Effect of Disrupting the Mitral Apparatus on Left Ventricular Function in Dogs

Hideo Shintani, MD, and Stanton A. Glantz, PhD

Background. The importance of the mitral apparatus to left ventricular function has been suggested in clinical studies. The effect of disruption of the mitral apparatus on left ventricular diastolic and systolic properties has not been fully documented.

Methods and Results. We investigated the end-diastolic and end-systolic pressure-volume and stroke work--end-diastolic volume relations and measured the isovolumic relaxation time constant ($\tau_e$) during nonfilling beats before and after disruption of the mitral apparatus under different loading conditions in 14 dogs using our recently developed volume-clamping technique for the in situ left ventricle. Disruption of the mitral apparatus increased left ventricular diastolic equilibrium volume ($V_{de}$) without changing the slope of the end-diastolic pressure-volume relation ($S_d$) and increased end-systolic pressure-volume relation dead volume ($V_{sa}$) and volume-axis intercept of stroke work--end-diastolic volume relation ($V_{max}$) without changing the slopes of these relations (maximum elastance, $E_{max}$, and $S_{max}$). Disruption of the mitral apparatus increased $\tau_e$.

Conclusion. Disruption of the mitral apparatus increases the equilibrium volume without changing left ventricular diastolic stiffness or contractility and slows left ventricular relaxation. These results support and help explain the clinical observation that it is desirable to maintain the mitral apparatus during mitral valve replacement surgery. (Circulation 1993;87:2001–2015)

Key Words • left ventricle • mitral valve

The importance of the mitral apparatus to left ventricular function has been suggested in many clinical studies. In 1964, Lillehei et al. introduced a technique of mitral valve replacement preserving the mitral leaflets and chordae tendineae that reduced surgical mortality and improved postoperative left ventricular systolic function and overall clinical outcome. Recently, surgical mitral valve replacement with preserving the mitral apparatus has been revived. Support for this procedure also comes from animal studies. Sarris et al. demonstrated that cutting the chordae tendineae depressed left ventricular systolic function in ejecting dog hearts as quantified with the end-systolic elastance and slope of stroke work--end-diastolic volume relation. Similarly, Yun et al. observed a decline in segmental left ventricular function after dividing the chordae tendineae as assessed by the slope of the segmental stroke work--end-diastolic wall thickness relation. They also reported that the influence of the anterolateral papillary muscle chordae tendineae predominated in local left ventricular systolic function. In contrast, Salter et al. reported that there was no significant change in systolic function measured by the end-systolic pressure-volume or stroke work--end-diastolic volume relations after detaching and reattaching the chordae tendineae. The effect of disrupting the mitral apparatus on left ventricular diastolic properties has not been extensively studied. Sarris et al. indicated that the stiffness coefficient of the end-diastolic pressure-volume relation did not change after cutting the chordae tendineae, but the effect of disrupting the mitral apparatus on left ventricular early diastolic properties, including relaxation and restoring forces, was not studied. Rozich et al. found that end-diastolic and end-systolic volumes fell in patients who had mitral valve replacement with chordal preservation but not in those whose valves were replaced with chordal transection.

To determine whether disruption of the mitral apparatus changes the left ventricular diastolic properties, we investigated the end-diastolic pressure-volume relation and measured the time constant of isovolumic relaxation of nonfilling beats before and after disrupting the mitral apparatus under different loading conditions in dogs using in situ left ventricular volume clamping.

To determine whether disruption of the mitral apparatus decreases left ventricular contractility, we studied the end-systolic pressure-volume relation and stroke work--end-diastolic volume relations.

Disrupting the mitral apparatus increased the diastolic equilibrium volume without affecting the diastolic stiffness as assessed by the slope of the end-diastolic pressure-volume relation and increased the time constant of isovolumic relaxation, indicating slower relaxation. Disruption also increased the volume-axis intercepts of the end-systolic pressure-volume and stroke work--end-diastolic volume relations, but it did not change left ventricular contractility as assessed by the slopes of these relations.

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Methods

Surgical Preparation

Fourteen adult mongrel dogs (mean±SD kg, 27.7±3.7) were premedicated with 0.15 mL/kg Innovar-Vet s.c. (20 mg droperidol, 0.4 mg fentanyl), administered 3 mg/kg pentobarbital sodium i.v., intubated, and put on mechanical ventilation with a mixture of oxygen (60%) and nitrous oxide (40%). Anesthesia was maintained with 0.5–1.5% methoxyflurane. The dogs were placed in the left-side-up position, and the left thorax was opened with ribs 5–7 removed. The pericardium was opened along the left phrenic nerve, and the heart was suspended in a pericardial cradle. The descending aorta was snared with 3-mm-wide tape (Umbilical Tape, Ethicon, Inc., Somerville, N.J.) to permit increasing aortic pressure by tightening the snare.

Insertion of the Mitral Valve and Volume Clamping

The hearts were instrumented with a remote-controlled mitral valve to clamp left ventricular volume in situ as previously described.11 A waterproof funnel made of a polyester-cotton blend fabric was sutured around the left atrial appendage with a running suture. A 1-0 braided polyester-fiber purse-string suture with the point of the needle blunted was pushed into the right atrium at its junction with the inferior vena cava, pushed out from the superomedial portion of the right atrium close to the left atrium, and anchored on the left atrial wall. After 200 units/kg heparin, the left atrium was opened, and our modified 25-mm Björk-Shiley mitral valve (Figure 1) was inserted through the funnel into the left atrium and secured by the purse-string suture between the native mitral valve and the pulmonary veins. The valve was improved over that described earlier11 by adding a bevel to the lower plastic ring that holds the valve in place to affix it more tightly just above the mitral annulus and provide a better seal as well as making the other changes shown in Figure 1. To obtain complete isovolumic relaxation throughout diastole, the control unit was set to trigger on the ECG R wave, wait until mid systole (80 msec delay from the R wave triggered at a heart rate of 100 beats per minute), and then occlude the valve for 400 msec.

The construction of the artificial valve and the surgical technique for implanting it very close to the native valve were designed to minimize regurgitation between the native mitral valve and the artificial valve. Close examination of the volume signals during filling volume clamping for two adjacent beats showed that the volume remained flat during clamping and confirmed that there was no or very little regurgitation or leakage between or around the artificial valve.

Methods of Manipulation and Measurement

Pressures were measured in the left ventricle, left atrium, and right ventricle by 5F Millar catheters in-
serted through the left ventricular apex, the funnel, and the right atrial appendage to obtain high-fidelity pressure recordings. In 11 of the 14 dogs, left ventricular volume was measured with a 7F eight-electrode conductance catheter12-14 (Webster Laboratories, Inc., Baldwin, Calif.; Stiching Leycom-Sigma-5 Controller, The Netherlands) placed in the left ventricle through the left carotid artery. Proper positioning of the conductance catheter was checked from the segmental volume signal contours throughout the experiment and confirmed postmortem.

The conductance catheter volume signal includes an offset, the parallel conductance volume, $\alpha V_C$, and a gain, $1/\alpha$, which relates the conductance catheter volume signal to the true left ventricular volume, which generally are assumed to be constant in a given animal. (Most investigators assume $\alpha$ constant for all animals.) The techniques for estimating the parallel conductance volume and $\alpha$ are not particularly accurate, so we previously recommended working with the raw conductance catheter volume signal,15,16 particularly when one is interested in changes in volume rather than absolute volume, as in this study. Although this approach avoids introducing additional uncertainty in the measurements associated with estimating $1/\alpha$ and $\alpha V_C$, it yields numerical values that appear too large compared with the actual left ventricular volume measured by more conventional technologies, such as ultrasonic crystals. To facilitate direct comparisons of the data we collected with the conductance catheter and ultrasonic crystals, we applied a constant calibration to the conductance catheter to match the average baseline end-diastolic and end-systolic volumes observed in all dogs instrumental with ultrasonic crystals in these experiments to obtain $1/\alpha=1.1$ and $\alpha V_C=32 \text{ mL}$. These values are similar to those obtained in our laboratory in direct calibrations of the conductance catheter against angiographic volumes in individual dogs of the same size.15

To assess changes in the shape and volume17-21 of the left ventricle and to validate conclusions based on the conductance catheter, left ventricular dimensions were measured in three approximately orthogonal axes using ultrasonic crystals with a Triton technology sonomicrotometer in five of the 14 dogs (Figure 2), two of which also were instrumented with the conductance catheter. In these dogs, the data were collected using each method with the other one turned off to avoid electrical interference. The anteroposterior dimension was measured by a pair of hemispherical crystals sewn to the epicardium adjacent to the anterior descending coronary arteries. The septal-free wall dimension was measured by a hemispherical crystal sewn to the epicardium of the lateral free wall and a cylindrical crystal tunneled 1-2 cm into the septum from a point adjacent to the left anterior descending coronary artery. Postmortem examination verified that this crystal was always in the septum. These two crystal dimensions approximated a planar section perpendicular to the left ventricular long axis, located one half to two thirds of the distance from the apex to the base. The base crystal was sewn to the left ventricle adjacent to the origin of the left circumflex coronary artery, and the spiral crystal was sewn to the epicardium at the left ventricular apex. Left ventricular volume ($V$) was modeled as two half-ellipsoids15:

$$V = \frac{\pi}{6} \cdot A S L$$

where $A$, $S$, and $L$ are the anteroposterior, septum-free wall, and base-apex (long-axis) dimensions. Note that this volume is based on epicardial dimensions without any correction for the (constant) left ventricular wall volume.

To obtain pressure-volume relations, we decreased preload by occluding the superior and inferior venae cavae with balloon catheters (8F Fogarty venous thrombectomy catheter) inserted from the external jugular and femoral veins into the superior vena cava and inferior vena cava, respectively. To be acceptable for analysis, the vena caval occlusion had to reduce maximum left ventricular pressure by at least 30 mm Hg. To determine the passive diastolic pressure–volume relation of the fully relaxed left ventricle, the equilibrium volume, and the relaxation time constant of nonfilling beats, we clamped the mitral valve to prevent left ventricular filling.

Heart rate was kept at approximately 100 beats per minute by administration of UL-FS4922 (1 mg/kg) or

FIGURE 2. Drawing of placement of the valve and catheters and orthogonal arrays of three pairs of ultrasonic crystals to measure left ventricular dimensions. Ao, aorta; PA, pulmonary artery; MV, native mitral valve; RV, right ventricle; Sp, ventricular septum.
atrial pacing from the right atrial appendage using a demand-type stimulator (Medtronic pulse generator model 5320, Minneapolis, Minn.).

Arterial blood gases were monitored, and the ventilator was adjusted to maintain pH 7.35–7.45; P_{O_2}, >100 mm Hg; and P_{CO_2}, 35–50 mm Hg. Left ventricular pressure was maintained at >100 mm Hg by infusion of lactated Ringer’s solution. Data were recorded with the respirator off at end expiration (approximately 20–35 seconds).

Disruption of the Mitral Apparatus

The mitral apparatus was disrupted by cutting the chordae tendineae using a special metal hook (Figure 3, left). The hook was made of 20-gauge piano wire and was 10 cm long. The end of the hook was made into a J shape (approximately 3.0 mm wide and 3.0 mm long). The inside of the curve was sharpened to cut the chordae tendineae. An 8F catheter sheath introducer system (Cordis Corp., Miami, Fla.) was used to insert the hook into the left ventricle. The sheath, which was cut to approximately 30 mm long including the entry portion, was passed through the left ventricular anterior wall 2 cm below the circumflex branch of the left coronary artery and affixed (Figure 3, right). The hook was inserted through the sheath into the left ventricle and advanced deep enough to capture the chordae attached to the anterolateral and posteromedial papillary muscles. After the chordae were hooked, they were cut by pulling and twisting the hook. This procedure was repeated several times until no chordae could be captured.

In postmortem examination, we confirmed that at least 90% of the chordae were cut in each dog and that the residual chordae, if any, were from the ventricular free wall, finer and shorter than those that were cut, and closer to the wall than those that were cut. We also confirmed that the endocardium of the adjacent myocardium was not injured. Disruption of the mitral apparatus was attempted in all 14 dogs and accomplished in nine (four with a conductance catheter, three with ultrasonic crystals, and two with both a conductance catheter and ultrasonic crystals).

Protocol

Before disrupting the mitral apparatus, we recorded hemodynamic variables in steady state and then during occlusion of both venae cavae. In this baseline condition, left ventricular peak systolic pressure was kept at about 100 mm Hg. After recording the data with an intact mitral apparatus, the chordae tendineae were cut, and data were recorded in steady state and then during venous caval occlusion. Because the left ventricular pressure was no longer maintained at about 100 mm Hg after cutting the chordae tendineae, we targeted the pressure changes for each intervention from the pressure observed immediately after cutting the chordae tendineae. In all recordings, we clamped the mitral valve to prevent left ventricular filling for one beat every five or six beats.

The hemodynamic variables recorded were heart rate, left ventricular pressure, left atrial pressure, right ventricular pressure, left ventricular volume for dogs instrumented with a conductance catheter, left ventricular dimensions for dogs instrumented with ultrasonic crystals, and duration of mitral valve clamping. These
data were digitized on-line with a 12-bit AD converter sampling at 200 Hz.

In addition, to elicit a wide range of responses, we altered afterload before and after disrupting the mitral apparatus. To reduce afterload, nitroprusside (3–10 μg · kg\(^{-1}\) · min\(^{-1}\)) was infused intravenously until the left ventricular peak systolic pressure was reduced to about 80 mm Hg. Volume loading with saline was used to keep pressure above 80 mm Hg, if necessary. To increase afterload, the descending aorta was partially occluded by tightening the snare around it until left ventricular peak systolic pressure was increased by about 30 mm Hg.

**Data Analysis**

**End-diastolic pressure–volume relation.** To define the end-diastolic pressure–volume relation and calculate the stiffness coefficient \(S_0\) and the equilibrium volume \(V_{eq}\), left ventricular end-diastolic pressure \(P_{ed}\) and volume \(V_{ed}\) points were determined in both filling and nonfilling beats for each cardiac cycle during vena caval occlusion. End diastole was defined as the point of rapid upstroke of the time derivative of left ventricular pressure. The points at end diastole of the clamped beats fell on the same line, at lower volumes, as the end-diastolic points for filling beats; therefore, filling and nonfilling beats were included in one linear regression analysis. The end-diastolic pressure–volume relation for each caval occlusion appeared linear over the range of relatively low pressures we observed in most cases, in agreement with previous reports,\(^{23–27}\) so stiffness was defined as the slope of a simple linear regression of end-diastolic pressure \(P_{ed}\) on volume \(V_{ed}\):

\[
P_{ed} = S_0 (V_{ed} - V_{eq})
\]

(2)

where \(S_0\) is the stiffness coefficient, and \(V_{eq}\) is the diastolic equilibrium volume.

**Time constant of isovolumic relaxation.** We computed the time constant of left ventricular isovolumic relaxation in nonfilling beats from a monoexponential equation with nonzero-pressure asymptote using the following model:

\[
P = (P_0 - P_r) \exp(-t/\tau_r) + P_r
\]

(3)

where \(P_0\) is pressure at time of \(dP/dt_{min}\), \(\tau_r\) is the relaxation time constant, and \(P_r\) is nonzero-pressure asymptote. The pressure data from the time of \(dP/dt_{min}\) through the next end diastole were used to fit this equation using nonlinear least squares.\(^{11}\)

**End-systolic pressure–volume relation.** To define the end-systolic pressure–volume relation and calculate end-systolic elastance \(E_s\) as an index of left ventricular contractility, left ventricular end-systolic pressure \(P_{es}\) and volume \(V_{es}\) points were determined for each cardiac cycle during vena caval occlusion. End systole was defined as the time at which time varying elastance \(E(t)\) was maximal according to:

\[
E(t) = P(t)/[V(t) - V_{es}]
\]

(4)

where \(P(t)\) and \(V(t)\) are instantaneous left ventricular pressure and volume. The volume intercept \(V_{es}\) of the end-systolic pressure–volume relation was determined with an iterative algorithm.\(^{28}\) Once \(V_{es}\) was determined, \(E_s\) was estimated as the slope of the end-systolic pressure–volume relation:

\[
P_{es} = E_s (V_{es} - V_{equ})
\]

(5)

**Stroke work–end-diastolic volume relation.** Stroke volume (SV) was calculated as

\[
SV = V_{ed} - V_{es}
\]

(6)

Stoke work (SW) was calculated as:

\[
SW = \int PdV = \int VdP = \int V \frac{dP}{dt}
\]

(7)

The stroke work–end-diastolic volume relation was determined as another measure of contractility\(^{29,30}\) during each caval occlusion using linear regression to fit:

\[
SW = S_{a2} (V_{ed} - V_{eq})
\]

(8)

where \(S_{a2}\) is the slope of the linear stroke work–end-diastolic volume relation, and \(V_{eq}\) is the volume–axis intercept.

**Left ventricular shape changes.** An ellipsoidal model was used to investigate shape changes of the left ventricle. To evaluate shape changes after disruption of the mitral apparatus, we calculated eccentricity \(e\) for the three ellipsoidal planes that were constructed by any two of the three crystal dimensions according to:

\[
e = \frac{a^2 - b^2}{a}
\]

(9)

where \(a\) is the semimajor axis of the ellipsoid, and \(b\) is the semiminor axis of the ellipsoid \((e=0\) for a circle, and \(e=1\) for a straight line). Thus, a decrease in the eccentricity indicates a more circular (spherical) ventricle. Eccentricity was defined for the ellipsoids constructed with the base–apex axis and septum–free wall axis \((e_{s,b})\), base–apex axis and anteroposterior axis \((e_{s,a})\), and anteroposterior axis and septum–free wall axis \((e_{a,s})\). In general, the anteroposterior dimension was larger than the septum–free wall dimension, so the anteroposterior dimension generally was taken as the major axis to compute \(e_{As}\); when the septum–free wall dimension was longer than the anteroposterior dimension, the septum–free wall dimension was taken as the major axis, and a negative value was assigned to \(e_{As}\).

**Statistical Analysis**

To test for significant changes in hemodynamic variables after disruption of the mitral apparatus or the afterload interventions, we used a multiple linear regression implementation of a repeated-measures ANOVA with dummy variables that accounted for disruption of mitral apparatus, the afterload interventions, and differences between dogs.\(^{18,31,32}\) The specific regression model was:

\[
y = b_0 + b_{dmitral} \cdot mitral + b_{dnitro} \cdot nitro + b_{AcCp} \cdot AoCp + \Sigma D_i
\]

(10)

where \(y\) is the dependent variable. The dummy variable mitral equals 0 before disruption of the mitral apparatus and 1 later. The intervention dummies nitro (afterload reduction with nitroprusside) and AoCp (afterload increase with partial aortic clamp) were also defined according to the \((0,1)\) convention, set to 1 when the
Figure 4. Typical analog data before and after disruption of mitral apparatus in dogs instrumented with conductance catheter (panel A) and ultrasonic crystals (panel B). In nonfilling beats, left ventricular pressure (LVP) fell lower than that in filling beats, and conductance volume signal and dimension signals became more flat. After disruption of mitral apparatus, left ventricular systolic pressure fell in dogs with both conductance catheter and ultrasonic crystals. After disrupting the mitral apparatus, left ventricular volume in dogs with conductance catheter and dimensions in dogs with ultrasonic crystals increased. LAP, left atrial pressure.
condition was present. The $n-1$ dummy variables $D_i$ account for between-dog differences by allowing the $n$ dogs to have different mean responses. These dummy variables are defined according to

$$D_i = \begin{cases} 1 & \text{if dog } i \ (i \leq n-1) \\ -1 & \text{if dog } n \\ 0 & \text{otherwise} \end{cases}$$

The $b_i$ represents the deviation from the overall mean value for dog $i \ (i=1, \ldots, n-1)$. Using this coding, $b_0$ is the mean value for all dogs under baseline conditions with the mitral apparatus intact, and the coefficients $b_{\text{mitral}}, b_{\text{Nitro}},$ and $b_{\text{AoClp}}$ estimate the changes from the steady-state baseline during the corresponding interventions. We also report $s_d$, the square root of the mean square associated with the $b_i$, as a measure of between-dog variability.

All regression coefficients are reported with their associated standard errors (SEE). Computations were done with MINTAB Release 7.2. We considered differences significant when $p<0.05$.

**Results**

The results of analyses using Equation 10 are summarized in Tables 1–6. Each dependent variable is shown as a column heading, with the baseline value with intact mitral apparatus ($b_0$ in Equation 10), followed by the changes from baseline that accompany the different interventions derived from the regression models. All values in the row “Mitrail” represent the average change associated with disrupting the mitral apparatus, allowing for the effects of these different conditions (baseline, nitro, AoClp) and between-dog differences. For example, values in the row “Nitro” quantify the average change with afterload reduction with nitroprusside, allowing for the effects of mitral disruption.

**Effect of Disrupting the Mitral Apparatus**

Recordings before and after disruption of the mitral apparatus in dogs instrumented with the conductance catheter or ultrasonic crystals are shown in Figure 4. After disruption of the mitral apparatus, left ventricular systolic pressure fell. In nonfilling beats, left ventricular diastolic pressure fell lower than in filling beats, and the conductance volume signal became flat during volume clamping (Figure 4A). The volume signal calculated from dimensions also became flat, but the three-dimension signals changed during volume clamping, indicating isovolumic shape change of the left ventricle despite the fact that there was no filling (Figure 4B). Left ventricular volume increased following disruption of the mitral apparatus according to both the conductance catheter and ultrasonic crystals.

Hemodynamics were affected by disruption of the mitral apparatus (Tables 1 and 2). End-diastolic left ventricular pressure increased slightly, by 1±0.3 mm Hg. Maximum left ventricular pressure decreased by −12±2 mm Hg below baseline values of about 90 mm Hg after disruption of mitral apparatus. dP/dt max fell by −44±67 mm Hg/sec. End-diastolic and end-systolic left ventricular volumes increased by 17±2 mL and 13±2 mL, respectively, in dogs with the conductance catheter and by 11±1 mL and 7±1 mL, respectively, in dogs with ultrasonic crystals. Stroke volume also increased in dogs with both the conductance catheter and ultrasonic crystals. Mitral apparatus disruption decreased left ventricular systolic pressure and increased left ventricular volume. These changes suggest depressed systolic function.

In all dogs, disruption of the mitral apparatus increased the diastolic equilibrium volume ($V_d$), by 13±4 mL according to the conductance catheter and 9±2 mL according to ultrasonic crystals, as indicated by a shift to the right of the end-diastolic pressure–volume relation, but the stiffness coefficient ($S_d$) did not change significantly (Table 3). Typical pressure–volume loops before and after mitral apparatus disruption under baseline conditions appear in Figure 5. Figure 6 shows the corresponding end-diastolic pressure–volume relations together with the linear fits before and after mitral apparatus disruption. Disrupting the mitral apparatus increased left ventricular volume without changing the diastolic stiffness.

In addition, the left ventricular isovolumic relaxation time constant increased significantly following mitral apparatus disruption, averaging 8±2 msec more than the overall baseline mean, indicating slower relaxation (Table 4). Disruption of the mitral apparatus slightly, but significantly, increased (by 1±0.3 mm Hg) the fully
TABLE 2. Baseline Volume Data and Changes After Interventions in Dogs

<table>
<thead>
<tr>
<th></th>
<th>Conductance catheter</th>
<th>Ultrasound crystals</th>
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<tbody>
<tr>
<td></td>
<td>LVEDV (mL)</td>
<td>LVESV (mL)</td>
</tr>
<tr>
<td>Baseline</td>
<td>128±2</td>
<td>103±2</td>
</tr>
<tr>
<td>Changes from baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral</td>
<td>17±2*</td>
<td>13±2*</td>
</tr>
<tr>
<td>Nitro</td>
<td>-3±3</td>
<td>-2±2</td>
</tr>
<tr>
<td>AoClp</td>
<td>4±3</td>
<td>2±3</td>
</tr>
<tr>
<td>s&lt;sub&gt;d&lt;/sub&gt;</td>
<td>89</td>
<td>69</td>
</tr>
<tr>
<td>SEE</td>
<td>12</td>
<td>10</td>
</tr>
</tbody>
</table>

LVEDV and LVESV, end-diastolic and end-systolic left ventricular volumes; SV, stroke volume; SW, stroke work; Mitral, disruption of mitral apparatus; Nitro, afterload reduction induced by nitroprusside; AoClp, afterload increase induced by partial aortic clamp; s<sub>d</sub>, between-dog variability; SEE, standard error of estimate. *p<0.001, †p<0.01, ‡p<0.05 vs. baseline. n=11 for conductance catheter; n=5 for ultrasonic crystals.

relaxed left ventricular pressure (P<sub>r</sub>) in nonfilling beats (Table 4). The mean pressure asymptote, over all dogs, was 2.0±1.8 mm Hg at baseline. Under baseline conditions, before disruption of the mitral apparatus, negative left ventricular pressures were observed in only two of 14 dogs (−0.4 mm Hg and −0.9 mm Hg). Mitral apparatus disruption did not make left ventricular diastolic pressure more negative but rather less negative or more positive.

Disruption of the mitral apparatus did not change left ventricular muscle contractility, defined as the slopes of the end-systolic pressure–volume or stroke work–end-diastolic volume relations (Figure 7). The volume–axis intercepts increased for both the end-systolic pressure–volume relation (V<sub>se</sub>, by 27±7 mL in the conductance catheter experiments and 10±5 mL in the crystal experiments) and the stroke work–end-diastolic volume relation (V<sub>sw</sub>, by 35±4 mL in the conductance catheter experiments and 15±2 mL in the crystal experiments) after disruption of the mitral apparatus, whereas the slopes of both relations did not change significantly (Table 5). Left ventricular shape changed after disrupting the mitral apparatus. End-systolic and end-diastolic base–apex dimensions (L<sub>e</sub>,L<sub>s</sub>), end-diastolic septum–free wall dimension (S<sub>d</sub>), and end-diastolic anteroposterior dimensions (A<sub>d</sub>,A<sub>s</sub>) all significantly increased after disruption of mitral apparatus (Table 6), indicating global enlargement of the left ventricle. End-systolic e<sub>Ls</sub> and end-diastolic and end-systolic e<sub>L</sub>s<sub>LA</sub> slightly, but significantly, increased. Thus, the left ventricle enlarged and became slightly more ellipsoidal after disruption of mitral apparatus.

TABLE 3. End-Diastolic Pressure–Volume Relation Data and Changes After Interventions in Dogs

<table>
<thead>
<tr>
<th></th>
<th>Conductance catheter</th>
<th>Ultrasound crystals</th>
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<tr>
<td></td>
<td>s&lt;sub&gt;d&lt;/sub&gt; (mm Hg/mL)</td>
<td>V&lt;sub&gt;se&lt;/sub&gt; (mL)</td>
</tr>
<tr>
<td>Baseline</td>
<td>0.207±0.024</td>
<td>94±3</td>
</tr>
<tr>
<td>Changes from baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral</td>
<td>-0.004±0.027</td>
<td>13±4*</td>
</tr>
<tr>
<td>Nitro</td>
<td>0.035±0.004</td>
<td>-3±4</td>
</tr>
<tr>
<td>AoClp</td>
<td>0.199±0.035*</td>
<td>9±4</td>
</tr>
<tr>
<td>s&lt;sub&gt;v&lt;/sub&gt;</td>
<td>0.346</td>
<td>50</td>
</tr>
<tr>
<td>SEE</td>
<td>0.096</td>
<td>12</td>
</tr>
</tbody>
</table>

s<sub>d</sub>, stiffness measured as slope of the end-diastolic pressure–volume relation; V<sub>se</sub>, equilibrium volume; Mitral, disruption of mitral apparatus; Nitro, afterload reduction induced by nitroprusside; AoClp, afterload increase induced by partial aortic clamp; s<sub>v</sub>, between-dog variability; SEE, standard error of estimate.

*p<0.001, †p<0.01, ‡p<0.05 vs. baseline. n=11 for conductance catheter; n=5 for ultrasonic crystals.

Discussion

We found that disruption of the mitral apparatus alters the left ventricular end-diastolic pressure–volume relation. The diastolic equilibrium volume (volume–axis intercept) increased; the diastolic stiffness (the slope of the diastolic pressure–volume relation) did not change. Likewise, disruption created similar but larger increases in the volume–axis intercepts of the end-systolic pressure–volume and stroke work–end-diastolic volume relations without changing the end-systolic elastance or slope of the stroke work–end-diastolic volume relation.

Effect of Disrupting the Mitral Apparatus on Pump Performance

These findings help explain why preserving the mitral apparatus improves hemodynamic performance and clinical outcome in mitral valve replacement surgery. End-diastolic volume increased after disruption of the mitral apparatus by the same amount as the diastolic equilibrium volume (Tables 2 and 3). Stroke volume, on the other hand, slightly, but significantly, increased after disrupting the mitral apparatus. Because stroke volume depends on both inotropic state and afterload, this modest increase in stroke volume following disruption of the mitral apparatus probably was due to the fall in aortic pressure in this study. Increased stroke volume and decreased systolic pressure probably reflect a reduction in peripheral resistance. Yun et al also observed a similar drop in peripheral resistance without changing stroke volume. The reason for this finding is not clear. Rozich et al did not observe differences in mean arterial blood pressure before or after mitral valve...
FIGURE 5. Pressure-volume loops drawn at high- and low-pressure gain in dog 335 instrumented with conductance catheter (panel A) and in dog 342 instrumented with ultrasonic crystals (panel B) during vena caval occlusion under baseline conditions before and after disruption of mitral apparatus. Loops shifted to the right after disruption of mitral apparatus. LVP, left ventricular pressure.
replacement in patients with or without cutting the chordae tendineae.

Disruption of the mitral apparatus does not change the slope of the end-systolic pressure–volume or stroke work–end-diastolic volume relations, whereas the volume–axis intercepts of the both relations, \( V_{end} \) and \( V_{syst} \), increased after disrupting the mitral apparatus. Thus, the ventricular systolic function curves shifted rightward without changing the slopes.

The lumped model of the left ventricle proposed by Sunagawa et al. to describe the global function of the regionally ischemic ventricle using the concept of time-varying volume elastance can be used to explain these results. Sunagawa et al. found a parallel rightward shift of the end-systolic pressure–volume relation in acute regional ischemia and used this model to explain the result. We believe that this model also can explain our data because the effective stiffness in the apical region is reduced by disrupting the mitral apparatus. Sunagawa et al.'s model divided a regionally ischemic ventricle into two compartments, in which volume from the “normal” compartment would be displaced into a greater capacitance “ischemic” compartment. After disruption of the mitral apparatus, it may be possible that the apical region becomes more compliant in terms of chamber properties because the connections of the base of the ventricle have been released, producing a similar rightward shift of the end-systolic pressure–volume relation.

Our findings on global function disagree with the findings of Hansen et al. and Yun et al. First, we did not observe a change in the systolic function curves (\( E_a \) and \( S_w \)) after disruption of the mitral apparatus, whereas Hansen et al. reported a change in the slope of the isovolumic peak pressure–volume relation in isovolumically beating left ventricles without any change in the diastolic equilibrium volume. Second, although we found that disruption of the mitral apparatus increased the diastolic equilibrium volume, Sarris et al. found no significant change in the equilibrium volume. They reported that disruption of the mitral apparatus did not significantly change volume–axis intercepts and the stiffness coefficients of both linear and nonlinear descriptions of the end-diastolic pressure–volume relation. Third, despite measuring the

![Figure 6. Scatterplots of end-diastolic pressure–volume relation for caval occlusion in dog 335 and dog 348 under baseline conditions before and after disruption of mitral apparatus. The end-diastolic pressure–volume relation was defined by fitting simple linear regression. The end-diastolic pressure–volume line shifted to the right when the chordae were cut. The volume–axis intercept increased but the slope remained unchanged after disruption of mitral apparatus. The disruption of mitral apparatus increased the equilibrium volume without affecting left ventricular stiffness.](image-url)
dimensions in the same manner we used with epicardial crystals, we found that the left ventricle became slightly less ellipsoidal than reported by Yun et al. The changes in dimensions and eccentricities after disruption of the mitral apparatus reported by Yun et al (3.9% increase in base–apex dimension, 2.0% increase in end-diastolic eccentricity) were slightly larger than ours (2.5% increase in dimension, 1.1% increase in eccentricity). As will be discussed, this difference may reflect differences in the techniques used to implant the values and the presence or absence of cardiopulmonary bypass. Our data are, however, consistent with changes in regional function observed by Sarris et al. They observed a pronounced rightward offset of the stroke work–end-diastolic volume relation after severing the chordae in the left ventricular major (base–apex) axis but no such change in the two left ventricular minor axes. This particular finding is consonant with our results.

**Effect of Disrupting the Mitral Apparatus on the Diastolic Pressure–Volume Relation**

The reason for the increase in the diastolic equilibrium volume after disruption of the mitral apparatus is not clear. One possible reason could be a change in the shape of the left ventricle because cutting the chordae tendineae prevented the left ventricle from maintaining its shape. After disrupting the mitral apparatus, the ventricular free-wall segments are no longer tethered by
the fibrous endocardial skeleton of the mitral apparatus, so the ventricle fails to maintain its normal radius of curvature and optimal elliptical geometry. If the left ventricle had become more spherical after disruption of mitral apparatus, the increase in equilibrium volume could have been attributed to the shape change because a sphere has the highest volume for a given wall (surface) area. Unfortunately, the entire left ventricle became more ellipsoidal, so shape change cannot explain the increase in diastolic equilibrium volume. In addition, the shape change is small; the shape change quantified by eccentricity was less than 10% after disruption of mitral apparatus. Thus, it is unlikely that the ventricular shape change increased the equilibrium volume.

A second possible explanation for the increase in the equilibrium volume could be that transient ischemia due to low coronary perfusion pressure secondary to lower systolic pressure after mitral apparatus disruption affected the end-diastolic pressure–volume relation. It has been reported that during brief coronary occlusion, the ischemic region shows rightward shift of end-diastolic pressure–volume relations, indicating increased equilibrium volume.\(^{26,34}\) However, because systolic pressures were kept above 80 mm Hg even after mitral apparatus disruption, the possibility of transient ischemia seems remote. The finding that the slopes of the end-diastolic pressure–volume curve \(S_d\) and the systolic function curves \(E_{es}\) and \(S_{ew}\) did not change after disruption of the mitral apparatus also argues against transient ischemia as the mechanism for the increase in the equilibrium volume.

### Effect of Disrupting the Mitral Apparatus on Relaxation

This study shows that disruption of the mitral apparatus slows early diastolic relaxation, although it does not change diastolic stiffness of the left ventricle. In our dogs, time constant of isovolumic relaxation increased

### Table 5. Left Ventricular Contractility Data and Changes after Interventions in Dogs

<table>
<thead>
<tr>
<th>Conductance catheter</th>
<th>Ultrasound crystals</th>
</tr>
</thead>
<tbody>
<tr>
<td>(E_{es}) (mm Hg/mL)</td>
<td>(V_{os}) (mL)</td>
</tr>
<tr>
<td>Baseline</td>
<td>1.23±0.19</td>
</tr>
<tr>
<td>Changes from baseline</td>
<td>Mitral</td>
</tr>
<tr>
<td></td>
<td>Nitro</td>
</tr>
<tr>
<td></td>
<td>AoClp</td>
</tr>
<tr>
<td></td>
<td>(S_4)</td>
</tr>
<tr>
<td></td>
<td>SEE</td>
</tr>
</tbody>
</table>

\(E_{es}\), slope of end-systolic pressure–volume relation; \(V_{os}\), volume–axis intercept of end-systolic pressure–volume relation; \(S_{ew}\), slope of stroke work–end-diastolic volume relation; \(V_{ow}\), volume–axis intercept of stroke work–end-diastolic volume relation; Mitral, disruption of mitral apparatus; Nitro, afterload reduction induced by nitroprusside; AoClp, afterload increase induced by partial aortic clamp; \(S_4\), between-dog variability; SEE, standard error of estimate.

\(\ddagger p<0.001, \ddagger\ddagger p<0.01, \ddagger\ddagger p<0.05\) vs. baseline.

\(n=11\) for conductance catheter; \(n=5\) for ultrasonic crystals.

### Table 6. Left Ventricular Dimensions and Eccentricity Data and Changes after Interventions

<table>
<thead>
<tr>
<th>L (mm)</th>
<th>S (mm)</th>
<th>A (mm)</th>
<th>(e_{ls})</th>
<th>(e_{1a})</th>
<th>(e_{as})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(L_d)</td>
<td>(L_s)</td>
<td>(S_d)</td>
<td>(S_s)</td>
<td>(A_d)</td>
<td>(A_s)</td>
</tr>
<tr>
<td>Baseline</td>
<td>81±0.2</td>
<td>79±0.3</td>
<td>54±0.2</td>
<td>46±0.3</td>
<td>56±0.2</td>
</tr>
<tr>
<td></td>
<td>0.002</td>
<td>0.003</td>
<td>0.002</td>
<td>0.003</td>
<td>0.010</td>
</tr>
<tr>
<td>Changes from baseline</td>
<td>Mitral</td>
<td>2±0.2(\dagger)</td>
<td>4±0.3(\dagger)</td>
<td>2±0.2(\dagger)</td>
<td>0±0.2</td>
</tr>
<tr>
<td></td>
<td>0.002</td>
<td>0.002(\dagger)</td>
<td>0.003</td>
<td>0.003(\dagger)</td>
<td>0.003</td>
</tr>
<tr>
<td>Nitro</td>
<td>0±0.3</td>
<td>0±0.4</td>
<td>0±0.2</td>
<td>-1±0.3(\dagger)</td>
<td>-1±0.2(\dagger)</td>
</tr>
<tr>
<td></td>
<td>0.003</td>
<td>0.003(\dagger)</td>
<td>0.003</td>
<td>0.003</td>
<td>0.013(\dagger)</td>
</tr>
<tr>
<td>AoClp</td>
<td>0±0.3</td>
<td>1±0.4</td>
<td>1±0.2(\dagger)</td>
<td>1±0.3(\dagger)</td>
<td>0±0.2</td>
</tr>
<tr>
<td></td>
<td>0.003(\dagger)</td>
<td>0.003</td>
<td>0.003</td>
<td>0.003</td>
<td>0.013</td>
</tr>
<tr>
<td>(S_4)</td>
<td>29.8</td>
<td>33.2</td>
<td>18.7</td>
<td>22.4</td>
<td>25.6</td>
</tr>
<tr>
<td>SEE</td>
<td>1.0</td>
<td>1.4</td>
<td>0.8</td>
<td>1.1</td>
<td>0.7</td>
</tr>
</tbody>
</table>

\(L\), base–apex dimension; \(S\), septum–free wall dimension; \(A\), anteroposterior dimension; \(e_{ls}\), eccentricity for base–apex dimension vs. septum–free wall dimension; \(e_{1a}\), eccentricity for base–apex dimension vs. anteroposterior dimension; \(e_{as}\), eccentricity for anteroposterior dimension vs. septum–free wall dimension; \(S\), end systole; \(d\), end diastole; Mitral, disruption of mitral apparatus; Nitro, afterload reduction induced by nitroprusside; AoClp, afterload increase induced by partial aortic clamp; \(S_4\), between-dog variability; SEE, standard error of estimate.

\(\dagger p<0.001, \ddagger p<0.01, \ddagger\ddagger p<0.05\) vs. baseline.

\(n=5\).
by 8±2 msec (above a 34±1-msec baseline) in nonfilling beats, indicating significantly slower relaxation.

The slower relaxation may reflect a less-coordinated relaxation pattern because of the failure to maintain optimal elliptical left ventricular geometry.\textsuperscript{35-39} Aoyagi et al\textsuperscript{35} reported that the time constant of left ventricular relaxation was prolonged with wall motion asynchrony induced by atrioventricular sequential pacing with the second stimulation at six epicardial sites. They suggested that when the time constant is assessed in situations with wall motion asynchrony, such as ischemic heart disease and hypertrophic cardiomyopathy, not only the failure of inactivation but also the effect of wall motion asynchrony should be taken into consideration. Lew and Rasmussen\textsuperscript{36} also demonstrated that nonuniformity of regional ventricular function produced by selective isoproterenol infusion into a coronary artery increased the time constant of isovolumic relaxation, whereas the heart rate, end-diastolic pressure, and peak systolic pressure remained constant. Thus, although the shape changes were small, these studies suggest that wall motion asynchrony or nonuniformity of left ventricular function produced by the shape change following disrupting the mitral apparatus might explain the increased time constant in our study.

**Effect of Disrupting the Mitral Apparatus on Elastic Recoil**

In this study, using in situ left ventricular volume clamping at end systole, we observed small negative fully relaxed left ventricular pressures (\(P_s\)) in some nonfilling beats, which is evidence for stored elastic energy because the left ventricle contracted below its diastolic equilibrium volume. Disruption of the mitral apparatus did not make the negative pressure more negative; the pressure became less negative or more positive. After disruption, if the end-systolic volume was further below the equilibrium volume than before disruption, the negative pressure should become more negative because of the increase in the diastolic equilibrium volume, and more compressive forces should be present in the wall. However, despite the increased diastolic equilibrium volume after disruption of mitral apparatus, we did not observe more negative pressure. Stroke volume also increased by almost the same amount as the increase in \(V_{es}\). Taking this argument one step further suggests that severing the chordae tendineae interferes with potential energy storage in the myocardium and interstitium at end systole, which reduces elastic recoil and could impair left ventricular filling by decreasing diastolic suction.

The results of the negative pressure in our preparation contrast with those obtained by Nikolic et al.\textsuperscript{36-40} who found large (=−10 mm Hg) negative left ventricular pressures in fully relaxed ventricles volume clamped at end-systolic volume. In one study,\textsuperscript{38} \(P_s\), was −5.1±4.1 (±SD) mm Hg in baseline condition, which is much more negative than what we observed. The reasons for this difference are unknown. One possibility is that there are two differences in design between our technique and those of Yellin et al\textsuperscript{27,41}: we maintain an intact mitral apparatus and place the valve used for volume clamping without cardiopulmonary bypass, whereas Yellin et al replace the native valve with an artificial valve, which requires putting the dog on car-
diopulmonary bypass. Disruption of the mitral apparatus did not make the fully relaxed left ventricular pressure more negative but rather made it less negative. Thus, this difference in the status of the mitral apparatus cannot explain the different physiological responses observed in these two preparations.

**Study Limitations**

Four potential limitations of this study should be considered. One is the method of cutting the chordae tendineae. Cutting was done blindly by a hook inserted through the anterior wall into left ventricle. We believe that the influence of the residual chordae tendineae is negligible for evaluation of left ventricular function because we confirmed that more than 90% of chordae tendineae were severed and that all the chordae tendineae that belonged to large anterolateral and posteromedial papillary muscles were completely severed in all dogs, as verified by postmortem examination. The second limitation is that we did not calibrate the conductance catheter for each experiment but instead applied a constant calibration for all animals. This approach also assumes that the parallel conductance volume does not change when the chordae are cut. Such artifacts probably are not a problem because the behavior of the end-systolic and end-diastolic pressure-volume relations assessed by ultrasonic crystals were consistent with those obtained with the conductance catheter. Moreover, as discussed, we believe that the calibration procedure we used actually is less artifact prone than those based on calibrations in individual animals, particularly because we were able to account for between-animal variation in the statistical analysis. Indeed, we had thought that a problem may have arisen because of an artifact in the conductance catheter, perhaps secondary to odd shape changes in the heart or length change that would lead to misalignment of the upper stimulating electrode or changes in parallel conductance volume, which led us to different conclusions than those reached by other investigators. To determine whether the results we found were not artifacts and could be replicated using a different method, we did a second complete set of experiments using ultrasonic crystals. The results were totally consistent. In addition, we found that the shape changes and long-axis length change that accompanied disruption of the mitral apparatus were sufficiently small that we did not have to worry about catheter malplacement or major changes in the shape of the ventricle that hypothetically could affect the volume conductance signal. The third limitation is that we might not have had a large enough sample to overcome the “noise” in the data and that the attendant low power led us to a false-negative conclusion regarding the lack of change in contractility after mitral apparatus disruption. (The power of our experiments to detect a 50% change in the slope of the end-systole pressure–volume relationship, \(E_{es}\), was about 0.40 with \(n=0.05\).) The fourth limitation is that the volume between the artificial valve and the native valve might affect the slopes and intercepts we measured for the systolic and diastolic function curves. There definitely is some volume that is not included in the measured left ventricular volume. If the volume in question is affected by changes in left ventricular pressure, it might lead to errors in assessing the slopes and volume–axis intercepts of the relations...
Clinical Significance

Our findings in dogs imply that because of the increase in the equilibrium volume, the slowing of early diastolic relaxation, and decreased peak systolic pressure that accompany cutting the chordae tendineae, preservation of the mitral apparatus is recommended to maintain pump function of the left ventricle in valve reconstructive surgery such as mitral annuloplasty or valvuloplasty and mitral valve replacement. Although these findings in dogs cannot necessarily be applied to patients with mitral valve diseases, particularly for patients with hearts with impaired diastolic function by fibrosis and myopathy, preservation of mitral apparatus appears desirable in terms of preserving left ventricular pump function.

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References

Effect of disrupting the mitral apparatus on left ventricular function in dogs.
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