypothesize that the implantation of an endoventricular elastic ring at the left ventricle (LV) equatorial site will positively affect the cardiac mechanics in an experimental model of acute LV dysfunction.

Background Changes in the elastic properties of LV occur in the dilated and failing heart, contributing to overall cardiac mechanical dysfunction. No interventions are as yet specifically designed to improve LV elasticity in failing hearts.

Methods Acute LV enlargement and dysfunction was induced in 13 healthy sheep via the insertion of a large Dacron patch into the lateral wall. In 6 of these sheep, a customized elastic ring was implanted at the inner surface of the LV equator (ring group), and the remaining 7 served as control subjects (dysfunction group). Systolic and diastolic function was evaluated using echocardiography and pressure–volume (P–V) analysis.

Results In the ring group, both the maximum rate of pressure increase and the slope of end-systolic P–V relationship were significantly different from those without ring (1,718 ± 726 vs. 1,049 ± 269 and 1.25 ± 0.30 vs. 0.88 ± 0.19; both $p < 0.05$). Preload recruitable stroke work changed even more prominently (33 ± 11 vs. 17 ± 5; $p = 0.005$), along with stroke volume, ejection fraction, and stroke work. Although ring implantation had no effect on end-diastolic P–V relationship, it positively affected the active component of diastole: the maximum rate of pressure decrease declined significantly ($p = 0.037$). The time constant of relaxation tended to decrease (37 ± 8 vs. 44 ± 6; $p = 0.088$).

Conclusions Improving the elastic component of the LV at its equatorial site substantially augments contractility and early relaxation in acute systodiastolic LV dysfunction. (J Am Coll Cardiol 2007;50:1791–8) © 2007 by the American College of Cardiology Foundation

Heart failure (HF) can be viewed as a biomechanical model in which systodiastolic left ventricular (LV) dysfunction progresses after changes in cardiac structure and mechanics (1). Several factors can lead to maladaptive cardiac remodeling, LV dilation, and poor contractile function (2). A failing, dilated heart is the outcome of changes in the contractile machinery, disarrangements in the extracellular matrix (ECM), and structural properties of cardiomyocytes. The elastic component of both ECM and myocytes is essential to providing the cardiac tissue with the elasticity and resilient recoil required to keep a normal cardiac architecture against changes in LV volume. Myocardial elasticity is altered in HF, at both micro and macro levels (3–8). Abnormal passive elastic properties contribute to alter LV function, with worsening effects on heart pumping (1–8). The increase in LV size and changes in its geometry, i.e., from the normal prolate ellipse to a more spherical shape, decreases cardiac efficiency, mostly via increased wall stress (1–3,8). Regional LV wall stress is higher in the endocardium compared with the epicardium and at the equator level more than in the apex (9). Thus, the inner layer of the LV equator in a spherical chamber is the most subjected to wall stress.

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
devP = developed pressure
dP/dt_{max} = maximum rate of pressure increase
dP/dt_{min} = maximum rate of pressure decrease
EDP = end-diastolic pressure
EDPVR = end-diastolic pressure–volume relationship
EDV = end-diastolic volume
EF = ejection fraction
ESP = end-systolic pressure
ESPVR = end-systolic pressure–volume relationship
ESV = end-systolic volume
HF = heart failure
LV = left ventricular/ventricle
PRSW = preload recruitable stroke work
P–V = pressure–volume
SV = stroke volume
SW = stroke work

Surgical volume reduction has developed to reduce LV stress as determinant of chamber remodeling (10,11), but almost no efforts have been generated to improve the elastic properties. Here we hypothesize that adding an elastic ring in the equatorial LV region of the failing heart would benefit global cardiac performance independently of changes in chamber volume. To test this, we used an ovine model of acute LV dysfunction in which chamber dilation and systodiastolic dysfunction were achieved via the insertion of a large Dacron patch into the LV lateral wall. This intervention transforms the elliptical LV into a spherical chamber, leading to increased end-diastolic volume and systodiastolic dysfunction (12,13). In a separate group, concomitantly with the insertion of the Dacron patch, a customized elastic ring was implanted on the inner surface of LV equator. The ring is conceived to store energy in 2 different moments of the cardiac cycle: in diastole ("ring expansion") and in the last part of systole ("ring contraction") (Fig. 1). Our prediction was that the energy stored by the ring would be returned first during the onset of systole, when the work efficiency of the LV is at the lowest peak, and later during the early diastolic phase. This should positively impact contractile force generation as well as relaxation, drawing the dysfunctional model closer to the physiologic elastic behavior of a normal LV chamber.

Methods

Study design. We have selected the acute animal model of LV dysfunction previously described by Nicolosi et al. (12) and Baretti et al. (13) in swine and then adopted by Batista et al. (14) in sheep, with some modifications. This model allows the evaluation of the pure mechanical effects of the equatorial elastic element. Furthermore, the choice was dictated to surgically accommodate a mechanical device of preset size inside the LV. Thirteen healthy sheep were included and divided into 2 groups: dysfunction group: 7 sheep (control); and ring group: 6 sheep (treated). Acute LV dysfunction was obtained by sphericalization and enlargement of the LV through the insertion of a large Dacron patch into the lateral wall (Fig. 2), transforming the LV into a spherical chamber with a consistent increase in end-diastolic volume (EDV) (12,13). The insertion of the Dacron patch, mimicking the presence of a large damaged area, alters the geometry, systolic and diastolic function, and the elastic property of LV chamber with a significant increase in LV wall stress (15,16). In the ring group, the animals underwent the same procedure (LV patch enlargement), and an elastic ring was sutured inside LV at equatorial level. The analysis of LV function was carried out by echocardiography and pressure–volume (P–V) loop analysis after thoracotomy and pericardiotomy and before cardiopulmonary bypass (CPB) (basal) and after weaning from the CPB.

Elastic ring. The elastic ring consists of 2 components: ring-shaped torsional spring, made of cold-forged stainless steel wire (ASTM TP 302 Sandvik 12R10, Sandvik, Sandviken, Sweden), and an oversized knitted low-weight Dacron fabric ring (Biomateriali, Brindisi, Italy). The latter allows suturing the device to the inner ventricular surface by means of an ad hoc holder allowing the insertion of the expanded ring (Fig. 3). The minimum spring ring diameter was 25 mm, which corresponded to the mean value of the end-systolic LV equatorial diameter measured by echocardiography in a similar normal animal population. The elastic constant of the spring was k = 294 dyne·mm in circumferential direction. The maximal diameter of Dacron suturing ring was 64 mm, which corresponds to more than 15 mm of the maximum end-diastolic diameter of a dysfunctional patched LV (49 ± 5 mm).

The elastic constant, the diameter at rest of the spring, and the dimension of the suturing ring were selected on the assumption that the spring joined together with the LV wall and patch would acquire a final slack size approximately in between the end-systolic and the end-diastolic dimension of LV. This should make possible elastic systodiastolic loading-recoiling, free expansion of the LV wall (Fig. 1), and evaluating the effect of an elastic element insertion on cardiac mechanics without any confounding factor due to a predetermined volume reduction.

Surgical protocol. All animals in this study received care according to the Guide for Care and Use of Laboratory Animals by the Institute of Laboratory Animal Research, National Research Council (revised in 1996, National Academy Press, Washington, DC), and following Italian Guidelines (D.L.G.S. 27/01/1992, no. 116). The local ethical committee approved the study in compliance with the European Convention on Animal Care.

The 13 sheep, weighting 60 ± 6.2 kg, were medicated 30 min before surgery with 0.01 mg/kg atropine and 1 mg/kg diazepam. General anesthesia was induced with 10 mg/kg ketamine and maintained with 4 mg/kg propofol and 5 mg/kg ketamine. Mechanical ventilation (Sirecust 50, Siemens, Germany) was maintained with air/oxygen mixture and a tidal volume of 20 ml/kg. Body temperature was maintained with a thermal blanket. All data were collected with the ventilator held at the end of the expira-

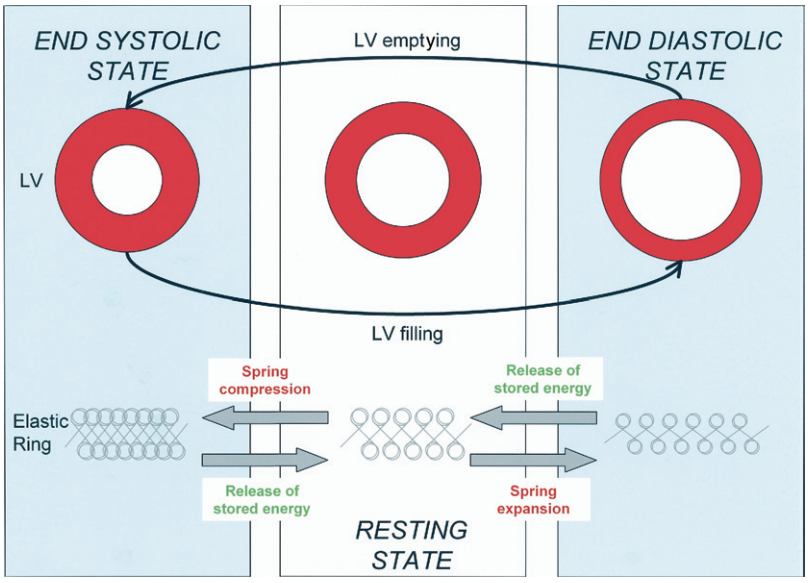

Figure 1 **Schematic Representation of a Portion of the Elastic Ring During Diastole and Systole**

The elastic ring is conceived to store energy in 2 different moments of the cardiac cycle: in diastole (ring expansion) and in the last part of systole (ring compression). The theoretic behavior of the elastic ring predicts that the energy stored by the ring would be returned at first during the onset of systole and later during the early diastolic phase, according to physiologic elastic behavior of a normal left ventricle (LV) chamber.

tion. The heart was exposed through a left anterolateral thoracotomy in the fourth intercostal space. A CPB with moderate hypothermia (34°C) was instituted cannulating the right carotid artery with a 20-F cannula and the right ventricle through the pulmonary artery with a 28-F cannula. The pump flow was kept at a rate of >50 ml/kg/min using a roller heart-lung machine primed with 1,000-ml lactated Ringer solution and bicarbonate. Blood gases were maintained in the physiologic range using a membrane oxygenator. The aorta was cross-clamped and cardioplegic arrest achieved by infusing into the aortic root 1,000-ml cold St. Thomas crystalloid solution and by topical hypothermia. After the papillary muscles were identified through a small cut in the LV apical region, the incision was carried out longitudinally toward the left atrial appendage for a total opening of 6 cm. An elliptic woven knitted Dacron patch (4.5 × 6.5 cm) cut from a vascular prosthesis (Gelseal, Vascutek Terumo, Renfrewshire, Scotland) was sutured to this incision, causing enlargement and sphericalization of the physiologic elliptical ventricle. In the 6 sheep with the elastic ring, after insertion of the Dacron patch, the ring was implanted at the equatorial level. The anatomic LV equator was identified as a line passing through the middle of ventricular attachment of the anterior papillary muscle and perpendicular to the longitudinal axis. The ring was secured for one-third of its circumference to the patch by means of 4 U-stitches and for the remaining two-thirds to the LV endocardium by means of 9 U-stitches.

After cross-clamp removal and heart de-airing, CPB was discontinued. An average time of 23 min was necessary for hemodynamic stabilization; at that time, heart rate and end-diastolic pressure (EDP) of the 2 groups were comparable. None of the animals were supported by inotropes. The pressure transducer-tipped catheter was repositioned in the LV, tip position assessment and recalibration was performed by epicardial echocardiography, and P–V loop and echocardiographic data analysis were carried out in all of the animals. The animals were then killed by phenobarbital and potassium chloride bolus injection.

Echocardiographic measurements. All epicardial Doppler echocardiographic studies were performed with a multifrequency transducer attached to a Vivid 3 instrument (General Electric, Fairfield, Connecticut). The images were obtained with the probe directly on the surface of the heart. Fine epicardial sutures were used to mark the probe position and to allow proper late repositioning. Long-axis, short-axis, 4-chamber, and 5-chamber views were obtained. Three sets of measurements were made in each echocardiographic view at predetermined steps. The mean value of three measurements was used to describe the quantitative data for each animal at each step. The same operator analyzed all the images. End-diastolic measurements were obtained at the peak of the R-wave on the electrocardiogram. End-systolic measurements were obtained at the end of the T-wave. Ejection fraction (EF) and LV volumes were calculated with a modified Simpson's rule. The mitral regurgitation and LV outflow tract obstructions were checked with color flow Doppler echocardiography. All images were obtained in real time.

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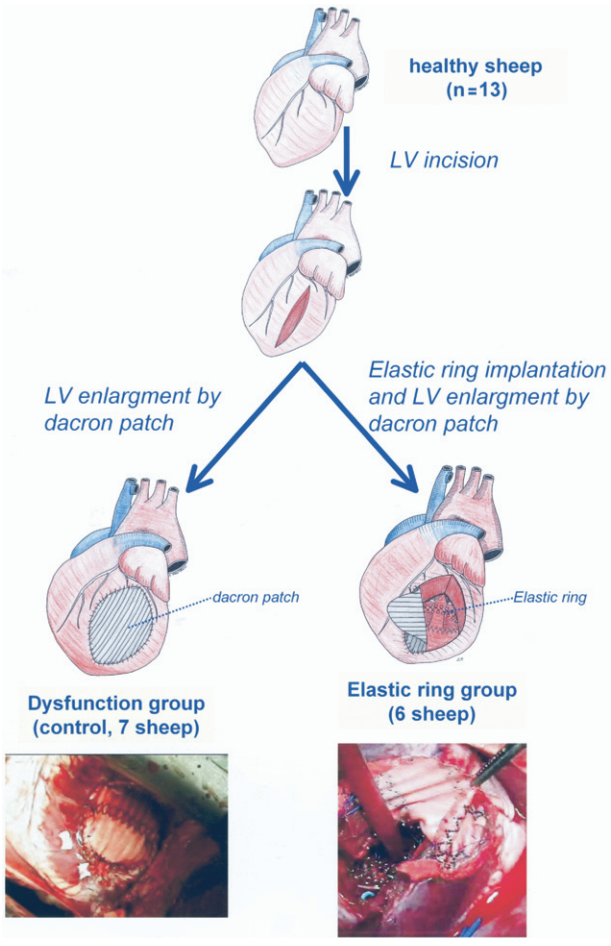

Figure 2 **Experiment Design and Photographs Showing Enlargement of LV and Implantation of the Elastic Ring**

The dacron waves are parallel to long axis of the LV chamber, allowing the expansion of the patch during cardiac cycle. The elastic ring was surgically implanted at the inner surface of the LV equator. LV = left ventricle.

P–V loop measurements. The cardiac function analyzer Leycom CFL512 (CD Leycom, Zoetermeer, the Netherlands) used a conductance catheter to measure ventricular P–V curves. This catheter was calibrated by 2-dimensional echocardiography performed before and after CPB (17). Steady-state hemodynamic measurements were determined from signal-averaged cardiac cycles, combining 5 to 20 sequential beats. Electrocardiogram, LV pressure, and volume signals were digitized at a sampling rate of 250 Hz. The following variables were recorded: EDP, end-systolic pressure (ESP), maximum rate of pressure increase (dP/dt_{max}), maximum rate of pressure decrease (dP/dt_{min}), and the time required for LV pressure at dP/dt_{min} to be reduced by half (tau). Owing to the complexity of the model, the acute preload reduction via vena cava occlusion was not performed. Referring to recent methods validated by other authors, we calculated the following variables: stroke volume (SV) as the difference between EDV and end-systolic volume (ESV) (18), developed pressure (devP) as the difference between the ESP and EDP (7,19), and stroke work (SW) as the product of SV and devP (18). The slope of end-systolic pressure–volume relationship (ESPVR) and its intersection with the volume axis (V_0), the end-diastolic pressure–volume relationship (EDPVR) α and β parameters, and the EDV_{30} (defined as the capacitance at 30 mm Hg) were calculated as a single-beat estimation (20,21). The stiffness was calculated at the end of diastole as described by Burkhoff et al. (22) by the formula: $\mu = \beta EDP/EDV$.

The preload recruitable stroke work (PRSW) was also single-beat determined (23,24); V_w and M_w (PRSW slope) values were calculated.

Statistical analysis. All variables were tested not to violate the normality assumption by the Kolmogorov-Smirnov test and were reported as mean ± SD. Comparisons between means were performed by paired- or independent-sample 2-sided *t* test as appropriate. When independent-samples *t* test were performed, the equality of variance between samples was assessed by Levene test, and the *t* test statistic was adjusted in the presence of homoscedasticity (25). A p value of <0.05 was considered to be statistically significant. Statistical analyses were performed using SPSS version 13.0 software package (SPSS Inc., Chicago, Illinois).

Results

The 2 groups were hemodynamically homogeneous, as demonstrated by the baseline parameters and the LV function indexes recorded after the thoracotomy and before the CPB (Table 1). Mitral regurgitation more than mild never occurred. In the elastic ring group, the implantation of the device was carried out uneventfully in all 6 cases; temporary paroxysmal atrial fibrillation occurred and resolved spontaneously in 1 sheep.

Experimental model of acute LV dysfunction. According to a previously described model in swine (12), a wide

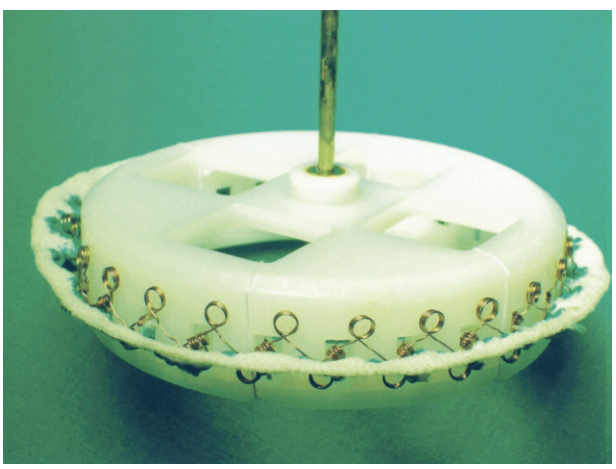

Figure 3 **The Elastic Ring Device Mounted on the Holder**

Table 1 Comparison of Baseline Hemodynamic and Left Ventricular Function Parameters in Dysfunction (n = 7) and Elastic Ring (n = 6) Groups After Thoracotomy and Before Cardiopulmonary Bypass

	Dysfunction Group	Elastic Ring Group	p Value
Weight (kg)	60.9 ± 7	59.0 ± 6	0.609
HR (beats/min)	98 ± 21	99 ± 24	0.924
EF (%)	57 ± 13	60 ± 11	0.636
EDP (mm Hg)	6 ± 3	7 ± 2	0.412
ESP (mm Hg)	87 ± 13	89 ± 33	0.846
devP (mm Hg)	80 ± 13	82 ± 32	0.905
EDV (ml)	74 ± 12	68 ± 24	0.558
ESV (ml)	32 ± 10	25 ± 8	0.251
SV (ml)	41 ± 14	45 ± 20	0.663
SW (ml × mm Hg)	3,010 ± 1,115	3,134 ± 2,241	0.899
dP/dt_{max} (mm Hg/s)	1,806 ± 547	1,550 ± 263	0.318
dP/dt_{min} (mm Hg/s)	−1,289 ± 499	−1,323 ± 293	0.888
tau (ms)	27 ± 10	34 ± 6	0.188

devP = developed pressure; dP/dt_{max} = maximum rate of pressure increase; dP/dt_{min} = maximum rate of pressure decrease; EDP = end-diastolic pressure; EDV = end-diastolic volume; EF = ejection fraction; ESP = end-systolic pressure; ESV = end-systolic volume; HR = heart rate; SV = stroke volume; SW = stroke work; tau = time required for left ventricular pressure at dP/dt_{min} to be reduced by half (time constant of relaxation).

separation of ventriculotomy edges by patch interposition creates an acute LV dysfunction. In a normal ellipsoidal LV with EDV of 70 ml, an endocardial surface area of 82 cm^2 is expected. The insertion of a 4.5 × 6.5 cm ellipsoid patch (total area of 23 cm^2) will increase this area of 28%. Theoretically, the predicted EDV would acutely increase to 101 ml (44% more). After patch insertion, we observed a 40% increase of EDV, as expected. The changes in LV geometry were associated with severe worsening of diastolic and systolic function in all of the animals (Table 2).

Elastic ring. A full assessment of global mechanics of the LV required the combined use of indexes that reflected LV systolic and diastolic properties (18–24). We compared these parameters in the 2 groups (Table 3).

Effects on LV diastolic properties. Diastole encompasses the isovolumic relaxation and filling phases. It has active and passive components (5). The active component of diastole involves the rate of myocardial relaxation and thus the rate of ventricular pressure decrease that typically is defined by the time constant of relaxation (tau) and dP/dt_{min}. The early-diastolic function was positively affected by the endoventricular elastic ring compared with animals implanted with Dacron patch alone. A significantly lower dP/dt_{min} and a trend to reduction for tau were noticed. After relaxation, the mechanical behavior of LV is determined by geometric and passive factors that contribute to create the EDPVR, an expression of LV passive chamber properties (22). Because EDV and EDP were not dissimilar in the 2 groups, EDPVR was not different as well, as demonstrated by α and β values, the ventricular capacitance (EDV_{30}), and the end diastolic stiffness. This suggests that adding the elastic ring on the dysfunctional model did not negatively affect late-diastolic function (Fig. 4).

Effects on LV systolic properties. The systolic properties of the LV were evaluated by indexes that reflect LV performance, contractility, and function (24). Developed pressure, SV, and SW were measured as indexes of LV systolic performance. Heart rate was similar in the 2 groups. In contrast, SV and devP were higher in the elastic ring group. Therefore, SW, the integrated index of pressure and shortening work, was significantly increased. Indexes of ventricular contractility have conventionally been divided into isovolumic phase indexes (dP/dt_{max}), ejection phase (EF) indexes, and those determined at the end of ejection (ESPVR) (Fig. 4) (24). The equatorial elastic ring had a positive impact on LV global contractility. The PRSW was determined, relating LV stroke work and end-diastolic volume. With similar preload but higher SW, the elastic ring group had a better PRSW linear relationship (Fig. 4).

Discussion

We show that in an acute model of LV dysfunction, implementing the elasticity of LV at its equatorial site via a juxtaposed elastic (spring) element has a positive impact on global cardiac mechanics. These beneficial effects were obtained in absence of significant changes in LV volumes, thereby validating the concept that elasticity is an essential contributor to LV mechanics.

Table 2 Comparison of Global Mechanics Indexes in Dysfunction Group (n = 7) at Baseline and After the Insertion of the Patch

	Basal	Patch	p Value
HR (beats/min)	98 ± 21	106 ± 19	0.495
EDP (mm Hg)	6 ± 3	9 ± 3	0.029
ESP (mm Hg)	87 ± 13	61 ± 13	<0.001
EDV (ml)	74 ± 12	103 ± 19	<0.001
ESV (ml)	32 ± 10	76 ± 14	<0.001
Diastolic parameters			
tau (ms)	27 ± 10	44 ± 6	0.010
dP/dt_{min} (mm Hg/s)	−1,289 ± 499	−686 ± 200	0.007
EDPVR α (mm Hg 10^{-10})	1.87 ± 1.94	0.34 ± 0.58	0.028
EDPVR β	5.71 ± 0.13	5.84 ± 0.10	0.034
EDV_{30} (ml)	99 ± 14	128 ± 22	<0.001
End-diastolic stiffness (mm Hg/ml)	0.48 ± 0.20	0.54 ± 0.22	0.353
LV performance parameters			
SV (ml)	41 ± 14	27 ± 7	0.040
devP (mm Hg)	80 ± 13	52 ± 10	<0.001
SW (ml × mm Hg)	3,010 ± 1,115	1,419 ± 519	0.015
LV contractility parameters			
EF (%)	57 ± 13	26 ± 4	0.001
dP/dt_{max} (mm Hg/s)	1,806 ± 547	1,049 ± 269	0.016
ESPVR V_0 (ml)	−32 ± 21	5 ± 17	0.004
ESPVR slope	1.32 ± 0.10	0.88 ± 0.19	0.006
LV function parameters			
PRSW V_w (ml)	−0.3 ± 3.8	20.9 ± 9.6	<0.001
PRSW M_w, slope	40 ± 12	17 ± 5	0.006

EDPVR = end-diastolic pressure–volume relationship; ESPVR = end-systolic pressure–volume relationship; LV = left ventricular; PRSW = preload recruitable stroke work; other abbreviations as in Table 1.

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Table 3 Comparison of Global Mechanics Parameters in Dysfunction (n = 7) and Elastic Ring (n = 6) Groups

	Dysfunction Group	Elastic Ring Group	p Value
HR (beats/min)	106 ± 19	118 ± 24	0.333
EDP (mm Hg)	9 ± 3	10 ± 3	0.604
ESP (mm Hg)	61 ± 13	76 ± 12	0.045
EDV (ml)	103 ± 19	97 ± 28	0.631
ESV (ml)	76 ± 14	56 ± 21	0.068
Diastolic parameters			
tau (ms)	44 ± 6	37 ± 8	0.088
dP/dt_{min} (mm Hg/s)	−686 ± 200	−977 ± 245	0.037
EDPVR α (mm Hg 10^{-10})	0.34 ± 0.58	0.98 ± 0.17	0.358
EDPVR β	5.84 ± 0.10	5.86 ± 0.09	0.806
EDV_{30} (ml)	128 ± 22	118 ± 37	0.592
End-diastolic stiffness (mm Hg/ml)	0.54 ± 0.22	0.68 ± 0.29	0.347
LV performance parameters			
SV (ml)	27 ± 7	43 ± 14	0.023
devP (mm Hg)	52 ± 10	66 ± 10	0.026
SW (ml × mm Hg)	1,419 ± 519	2,573 ± 1,152	0.035
LV contractility parameters			
EF (%)	26 ± 4	44 ± 10	0.001
dP/dt_{max} (mm Hg/s)	1,049 ± 269	1,718 ± 726	0.044
ESPVR V_0 (ml)	5 ± 17	−6 ± 22	0.320
ESPVR slope	0.88 ± 0.19	1.25 ± 0.30	0.020
LV function parameters			
PRSW V_w (ml)	20.9 ± 9.6	19.4 ± 10.4	0.792
PRSW M_w, slope	17 ± 5	33 ± 11	0.005

Abbreviations as in Tables 1 and 2.

The sphericalization and enlargement of LV with a patch creates an acute dysfunction, increasing the wall stress and varying the LV elastic properties (12,15,16), even though the myocardium is normal. Such an acute dysfunctional model is likely the best fit to show the potential beneficial effect of this elastic passive device. The insertion of the elastic ring in the patch-induced LV-dysfunctioning animals not only improves LV contractility but also ameliorates the active component of the diastolic period, with no net change in the passive one. Comparing the 2 experimental groups, EDV is not significantly different, in agreement with the original intent of not changing LV volume. Likewise, EDP did not change, whereas devP and SV increased in the ring group.

The viscoelastic properties of the myocardiaum are likely to play a major role here. We understand that it is the blood that actually stretches the elastic ring during the passive phase of the diastole, returning part of the energy of previous systole stored as external work. We speculate that part of this energy would otherwise be lost in dysfunctional LV as entropic dissipation. This seems consistent with the fact that EDV and EDP of the 2 groups were similar. We envision that the elastic recoil during the initial part of systole returns part of the energy stored during filling phase to favor the development of active tension in one of the most crucial moments of the cardiac cycle, the onset of systole (i.e., maximum wall stress) (8). The other "momentum" is at the end of systole, a time in which tension development inside LV is at its nadir. Here, the spring may store some new elastic energy owing to systolic compression that is released during the early phase of diastole, helping the impaired relaxation and filling that certainly constitute early events of LV dysfunction (5,6). All in all, we propose that the energy stored by the spring during the filling period helps the onset of systole and

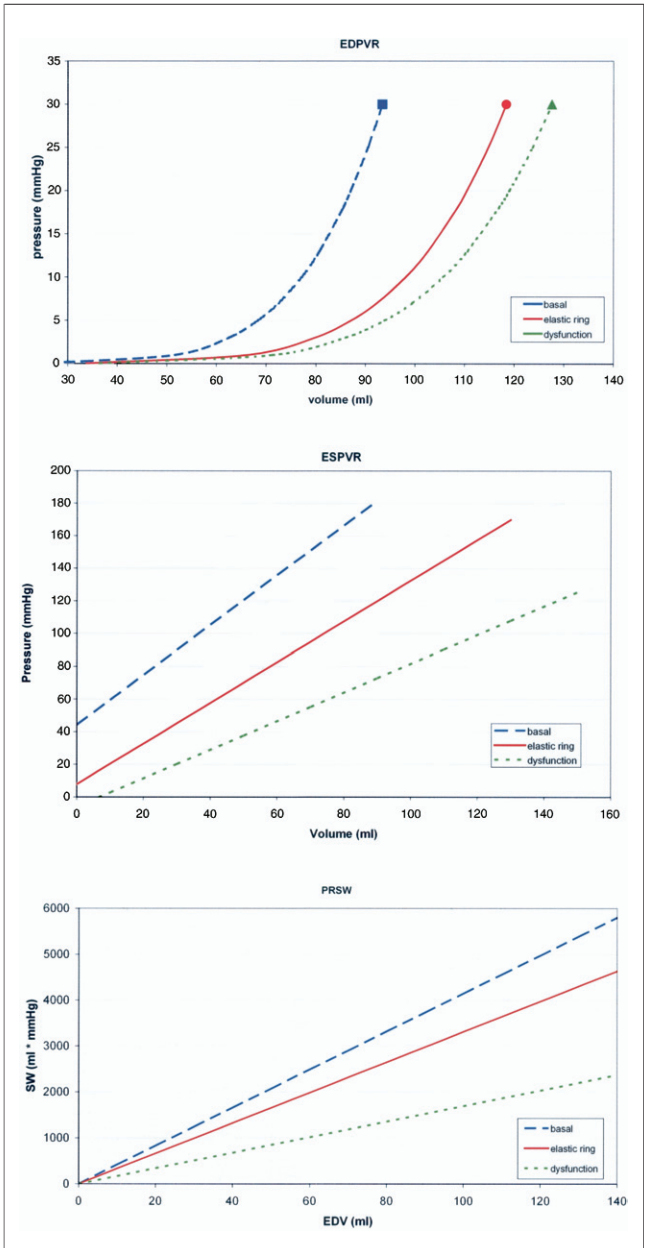

Figure 4 Comparison of EDPVR, ESPVR, and PRSW of Dysfunction Group and Elastic Ring Group Versus Basal

The **curves** represent the mean value for each group. The **top mark of each curve** represents the EDV_{30} value. EDPVR = end-diastolic pressure–volume relationship; EDV_{30} = end-diastolic volume at 30 mm Hg; ESPVR = end-systolic pressure–volume relationship; PRSW = preload recruitable stroke work.

during late systole it promotes early diastolic relaxation and filling, thus bridging systolic and diastolic phases effectively while optimizing the energy balance.

Part of relaxation and filling may reside in the properties of the giant molecular spring titin (3,5,6). Evidence suggests that titin modulates both systole and diastole and participates in the length-dependent activation of cardiomyocytes (6,26,27), as such contributing to the Frank-Starling phenomenon (6,26,27). The notion that titin's passive stretching can enhance contractility in relation to its mechanical response (6) suggests that the elastic device, at a more macroscopic level, may determine a better interplay between passive and active mechanical characteristics of the failing heart. Admittedly, this theory remains fairly speculative at the moment, given the lack of direct evidence that the elastic properties at cellular and intracellular levels can be translated tout court to the chamber level. Other factors may also have influence (26,27).

A new possible approach is to tackle increased systolic wall stress by acting on the LV elastic component, particularly at the LV equatorial region. This idea is based on human and animal studies showing that LV wall stress distribution is not homogeneous at all: LV endocardium is more affected by wall stress compared with the epicardial region, whereas the LV equator is potentially subjected to the most relevant changes toward LV sphericalization (9,11). Furthermore, because the apex and the base rotate in opposite directions during the cardiac cycle, the LV equator represents the fulcrum of the chamber wringing motion (11,26,27). As such, we hypothesized that the juxtaposition of an elastic support at the endocardial surface of the LV equator, by affecting the inherent LV viscoelastic properties, would relieve or reduce wall stress, ultimately leading to a positive impact on cardiac mechanics.

Study limitations. The first limitation is the acute time-course. Yet the result is a promising starting point for future investigations on chronic LV dysfunction models to establish whether an elastic LV device can prevent or reverse LV remodeling and/or how the elastic ring would impact a chronically failing heart. Second, the use of CPB is mandatory and the overall procedure is complex, hampering the ability of performing PV relationship via inferior vena cava occlusion. Indeed, traditional methods of assessing ESPVR and EDPVR during transient acute preload reduction would have been inaccurate as if the spring was effective: systolic and diastolic properties would be changing as preload was decreased. Nevertheless, the single-beat approach is accepted as an alternative when dealing with groups of hearts (21). Third, the comparison was made between a few different animals. Performing serial studies in the same sheep would have had unbearable biologic cost for the animals, making the comparison unfeasible.

Despite these limitations, the present model is a first step necessary to gain the initial groundworking information about the possible benefits of such a device. The present experimental setting is relatively rapid and low cost while allowing a complete evaluation of the pure mechanical action of the elastic ring implantation on global cardiac mechanics. Moreover, the present setting avoids any confounding effects due to neurohormonal, cellular, and molecular alterations that characterize chronic heart failure models. We recognize that the measurement of O_2 uptake would have been extremely insightful to get initial hints on the energetic implications of the present device (efficiency/efficacy). We acknowledge the large amount of work remaining to establish mechanisms and potential clinical applicability, including the fact that the magnitude of changes as observed here are not predictable in chronic dysfunctioning ventricle. However, the present hemodynamic approach is paving the way for future studies to be performed in this direction.

Conclusions

The present study appraises the effect of an artificial elastic element on global cardiac mechanics in an acute ovine model of LV enlargement and dysfunction. The data show the improvement in systolic and early diastolic function (without negative impact on late diastolic function) after the insertion of an elastic component in acutely dysfunctional LVs. These findings strengthen the notion that the passive elastic properties of the LV chamber are crucial for proper and adequate LV function. They also raise new intriguing pathophysiologic issues, such as whether therapies using multiple passive elastic devices, implanted at different levels of LV (i.e., mitral annulus, apex), aiming to achieve a complete elastic restoration of a failing heart, would improve the natural history of heart failure.

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REFERENCES

1. Mann DL, Bristow MR. Mechanisms and models in heart failure: the biomechanical model and beyond. Circulation 2005;111:2837–49.
2. Colucci WS, Braunwald E. Pathophysiology of heart failure. In: Braunwald E, editor. Heart Disease. A Textbook of Cardiovascular Medicine. Philadelphia, PA: Elsevier Saunders, 2005:509–38.
3. Ferrazzi P, Iascone MR, Senni M, Quaini E. The titan can help titin: from micro to macro myocardial elasticity. J Cardiovasc Med (Hagerstown) 2006;7:153–8.
4. Gupta KB, Ratcliffe MB, Fallert MA, Edmunds LH Jr., Bogen DK. Changes in passive mechanical stiffness of myocardial tissue with aneurysm formation. Circulation 1994;89:2315–26.
5. Borlaug BA, Kass DA. Mechanisms of diastolic dysfunction in heart failure. Trends Cardiovasc Med 2006;16:273–9.
6. Granzier HL, Labeit S. The giant protein titin: a major player in myocardial mechanics, signaling, and disease. Circ Res 2004;94:284–95.

7. Mizuno T, Yau TM, Weisel RD, Kiani CG, Li RK. Elastin stabilizes an infarct and preserves ventricular function. Circulation 2005;112 Suppl:I81–8.
8. Opie LH and Perlroth MG. Ventricular function. In: Opie LH, editor. Heart Physiology: From Cell to Circulation. Philadelphia, PA: Lippincott, Williams & Wilkins, 2004:355–401.
9. Buchi M, Hess OM, Murakami T, Krayenbuehl HP. Left ventricular wall stress distribution in chronic pressure and volume overload: effect of normal and depressed contractility on regional stress-velocity relations. Basic Res Cardiol 1990;85:367–83.
10. Saavedra WF, Tunin RS, Paolocci N, et al. Reverse remodeling and enhanced adrenergic reserve from passive external support in experimental dilated heart failure. J Am Coll Cardiol 2002;39:2069–76.
11. Ferrazzi P, Matteucci ML, Merlo M, et al. Surgical ventricular reverse remodeling in severe ischemic dilated cardiomyopathy: the relevance of the left ventricular equator as a prognostic factor. J Thorac Cardiovasc Surg 2006;131:357–63.
12. Nicolosi AC, Weng ZC, Detwiler PW, Spotnitz HM. Simulated left ventricular aneurysm and aneurysm repair in swine. J Thorac Cardiovasc Surg 1990;100:745–55.
13. Baretti R, Mizuno A, Buckberg GD, Child JS. Batista procedure: elliptical modeling against spherical distension. Eur J Cardiothorac Surg 2000;17:52–7.
14. Batista RJ, Santos JL, Takeshita N, Bocchino L, Lima PN, Cunha MN. Partial left ventriculectomy to improve left ventricular function in end-stage heart disease. J Card Surg 1996;11:96–7.
15. Dang AB, Guccione JM, Zhang P, et al. Effect of ventricular size and patch stiffness in surgical anterior ventricular restoration: a finite element model study. Ann Thorac Surg 2005;79:185–93.
16. Spotnitz HM. Macro design, structure, and mechanics of the left ventricle. J Thorac Cardiovasc Surg 2000;119:1053–77.
17. Schreuder JJ, Steendijk P, Van der Veen FH, et al. Acute and short-term effects of partial left ventriculectomy in dilated cardiomyopathy: assessment by pressure volume loops. J Am Coll Cardiol 2000;36:2104–14.
18. Braunwald E. Heart Disease: A Textbook of Cardiovascular Disease. 5th edition. Philadelphia, PA: W. B. Saunders, 1997:432.
19. Holubarsch C, Ruf T, Goldstein DJ, et al. Existence of the Frank-Starling mechanism in the failing human heart. Investigations on the organ, tissue, and sarcomere levels. Circulation 1996;94:683–9.
20. Shishido T, Hayashi K, Shigemi K, Sato T, Sugimachi M, Sunagawa K. Single-beat estimation of end-systolic elastance using bilinearly approximated time-varying elastance curve. Circulation 2000;102: 1983–9.
21. Klotz S, Hay I, Dickstein ML, et al. Single beat estimation of the end-diastolic pressure-volume relationship: a novel method with the potential for noninvasive application. Am J Physiol Heart Circ Physiol 2006;291:H403–12.
22. Burkhoff D, Mirsky I, Suga H. Assessment of systolic and diastolic ventricular properties via pressure-volume analysis: a guide for clinical, translational, and basic researchers. Am J Physiol Heart Circ Physiol 2005;289:H501–12.
23. Karunanithi MK, Feneley MP. Single-beat determination of preload recruitable stroke work relationship: derivation and evaluation in conscious dogs. J Am Coll Cardiol 2000;35:502–13.
24. Baicu CF, Zile MR, Aurigemma GP, Gaasch WH. Left ventricular systolic performance, function, and contractility in patients diastolic heart failure. Circulation 2005;111:2306–12.
25. Morgan GA, Leech NL, Gloeckner GW, Barrett KC. SPSS for Introductory Statistics. Use and Interpretation. Mahwah, NJ: Lawrence Erlbaum Associates, 2004:136–8.
26. Foster E, Lease KE. New untwist on diastole. What goes around comes back. Circulation 2006;113:2477–9.
27. Notomi Y, Martin-Miklovic MG, Oryszak SJ, et al. Enhanced ventricular untwisting during exercise: a mechanistic manifestation of elastic recoil described by Doppler tissue imaging. Circulation 2006;113:2524–33.