IMPROVED EFFICIENCY OF ENERGY TRANSFER TO EXTERNAL WORK IN CHRONIC CARDIOMYOPLASTY BASED ON THE PRESSURE-VOLUME RELATIONSHIP

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Objective: Cardiomyoplasty is a surgical procedure to support the failing heart, in which a burst-stimulated latissimus dorsi muscle flap is transposed and wrapped around the ventricles. The effect of dynamic cardiac compression, implemented as cardiomyoplasty, on left ventricular performance remains controversial; the mechanism by which clinical symptoms are improved remains unclear. To investigate the mechanism for improvement of patients' symptoms, it is important to evaluate the effects of cardiomyoplasty on left ventricular energetics and on left ventricular systolic and diastolic function. We therefore evaluated the efficiency of energy transfer from the native pressure-volume area to external work under conditions of 1:3 skeletal muscle burst pacing in an animal model with chronic heart failure. **Methods:** In seven Merino-Wether sheep, cardiomyoplasty was performed after stable heart failure was induced by staged coronary embolizations (ejection fraction < 35%). Hemodynamic assessment including the assessment of the pressure-volume relationship was performed 8 weeks after cardiomyoplasty when the latissimus dorsi muscle was fully trained. Instantaneous left ventricular pressure and volume were measured with a catheter-tipped manometer and a conductance catheter during steady-state conditions and after a transient inferior vena cava occlusion. The effect of dynamic cardiac compression on left ventricular systolic function was assessed by comparing pre-assisted and assisted beats and on diastolic function by comparing assisted and post-assisted beats. **Result:** The slope of the end-systolic pressure-volume relationship decreased by $30.5\% \pm 27.8\%$ ($p = 0.02$) during assisted beats. However, left ventricular pump performance improved by increasing stroke volume and external work by $35.9\% \pm 36.0\%$ ($p = 0.03$) and $9.7\% \pm 6.8\%$ ($p = 0.03$), respectively, resulting in a reduction of the volume intercept. As a result, the end-systolic pressure-volume relationship shifted to the left. The efficiency of energy transfer from the native pressure-volume area to the overall external work improved by $7.6\% \pm 8.2\%$ ($p = 0.04$). Cardiomyoplasty did not affect the time constant of left ventricular isovolumic pressure decline or the maximal rate of pressure decay, which suggested that cardiomyoplasty did not affect left ventricular relaxation. **Conclusions:** Dynamic cardiac compression in the form of cardiomyoplasty enhanced left ventricular pump performance without interrupting left ventricular filling. The ratio of energy transfer from the native pressure-volume area to the overall external work suggests a myocardial oxygen-sparing effect of cardiomyoplasty. (J Thorac Cardiovasc Surg 1998;115:1358-66)

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Cardiomyoplasty uses a burst-paced latissimus dorsi muscle flap that is transposed and wrapped around the ventricles of the failing heart.^{1,2} It is currently being evaluated as a therapeutic option for patients with congestive heart failure.³⁻⁸ In the early clinical trials, despite significant subjective clinical improvements, objective benefits were inconsistently noted.³⁻⁵ Most previous studies focused on improvement of the heart's systolic function measured as ejection fraction, systolic pressure, stroke volume, cardiac output, or the load-independent contractility index, E_{max} .^{7,9,10}

When patients showed significant improvement of their symptoms without improvement of objective parameters, it was unclear whether it was attributable to a placebo effect or other factors not evaluated. The efficiency of the energy transfer from the total mechanical energy to external work in each beat could be an important factor in improving a patient's symptoms.¹¹ However, previous studies have not assessed the aspect of left ventricular (LV) energetics in dynamic cardiomyoplasty. Because pressure-volume area (PVA) linearly correlates with myocardial oxygen consumption, the pressure-volume diagram provides important information about LV energetics.^{12,13} We evaluated the effects of cardiomyoplasty on LV systolic and diastolic function together with the efficiency of energy transfer from the native PVA to the overall external work.

Materials and methods

All animals involved in this study received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Research and published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985).

Staged coronary embolization. In seven Merino-Wether sheep (57.4 ± 4.2 kg) (University of Sydney farm, Sydney, NSW, Australia), staged coronary embolizations were performed to induce moderate heart failure with an ejection fraction of less than 35%.^{14,15} In each procedure, the animals were anesthetized with 20 mg/kg of thiopental sodium as induction, intubated, and ventilated with 1 L/min of oxygen, 2 L/min of nitrogen dioxide, and isoflurane (1.2% to 1.5%) through a respirator (Bird model 8; Bird Australia, Pty., Ltd., Chatswood, NSW, Australia). Maintenance fluid was provided through peripheral venous access with Hartmann's solution. Electrocardiography was monitored with electrodes clipped to the extremities. A 2 cm diameter orogastric tube was passed to enable decompression of the ruminant stomach.

When the heart rate stabilized, a cutdown was performed in the left side of the neck followed by an injection

of heparin (5000 unit bolus), after which the carotid artery was exposed. A 6F pigtail catheter was passed into the left ventricle via the carotid artery. LV ejection fraction was assessed by ventriculography (Siremobil; Siemens Ltd., Artarmon, NSW, Australia). For selective coronary embolization, a 6F right Judkin's coronary catheter (Cordis Surgical Australia, Auburn, Sydney, NSW, Australia) was introduced into the left anterior descending or circumflex coronary artery, and a slow injection (total, 0.1 to 0.5 ml) of polystyrene microspheres (90 μ m in diameter; polybead polystyrene; Bio Scientific Pty. Ltd., Sydney, NSW, Australia) was performed. To prevent ventricular arrhythmias, 50 mg of lidocaine (Xylocaine) was given as a slow intravenous bolus before each microsphere injection. Immediately after the injection, the Judkin's catheter was replaced with a catheter-tipped manometer (5F; Millar Instruments, Inc., Houston, Texas) to monitor the aortic pressure until it stabilized in the physiologic range. Metaraminol bitartrate (INN: metaraminol [Aramine]; 0.3 to 0.5 mg bolus injection) was administered intravenously as needed to prevent critical hypotension. The coronary embolization was repeated every 2 to 3 weeks until ejection fraction was shown to be below 35%, based on the left ventriculogram. On average, 4 ± 2 embolizations were required to induce heart failure. When the ejection fraction was stable below 35% ($27\% \pm 7\%$, mean $\pm$ standard deviation) for 4 weeks, the animal was subjected to cardiomyoplasty.

Cardiomyoplasty. Through a left flank incision the left latissimus dorsi muscle was completely mobilized, leaving the thoracodorsal neurovascular pedicle intact. Two intramuscular pacing electrodes (model 050-003; Teletronics Pacing Systems, Inc., Englewood, Colo.) were secured into the proximal portion of the flap 5 to 10 cm apart by each other, and threshold and total recruitment stimulation amplitudes were assured. The latissimus dorsi muscle was passed into the left hemithorax through a window in the third rib, and the humeral insertion was anchored to the periosteum of the fourth rib. Through a left anterior thoracotomy (fifth intercostal space), the pericardium was opened and the muscle was wrapped around both ventricles in a clockwise fashion, with the costal surface of the latissimus dorsi muscle in contact with the epicardium. The spinal border of the flap was secured to the pericardium at the level of the atrioventricular groove behind the heart. The anterior edge of the muscle flap was sutured to itself. An intramyocardial sensing lead (Model 033-572; Teletronics Pacing Systems, Inc.) was implanted in the anterior wall of the right ventricle. All leads were tunneled to a pocket under the skin and connected to an implantable cardiosynchronous myostimulator (Myostim, Model 722; Teletronics Pacing Systems, Inc.).

Muscle stimulation protocol. For the first 2 weeks after cardiomyoplasty, the latissimus dorsi muscle remained unstimulated to allow for a vascular recovery period (Fig. 1). During the following 2 weeks, the implanted myostimulator was programmed to deliver an electrical burst of 2.5 volts amplitude, 100 μ sec pulse width, one pulse per burst, with a 1:2 synchronization ratio. After the fifth week, voltage was increased to 5 volts. The number of pulses (35 Hz pulse frequency) per burst was progressively increased every 2 weeks to a maximum of 6 pulses per

Fig. 1. Schematic diagram of the pacing protocol for the latissimus dorsi muscle. After a 2-week vascular recovery period, the pacing protocol was started at 2.5 volts and increased to 5 volts from week 5. The number of pulses per burst was progressively increased to 6.

burst over a 6-week period. At 8 weeks, the muscle was regarded as being fully trained, and hemodynamic assessment was performed with 1:3 burst pacing at 6 pulses per burst with 100 msec of delay (Fig. 1). Each heart beat was categorized as a pre-assisted, assisted, or post-assisted beat depending on the timing of the burst stimulation.

Hemodynamic assessment. The animal was anesthetized in the same manner as previously described. A cutdown was performed in the left neck, and the carotid artery and jugular vein were isolated. The Millar catheter (5F) and a 12-electrode conductance catheter (6F; CardioDynamics, Rijnsberg, The Netherlands) were placed longitudinally in the LV cavity (Fig. 2). The conductance catheter was connected to a Sigma 5 signal conditioner-processor (CardioDynamics). We corrected our volume measurement using a standard procedure (hypertonic saline solution injection and blood resistivity measurement) while the myostimulator was off. However, we did not correct a gain factor, α . The jugular vein was cannulated with an inferior vena cava (IVC) occlusion catheter. LV pressure, volume, and electrocardiogram were displayed and digitized at 200 Hz on a personal computer during steady-state conditions and during transient IVC occlusion. Ventilation was held at end-expiration during the measurements. Data were stored on hard disk and analyzed off-line with custom-designed software.

Data analysis. All hemodynamic parameters during steady-state 1:3 burst pacing were calculated as the average of 4 to 5 beats in each group. The end-systolic pressure-volume relationship was assessed from each set of pressure-volume data during abrupt preload reduction during a transient IVC occlusion.

LV performance. The effect of dynamic compression resulting from cardiomyoplasty was assessed during steady-state conditions with traditional hemodynamic parameters such as LV end-systolic pressure, volume, stroke volume, and external work.

LV contractility. Global LV contractility was assessed with a relatively load-insensitive index: the end-systolic pressure-volume relationship.¹² To define the end-systolic pressure-volume relationship, end-systolic pressure and volume points were determined with an iterative technique for each cardiac cycle analyzed. A straight line was

fitted to these points by least squares linear regression, yielding the equation:

$$P_{es} = E_{max}(V_{es} - V_0)$$

where E_{max} and V_0 are the slope and volume axis intercept, respectively, of the end-systolic pressure-volume relationship, and P_{es} and V_{es} are the end-systolic pressure and volume, respectively. In addition, external work was computed as the integral of LV pressure and volume.

Derived LV energetics. The total mechanical energy generated by the left ventricle was approximated as PVA, which includes the area bounded by the ejection segment of the pressure-volume loop, the diastolic pressure-volume curve, and the end-systolic pressure-volume relationship.^{12, 16} Note that PVA reflects both potential energy (a triangular area to the left of the pressure-volume loop) and external work and is directly related to myocardial oxygen consumption by the left ventricle. Efficiency of energy transfer from PVA of the native heart to external work was mathematically derived¹⁷: Efficiency of energy transfer from PVA to external work = external work/PVA. This represents the ability of the ventricle to convert the total energy generated during systole to mechanical energy for external work. However, in assisted beats, overall PVA includes mechanical energy transferred from the latissimus dorsi muscle. Therefore overall PVA overestimates myocardial oxygen consumption. Then, this efficiency was calculated from the overall external work and the PVA of the native heart (see appendix).

LV filling and relaxation. LV filling and relaxation were assessed with the time constant of LV isovolumic pressure decline (τ) and the maximal rate of pressure decay ($-dP/dt \max$) during steady-state conditions between assisted and post-assisted beats. We also analyzed the end-diastolic pressure-volume relationship to evaluate the diastolic function of the left ventricle after a transient IVC occlusion.

Statistical analysis. Mean values of parameters among groups were compared by two-way analysis of variance when the data passed the normality test; otherwise the Mann-Whitney rank sum test was applied. Comparison between two groups was performed by two-tailed Stu-

dent's *t* test. Data are presented as mean $\pm$ standard deviation unless otherwise indicated.

Results

The effect of dynamic cardiac compression by cardiomyoplasty on LV performance. Fig. 3 shows a representative tracing of parameters measured during steady-state conditions and during transient occlusion of the IVC. As shown by arrows in Fig. 3, *A*, LV systolic volume with the assisted beats was smaller than that with pre-assisted and post-assisted beats, with a slight increase in end-systolic pressure during both steady-state conditions and during the IVC occlusion. There was not much difference in dP/dt among the three groups. When the steady-state beats were plotted on the pressure-volume diagram (Fig. 3, *B*), the end-systolic volume decreased from 93.1 ml to 87.4 ml during the assisted beats. As a result, the pressure-volume loop shifted to the left, and external work increased from 1773 to 2308 mm Hg $\cdot$ ml. The pressure-volume loops plotted during the IVC occlusion produced two different sets of end-systolic pressure-volume relationships (Fig. 3, *C*).

Table I averages the steady-state hemodynamic parameters during pre-assisted, assisted, and post-assisted contractions resulting from 1:3 burst pacing. During assisted beats, end-systolic volume significantly decreased by $4.5\% \pm 5.0\%$ ($p = 0.03$), and stroke volume increased by $35.9\% \pm 36.0\%$ ($p = 0.03$) compared to pre-assisted beats. T_{max} decreased by $15.5\% \pm 17.1\%$ ($p = 0.03$) although dP/dt max did not change. External work significantly increased by $9.7\% \pm 6.8\%$ ($p = 0.03$).

Effect on LV contractility. When the end-systolic pressure-volume relationships of pre-assisted and assisted beats were plotted (Fig. 3, *D*), the volume intercept (V_0) decreased from 10.8 ml to 0.8 ml; the slope (E_{max}) did not change (1.07 vs 1.06 mm Hg/ml, respectively).

Table II averages the slope and intercept of the end-systolic pressure-volume relationship. E_{max} decreased by $30.5\% \pm 27.8\%$ ($p = 0.02$); V_0 decreased by $144\% \pm 172\%$ ($p = 0.02$). As a result, the end-systolic pressure-volume relationship shifted to the left.

Effect on the efficiency of energy transfer. As shown in Fig. 4, dynamic cardiac compression applied via cardiomyoplasty increased overall external work by $9.7\% \pm 6.8\%$ ($p = 0.03$) although PVA of the native heart remained unchanged. As a result, the efficiency of energy transfer from native PVA to

Fig. 2. Schematic diagram of the experimental setting. SVC, Superior vena cava; AO, aorta; PA, pulmonary artery; RA, right atrium; LA, left atrium.

overall external work significantly increased by $7.6\% \pm 8.2\%$ ($p = 0.04$). This implies that cardiomyoplasty improved the efficiency of energy transfer by substituting the skeletal muscle energy as a burst support for the left ventricle.

Effect on LV filling. There was a small but significant difference of $1.0\% \pm 1.0\%$ ($p = 0.02$) in end-diastolic volume between assisted and post-assisted beats (Table I). Slow muscle relaxation after the assisted beat could impair venous return and reduce the next end-diastolic volume. When LV relaxation was assessed by LV isovolumic pressure decline (τ) and the maximal rate of pressure decay ($-dP/dt$ max), it was found not to be affected by burst pacing.

Fig. 5 shows the representative end-diastolic pressure-volume relationship. Although in this study we applied 100 msec of delay for burst pacing, which is longer than in the traditional clinical setting, there was no significant difference in the end-diastolic pressure-volume relationship. Therefore the reduction of the end-systolic volume would be related to the unloading effect rather than any compromise in LV filling.

Discussion

Conceptually, dynamic cardiomyoplasty has many features of an ideal cardiac support in the setting of

Fig. 3. Representative tracings of data acquired to derive the pressure-volume relationship during 1:3 muscle stimulation. **A**, LV volume and pressure with ECG synchronization signal and raw dP/dt values. Arrows indicate the assisted beats. **B**, Steady-state LV pressure-volume loop. Closed squares indicate values during the assisted beat. Open circles and triangles represent pre-assisted and post-assisted beats, respectively. **C**, Pressure-volume loops during transient IVC occlusion. Two different sets of end-systolic pressure-volume relationship were derived, as indicated with solid and dashed lines. The solid line is the end-systolic pressure-volume relationship of assisted beats. **D**, End-systolic pressure volume relationship. Closed squares represent end-systolic pressure-volume data points, and the solid line represents the end-systolic pressure-volume relationship of assisted beats. Open circles represent end-systolic pressure-volume data points, and the dashed line represents the end-systolic pressure-volume relationship of pre-assisted beats. Dotted lines indicate 95% confidence intervals of each relationship.

chronic heart failure. It has the advantages of being non-blood contacting and making use of a biologic power source. However, in contrast to significant improvement of clinical symptoms, only small objective hemodynamic changes have been reported.^{3-5, 18-21} Therefore the mechanism by which dynamic cardiac compression in cardiomyoplasty improves the LV performance and clinical symptoms is still unclear.

In many previous studies, comparisons were made between assisted and non-assisted beats in the 1:2 pacing mode.^{9, 20, 22, 23} When the average hemodynamic parameters in 1:2 mode were compared, it was not always sensitive enough to detect significant

differences. In addition, such a comparison has disadvantages including the possibility that slow muscle relaxation after the assisted beat could impair venous return, resulting in a reduction of the next end-diastolic volume. Therefore, in this study, comparison was made in the 1:3 mode, when the assisted beats cause no impairment of LV filling.

LV contractility and hemodynamic change. In this study, cardiomyoplasty improved LV performance by increasing stroke volume and external work without compromising LV filling. The increase in stroke volume and stroke work with a significant leftward shift of the end-systolic pressure-volume

Fig. 4. Changes in the efficiency of energy transfer to stroke volume. *EW*, External work; *C*, control; *O*, overall; *NS*, not significant; *N*, native heart; *EW/PVA*, efficiency of energy transfer to external work. * $p < 0.05$.

Table I. Hemodynamic change induced by cardiomyoplasty

	Pre-assisted	Assisted	Post-assisted	Statistics
End-systolic volume (ml)	118.0 ± 38.7	111.9 ± 34.8	118.5 ± 39.1	$p = 0.03$
End-systolic pressure (mm Hg)	96.8 ± 13.2	97.9 ± 11.8	97.3 ± 13.3	NS
Stroke volume (ml)	20.5 ± 6.3	26.6 ± 7.7	18.9 ± 5.8	$p = 0.03$
External work (mm Hg · ml)	1863 ± 339	2013 ± 393	1756 ± 298	$p = 0.03$
dP/dt max (mm Hg · sec ⁻¹)	1071 ± 280	1058 ± 263	1041 ± 266	NS
T_{max} (msec)	276 ± 21	259 ± 30	276 ± 23	$p = 0.03$
End-diastolic volume (ml)	138.5 ± 35.4	138.5 ± 35.7	137.4 ± 36.4	$p = 0.02^*$
End-diastolic pressure (mm Hg)	17.9 ± 2.6	18.0 ± 3.1	18.4 ± 1.7	NS*
-dP/dt max (mm Hg · sec ⁻¹)	1241 ± 284	1254 ± 297	1252 ± 292	NS*
Tau (msec)	54.6 ± 8.5	56.4 ± 9.7	55.1 ± 9.1	NS*

Values are means ± standard deviation.

NS, Not significant; dP/dt max, the maximal rate of pressure rise in the LV; T_{max} , time to end-systole; -dP/dt max, maximal pressure decay in the LV; Tau, time constant of isovolumic LV pressure decline.

*Comparison between assisted and post-assisted beats; all other comparisons are between pre-assisted and assisted beats.

relationship (decreased V_0) resulted in the observed decrease in E_{max} . E_{max} , the slope of the end-systolic pressure-volume relationship, is accepted as a load-independent index of LV contractility. However, because E_{max} practically decreased during assist, we found a discrepancy between LV performance and E_{max} .

Kawaguchi and coworkers^{24, 25} reported the enhancement of E_{max} with dynamic cardiac compression by using excised, cross-circulated dog hearts. E_{max} was calculated as a slope from V_0 to end-systole in the excised heart preparation; a linear regression was applied to calculate E_{max} in this study. Although we did not find any significant curvilinearity in the measured pressure-volume data, this relationship might be curvilinear in a subphysiologic pressure range. In that case, the linear regression analysis of pressure-volume data in the physiologic pressure range might result in the underestimation of V_0 and E_{max} .

They also reported the improvement of LV contractile efficiency calculated by PVA and myocardial

oxygen consumption.²⁶ Despite a discrepancy in E_{max} change with dynamic cardiac compression where E_{max} increased with dynamic cardiac compression although it reduced in this study, the effect of dynamic cardiac compression on the pressure-volume loop (leftward shift) in the in situ heart is as they expected. No matter how E_{max} changes with dynamic cardiac compression, mechanical efficiency should improve when the pressure-volume loop shifted to the left. Myocardial oxygen consumption is smaller for a given external work with cardiomyoplasty.

The pressure-volume relationship during cardiomyoplasty has been assessed in dogs and human beings. Although the slope change was not consistent, the consistent result has been the leftward shift of the end-systolic pressure-volume relationship.^{9, 20, 22, 23, 27} However, the physiologic role of the leftward shift of the pressure-volume relationship during dynamic cardiomyoplasty has not been discussed. Although PVA linearly correlates with the myocardial oxygen consumption under a steady

Fig. 5. Representative end-diastolic pressure-volume relationship during 1:3 burst pacing with cardiomyoplasty. There are no differences among the three relationships. Open circle, Pre-assisted; closed square, assisted; open triangle, post-assisted beats.

state contractile condition, the effect of a leftward shift of the pressure-volume relationship on the myocardial oxygen consumption in the in situ heart is unclear. When the heart is capable of generating a larger amount of external work resulting from the smaller end-diastolic volume, the wall tension must be smaller. Therefore when the native LV contractility did not change during assist, myocardial oxygen consumption will be reduced. In addition, because a part of the mechanical energy is provided by dynamic cardiac compression, an improvement in the oxygen cost of contractility is likely to result.²⁶ However, further study is needed to elucidate the effect of dynamic cardiac compression in cardiomyoplasty on myocardial oxygen consumption.

Benefit to the efficiency of energy transfer. There is a linear relationship between PVA and myocardial oxygen consumption. Therefore, although we did not directly measure the myocardial oxygen consumption in this study, we used PVA as an index of myocardial oxygen consumption. When the ratio of external work from PVA of the native heart to overall external work during assist is calculated, the ratio is found to be significantly smaller in the assisted beats (Fig. 4). In other words, in non-assisted beats, more PVA is needed to generate a given external work, or less external work is generated from a given PVA. This finding supports the myocardial oxygen-sparing effect of cardiomyoplasty.

To estimate myocardial oxygen consumption from PVA, assessment of PVA of the native heart is

Table II. Hemodynamic change induced by cardiomyoplasty

	Pre-assisted	Assisted	Statistics
$E_{\max}$ (mm Hg/ml)	1.53 ± 0.56	1.22 ± 0.53	$p = 0.02$
V_0 (ml)	48.8 ± 44.4	23.1 ± 42.2	$p = 0.02$
Correlation coefficient*	$0.998 - 0.961$ (0.991)	$0.97 - 0.692$ (0.943)	

Values are means $\pm$ standard deviation.

*Lists the range and median.

essential. Because there are difficulties in measuring the pressure transferred from the latissimus dorsi muscle to the left ventricle, the native heart's PVA cannot be estimated with traditional PVA calculation methods.¹⁶ However, when we assume the end-systolic pressure-volume relationship of the native heart is constant, the end-systolic pressure is derived from the end-systolic pressure-volume relationship; and end-systolic volume is measured. The native heart's PVA is reasonably derived by proportionally reducing the measured PVA depending on the estimated end-systolic pressure.

Effect on LV filling. In previous studies,^{6,7,9} a significant difference in end-diastolic volume was found between assisted and post-assisted beats. However, the magnitude of the difference between such beats was much smaller in this study. Therefore any possible effect of slow muscle relaxation in impairing LV filling is minimal. Enhanced stroke volume and external work by the compression is attributable to the mechanical work provided by the latissimus dorsi muscle instead of the preload effect operative in Starling's mechanism.

Although the magnitude of rise of the end-systolic pressure was small, the end-diastolic pressure-volume relationship should be elevated if delayed muscle relaxation in cardiomyoplasty impairs LV filling. However, cardiomyoplasty reduced end-diastolic volume in the way that the end-diastolic pressure-volume relationship remained unchanged. Therefore the possibility of impaired venous return related to slow muscle relaxation after the assisted beat is negated in this study. Instead, it indicates that dynamic cardiac compression has the potential to unload the left ventricle, which could be the mechanism of the girdling effect.²⁸

Heart failure model induced by microembolization. Our heart failure model takes a longer period to achieve stable heart failure (average, 14 ± 2 weeks) compared with the continuous ventricular pacing model. However, it is more comparable to

the cause of most human heart failure and is not readily reversible. A stable ejection fraction at less than 35% for 4 weeks confirmed this. In addition, staged microembolization induced global LV damage without severe mitral regurgitation although the coronary ligation heart failure model results in an LV aneurysm with/without mitral regurgitation.

Limitations. Volume measurement of the left ventricle with a conductance catheter involves a parallel volume component that is important to estimate the absolute LV volume. To exclude the parallel volume component, we corrected our volume measurement using hypertonic saline solution injection in the steady-state control status. We did not correct a gain factor, α . Because there is a possible error in absolute volume measurement in conductance methods, we compared the beat-to-beat data after IVC occlusion in 1:3 muscle stimulation. Because $E_{\max}$, PVA and external work are determined by relative volume from V_0 , the error of analysis resulting from the conductance volume measurement is negligible. However, there still is a possibility that muscle stimulation changes the parallel volume component during the contraction. Further study is needed to clarify this parallel volume change in the conductance method in cardiomyoplasty.

In conclusion, dynamic cardiac compression as used in cardiomyoplasty-enhanced LV pump performance without interrupting LV filling despite reduced contractility indices. The ratio of energy transfer from native PVA to overall external work suggested myocardial oxygen-sparing effect of a significant leftward shift of the end-systolic pressure-volume relationship in cardiomyoplasty.

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Appendix

End-systolic pressure generated by the native heart was calculated as the cross point of the pre-assisted end-systolic pressure-volume relationship and the assisted pressure-volume loop (P1 in Fig. 6). As the end-systolic pressure-volume data sit on the native heart's end-systolic pressure-volume relationship, the end-systolic pressure generated by the heart is calculated when the end-systolic volume is given. The native heart's pressure-volume loop was estimated from changes in pressure and volume in the

Fig. 6. Schematic diagram of PVA of the native heart (shaded area). *ESPVR*, end-systolic pressure-volume relationship; *P2*, end-systolic pressure of the assisted beat; *P-V*, pressure-volume; *P1*, end-systolic pressure of the native heart in the assisted beat; *EDPVR*, end-diastolic pressure-volume relationship; *V₀*, volume intercept of the end-systolic pressure-volume relationship.

native heart during the assisted beat. We hypothesized that the pressure generated by the native heart in the assisted beat is proportional to the assisted pressure according to the ratio: $P1/(\text{end-systolic pressure in assisted beat, } P2)$. With the V_0 of the pre-assisted beat and the native heart's pressure-volume loop, the PVA of the native heart in the assisted beat was calculated as shown in the shaded area of Fig. 6.