The Effect of Cardiomyoplasty on Left Atrial Function in Experimental Canine Models*

Yoshio Ootaki, MD; Masayoshi Okada, MD; Takuro Tsukube, MD; and Yutaka Okita, MD

**Background:** Cardiomyoplasty utilizes the latissimus dorsi muscle to boost the failing ventricle. However, the mechanism for clinical improvement still remains controversial. We have previously shown that left ventricular contraction was improved in the long-term periods after cardiomyoplasty in the normal canine heart model and in the dilated failing heart model. On the other hand, right ventricular filling was impaired if a rapid volume loading test was employed in the long-term period after cardiomyoplasty. The purpose of the present study was to determine whether cardiomyoplasty impairs the left atrial function and affects ventricular filling.

**Method:** Eleven mongrel dogs that had undergone cardiomyoplasty (study group, n = 5) or a sham operation (control group, n = 6) were studied for 12 weeks postoperatively. An IV 4.5% albumin solution (10 mL/kg) was infused into the right atrium, and hemodynamic changes in right cardiac catheterization and left atrial volume (LAV) were obtained by two-dimensional echocardiography. Atrial function was assessed by hemodynamic changes in Doppler echocardiography and hormonal changes.

**Results:** Stroke volume was significantly increased, from 17.0 ± 4.4 to 21.1 ± 7.0 mL, respectively, before and 15 min after albumin infusion in the control group (p < 0.05). Heart rate and cardiac output were significantly increased, from 131.2 ± 18.1 to 152.0 ± 9.8 beats/min and 2.72 ± 1.29 to 4.03 ± 1.67 L/min, respectively, before and 15 min after albumin infusion in the study group (p < 0.05). No changes were observed in mean right atrial pressure and pulmonary capillary wedge pressure. LAV and atrial natriuretic peptide (ANP) levels increased significantly, from 5.8 ± 2.1 to 8.5 ± 3.8 mL and 22.5 ± 7.5 to 44.5 ± 31.7 pg/mL, respectively, before and 15 min after albumin infusion in the control group (p < 0.05). In the study group, LAV and ANP levels were also increased, from 10.1 ± 2.4 to 12.7 ± 2.8 mL and 64.2 ± 60.6 to 232.6 ± 272.2 pg/mL, respectively, before and 15 min after albumin infusion (p < 0.05). The peak velocities and the time-velocity integrals in the pulmonary venous flow of the systolic and diastolic waves, as well as their ratios (systolic to diastolic peak velocity ratio and systolic to diastolic time-velocity integral ratio) showed no significant differences between the two groups.

**Conclusions:** Cardiomyoplasty preserves left atrial filling and transport function; therefore, cardiomyoplasty may also activate ANP production by stimulating the atrium in the long-term period after cardiomyoplasty.

**Key words:** atrial function; atrial natriuretic peptide; cardiomyoplasty; volume loading

**Abbreviations:** AFF = atrial filling fraction; Ai = time-velocity integral of atrial filling; ANP = atrial natriuretic peptide; A wave = atrial filling wave; CHF = congestive heart failure; Ei = time-velocity integral of early ventricular filling; E wave = early filling wave; LAV = left atrial volume; LDMF = latissimus dorsi muscle flap; MPAP = mean pulmonary artery pressure; MRAP = mean right atrial pressure; PCWP = pulmonary capillary wedge pressure; peak E/A = ratio of peak E-wave and peak A-wave velocities; S/D ratio = systolic to diastolic peak velocity ratio; S/Di ratio = systolic to diastolic time-velocity integral ratio; Tdi = diastolic time-velocity integral;

Despite recent advances in medical and surgical therapy, congestive heart failure (CHF) continues to be a major cause of morbidity and mortality. Cardiomyoplasty utilizes the latissimus dorsi muscle flap (LDMF) to boost the failing ventricle, and approximately 700 procedures have been performed worldwide since Carpentier and Chachques reported it in 1985. Generally, the patients seem to have improved physical capacity, but objective measures do not always reflect this improvement, and the mechanism for clinical improvement remained...
controversial. In experiments, enhancement of left ventricular function with this procedure has been proved in both long-term models and heart failure models. In previous studies, we have also found that cardiomypoplasty improved left ventricular function in doxorubicin-induced dilated canine hearts. However, if rapid volume loading was applied, right ventricular compliance was decreased in the heart with cardiomypoplasty, and the mechanism for this impairment was suggested as the constrictive effect of the LDMF surrounding the right ventricle. In cardiomypoplasty, as the LDMF is wrapped around both ventricles and also covers part of the left atrium, left atrial pressure and left atrial volume (LAV) both might vary over a considerable range; if so, atrial contribution to the ventricular filling might be decreased. We therefore investigated whether LAV and left atrial pressure may increase with rapid albumin loading, and the effect of cardiomypoplasty on atrial contraction.

**Materials and Methods**

Eleven adult mongrel dogs, weighing 10 to 15 kg, were used in this study. All animals received humane care in compliance with the guidelines for animal experimentation at Kobe University School of Medicine.

**Experimental Preparation**

Five adult mongrel dogs (the study group) were anesthetized and prepared for the following sterile surgical procedures. General anesthesia was induced with ketamine hydrochloride, 5 mg/kg, and thiamylal sodium, 30 mg/kg, and was maintained with doses of sodium pentobarbital given IV as needed. Endotracheal intubation and positive-pressure mechanical ventilation (MA-1; Acoma; Tokyo, Japan) were performed. Then, 1.5 to 2.5% of sevoflurane was introduced to maintain anesthesia. Perioperative antibiotics were administered routinely. The dogs were placed in a right decubitus position, and a longitudinal skin incision was made from the left axilla toward the costovertebral angle. The left latissimus dorsi muscle was dissected free from all attachments, except for the neurovascular pedicle, which was carefully preserved for good circulation and nerve response. A 3-cm portion of the lateral aspect of the second rib was resected to permit passage of the dissected muscle flap into the thoracic cavity. The proximal tendinous humeral insertion of the LDMF was secured to the lateral aspect of the second rib to prevent tension on the neurovascular bundle. A left anterolateral thoracotomy was performed in the fifth intercostal space using the same anesthetic technique with pericardectomy through a left anterolateral thoracotomy in the fifth intercostal space using the same anesthesia. The effects of cardiomypoplasty were then studied in these five dogs. Six adult mongrel dogs (the control group) underwent a sham operation with pericardectomy through a left anterolateral thoracotomy in the fifth intercostal space using the same anesthesia.

**Hemodynamic Evaluation**

For each hemodynamic measurement, the dogs were anesthetized with IV sodium pentobarbital, 30 mg/kg, and permitted to breathe spontaneously with diminished eyelash reflex. Each study took place after the dogs had rested supine in a quiet laboratory for a minimum of 20 min at room temperature (20° to 24°C). Under sterile conditions, a 7.5F Swan-Ganz catheter (Baxter Healthcare; Irvine, CA) was advanced from the femoral vein to the pulmonary artery under fluoroscopic guidance. Pressure was monitored continuously on an oscillograph (model 363; NEC San-ei Instruments; Tokyo, Japan). Mean right atrial pressure (MRAP), mean pulmonary arterial pressure (MPAP), and pulmonary capillary wedge pressure (PCWP) were measured before and 15 min after volume loading. In order to volume load, a 4.5% albumin solution was infused into the central vein at a dose of 10 mL/kg for 5 min. Cardiac output was measured by the thermodilution technique using five 5-mL injections of 0.9% saline solution (1° to 5°C). All hemodynamic parameters were monitored using a polygraph (model 363; NEC San-ei Instruments) and were continuously recorded (model 8M14; NEC San-ei Instruments).

**Echocardiographic Evaluation**

An echocardiographic study was performed (Toshiba SSA-260A CE Sector Scan; Toshiba Medical; Tokyo, Japan), and routine parasternal long-axis and parasternal short-axis views were obtained with the transducer placed at the level of the right sternal border, usually in the third intercostal space, and recorded on videotape at 30 frames per second. End-systolic LAV was calculated using the single-plane area-length method before and after volume loading, which has been described in detail elsewhere. Briefly, LAV was calculated as follows: LAV = πD²L/6, where D = minor-axis length of the left atrium and L = major-axis length of the left atrium.

Pulsed Doppler echocardiography was performed using a 2.5-MHz or 5-MHz imaging transducer before volume infusion. The study was carried out from the apical four-chamber view with the sample volume positioned at the level of the tip of the mitral valvular leaflets. Subsequently, the sample volume was placed at the entrance of the right superior pulmonary vein connecting to the left atrium. Flow-velocity spectra were recorded on videotape at a display speed of 100 mm/s. To characterize the transmitial flow, the peak velocities of the early filling wave (E wave) and atrial filling wave (A wave) and their ratio (peak E/A) were determined. The total diastolic time-velocity integral (Tdi) and the time-velocity integral of early ventricular filling (Ei) were measured directly by planimetry of the diastolic mitral flow-velocity spectra. The time-velocity integral of atrial filling (Ai) was calculated as the difference between the integrals (Ai = Tdi − Ei). Each measurement was obtained as an average of three to five cardiac cycles. The atrial filling fraction (AFF), as an expression of atrial transport flow, was then derived as the percentage of the Ai in relation to the total Tdi (AFF = 100 × Ai/Tdi). From the pulmonary venous flow-velocity spectra, the peak velocities of the systolic and diastolic flow components were obtained. The time-velocity integrals of the systolic and the diastolic flow components were also measured by planimetry of the flow-velocity spectra waves. The systolic to diastolic peak velocity ratio (S/D ratio) and the systolic to diastolic time-velocity integral ratio (Si/Di) ratio were determined.

**Evaluation of the LDMF Wrapping**

At the end of the study, the dogs were killed. The degree of LDMF wrapped around the heart is expressed by the ratio of the
length of the external circumference of both ventricles covered with LDMF to the length of the total external circumference of both ventricles (the cover ratio), as we previously reported.12

Measurement of Plasma Level of Atrial Natriuretic Peptide

Plasma atrial natriuretic peptide (ANP) was measured by radioimmunoassay. Briefly, venous blood samples were obtained from the pulmonary artery through the Swan-Ganz catheter before and 15 min after albumin infusion. Blood samples were then transferred to chilled disposable tubes containing aprotextin (500 kallikrein inactivator units/mL) and immediately placed on ice and centrifuged at 4°C as previously reported. One milliliter of plasma was extracted on a C18 Sep Pak cartridge (Waters Associates; Milford, MA). The cartridges were prewashed with 10 mL of methanol and 10 mL of 4% acetic acid. After the plasma was applied, the cartridges were washed three times with 5 mL of 0.1% vol/vol trifluoroacetic acid, and the absorbed peptide was eluted with 2 mL of 60% acetonitrile/0.1% trifluoroacetic acid into plastic tubes. The extracts were dried down and reconstituted in 0.1% vol/vol trifluoroacetic acid, and the absorbed peptide was eluted with 2 mL of 60% acetonitrile/0.1% trifluoroacetic acid into plastic tubes. The extracts were dried down and reconstituted in a 1.0-mL buffer and measured by radioimmunoassay with use of a specific antibody against α-ANP (Shionoria-ANP, Tokyo, Japan).

Statistical Analysis

Statistical analyses were performed with a statistical program (Statview 4.0; Cricket Software; Philadelphia, PA). All values were expressed as mean ± SD. Analysis of variance for repeated measures was performed to determine the significance of changes of hemodynamic, echocardiographic, and humoral variables. A paired t test was used to assess the differences in hemodynamics, LAV, and serum ANP levels before and 15 min after albumin infusion. Differences were considered significant at p < 0.05.

RESULTS

Hemodynamic Parameters

The effects of volume loading in the control group on hemodynamic parameters are shown in Table 1. After rapid infusion of the 4.5% albumin solution, stroke volume was significantly increased. However, the MRAP, MPAP, PCWP, heart rate, and cardiac output did not change significantly. Table 2 summarizes hemodynamic changes in the study. Volume loading induced a significant increase in the heart rate and cardiac output. However, the MRAP, MPAP, PCWP, and stroke volume did not change significantly.

LAV

End-systolic LAV measurements before and after volume loading are shown in Table 3. Rapid infusion of the 4.5% albumin solution produced a significant increase in both the control and study groups, compared with preinfusion values. In addition, LAV before albumin infusion was higher in the study group, as compared to that in the control group, respectively; and LAV after albumin infusion was higher in the study group, as compared to that in the control group, although statistical significance was not shown (p = 0.07). These results suggested that the left atrial filling was well preserved in cardiomyoplasty and that the left atrium could dilate sufficiently by an acute volume loading.

Transmitral Flow Velocity

The E wave and A wave of the transmitral flow were detected in all dogs in both groups. The peak velocities of the E wave and A wave across the mitral valve, the peak E/A, the time-velocity integrals of the E wave and A wave across the mitral valve, and the AFF are shown in Table 4. There were no significant differences between the two groups.

Pulmonary Venous Flow

The peak velocities and the time-velocity integrals of the systolic and diastolic waves, as well as their ratios (S/D ratio and Si/Di ratio), are shown in Table 5. There were no significant differences between the two groups.

Structure Changes of the LDMF

In all models, LDMF around the heart did not cover both atria. In each case, the cover ratio was >30% (Fig 1)

Table 1—Cardiac Catheterization Data of Control Group*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Preinfusion Values</th>
<th>Values 15 min After Infusion</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRAP, mm Hg</td>
<td>0.7 ± 0.5</td>
<td>1.7 ± 1.5</td>
<td>NS</td>
</tr>
<tr>
<td>MPAP, mm Hg</td>
<td>13.7 ± 4.6</td>
<td>17.3 ± 3.2</td>
<td>NS</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>5.5 ± 2.4</td>
<td>6.3 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>151.2 ± 2.7</td>
<td>155.3 ± 31.1</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>2.52 ± 0.08</td>
<td>3.29 ± 1.22</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>17.0 ± 4.4</td>
<td>21.1 ± 7.0</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD. NS = not significant.

Table 2—Cardiac Catheterization Data of Study Group*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Preinfusion Values</th>
<th>Values 15 min After Infusion</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRAP, mm Hg</td>
<td>0.6 ± 0.9</td>
<td>1.8 ± 2.0</td>
<td>NS</td>
</tr>
<tr>
<td>MPAP, mm Hg</td>
<td>10.6 ± 3.4</td>
<td>14.0 ± 4.5</td>
<td>NS</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>4.4 ± 2.9</td>
<td>7.4 ± 5.0</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>131.2 ± 18.1</td>
<td>152.0 ± 9.8</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>2.72 ± 1.29</td>
<td>4.03 ± 1.67</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>20.4 ± 7.8</td>
<td>26.9 ± 12.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD. See Table 1 for expansion of abbreviation.
Control 5.8 6 6 Study 10.1 6 6 other alternatives, such as cardiac transplantation and many patients die await-

Surgical reduction of cardiac size to improve heart failure for end-stage CHF is being popularized by Batista and associates13 with a partial ventriculectomy operation. Although an early in-

Plasma Level of ANP

ANP levels before and after albumin infusion in the two groups are shown in Table 6. After rapid infusion, plasma ANP was significantly elevated in both groups as compared to the preinfusion values. Also, ANP levels in the study group were higher than those of the control group, although statistical significance was not shown.

Table 3—End-Systolic LAV*

<table>
<thead>
<tr>
<th>Groups</th>
<th>Preinfusion Values, mL</th>
<th>Values 15 min After Infusion, mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5.8 ± 2.1</td>
<td>8.5 ± 3.8†</td>
</tr>
<tr>
<td>Study</td>
<td>10.1 ± 2.4†</td>
<td>12.7 ± 2.8†§</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
†p < 0.05, before vs after infusion.
‡p < 0.05, control group vs study group.
§Not significant, control group vs study group.

Table 4—Peak Velocity and Time-Velocity Integral of Transmitral Doppler Echocardiographic Flow*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak E wave, cm/s</td>
<td>35.0 ± 3.7</td>
<td>51.8 ± 6.8†</td>
</tr>
<tr>
<td>Peak A wave, cm/s</td>
<td>44.7 ± 8.0</td>
<td>47.0 ± 8.7†</td>
</tr>
<tr>
<td>Peak E/A</td>
<td>1.27 ± 0.23</td>
<td>1.12 ± 0.08†</td>
</tr>
<tr>
<td>Ei, cm</td>
<td>4.45 ± 0.34</td>
<td>4.35 ± 0.57†</td>
</tr>
<tr>
<td>Ai, cm</td>
<td>2.79 ± 0.72</td>
<td>3.29 ± 0.73†</td>
</tr>
<tr>
<td>AFF, %</td>
<td>38.1 ± 7.4</td>
<td>42.9 ± 3.3†</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
†Not significant, control group vs study group.

Table 5—Peak Velocity and Time-Velocity Integral of Pulmonary Venous Flow*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak systolic, cm/s</td>
<td>26.7 ± 4.0</td>
<td>35.7 ± 8.3†</td>
</tr>
<tr>
<td>Peak diastolic, cm/s</td>
<td>42.0 ± 2.0</td>
<td>46.0 ± 3.5†</td>
</tr>
<tr>
<td>S/D ratio</td>
<td>0.64 ± 0.1</td>
<td>0.77 ± 0.14†</td>
</tr>
<tr>
<td>Systolic, cm</td>
<td>3.9 ± 1.2</td>
<td>5.1 ± 0.8§</td>
</tr>
<tr>
<td>Diastolic, cm</td>
<td>5.6 ± 0.8</td>
<td>7.2 ± 1.6†</td>
</tr>
<tr>
<td>S/D ratio</td>
<td>0.69 ± 0.14</td>
<td>0.74 ± 0.17†</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
†Not significant, control group vs study group.

Discussion

End-stage CHF carries a very poor prognosis, and patients have few options once conventional surgical options have failed and medical therapy has not been effective. Although cardiac transplantation remains the procedure of choice for end-stage CHF refractory to medical treatment, its usefulness is limited by donor supply and recipient suitability. Because of strict selection criteria and donor shortage, only a small percentage of end-stage CHF patients undergo cardiac transplantation and many patients die awaiting organ transplantation. Other alternatives, such as ventricular-assist devices, are hampered by their dependence on external power sources and the inherent problems of thromboembolism, infection, and cost. Surgical reduction of cardiac size to improve heart failure for end-stage CHF is being popularized by Batista and associates13 with a partial ventriculectomy operation. Although an early in-
crease in ejection fraction has been noted in many surviving patients,14,15 the long-term outcome after this operation and its mechanism are still unknown.

The efficacy of cardiomyoplasty, which relies on an electrically simulated autologous skeletal muscle to augment cardiac function, is currently being investigated both experimentally and clinically. Although patients have reported a subjective improvement in exercise tolerance, the hemodynamic benefit derived from cardiomyoplasty has yet to be consistently demonstrated.5–8 The effect of cardiomyoplasty is mainly considered to protect further dilatation of the left ventricle (the so-called "girdling effect"), rather than direct cardiac assistance.16–18 We have previously shown that left ventricular function continued to be enhanced by stimulated cardiomyoplasty for 6 weeks after cardiomyoplasty in the experimental canine model.9 After adhesion of both LDMF and myocardium, the effect of cardiomyoplasty on cardiac assistance was remarkably enhanced, and disturbance of the left ventricular systolic function was not observed in the study.9 However, we have also shown that right ventricular filling in nonstimulated cardiomyoplasty was impaired when rapid volume loading was employed.10 In that study, the MRAP and right ventricular end-diastolic pressure were significantly increased within 1 min after volume loading in the nonstimulated cardiomyoplasty group. These conflicting results, enhancing left ventricular function but disturbing right ventricular filling, raised the question of the effect of cardiomyoplasty on the atrial function, and we hypothesize that cardiomyoplasty might have an adverse effect on the atrial functions by impairing the atrial passive dilatation or reducing the response of ANP production. Therefore, we investigated the atrial function by means of changes in hemodynamics, the atrial volume, and serum ANP levels after volume loading.

In the present study, the MRAP and MPAP normalized within 15 min after albumin infusion in the study group. These results were not consistent with our previous study,10 in which the MRAP and...
MPAP were significantly increased within 1 min after volume loading in the cardiomyoplasty group. These differences were explained by the time differences of hemodynamic measurements after albumin infusion. In the present study, after an initial increase of right atrial pressure and right ventricular pressure were observed, we used hemodynamic changes 15 min after albumin infusion, when initial hemodynamic changes were stabilized and atrial volume became stable. Moreover, and most importantly, the serum ANP level was shown to increase enough 15 min after volume loading, and serum ANP played an important role in atrial function.

With respect to left atrial function, as we described before, pericardial constraint is one of the most important factors influencing both ventricular function and left atrial dilatation performance. As the skeletal muscle inevitably adheres to the epicardium in cardiomyoplasty, it may have effects similar to the pericardial constraint seen in constrictive pericarditis. Also, we concluded that impaired right ventricular filling was caused by external constraint resulting from cardiomyoplasty. However, although initial increases in MRAP, right ventricular pressure, pulmonary arterial pressure, and PCWP were observed, there was no significant increases 15 min after volume loading in cardiomyoplasty. This change correlated with increases in LAV and cardiac output in cardiomyoplasty.

The study group responded to volume with increased heart rate and cardiac output, with stroke volume remaining the same, possible because of decreased compliance of the left atrium that is compensated by increased heart rate. However, the left atrium could dilate easily after albumin infusion, whereas left atrial pressure was not changed. Furthermore, heart rate was influenced by various factors, and the ANP levels of the study group increased surprisingly. The findings of the present study suggest that the left atrium can maintain sufficient dilatation in response to increases of volume loading in cardiomyoplasty, and cardiomyoplasty does not impair left atrial compliance.

These results are well consistent with autopsy specimen findings, which demonstrated that the LDMF covers both ventricles, resulting in external constraint of the ventricles. On the contrary, the left atrium has no direct external influence from the skeletal muscle. Accordingly, it is reasonable to say that cardiomyoplasty may not impair the distensibility of the left atrium during volume loading.

The left atrial contribution to ventricular filling is not only determined by the mechanical left atrial contraction, but is also affected by diastolic function of the left ventricle. In a heart with increased ventricular stiffness, diastolic filling of the ventricle is impaired. Elevated left ventricular end-diastolic pressure diminishes the pressure gradient between the left ventricle and the left atrium, thus impairing passive filling of the ventricle, which occurs in early diastole. Ventricular filling is compensated by atrial contraction in late diastole, leading to a larger A wave, and thus a smaller peak E/A. In the present study, there were no significant differences between the two groups in peak velocities of E wave and A wave, and peak E/A. These results show that cardiomyoplasty may not impair the distensibility of the left ventricle.

We also measured the AFF as an index of atrial

### Table 6—Plasma Level of ANP*

<table>
<thead>
<tr>
<th>Groups</th>
<th>Preinfusion Values, pg/mL</th>
<th>Values 15 min After Infusion, pg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>22.5 ± 7.5</td>
<td>44.5 ± 31.7†</td>
</tr>
<tr>
<td>Study</td>
<td>64.2 ± 60.6†</td>
<td>232.6 ± 272.2†‡</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
†p < 0.05, before vs after.
‡Not significant, control group vs study group.

![Figure 1. Photograph of the autopsy specimen in the study group. RV = right ventricle; LV = left ventricle.](image.png)
contribution to ventricular filling. Although it is theoretically possible to quantify the relative amount of flow occurring at a given phase in diastole by measuring the flow-velocity integral at the level of the atrioventricular annulus, precise assessment of the flow volume requires accurate measurement of annular area and the assumption that the annular size remains constant, which is not the case. Therefore, we expressed the relative ratio of flow (AFF) rather than actual flow by sampling ventricular inflow at the level of the leaflet tips in this study. The AFF was 38.1% in the control group and 42.9% in the study group in the present study, a value similar to that in the canine model of another study. These results show that cardiomyoplasty may not impair the atrial contribution to ventricular filling.

Pulmonary venous systolic inflow occurs with atrial relaxation simultaneously with the reduction of left atrial pressure, whereas diastolic inflow occurs with ventricular relaxation and rapid transmural filling of the ventricle. Systolic inflow is closely related to left atrial pressure and atrial compliance. Diastolic inflow follows the pattern of mitral inflow into the left ventricle. During this time, the left atrium acts as a passive conduit between the pulmonary veins and the left ventricle. In the present study, there is no significance in the pulmonary venous flow pattern between the two groups. These results show that cardiomyoplasty may not impair the atrial reservoir function.

In all autopsy specimens, the cover ratio of the study group was > 30% (Fig 1). These results show that, although the LDMF of our models were unstimulated for 3 months, the LDMF might be viable, as we previously reported. ANP is a hormone with a wide range of potent biological effects, including natriuresis, diuresis, vasodilatation, and inhibition of the renin-angiotensin-aldosterone system and the sympathetic nervous system. There is a positive linear relation between serum ANP levels and atrial pressure, indicating that atrial pressure or stretch plays an important role in regulating secretions of ANP. Our data also pointed out that serum ANP in the study group after cardiomyoplasty was higher than that in the control group. These elevations of ANP might reflect the relative ratio of flow (AFF) rather than actual flow by sampling ventricular inflow at the level of the leaflet tips in this study. The AFF was 38.1% in the control group and 42.9% in the study group in the present study, a value similar to that in the canine model of another study. These results show that cardiomyoplasty may not impair the atrial contribution to ventricular filling.

In conclusion, our results suggest that cardiomyoplasty preserves left atrial filling and transport function. In addition, cardiomyoplasty may activate ANP production by stimulating the atrium in the long-term phase.

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