The Effects of Left Ventricular Load and Contractility on Mitral Regurgitant Orifice Size and Flow in the Dog

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SUMMARY Acute mitral regurgitation (MR) was produced in 12 dogs by closed chest partial valvulotomy and the relative contributions of MR pressure gradient (MRG), the time for regurgitant flow (VSI), and the MR orifice area (MRA) to mitral regurgitant volume (MRV) assessed. Aortic and left atrial pressures, biplane left ventricular (LV) angiography, forward flow and mitral regurgitant flow (MRF) were measured following MR induction and following augmentation of left ventricular end-diastolic volume (EDV), increased aortic resistance (angiotensin), and in the presence of increased ventricular contractility (calcium or epinephrine). Mitral regurgitation orifice area was determined by calculation and the diameters of the mitral anulus and subvalvular areas measured angiographically. Angiotensin and volume infusion induced a substantial increase in MRF which was largely dependent on an increase in MRA but not MRG, while augmentation of contractility decreased MRF accompanied by a decrease in MRA, relatively independent of MRG. Left ventricular size and shape are major determinants of MRA and resultant MRF in acute mitral regurgitation. These findings may help to explain the effects of such factors as ventricular loading and volume on the clinical course of mitral regurgitation in man.

THE LESION IN MITRAL VALVULAR INSUFFICIENCY results from incomplete apposition of the mitral leaflets, whether due to abnormalities of the leaflets themselves or to dysfunction of their supporting structures. Traditional concepts relate regurgitant flow across the lesion to the systolic pressure gradient between the left ventricle and left atrium, to the size of the defect of mitral closure, or regurgitant orifice, and to the duration of ventricular systole, or the time interval for regurgitation. Moreover, the orifice in mitral insufficiency has been thought to be relatively static, except in the clinical syndrome of papillary muscle dysfunction in which the properties of the supporting structure may change with time.

However, recent observations suggest that this formulation may be oversimplified. The circumference of the mitral anulus in normal dogs is known to be reduced by atrial contraction, while relaxation of the atrium prior to ventricular systole can close the mitral valve. The leaflets themselves contain muscle fibers which contract synchronously with atrial systole. The circumference of the anulus is known to be reduced further by ventricular systole and it has been suggested that the size of the mitral lesion may change with alterations in ventricular shape.

Previous models of mitral insufficiency have been limited to the study of hemodynamics or have utilized shunts with a fixed orifice between the left ventricle and left atrium. This latter approach has vitiated analysis of the influence of left ventricular size on the anulus, the orifice, and regurgitant flow. In the present study, mitral insufficiency has been created in intact dogs by partial valvulotomy and chordotomy, which produces a lesion similar to that of an acutely ruptured chordae tendineae. Hemodynamic and cineangiographic studies have been performed and the influence of left ventricular size on the area of the mitral lesion and the volume of orifice flow has been analyzed. Evidence is presented that the size of the subvalvular cavity of the ventricle and the circumference of the mitral anulus greatly influence the size of the regurgitant orifice and resultant regurgitant flow.

Materials and Methods

Twelve mongrel dogs weighing 20 to 31 kg (mean 25 ± 1 kg) were sedated and anesthetized with either morphine (0.8–1.2 mg/kg) and sodium pentobarbital (10–20 mg/kg), or fentanyl-droperidol (Inovar-Vet) (0.1 ml/kg) and alphachloralose (40–60 mg/kg). An uncuffed endotracheal tube was inserted into the trachea and respiration assisted by a Harvard ventilation pump.

Right and left heart catheterization was performed. Closed tip catheters were inserted via a carotid artery into the central aorta and left ventricle for measurement of pressure and injection of angiographic contrast medium. An open-tip catheter was passed via a jugular vein into the coronary sinus and attached externally to a physiologic stimulator. Another open-tip catheter was inserted into the right atrium via the jugular vein and passed trans-septally into the left atrium for the measurement of the left atrial pressure. A catheter was inserted via a femoral vein into the main pulmonary artery.

Statham P23 Db strain gauge transducers were used for pressure measurements. In most animals a transducer tip catheter was introduced into the left ventricle for high fidelity pressure measurements. A high frequency physiologic recorder designed from instruments manufactured by Honeywell, Inc., and Grass Instruments Co. was used to record physiologic data on photographic recording paper at paper speeds of 0.25, 25 and 200 mm/sec. The first derivative of left ventricular pressure was obtained using an active R-C differentiator employing an operational amplifier.

Effective forward ventricular stroke volume was determined by dye dilution method. Indocyanine green (0.7 ml) was injected as a bolus into the coronary sinus and blood sampled simultaneously from the pulmonary artery using a Harvard withdrawal pump set at 15 ml/min. A Gilson densitometer and DTL-M dye tracer were used to detect in-

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Supported in part by HE 11306, GM 18674, HL 20895, and HL 05832.

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Received December 1, 1976; revision accepted February 28, 1977.
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dicator concentration and to record dilution curves.

Left ventricular biplane cineangiography was performed in right anterior oblique (60° RAO) and left anterior oblique (30° LAO) projections at 100 frames per second employing a biplane cine X-ray unit manufactured by Siemens Corp. A Via-monte/Hobbs injector (Barber-Colman Co.) was used to deliver angiographic contrast medium (megumine diatrizoate) (1.2 ml/kg/2.5-4 sec) into the left ventricular cavity. Pressures, flow, and angiographic data were obtained sequentially within 3-5 min at constant heart rate.

Volumes (V), of the left ventricle at end-diastole (ed), mid-systole (ms), and end-systole (es), were calculated from measurements of cineangiographic sagittal (RAO) and transverse (LAO) images of the ventricle. The following formula for volume of an ellipsoid of revolution was used:

\[ V = \frac{4}{3} \pi \left( \frac{D_{\text{rao}}}{2} \right) \left( \frac{D_{\text{lao}}}{2} \right) \left( \frac{l_{\text{lao}}}{2} \right) \]

where \( D_{\text{rao}} \) and \( D_{\text{lao}} \) are calculated diameters of the sagittal (rao) and transverse (lao) ventricular images and \( l_{\text{lao}} \) is the measured length of the sagittal (rao) image.\(^{15, 18}\)

A valvullectome (KIFA, Sweden) was then passed through the intraatrial septum over a flexible guide wire and into the region of the mitral valve and subvalvular ventricle. Portions of the free edge of a leaflet and chordae tendineae were excised. A semi-quantitative estimate of the degree of mitral regurgitation produced by the procedure was made by injection of 5-10 ml of contrast medium into the ventricle under fluoroscopic observation.

The mean pressure gradient in mm Hg across the mitral orifice during ventricular systole (MRG) was calculated as the difference between mean systolic pressure in the left ventricle and mean systolic pressure in the left atrium. The ventricular systolic interval (VSI), expressed in milliseconds, was measured from ventricular pressure curves recorded at high paper speed. The systolic interval represents the time from the upstroke of ventricular pressure to the inscription of the dicrotic notch on the corresponding aortic pressure curve. Effective forward ventricular stroke volume in ml/beat (SV\(_{\text{def}}\)) was calculated from indicator dilution cardiac output/minute and heart rate.

Total ventricular stroke volume (SV\(_{\text{tot}}\)) was calculated as the difference between end-diastolic ventricular volumes (ed V - es V) obtained angiographically. The fraction of end-diastolic volume ejected during total systole was expressed as:

\[ \frac{\text{ed V} - \text{es V}}{\text{ed V}} \]

Mitral regurgitant volume (MR V) was calculated as the difference between total left ventricular stroke volume and effective forward ventricular stroke volume obtained by green dye: SV\(_{\text{tot}}\) - SV\(_{\text{def}}\). The mitral regurgitant fraction of total ventricular stroke volume was expressed by the ratio: MR V/SV\(_{\text{tot}}\). The mean area of the regurgitant orifice, MRA, during ventricular systole was calculated from the hydraulic equation:

\[ \text{MRA} = \frac{\text{MR V}}{\text{VSI} \times 36 \times \sqrt{\text{MRG}}} \]

where MRV is regurgitant volume in ml/beat; VSI is the ventricular systolic time interval in sec/beat, and MRG is the mean regurgitant pressure gradient in mm Hg.\(^{8}\)

The following measurements of sagittal (RAO) or transverse (LAO) images were made at end-diastole, mid-systole, and end-systole: length, l; subvalvular diameter, \( d_{\text{sub}} \); mid-ventricular diameter, \( d_{\text{mid}} \); apical diameter, \( d_{\text{ap}} \); and mitral annular diameter, \( d_{\text{ann}} \). In the sagittal view of the ventricle (fig. 1), the length extends from the midpoint of the aortic valve to the apex; ventricular diameters are quadrisections of this length; the subvalvular diameter extends from the superior margin of the left ventricular outflow tract to the inferior wall of the left ventricle near the inferior margin of the mitral anulus; the midventricular and apical diameters extend from superior to inferior ventricular wall; the mitral annular diameter extends from the insertion point superiorly of the anterior mitral leaflet into the fibrous skeleton of the heart to the insertion point inferiorly of the posterior leaflet into the anulus itself. In the transverse view of the ventricle the length extends from the midpoint of the aortic valve to the apex of the ventricle; diameters represent quadrisections of the length; the subvalvular diameter extends from the posterior wall of the ventricle near its junction with the posterior margin of the mitral anulus to the interventricular septum at a point along the septal margin of the ventricular outflow tract.

Average values for subvalvular and apical diameters, \( d_{\text{sub}} \) and \( d_{\text{ap}} \), were expressed as the average of sagittal and transverse subvalvular diameters and of sagittal and transverse apical diameters, respectively. The ratio of subvalvular to apical diameter (\( d_{\text{sub}}/d_{\text{ap}} \)) was determined using average, or \( D \), values. Eccentricity index (E) was determined by relating the average of the mid-diameters, \( D_{\text{mid}} \), to the

![Figure 1. Diagram of the angiographic measurements made in the right anterior oblique (RAO) view.](http://circ.ahajournals.org/content/107/4/107/F1.large.jpg)
length of the ventricle on the sagittal image, $l_{\text{rao}}$, according to the mathematical relationship:

$$E = \sqrt{\left(\frac{l_{\text{rao}}}{2}\right)^2 - \left(\frac{D_{\text{mono}}}{2}\right)^2}$$

As the index approaches 0.0, the ventricle approaches a sphere in shape; as the index approaches 1.0, ventricular shape approaches a straight line.10

Assumptions inherent in experimental design were examined in a separate series of experiments. To test the assumption that right and left stroke volumes were equal in the steady state, consecutive right and left ventricular indicator dilution curves were obtained and compared in nine animals before production of mitral valvular insufficiency. Right ventricular curves were obtained by injecting indocyanine green into the coronary sinus and simultaneously sampling blood from the pulmonary artery. Left ventricular curves were obtained by injecting into either pulmonary artery, left atrium, or left ventricle and sampling blood from the aorta. Green dye dilution stroke volumes measured from the right heart averaged 27.6 ± 4.5 (se) ml while simultaneous stroke volumes from the left side averaged 28.2 ± 4.3 ml ($r = 0.94$). To test the assumption that values for ventricular stroke volume determined by indicator dilution and cineangiographic analysis were equal, values for ventricular stroke volume determined by each method before production of valvular insufficiency in 16 animals were compared.10 Stroke volumes calculated from the left ventricular angiograms averaged 26.1 ± 2.0 ml while the simultaneously measured stroke volumes calculated from green dye curves on the right side of the heart averaged 24.7 ± 2.2 ml ($r = 0.93$).

The basic protocol of study is outlined below. Before production of mitral valvular insufficiency, control central aortic, left ventricular and left atrial pressures, forward blood flow, and ventricular cineangiography were obtained.

Thirty to 45 minutes after production of mitral valvular insufficiency hemodynamic and angiographic data were collected in a control, or ambient state. Forty-five to 60 minutes after control measurements, hemodynamic and angiographic data were again collected at the same heart rate, but during intravenous infusion of either angiotensin (5–10 μg/min); or an agent with inotropic properties, calcium chloride (2 g/30 ml normal saline/5–10 min), or epinephrine (15–30 μg/min; or immediately after intravenous infusion of low molecular weight dextran (250-200 ml/5-10 min). During these interventions, heart rate was kept constant by right atrial pacing via the coronary sinus.

Results

Effect of Acute Mitral Insufficiency

Following the production of mitral insufficiency, total left ventricular stroke volume was increased from 26 ± 2 (se) ml to 40 ± 3 ml ($P < 0.05$) while effective stroke volume was decreased from 24 ± 2 ml to 18 ± 2 ml. Total ejection fraction was increased from 0.48 ± 0.04 to 0.60 ± 0.03 ($P < 0.05$) and regurgitant volume represented 54 ± 3% (range 42 to 74%) of total left ventricular stroke volume. Left ventricular volume at end-diastole was increased from 57 ± 6 ml to 68 ± 5 ml ($P < 0.05$) while end-diastolic pressure was not significantly different. Mean left atrial pressure averaged 8 ± 1 mm Hg immediately following the induction of mitral insufficiency with the V waves peaking to 13 ± 2 mm Hg. Mean heart rate was increased from 143 ± 8 beats/min to 157 ± 6 beats/min ($P < 0.05$).

The Effects of Ventricular Load

Increments in Volume

When blood volume was expanded by infusion of low molecular weight dextran, mean aortic pressure was not increased significantly. Peak left ventricular pressure was increased from 121 ± 12 mm Hg to 138 ± 9 mm Hg ($P < 0.05$), while end-diastolic ventricular pressure was increased from 5 ± 1 mm Hg to 12 ± 2 mm Hg ($P < 0.05$). Mean atrial pressure was increased from 5 ± 1 mm Hg to 13 ± 2 mm Hg, and the V wave, from 8 ± 1 to 20 ± 3 mm Hg. Left ventricular dP/dt was not changed significantly.

Hydraulic Calculations. The systolic ventricle-atrial pressure gradient (MRG) was increased 6% from 108 ± 12 to 115 ± 8 (fig. 2, panel A) and the VSI from 150 ± 10 to 170 ± 10 msec ($P < 0.05$). The volume of regurgitant flow was increased from 19 ± 2 to 32 ± 5 ml ($P < 0.05$) (fig. 2B). The calculated area of the mitral regurgitant lesion was increased from 0.34 ± 0.03 cm² to 0.49 ± 0.08 cm² ($P < 0.05$) (fig. 2, panel C). The 68% increase in regurgitant volume is four times greater than the 17% increase in regurgitant volume predicted from the hydraulic formula on the basis of MRG and VSI alone.

Angiographic Studies. Ventricular volume at end-diastole was increased from 60 ± 7 ml to 88 ± 9 ml ($P < 0.05$) (fig. 2D). Total stroke volume was increased from 38 ± 4 to 57 ± 6 ml; effective stroke volume, from 18 ± 2 to 26 ± 5 ($P < 0.05$); while total ejection fraction' was not changed significantly (0.63 vs 0.65). However, with the large increase in MRV, effective ejection fraction was actually unchanged at 30%. The ratio MRV/SV total increased from 0.52 ± 0.03 to 0.56 ± 0.06 ($P < 0.05$).

The average of the biplanar diameters of the subvalvular region of the end-diastolic ventricular cavity was increased from 4.08 ± 0.17 cm to 4.89 ± 0.16 cm ($P < 0.05$) (fig. 2E); and the end-diastolic diameter of the mitral anulus, from 2.48 ± 0.17 cm to 2.96 ± 0.25 cm ($P < 0.05$) (fig. 2F). The eccentricity index was reduced from 0.78 ± 0.02 to 0.71 ± 0.02, ($P < 0.05$) indicating that the ventricle became more globular in shape.

Increments in Pressure

When systemic pressure was raised by infusion of angiotensin, mean aortic pressure was increased from 117 ± 8 mm Hg to 144 ± 5 mm Hg ($P < 0.05$); peak left ventricular pressure from 130 ± 8 mm Hg to 156 ± 5 mm Hg ($P < 0.05$); and the end-diastolic ventricular pressure, from 9 ± 2 mm Hg to 12 ± 3 mm Hg ($P < 0.05$). Mean atrial pressure increased from 8 ± 2 mm Hg to 11 ± 3 mm Hg ($P < 0.05$), while the V wave increased from 13 ± 2 to 18 ± 3 mm Hg. Left ventricular dP/dt increased from 3100 ± 200 to 3700 ± 400 mm Hg/sec ($P < 0.05$).
Hydraulic Calculations

The MRG was increased from 114 ± 5 mm Hg to 137 ± 2 mm Hg (P < 0.05) (fig. 3, panel A), an increase of 20%. The VSI was decreased from 120 ± 5 msec to 110 ± 5 msec (P < 0.05). Nevertheless, regurgitant volume was increased from 18 ± 4 ml to 31 ± 3 ml (fig. 3B). This 72% increase in MRV is vastly greater than the 1% increase predicted by the hydrodynamic formula, were MRA to remain constant. The calculated area of the mitral lesion was increased from 0.39 ± 0.08 cm² to 0.64 ± 0.04 cm² (fig. 3C).

Angiographic Studies

Ventricular volume at end-diastole was increased from 68 ± 10 ml to 79 ± 13 ml (P < 0.05) (fig. 3D). Total stroke volume increased from 35 ± 5 to 45 ± 6 (P < 0.05) while effective stroke volume was decreased from 18 ± 3 to 14 ± 3 ml (P < 0.05) and total ejection fraction changed from 0.52 ± 0.05 to 0.63 ± 0.03 (NS). However the effective ejection fraction was reduced from 26 ± 3 to 18 ± 3% (P < 0.05) due to the large increase in MRV. The ratio MRV/SVtot rose from 0.50 ± 0.05 to 0.65 ± 0.06 (P < 0.05). The average of biplanar diameters of the subvalvular region of the end-diastolic ventricular cavity increased from 4.21 ± 0.15 cm to 4.69 ± 0.17 cm (P < 0.05) (fig. 3E); and the end-diameter of the anulus, from 2.60 ± 0.20 cm to 2.97 ± 0.10 cm (P < 0.05) (fig. 3F). The eccentricity index was reduced from 0.78 ± 0.02 to 0.74 ± 0.03.

The Effects of Ventricular Contractility

When calcium chloride or epinephrine was infused, mean aortic pressure, peak and end-diastolic ventricular pressures, and mean atrial pressure were changed insignificantly. Left ventricular dP/dt rose substantially from 3400 ± 500 to 4500 ± 700 mm Hg/sec (P < 0.05).
Figure 3. The effects of augmenting aortic pressure with angiotensin infusion. Notation as in figure 1.

Figure 4. The effects of augmenting ventricular contractility. Notation as in figure 1.
forward stroke volume rose slightly from 18 ± 3 to 20 ± 5. Although total ejection fraction changed little (0.65 vs 0.67), effective ejection fraction increased from 25 to 37%, while MRV/SV, decreased from 0.63 ± 0.05 to 0.49 ± 0.06 (P < 0.05).

The average of biplanar diameters of the subvalvular region of the end-diastolic cavity was reduced from 4.54 ± 0.23 cm to 3.89 ± 0.21 cm (P < 0.05) (fig. 4E); and the end-diastolic anular diameter, from 2.62 ± 0.14 cm to 2.16 ± 0.08 cm (P < 0.05) (fig. 4F). The eccentricity index was increased from 0.80 ± 0.01 to 0.84 ± 0.01 (P < 0.05).

Relative Effects of the Area of the Mitral Lesion and the Pressure Gradient Across the Lesion

With altered ventricular load and contractility, the change in MRV was correlated with changes in either the end-diastolic diameter of the subvalvular cavity (fig. 5) or the diameter of the mitral anulus (fig. 6). The MRV was well correlated with MRG only when alteration in subvalvular diameters was not a dominant factor (fig. 7). When load and contractility were not altered, regurgitant mitral flow was highly correlated with the diameters of the subvalvular cavity and mitral anulus at end-diastole, but could not be correlated with either the pressure gradient or the time interval for regurgitation. The MRF was highly correlated with LV end-diastolic basilar diameter (r = 0.85), LV end-diastolic anular diameter (r = 0.69), and LV end-diastolic volume (r = 0.68).

There was no correlation between regurgitant flow and the subvalvular or anular diameters at mid-systole or end-systole under control conditions or when load or contractility was changed.

A good correlation was found between MRA calculated from the hydraulic formula and the angiographically measured mitral anular diameter (fig. 8). This relationship supports conclusions concerning changes in the regurgitant orifice consequent to ventricular volume.

Effect of Ventricular Loading and Contractility on the Shape of the Ventricle

When ventricular load and contractility were altered, the shape of the ventricle at end-diastole was also altered. When dextran was infused and blood volume augmented, the eccentricity index decreased from 0.78 ± 0.02 to 0.71 ± 0.02 (P < 0.05), indicating the assumption of a more spheroidal shape. During an angiotensin infusion, the eccentricity index also decreased from 0.78 ± 0.02 to 0.74 ± 0.03 (P < 0.05). Thus, the ventricle assumed a less eccentric shape, or became more spherical, when volume or pressure was augmented. When calcium or epinephrine was infused, the eccentricity index increased from 0.80 ± 0.01 to 0.84 ± 0.01 (P < 0.05); hence, the ventricle became more eccentric at end-diastole when contractility was augmented and a decrease in ventricular end-diastolic volume occurred.

Discussion

In the present study it has been demonstrated that when acute mitral regurgitation is induced in the normal dog heart.
by section of a chordae tendineae, the amount of regurgitation is highly dependent on the geometry of the mitral orifice and subvalvular area of the ventricle and is not determined primarily by the systolic pressure gradients between the left ventricle and the atrium. Thus, the mitral area for regurgitation is not fixed in such a lesion but is actively determined by ventricular dynamics.

Accordingly, factors which tend to enlarge the diastolic volume of the ventricle will also increase the subvalvular mitral area and diameter of the mitral ring, and hence augment the amount of mitral regurgitation. Indeed the major mechanism by which an increase in arterial pressure leads to an increase in mitral regurgitation is not due to a significant increase in the gradient for regurgitation but rather to a compensatory increase in diastolic ventricular volume and thus secondarily to an enlargement of the regurgitant area. That this should be the case is further emphasized by the fact that the amount of regurgitation depends on the square root of the pressure gradient and directly on the area. Thus a very large increment in left ventricular systolic pressure and the resultant pressure gradient would create only a relatively minor effect on regurgitant flow, were the area for regurgitation to remain fixed. Alternatively, factors which tend to reduce ventricular size were shown in the present study to reduce mitral regurgitation, again largely independent of changes in transvalvular gradients.

We have shown that the diameter of the subvalvular ventricular cavity is related to the diastolic volume of the heart and changes with alterations in volume. Likewise the mitral regurgitant area calculated from hemodynamic measurements correlates reasonably well with the area measured from left ventricular angiograms (fig. 8).

During ventricular systole, the subvalvular mitral region contracts along with the remainder of the ventricle and may help to bring components of the mitral apparatus closer together, thereby helping to maintain or improve valve closure. We have no direct evidence as to how this contributes to the dynamic regurgitant area we have measured.

Alternative explanations of the present data were also considered. With altered ventricular load and contractility, alterations in the shape of the left ventricle have been documented. At end-diastole the left ventricle is more spherical during angiotensin and volume infusion, and more eccentric during calcium or epinephrine infusion. Thus, in addition to ventricular size, ventricular shape and the orientation of papillary muscles and forces acting on the mitral leaflets during valvar closure may have influenced the effective area of the mitral lesion. However, no good correlation has been found between the rate of left ventricular pressure development and the volume of regurgitant flow. Furthermore, we have assumed that as thin and mobile structures, the mitral leaflets were fully deflected over the observed range of pressure gradients, although theoretically, pressure-related variation in deflection of a free leaflet edge could further alter the size of the regurgitant orifice. In addition, in the present study, valve gradients and flows were measured as mean values. Whether or not the same results would obtain with measurements of instantaneous pressures and flows and the use of these values to calculate valve orifice areas remains to be determined.

In earlier studies of experimental mitral regurgitation, Wiggers demonstrated that acute mitral insufficiency produced a major increase in total left ventricular stroke volume with little change in either forward blood flow or arterial blood pressure. When regurgitant volume became immense, pulmonary edema and death ensued. Later studies employed an external cannula between the left ventricle and left atrium to produce a controlled level of mitral insufficiency. Ventricular compensation was obtained by an augmentation of end-diastolic volume (Starling mechanism) combined with a fall in impedance which tended to augment ventricular emptying. The dynamic component provided
by a varying mitral regurgitant orifice was vitiated by the experimental arrangement. Nevertheless, the principles of the hemodynamic formulæ were affirmed in that the orifice of the cannula was more important than the pressure gradient in determining regurgitant flow.  

The relation of the present animal model to mitral disease in man remains speculative. The experimental model itself resembles the clinical syndrome of ruptured chordae tendineae. As a model of mitral regurgitation due to a variable orifice, it also resembles the syndrome of papillary muscle dysfunction due to ischemia. Mitral regurgitation may also develop, but not invariably, in the absence of organic valvular disease in cardiomyopathies with ventricular dilatation, whether due to coronary artery disease, infection, or inflammation of the myocardium, chronic alcohol ingestion, or ventricular outflow obstruction. In these circumstances, where the mitral apparatus is not rigid, alterations in the size of the subvalvular cavity and the circumference of the anulus may be translated into changes in regurgitant orifice, and hence orifice flow. According to this hypothesis, net augmentation of ventricular afterload and/or preload tends to enlarge the ventricle, widen the anulus and orifice, and increase flow. Conversely, reduction in ventricular volume tends to narrow the anulus and orifice, and decrease regurgitant flow. Moreover, several clinical observations may be explained by this phenomenon such as systolic murmurs that diminish or intensify with time; patients with chordal rupture and pulmonary edema who respond promptly to therapy with digitalis and diuresis; and patients with cardiomyopathy complicated by mitral regurgitation which diminishes or disappears entirely when ventricular function is improved and heart size reduced.

These findings form further support for the view that a reduction in left ventricular volume is beneficial in mitral insufficiency and that ventricular dilatation may be detrimental. Previous studies have emphasized that the rapid reduction in ventricular size resulting from decompression of the left ventricle into the left atrium may reduce force in the wall via the LaPlace relation and thus permit even faster muscle shortening. This same process may also help to reduce regurgitation itself by reducing the orifice for regurgitation. The same mechanism would help to explain the beneficial effects of reducing systemic vascular resistance in mitral insufficiency where the actual changes in arterial pressure are relatively small. During therapy with vasodilators such as nitroprusside, the loss of large V waves appears to occur without a significant decrease in the ventriculo-atrial gradient. Indeed with the loss of the V wave and a modest fall, if any, in ventricular pressure, this gradient is actually increased. According to our hypothesis the major benefit may be from reduction in ventricular volume and hence regurgitant orifice size but this speculation remains to be explored.

Whether the degree of mitral regurgitation can also be altered on the basis of changes in the subvalvular area in rheumatic mitral disease remains to be explored. Nevertheless, the principles developed from the present animal model may play a role.

Acknowledgment

The authors are indebted to Patricia Sullivan, Maureen Campbell, Irene Dowgiato, Robert U. Johnson, John Klopping and Stephen Fischel. Dr. Fischel provided casts of canine hearts for calibration of the experimental system.

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Circulation. 1977;56:106-113
doi: 10.1161/01.CIR.56.1.106

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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