The effects of dynamic cardiac compression on ventricular mechanics and energetics

Role of ventricular size and contractility

The purpose of this study was to determine the role of ventricular size or contractility in the effectiveness of dynamic cardiac compression in terms of the pressure-volume relationship and myocardial oxygen consumption. In 10 isolated cross-circulated dog hearts, the ventricle was directly compressed during systole. For the volume run, measurements for slope of the end-systolic pressure-volume relation, pressure-volume area, external work, coronary blood flow, and myocardial oxygen consumption were achieved before and during a fixed amount of dynamic cardiac compression. Left ventricular volume was then increased while stroke volume was kept constant, and measurements were repeated. For the contractility run, after the control measurements were taken, left ventricular contractility was significantly increased or decreased by infusion of either dobutamine or propranolol into the coronary circulation. Measurements were repeated before and during dynamic cardiac compression at the control level of end-diastolic and stroke volumes. Dynamic cardiac compression significantly increased slope of the end-systolic pressure-volume relation, pressure-volume area, and external work ($p < 0.01$), whereas coronary blood flow and myocardial oxygen consumption were not affected. The increase in pressure-volume area caused by dynamic cardiac compression was greater with the larger volume. Despite the significant differences in the native left ventricular contractility, the increases in slope of the end-systolic pressure-volume relation, pressure-volume area, and external work did not differ among the three groups. We conclude that dynamic cardiac compression enhances left ventricular systolic function independent of ventricular contractility and without affecting coronary blood flow or myocardial oxygen consumption. Mechanical enhancement is more effective in the dilated heart. (J THORAC CARDIOVASC SURG 1994;107:850-9)

Osamu Kawaguchi, MD, Yoichi Goto, MD, Shiho Futaki, MD, Yuichi Ohgoshi, MD, Hitoshi Yaku, MD, and Hiroyuki Suga, MD,^a *Osaka and Okayama, Japan*

From the Department of Cardiovascular Dynamics, National Cardiovascular Center Research Institute, Osaka, and the Second Department of Physiology,^a Okayama University Medical School, Okayama, Japan.

Supported in part by grants-in-aid for scientific research (04237219, 04454267, 04557041) from the Ministry of Education, Science and Culture; research grants for cardiovascular diseases (3A-2, 4C-4) from the Ministry of Health and Welfare; and a grant from Japan Cardiovascular Research Foundation and Nakatani Electric Measuring Technology Association of Japan.

Received for publication Feb. 18, 1993.

Accepted for publication Aug. 19, 1993.

Address for reprints: Osamu Kawaguchi, MD, Department of Cardiovascular Dynamics, National Cardiovascular Center Research Institute, 5-7-1 Fujishirodai, Suita, Osaka 565, Japan.

Copyright © 1994 by Mosby-Year Book, Inc.

0022-5223/94 \$3.00 + 0 12/1/50930

Clinically, latissimus dorsi muscle wraps have been used as a therapeutic tool for patients with severe left ventricular dysfunction.¹⁻⁶ Experimental studies of cardiomyoplasty have shown significant increases in cardiac output,⁷⁻⁹ ejection fraction,¹⁰ rate of pressure rise,^{8, 10, 11} and stroke volume.^{7, 8, 11} In isometric contraction, cardiomyoplasty increased left-ventricular pressure.⁸ Right ventricular wrapping significantly increased right ventricular systolic pressure.^{12, 13} However, in the in situ heart no blood pressure change was noted by left ventricular wrapping¹⁴ unless the left ventricle was damaged.^{5, 9, 10} Although a great improvement in cardiac function has not been detected, most of the patients who have dilated ventricles have shown a remarkable improvement in activity.^{5, 6, 15} Patients with dilated cardiomyop-

athy or Chagas' disease have been considered to be good candidates for cardiomyoplasty.¹⁵ These findings suggest that the contractility or size of the ventricle potentially affects the effectiveness of cardiomyoplasty. However, the role of ventricular contractility or size in the effectiveness of cardiomyoplasty is still unknown.

Materials and methods

by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

The surgical procedure of the heart preparation has been described previously.²¹ In brief, two dogs were anesthetized with sodium pentobarbital (25 mg/kg intravenously) after premedication with ketamine hydrochloride (7 mg/kg intramuscularly). The dogs were heparinized (10,000 IU per dog intravenously). Arterial and venous cross-circulation cannulas were inserted into both common carotid arteries and into the right jugular vein of the larger dog (supporter), respectively. The chest of the smaller dog (heart donor) was opened midsternally with the animal supported by artificial ventilation. The left subclavian artery was cannulated and connected to the arterial cross-circulation tube from the support dog. The right ventricle was cannulated through the right atrial appendage to collect coronary venous blood flow. By ligation of the descending aorta, superior and inferior vena cavae, azygos vein, and pulmonary hili, the beating heart was isolated from the systemic and pulmonary circulations. The heart was excised from the chest after cross-circulation was started.

Indomethacin solution (0.3 mg/kg intravenously) was administered to prevent hypotension of the support dog after the initiation of cross-circulation. Although its effect on the stability of blood pressure of the support dog was substantial, its direct effects on cardiac contractility and VO_2 were negligible.²² Fresh blood collected from the donor dog or 10% dextran 40 solution was infused intravenously to the support dog if necessary. The lungs of the support dog were ventilated with room air mixed with oxygen to maintain the arterial pH, oxygenation, and carbon dioxide tension within physiologic ranges.

The left atrium was opened wide and all chordae tendineae were cut from the mitral valve leaflets. A water-filled latex balloon (unstressed volume of 60 ml) was placed in the left ventricle and secured to the mitral annulus. The balloon was connected to a servo-controlled pump system,²¹ which precisely controlled and accurately measured left ventricular volume (Fig. 1). A miniature pressure gauge (Konigsberg P-7, Konigsberg Instruments Inc., Pasadena, Calif.) was placed inside the apical end of the balloon to measure left ventricular pressure.

Fig. 2. Schematic illustration of ventricular P-V loop, systolic PVA, EW, and end-systolic potential energy (PE). ESPVR, End-systolic P-V relation; EDPVR, end-diastolic P-V relation; V_0 , volume axis intercept of ESPVR.

Total coronary blood flow (except for the small amount of left ventricular thebesian flow) was continuously measured with an electromagnetic flowmeter (MFV-2100, Nihon Kodan, Tokyo, Japan) placed in the middle of the venous drainage tube from the right ventricle. The thebesian blood flow was negligible (1% to 2%) compared with the total coronary blood flow. The difference in oxygen content between arterial and coronary venous blood was continuously measured with a PWA-200S oximeter (Erma Optical Works Ltd., Tokyo, Japan) by bypassing parts of both arterial and venous blood from the cross-circulation tubes through the cuvettes of the oximeter. The oximeter was calibrated against an IL-282 CO-Oximeter (Instrumentation Laboratory, Lexington, Mass.) at the beginning of each experiment. The coronary venous blood that passed through the oxygen cuvette was returned upstream of the flowmeter. The right ventricle was kept collapsed by continuous hydrostatic drainage of the coronary venous blood to minimize the contribution of right ventricular VO_2 to the measured total VO_2 .

Mean coronary perfusion pressure was 112 ± 23 (standard deviation) mm Hg during experiments. The temperature of the heart was maintained at 35° to 37° C with a heater around the arterial cross-circulation tube and under the box containing the heart. At the end of each experiment, the left ventricle (with the interventricular septum) and the right ventricle (free wall only) were weighed. They weighed 72.5 ± 11.0 gm and 21.5 ± 5.4 gm, respectively.

Creation of DCC. The ventricular portion of the isolated heart was placed in an airtight chamber (Fig. 1). The chamber was lined with a thin latex rubber sac to fit the ventricle. An air cylinder (Super Pump, SP 3892, VIVITRO System Inc., Victoria, British Columbia, Canada) was actuated in synchrony with the left ventricular epicardial electrogram. The stroke volume of the cylinder was set constant during each experiment to keep dynamic compression pressure inside the air chamber constant. Dynamic compression pressure was monitored with a Gould-Statham P-50 pressure transducer (Viggo-Spectramed Inc., Critical Care Division, Oxnard, Calif.). Negative compression pressure was not effective because this caused the rubber sac to detach from the epicardium. The heart was firmly

connected to the volume servo pump and preserved from a displacement during DCC. We tried several settings of DCC pressure before data collection and determined DCC pressure to induce 30% to 40% increases in end-systolic pressure at the beginning of each experiment.

Experimental protocol. Each heart was paced at a constant rate slightly above the natural sinus rhythm observed at the beginning of each experiment. Measurements were started after all tracings of ventricular pressure, coronary blood flow, and arteriovenous oxygen content difference were stabilized.

Volume run. In different settings of end-diastolic volume (13.6 to 21.1 ml [17.9 ± 3.3 ml] for the small volume run and 21.0 to 28.1 ml [26.5 ± 2.2 ml] for the large volume run), ejection contraction was produced at the same stroke volume (3.8 to 5.0 ml). We selected the baseline ventricular volumes for the large volume run to be as large as possible within the range at which DCC did not induce arrhythmia. For the small volume run, we reduced the effective ventricular volume (end-diastolic volume minus left ventricular unloaded volume, V_0) by 50%. End-systolic pressure, $E_{\max}$, PVA, external work (EW), coronary blood flow, and VO_2 were measured during steady-state contractions. DCC was started in each setting of end-diastolic volume and measurements were achieved during steady-state contractions.

Contractility run. Ejecting contraction was produced at moderate end-diastolic volume (20 to 30 ml [25.5 ± 2.9 ml]) and stroke volume (3.8 to 5.0 ml). End-diastolic and stroke volumes were kept constant in each heart. End-systolic pressure, $E_{\max}$, PVA, EW, coronary blood flow, and VO_2 were measured during steady-state contractions before and during DCC (control run). Then, dobutamine (2.5 to 5.0 $\mu\text{g}/100$ gm left ventricular weight/min) was administered into the coronary arterial tube of each heart with an infusion pump (model STC-521, Terumo, Tokyo, Japan) to enhance left ventricular contractility. Measurements were achieved during steady-state contractions at the same end-diastolic and stroke volumes as in the control run. DCC was then started and measurements were repeated (dobutamine run). In 7 of 10 hearts that were subjected to both the control and dobutamine runs, propranolol (1.0 to 2.0 $\mu\text{g}/100$ gm left ventricular weight/min) was administered into the coronary arterial tube after the cessation of dobutamine administration. $E_{\max}$ was reduced to about half the control $E_{\max}$ level. When contractions became stable under propranolol administration, measurements were repeated before and during DCC (propranolol run).

Data analysis. All data were sampled at 2 msec intervals for 2 seconds, analyzed on-line with a signal processor (7T18, NEC San-ei, Tokyo, Japan), and stored on a floppy disk. Measurements were repeated twice at an interval of 0.5 to 1 minute under the same steady-state condition to confirm reproducibility of the data. The means of the two measurements were used for analysis.

Left ventricular mechanics. The contractile state of the beating left ventricle was assessed by ventricular systolic elastance, $E(t)$, where $E_{\max}$ was the maximum value of the ratio $E(t) = P(t)/[V(t) - V_0]$.¹⁶ $P(t)$ and $V(t)$ are left ventricular instantaneous pressure and volume and V_0 is the left ventricular volume at which peak isovolumic pressure is zero. Fig. 2 shows a schematic P-V diagram. $E_{\max}$ is the slope of the straight end-systolic P-V relationship line connecting V_0 and the left upper corner of each P-V trajectory. $E_{\max}$ was normalized for

Fig. 3. A, Simultaneous tracings of left ventricular pressure (LVP), left ventricular volume (LVV), dynamic compression pressure (DCP), left ventricular epicardial electrocardiogram (ECG), coronary blood flow (CBF), and coronary arteriovenous O₂ content difference (AVOX) in control and DCC contractions. P-V loops of control and DCC contractions. Dashed diagonal lines are E_{max} lines of these contractions.

Fig. 4. Comparison of incremental variables by DCC in small and large volume runs. ΔEW , Increases in external mechanical work; ΔPVA , increases in PVA; NS, statistically insignificant; L, large volume; S, small volume. Means $\pm$ standard error of mean are indicated ($n = 10$). $*p < 0.01$.

100 gm left ventricular weight. PVA is the area bounded by the end-systolic and end-diastolic P-V relations and the systolic segment of the P-V trajectory.¹⁷⁻²¹ PVA represents the total mechanical energy generated by a ventricular contraction on the basis of the time-varying elastance model of the ventricle.^{19,20} It consists of EW within the P-V loop and mechanical potential energy on the origin side of the loop. Potential energy is generated during contraction and has been assumed to dissipate as heat during relaxation.¹⁹

PVA of the beating left ventricle was determined by summing all small triangular areas swept by the lines connecting V_0 and instantaneous P-V data points drawing a P-V trajectory during every 2 msec interval between the onset of contraction and the time of E_{max}.^{16,17} The crescent area between the actual end-diastolic P-V curve and the straight line connecting V_0 and the end-diastolic P-V point was computed by approximating the end-diastolic P-V curve by a third power function.¹⁷ This area

was added to the sum of the small triangular areas to complete PVA. End-diastole was determined from the R wave of the epicardial electrocardiogram.

Myocardial VO_2 . VO_2 of the heart was determined as the product of mean coronary blood flow per minute and arteriovenous oxygen content difference; this value was divided by the heart rate to obtain VO_2 per beat. It was normalized for 100 gm left ventricular weight after subtracting the unloaded right ventricular free wall VO_2 from the measured total VO_2 in each heart. The unloaded right ventricular VO_2 was calculated as (total unloaded VO_2) $\times$ (right ventricular free wall weight)/(total ventricular weight). The total unloaded VO_2 was measured at V_0 with zero PVA.

Statistics. Differences of mean values between the contractions before and during DCC were analyzed by the paired t test. Two-way analysis of variance was applied to compare individual variables among the control, dobutamine, and propranolol

Table I. The role of ventricular volume in the left ventricular mechanics and energetics during DCC

	Small volume (n = 10)		Large volume (n = 10)	
	Baseline	DCC	Baseline	DCC
EDP (mm Hg)	4.7 ± 1.7	2.1 ± 1.3	7.1 ± 1.5	6.0 ± 1.2
EDV (ml)	17.9 ± 1.2	17.8 ± 1.2	26.5 ± 0.8	26.5 ± 0.8
ESP (mm Hg)	42 ± 8	71 ± 10*	91 ± 11	124 ± 12*
ESV (ml)	13.2 ± 3.3	13.4 ± 1.3	21.8 ± 0.8	21.9 ± 0.9
E _{max} (mm Hg/(ml/100 gm LV))	5.3 ± 1.4	9.3 ± 3.5*	4.4 ± 0.4	6.0 ± 0.5*
PVA (mm Hg · ml/100 gm LV)	516 ± 128	861 ± 170*	1561 ± 243	2104 ± 273*
EW (mm Hg · ml/100 gm LV)	282 ± 60	500 ± 74*	607 ± 89	806 ± 92*
BVO ₂ (ml O ₂ /beat/100 gm LV)	0.0358 ± 0.0047	0.0339 ± 0.0024	0.0477 ± 0.0043	0.0506 ± 0.0046*

Values are mean ± standard error of the mean. BVO₂, Myocardial oxygen consumption of the left ventricle per beat; EDP, end-diastolic pressure; EDV, end-diastolic volume; ESP, end-systolic pressure; ESV, end-systolic volume; LV, left ventricular weight.

*p < 0.05 versus each baseline value by two-way analysis of variance.

Table II. The role of ventricular contractile state in left ventricular mechanics and energetics during DCC

	Control (n = 10)	DCC	Dobutamine (n = 10)	Dobutamine + DCC	Propranolol (n = 7)	Propranolol + DCC
EDP (mm Hg)	9.0 ± 4.8	7.9 ± 4.2	9.8 ± 3.0	8.8 ± 3.6	12.7 ± 3.5	9.8 ± 3.3
ESP (mm Hg)	96 ± 27	131 ± 25*	133 ± 31†	163 ± 26*	60 ± 21†	91 ± 20*
E _{max} (mm Hg/(ml/100 gm LV))	4.3 ± 1.4	5.8 ± 1.5*	5.8 ± 1.5†	7.1 ± 1.5*	2.6 ± 0.8†	3.8 ± 0.8*
PVA (mm Hg · ml/100 gm LV)	1642 ± 586	2261 ± 590*	2297 ± 5753†	2842 ± 739*	1026 ± 460†	1634 ± 504*
EW (mm Hg · ml/100 gm LV)	605 ± 220	823 ± 210*	849 ± 263†	1042 ± 257*	330 ± 158†	549 ± 106*
CBF (ml)	65.2 ± 22.2	65.3 ± 22.5	94.6 ± 39.0†	89.4 ± 36.6	74.9 ± 28.0†	73.2 ± 26.3
BVO ₂ (ml O ₂ /beat/100 gm LV)	0.0487 ± 0.0111	0.0550 ± 0.0118*	0.0654 ± 0.0144†	0.0612 ± 0.0152	0.0374 ± 0.0128†	0.0388 ± 0.0110
DCP (mm Hg)	3 ± 3	36 ± 7*	2 ± 3	34 ± 11*	2 ± 3	37 ± 5

Values are mean ± standard error of the mean. BVO₂, Myocardial oxygen consumption of the left ventricle per beat; CBF, coronary blood flow; DCP, dynamic compression pressure; EDP, end-diastolic pressure; ESP, end-systolic pressure; LV, left ventricular weight.

*p < 0.05 versus each baseline value by two-way analysis of variance.

†p < 0.05 versus control value by two-way analysis of variance.

runs. When analysis of variance showed statistical significance by *F* test, mean values were compared by the least significant difference method. Probability values smaller than 0.05 were considered statistically significant. Data are presented as mean ± the standard deviation unless otherwise indicated.

Results

The effect of volume. Fig. 3, *A* shows representative tracings of the control and DCC measurements. End-diastolic and stroke volumes were kept constant at 28.0 ml and 4.8 ml, respectively. DCC was applied during systole in synchrony with the left ventricular epicardial electrocardiogram. In this example, DCC increased end-systolic pressure from 113 mm Hg to 146 mm Hg, while it did not change end-diastolic pressure or coronary blood flow. Fig. 3, *B* shows the P-V loops of the control and DCC contractions shown in Fig. 3, *A*. DCC increased E_{max} from 4.0 mm Hg/(ml/100 gm left ventricular weight) to

4.9 mm Hg/(ml/100 gm left ventricular weight). As a result, PVA and EW increased from 2435 mm Hg · ml/100 gm left ventricular weight and 856 mm Hg · ml/100 gm left ventricular weight in the control contraction to 3032 mm Hg · ml/100 gm left ventricular weight and 1117 mm Hg · ml/100 gm left ventricular weight in the DCC contraction, respectively.

Table I shows the changes in hemodynamic parameters and left ventricular mechanics and energetics in the volume run. End-diastolic and end-systolic volumes were kept constant in each run. In the small volume run, DCC significantly increased end-systolic pressure by 86% ± 58%, E_{max} by 79% ± 61%, PVA by 105% ± 67%, and EW by 115% ± 74%. In the large volume run, DCC significantly increased end-systolic pressure by 40% ± 18%, E_{max} by 39% ± 19%, PVA by 40% ± 20%, and EW by 37% ± 21%. Although VO₂ significantly increased in the

Fig. 5. Comparison of incremental variables by DCC in control, dobutamine, and propranolol runs. ΔDCP , Increases in dynamic compression pressure; ΔE_{max} , increases in E_{max} ; ΔEW , increases in EW; ΔPes , increases in end-systolic pressure; ΔPVA , increases in PVA; ΔVO_2 , increases in myocardial oxygen consumption; NS, statistically insignificant. Means plus or minus standard error of mean are indicated ($n = 7$).

large volume run, it was practically small ($6\% \pm 5\%$). There was no significant difference in VO_2 in the small volume run.

Fig. 4 compares the magnitudes of increases in E_{max} , PVA, and EW with DCC between the small and large volume runs. Although the increase in E_{max} was greater in the small volume run, the increase in EW was not different between the small and large volume runs as shown in Fig. 4, C, and the increase in PVA was greater in the large volume run.

The effect of contractility. Table II summarizes variables of left ventricular mechanics and energetics in the contractility run. In the control run, dynamic compression pressure averaged 32.2 ± 6.7 mm Hg. DCC significantly increased E_{max} by $41\% \pm 21\%$ ($p < 0.01$). PVA and EW significantly increased by $44\% \pm 21\%$ and $43\% \pm 23\%$ during the control plus DCC contractions, respectively ($p < 0.01$). Coronary blood flow was the same in the control plus DCC contractions. Although DCC significantly increased VO_2 , the difference was practically small ($5\% \pm 7\%$). In the dobutamine run, dynamic compression pressure averaged 31.6 ± 12.0 mm Hg. Although left ventricular contractility before DCC was enhanced by a dobutamine administration, DCC further increased E_{max} by $26\% \pm 13\%$ ($p < 0.01$). PVA and EW significantly increased by $27\% \pm 14\%$ and $26\% \pm 12\%$ during the dobutamine plus DCC contractions, respectively ($p < 0.01$). DCC did not affect coro-

nary blood flow or VO_2 . In the propranolol run, dynamic compression pressure averaged 32.9 ± 6.1 mm Hg. DCC significantly increased E_{max} by $54\% \pm 23\%$ ($p < 0.01$). PVA and EW significantly increased by $76\% \pm 40\%$ and $87\% \pm 45\%$ in the propranolol plus DCC contractions, respectively ($p < 0.01$). Again, coronary blood flow and VO_2 were not significantly different between the propranolol and propranolol plus DCC contractions.

Fig. 5 compares the dynamic compression pressure and the magnitudes of increases in E_{max} , PVA, and EW with DCC in seven hearts that were subjected to all three contractile states. Dynamic compression pressures were not significantly different among the three runs (Fig. 5, A). Although E_{max} values before DCC were significantly different among the three runs (control, 4.8 ± 1.2 mm Hg/[mm Hg/100 gm left ventricular weight]; dobutamine, 6.2 ± 1.2 mm Hg/[mm Hg/100 gm left ventricular weight]; propranolol, 2.6 ± 0.8 mm Hg/[mm Hg/100 gm left ventricular weight]; $p < 0.05$), the increases in E_{max} with DCC did not significantly differ among the control, dobutamine, and propranolol runs (Fig. 5, B). DCC increased end-systolic pressure by 31 ± 4 mm Hg, 27 ± 6 mm Hg, and 29 ± 5 mm Hg in the control, dobutamine, and propranolol runs, respectively (Fig. 5, C); these values did not significantly differ from that of the dynamic compression pressure value in each run. In addition, the increases in PVA and EW were not different among these three runs (Fig. 5, D and E).

Fig. 6. A, Schematic diagram of changes in P-V loop during DCC. Dashed area represents native heart PVA during DCC. B and C, Schematic diagram of changes in P-V loop at constant stroke volume in small-sized and dilated hearts. D and E, Schematic diagram of changes in P-V loop at constant end-diastolic volume in small-sized and dilated hearts. P-V loop under DCC is estimated from native end-systolic P-V relationship. Dashed area in B through E represents decrease in native heart PVA induced by DCC. Dotted area represents increased PVA during DCC. eES, Enhanced end-systolic P-V relation line; ED, end-diastolic P-V curve; nES, native end-systolic P-V relation line; V_0 , volume axis intercept of ES.

Discussion

The role of ventricular size or contractility in the effectiveness of cardiomyoplasty has not been previously studied. The ventricular size would be important to the success of cardiomyoplasty. Patients with dilated cardiomyopathy or Chagas' disease have significantly improved left ventricular function with cardiomyoplasty.^{5,6,15} Among the patients undergoing this procedure, those with dilated hearts seemed to derive the greatest benefit. On the other hand, hemodynamic improvement has not been shown to be as marked in patients with preoperative diagnoses of left ventricular aneurysm or ischemic cardiomyopathy.^{3,4} With the fixed amount of DCC pressure at fixed end-diastolic and stroke volumes for the volume run, the increase in PVA induced by DCC was greater in the large volume run without affecting coronary blood flow and VO_2 . VO_2 conservation by DCC may be different between smaller-sized and dilated hearts in the in situ heart for a given DCC.

A previous study suggested a significant leftward shift of the P-V loops during cardiomyoplasty.²³ Although we

used fixed end-diastolic and stroke volumes in this study, the role of left ventricular volume in the effectiveness of cardiomyoplasty in the in situ heart can be explained in the P-V diagram. Fig. 6 illustrates the schematic diagrams of P-V loop change during DCC. Cardiomyoplasty predominates systolic augmentation by dynamically altering the left ventricular loading condition rather than by increasing the developed pressure. As a result, the P-V loop shifts from area ABCD to GHIJ instead of changing to AEFD as illustrated in Fig. 6 A. Because unchanged VO_2 suggests that the native heart contractile state stays the same during DCC, the native heart PVA can be estimated as the dashed area. For a given mechanical enhancement achieved by DCC, leftward shift of the P-V loop is greater in the dilated heart than in the smaller-sized heart for a given end-systolic pressure and the constant stroke volume as shown in Fig. 6, B through C. The greater reduction of the end-diastolic volume in the dilated heart results in the greater increase in ejection fraction than in the smaller heart. Furthermore, although EW stays the same between them, the decreases in the native heart PVA (dashed area) in the dilated heart are greater than in the smaller-sized heart. Because PVA correlates linearly with VO_2 ,¹⁷⁻²¹ the VO_2 conservation would be thus greater in the dilated heart than in the smaller-sized heart. Even if end-diastolic volume remains constant, increases in stroke volume and ejection fraction are larger in the dilated heart than in the smaller-sized heart, as shown in Fig. 6, D through E, and decreases in native heart PVA are greater in the dilated heart. Increases in EW (dotted area) are much greater in the dilated heart than in the smaller-sized heart.

On the other hand, the mechanical energy provided by DCC can be estimated in the P-V diagram by subtracting the native heart PVA from the total PVA (area BEFV₀C at fixed end-systolic and diastolic volumes in Fig. 7, A) as illustrated in Fig. 7. When ventricular loading conditions are affected by DCC, the mechanical energy necessary for DCC to generate the same magnitude of EW is greater in the dilated heart than in the small-sized heart, as illustrated in Fig. 7, B and C. When the heart is too large, cardiomyoplasty could not generate such a large mechanical energy because of a limited power supply from skeletal muscle. We speculate that this would be the mechanism by which the effectiveness of cardiomyoplasty would be lost when a heart gets too large. Further study would be necessary to clarify the real effect of left ventricular volume on left ventricular energetics and muscle work in the ejecting heart.

In terms of the native left ventricular contractility in modulating DCC effect, we originally hypothesized that the relationship between the dynamic compression pres-

Fig. 7. A, Schematic diagram of changes in P-V loop during DCC. B and C, Schematic diagram of changes in P-V loop at constant stroke volume in small-sized and dilated hearts. P-V loop under DCC is estimated from native end-systolic P-V relationship. Dashed area represents mechanical energy provided by DCC. eES, Enhanced end-systolic P-V relation line; ED, end-diastolic P-V curve; nES, native end-systolic P-V relation line; V_0 , volume axis intercept of ES.

sure and the increase in intraventricular pressure might be affected by the stiffness of the ventricle. If the ventricular wall is rigid, external pressure applied by DCC would not be easily transmitted to the intraventricular pressure. Therefore we anticipated that the systolic stiffness (i.e., contractility) of the ventricle would have a negative influence on the effectiveness of DCC. However, despite significant differences in E_{max} before DCC among the three runs, DCC applied during systole enhanced left ventricular contractility (E_{max}) and mechanical performance (PVA and EW) without increasing the metabolic requirement of the myocardium (coronary blood flow and VO_2) at constant end-diastolic and stroke volumes. Similar magnitudes of the increases in E_{max} , PVA, and EW among the three different contractility runs mean that DCC has a constant effect on ventricular systolic function independent of ventricular contractility. Thus the unanticipated finding is that the contractile state of the ventricle does not affect the effectiveness of DCC.

In the in situ heart, it is difficult to separately measure pressure generated by enforced muscles from that generated by the native heart. Therefore the effects of cardiomyoplasty have been estimated by eliminating native heart performance (for example, by comparing parameters between muscle stimulation on and off^{4, 7, 12} or by fibrillating the heart¹⁴). However, DCC induced by skeletal muscle stimulation itself would also affect the ventricular loading conditions²³ and result in changes in

native heart work. Therefore improved function achieved by DCC cannot be correctly assessed by simply comparing data with the stimulation on and off. Such a protocol may result in underestimation of the effects of DCC on pump function.

The performance of skeletal muscles failed to produce enough pressure to maintain total circulation in the fibrillating heart.¹⁴ However, coincidence of the increase in end-systolic pressure with dynamic compression pressure in the present study indicates that mechanical enhancement of the ventricular systolic function by DCC is directly related to the external pressure applied by DCC. When the skeletal muscle is paced in synchrony with cardiac cycles, 30 mm Hg of pressure would increase ventricular pressure from 60 mm Hg to 90 mm Hg (Table II, propranolol run). Mechanical enhancement was shown to be simple summation of the native heart contractility and the work applied by DCC when DCC was given synchronously with cardiac contractions. Therefore the insufficient effectiveness of DCC in the fibrillating heart might be related to other factors such as impaired diastolic filling of the fibrillating heart, because the P-V relation of the fibrillating heart is located left and upward of the normal diastolic P-V relation.²⁴

Although mechanical enhancement of systolic pump function induced by DCC was consistent despite the differences in native heart contractility at fixed end-diastolic and stroke volumes, the effect of DCC on cardiac per-

formance may be different in the in situ heart. Our previous study has demonstrated that the effects of DCC are characterized as (1) enhancement of mechanical performance reflected by increased end-systolic pressure, PVA, and EW at constant end-diastolic and stroke volumes or (2) saving of VO_2 for a given EW.²⁵ In the right ventricle or the injured left ventricle, DCC applied by cardiomyoplasty has been reported to primarily enhance mechanical performance, resulting in a significant increase in end-systolic pressure.^{12, 13} However, our previous study suggested that DCC can save VO_2 regardless of left ventricular loading conditions even when a significant pressure increase is not observed.²⁵

There are two different mechanisms involved in the effect of DCC on coronary blood flow in the in situ heart: (1) a direct effect of squeezing action of DCC on epicardial coronary arteries, which might potentially decrease coronary blood flow and (2) an indirect effect via an elevation of coronary perfusion pressure caused by enhancement of left ventricular systolic function, which may potentially increase coronary blood flow. In the present study, unchanged coronary blood flow during DCC suggests that squeezing action of DCC does not compromise coronary circulation. Because most coronary arterial flow occurs during diastole, it is reasonable that DCC synchronized with cardiac cycles has little effect on coronary blood flow.²⁶ In contrast to DCC in the present study, a muscle wrapped around the heart would have nonuniformity and diastolic tension, which could potentially affect coronary circulation.

With regard to the indirect effect of DCC, coronary perfusion pressure was maintained constant by the support dog independent of left ventricular systolic function in the present study. In contrast, coronary perfusion pressure is generated by the left ventricle in the in situ heart, and coronary blood flow correlates with perfusion pressure when perfusion pressure is critically low.²⁷ Thus an enhancement of left ventricular systolic function during DCC will increase coronary perfusion pressure and, hence, blood flow. Because increased coronary perfusion pressure or blood flow has been reported to enhance left ventricular contractility, enhanced left ventricular pump function would also modify left ventricular contractility via coronary circulation and result in further improvement of pump function of the in situ failing heart.²⁸⁻³⁰ Therefore further study will be needed to clarify the effect of real cardiomyoplasty on coronary circulation.

Because the right ventricle was vented in our preparation, DCC was applied uniformly over the left ventricle. When DCC is applied in the in situ heart by dynamic cardiomyoplasty, muscle squeezes the heart predominantly in a circumferential fashion. Furthermore, because

part of the left ventricular wall is covered with right ventricle, the effect of DCC would be modified in the in situ heart. Although a recent study revealed the orientation of the skeletal muscle affects the effectiveness of cardiomyoplasty,³¹ quantitative assessment of the effect of the orientation of the skeletal muscle remains to be studied.

In conclusion, DCC applied during systole enhanced left ventricular systolic pump function regardless of baseline contractility of the ventricle and without affecting coronary blood flow or VO_2 . Mechanical enhancement by DCC is greater in larger hearts.

Dr. Kawaguchi acknowledges the continuous encouragement by Professor Toshio Abe of the Department of Cardiothoracic Surgery of Nagoya University School of Medicine.

REFERENCES

1. Carpentier A, Chachques JC. Myocardial substitution with a stimulated skeletal muscle: first successful clinical case [Letter]. *Lancet* 1985;1:1267.
2. Chachques JC, Grandjean PA, Carpentier A. Latissimus dorsi dynamic cardiomyoplasty. *Ann Thorac Surg* 1989; 47:600-4.
3. Magovern GJ, Heckler FR, Park SB, et al. Paced latissimus dorsi used for dynamic cardiomyoplasty of left ventricular aneurysms. *Ann Thorac Surg* 1987;44:379-88.
4. Macgovern GJ, Heckler RF, Park SB, et al. Paced skeletal muscle for dynamic cardiomyoplasty. *Ann Thorac Surg* 1988;45:614-9.
5. Molteni L, Almada H, Ferreira R. Synchronously stimulated skeletal muscle graft for left ventricular assistance. *J THORAC CARDIOVASC SURG* 1989;97:439-46.
6. Moreira LFP, Stolf NGA, Bocchi EA, et al. Latissimus dorsi cardiomyoplasty in the treatment of patient with dilated cardiomyopathy. *Circulation* 1990;82:IV257-63.
7. Chachques JC, Grandjean P, Schwartz K, et al. Effect of latissimus dorsi dynamic cardiomyoplasty on ventricular function. *Circulation* 1988;78(Suppl):III203-16.
8. Chachques JC, Grandjean PA, Tommasi JJ, et al. Dynamic cardiomyoplasty: a new approach to assist chronic myocardial failure. *Life Support Sys* 1987;5:323-7.
9. Kao RL, Christlieb IY, Magovern GJ, Park SB, Magovern GJ Jr. The importance of skeletal muscle fiber orientation for dynamic cardiomyoplasty. *J THORAC CARDIOVASC SURG* 1990;99:134-40.
10. Chagas ACP, Moreira LFP, da Luz PL, et al. Stimulated preconditioned skeletal muscle cardiomyoplasty: an effective means of cardiac assist. *Circulation* 1989;80(Suppl): III202-8.
11. Dewar ML, Drinkwater DC, Wittnich C, Chiu RC-J. Synchronously stimulated skeletal muscle graft for myocardial repair: an experimental study. *J THORAC CARDIOVASC SURG* 1984;87:325-31.
12. Soberman MS, Wornom IL III, Justicz AG, et al. Latissimus dorsi dynamic cardioplasty of the right ventricle:

- potential use as a partial myocardial substitute. *J THORAC CARDIOVASC SURG* 1990;99:817-27.
13. Guiraudon GM, Morell T, Boughner DR, et al. Right ventricular free wall dynamic cardiomyoplasty on a canine chronic right ventricular failure model: primary report. In: Chiu RC-J, Bourgeois I, eds. *Transformed muscle for cardiac assist and repair*. Mt. Kisco, N.Y.: Futura, 1990; 209-18.
  14. Anderson WA, Anderson JS, Acker MA, et al. Skeletal muscle grafts applied to the heart: a word of caution. *Circulation* 1988;78 (Suppl):III80-90.
  15. Jatene AD, Moreira LFP, Stolf NAG, et al. Left ventricular function changes after cardiomyoplasty in patients with dilated cardiomyopathy. *J THORAC CARDIOVASC SURG* 1992;103:573-81.
  16. Suga H, Sagawa K. Instantaneous pressure-volume relationships and their ratio in the excised, supported canine left ventricle. *Circ Res* 1974;35:117-26.
  17. Suga H, Hisano R, Goto Y, Yamada O, Igarashi Y. Effect of positive inotropic agents on the relation between oxygen consumption and systolic pressure volume area in canine left ventricle. *Circ Res* 1983;53:306-18.
  18. Suga H. Ventricular energetics. *Physiol Rev* 1990;70:247-77.
  19. Suga H. Total mechanical energy of a ventricle model and cardiac oxygen consumption. *Am J Physiol* 1979;236: H498-505.
  20. Suga H, Hayashi T, Shirahata M, Suehiro S, Hisano R. Regression of cardiac oxygen consumption on ventricular pressure-volume area in dog. *Am J Physiol* 1981;240: H320-5.
  21. Suga H, Hayashi T, Suehiro S, Hisano R, Shirahata M, Ninomiya I. Equal oxygen consumption rates of isovolumic and ejecting contractions with equal systolic pressure-volume areas in canine left ventricle. *Circ Res* 1981;49: 1082-91.
  22. Goto Y, Slinker BK, Lewinter MM. Decreased contractile efficiency and nonmechanical energy cost in hyperthyroid rabbit heart: relation between O_2 consumption and systolic pressure-volume area or force-time integral. *Circ Res* 1990;66:999-1011.
  23. Lee KF, Dignan RJ, Parmar JM, et al. Effects of dynamic cardiomyoplasty on left ventricular performance and myocardial mechanics in dilated cardiomyopathy. *J THORAC CARDIOVASC SURG* 1991;102:124-31.
  24. Yaku H, Goto Y, Futaki S, Ohgoshi Y, Kawaguchi O, Suga H. Equivalent pressure-volume area accounts for oxygen consumption of fibrillating heart. *Am J Physiol* 1991;261:H1534-44.
  25. Kawaguchi O, Goto Y, Futaki S, Ohgoshi Y, Yaku H, Suga H. Mechanical enhancement and myocardial oxygen saving by synchronized dynamic left ventricular compression. *J THORAC CARDIOVASC SURG* 1992;103:573-81.
  26. Katz SA, Feigl EO. Systole has little effect on diastolic coronary artery blood flow. *Circ Res* 1988;62:443-51.
  27. Mosher P, Ross J Jr, McFate PA, Shaw RF. Control of coronary blood flow by an autoregulatory mechanism. *Circ Res* 1964;14:250-9.
  28. Suga H, Goto Y, Yasumura Y, et al. O_2 consumption of dog heart under decreased coronary perfusion and propranolol. *Am J Physiol* 1988;254:H292-303.
  29. Sunagawa K, Maughan WL, Friesinger G, Guzman P, Change MS, Sagawa K. Effects of coronary arterial pressure on left ventricular end-systolic pressure-volume relation of isolated canine heart. *Circ Res* 1982;50:727-34.
  30. Goto Y, Slinker BK, Lewinter MM. Effects of coronary hyperemia on E_{max} and oxygen consumption in blood-infused rabbit hearts: energetic consequences of Gregg's phenomenon. *Circ Res* 1991;68:482-92.
  31. Kao RL, Christlieb IY, Magovern GJ, Park SB, Magovern GJ Jr. The importance of skeletal muscle fiber orientation for dynamic cardiomyoplasty. *J THORAC CARDIOVASC SURG* 1990;99:134-40.