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Evaluation of Myocardial Contractility Indices in Acute Experimental Mitral Regurgitation[1] (38278)

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A new method of producing acute reversible mitral regurgitation in the anesthetized, open-chested dog is described. Using this model, the effect of varying amounts of acute mitral regurgitation upon left ventricular peak dp/dt, peak V_{ce}, and V_{max} were determined. For small amounts of mitral regurgitation of a degree which causes mild hemodynamic derangement, no significant effects on contractility indices were noted. With more severe degrees of mitral regurgitation, significant falls in all indices were noted. For a given mitral defect, varying the level of ventricular contractility had a minimal influence on the effect of acute mitral regurgitation on the three contractility indices. While all indices of contractility were influenced to a comparable degree by acute mitral regurgitation, peak dp/dt was more sensitive to changes in inotropic state.

The rapid development of surgical techniques for valve replacement and myocardial revascularization during the last decade has allowed a group of patients with mitral regurgitation and myocardial disease to be considered for mitral valve replacement. However, contractility indices which accurately reflect the status of the myocardium independently of the degree of mitral regurgitation are badly needed in the preoperative assessment of such patients.

Recent publications have emphasized the significance of the maximum first derivative of the left ventricular pressure, peak *dp/dt*, the determination of the peak and the extrapolated maximum velocity of isometric contractile element shortening (peak V_{ce} and V_{max}) as indicators of myocardial contractility (1, 2). They have already been applied to a variety of clinical conditions (3, 4), but their significance and reliability in conditions of premature left ventricular unloading such as mitral regurgitation has been questioned (3).

This experimental study was designed primarily to determine and compare the effect on peak left ventricular *dp/dt*, peak V_{ce} and V_{max} of several degrees of acute mitral regurgitation both in the presence of normal and pharmacologically depressed and enhanced myocardial contractility.

Material and Methods. Mongrel dogs in a fasted state, weighing 14–22 kg, were anesthetized with an intravenous mixture of alpha-chloralose (80 mg/kg) and urethane (0.7 mg/kg). Respiration was controlled using a Harvard pump administering humidified room air via an endotracheal tube. Depth and rate of respiration were adjusted to maintain arterial pO_2 at 100 mm Hg, pH between 7.35 and 7.45, and pCO_2 between 25 and 35 mm Hg throughout the experiments; temperature was maintained with a heating pad. A left lateral thoracotomy at the 5th intercostal space was made, the pericardium exposed and opened, and the heart suspended in a pericardial cradle. Solid-state pressure cells precalibrated and balanced in water at 39°, with a flat frequency response to over 1000 Hz, were inserted through the apical dimple into the left ventricle and through the left atrial appendage into the left atrium to measure simultaneously left ventricular and left atrial pressures (both in mm Hg). A Honeywell differentiator with a linear amplitude response to 128 Hz was used in all the experiments to obtain *dp/dt*. A large-bore catheter was inserted into the left carotid artery and advanced to the ascending aorta; this was connected to a Statham P23Db pressure transducer for determination of central aortic pressure. A venous catheter was positioned in the

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right atrium via the jugular vein to measure central venous pressure (cm H_2O). Fluids lost during the surgical procedure were replaced, attention being directed to the maintenance of a stable central venous pressure. Cardiac output (minus coronary flow) was measured by means of an externally calibrated electromagnetic flow probe positioned around the proximal ascending aorta. The variability of this determination was ±10% when compared to dye dilution curves.

Recordings were made using a Honeywell visicorder ultraviolet optical recorder with high-frequency galvanometers, with one preamplifier set to register the electrocardiogram. Peak velocity of the contractile element (V_{ce} muscle-length/sec) was calculated from the simultaneously recorded left ventricular pressure and the *dp/dt* at 200 mm/sec paper speed; the formula:

$$V_{ce} = \frac{dp/dt}{32P}$$

(P = total pressure) was used in all calculations (1, 5). The maximum velocity of shortening V_{max}(muscle-length/sec) was obtained by linear extrapolation to zero pressure (best fitting line) of the pressure–velocity curve (1).

For production of experimental mitral regurgitation, a long, No. 18 gauge needle with a string passed through it was introduced through the apical left ventricular wall into the left ventricular cavity and across the mitral valve orifice, advancing carefully to avoid damaging a leaflet. A finger introduced into the left atrium cavity via the excised appendage guided the tip of the needle across the mitral valve and out the left atrial cavity. The needle was withdrawn, leaving only the string through the mitral valve with an end exteriorized through the left ventricular apical wall and the other end through the left atrial appendage. A hollow, short plastic tube of one of three diameters (7, 11, and 16 mm) was attached to the atrial end of the string and pulled into the left atrial cavity. The other end of the cylinder was attached to another string, which remained exteriorized through the left atrial appendage incision, which, in turn, was closed with a purse-string suture. Gentle pulling exerted on the left ventricular string interposed the cylinder between the mitral leaflets and allowed regurgitant flow to reach the left atrium through the hollow lumen without causing ventricular extrasystoles (Fig. 1). Immediate normal valve closure, with return to control conditions, was restored when the ventricular string was released and the cylinder was retracted back into the left atrial cavity.

After instrumentation was completed, a period of stable recordings was obtained. Two types of experiments were conducted. In the first group of dogs, the effects of several degrees of mitral regurgitation in the presence of normal contractility were studied; controls were taken at 200 mm/sec paper speed with the respirator off for a brief period of time to avoid respiratory variations in pressures; mitral regurgitation was then induced by the method described above, using different sized cylinders (Fig. 2). Records were taken during the mitral regurgitation as soon as stabilization was apparent, usually in less than 2 min. After recording of at least five sequences of mitral regurgitation (with return to control conditions after each sequence) with the initial cylinder, it was interchanged by another of different diameter and the sequences repeated. In most dogs, hemodynamic stability after completion of these two sequences permitted the interchange of a third different diameter cylinder, and the same sequences were repeated. Mitral regurgitation was maintained for a few minutes only, the hemodynamic changes return-

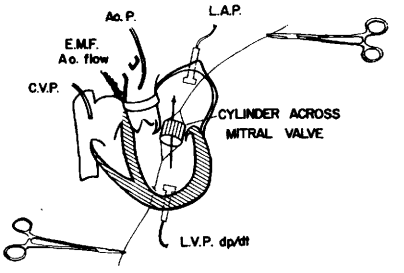

FIG. 1. Diagram showing experimental method of producing acute mitral regurgitation. C.V.P. = central venous pressure line; E.M.F. = electromagnetic flow probe on ascending aorta; Ao.P. = aortic pressure catheter; L.A.P. - left atrial manometer; L.V.P. dp/dt = manometer used to obtain left ventricular pressure and dp/dt. The arrow indicates regurgitant flow induced by positioning the cylinder across the mitral valve by means of threads attached to the cylinder ends.

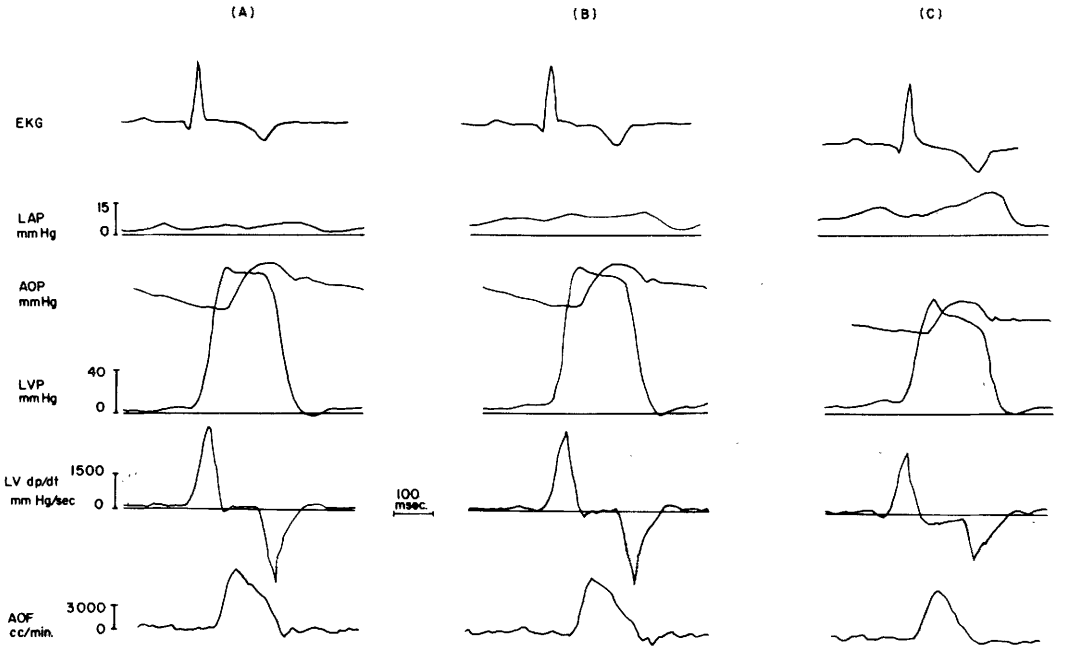

FIG. 2. Records from a single dog demonstrating control recordings (A) and subsequent induction of mitral regurgitation with a small (7 mm) cylinder (B), and a medium-sized (11 mm) cylinder (C).

ing to control levels soon after normal mitral competence was restored. We rarely observed extra beats during these maneuvers; whenever they occurred, the sequence was discarded and repeated.

In the second group of dogs, the changes in contractile indices produced by mitral regurgitation in the presence of enhanced and depressed contractility were studied; controls were taken as in Group I, and only one size of cylinder was used to produce mitral regurgitation (11 mm). Five sequences of mitral regurgitation were recorded in conditions of normal contractility. Dogs were then given intravenous norepinephrine (4 μg/kg/min) and sequences repeated in the same fashion. Similar measurements were taken 15 min after administration of a bolus of 2 mg/kg propranolol intravenously and 5 min after giving 20 mg/kg of diabutal. Calculations of V_{ce} and V_{max} were performed as described previously.

Changes in left ventricular systolic pressure, left ventricular diastolic pressure, left atrial V wave, aortic diastolic pressure, and cardiac output were used to assess the hemodynamic effects of mitral regurgitation. Although it was not possible to make an accurate measurement of the regurgitant flow with our model (as opposed to the left ventricular to left atrial shunt model), attempts were made to roughly estimate the regurgitant volume using the following formula (6):

$$\text{Regurgitant flow} = 350 \times (\text{regurgitant LA V wave} - \text{control LA V wave}).$$

The degree of mitral regurgitation was expressed as a ratio of the estimated regurgitant flow to the forward flow.

Standard statistical techniques such as paired and nonpaired Student's t tests were applied to data in order to assess significance.

Results. Effects of mitral regurgitation of varying degrees. In the first group of 8 dogs with normal contractility, 43 sequences with the small cylinder (7 mm i.d.), 16 sequences with the mid-sized cylinder (11 mm i.d.), and 21 sequences with the large-sized cylinder (16 mm i.d.) were recorded. Results are summarized in Tables IA and IB.

With "mild" mitral regurgitation (small-sized cylinder), no significant changes were observed in heart rate; there were significant decreases in left ventricular systolic pressure (9%), aortic systolic pressure (6%), aortic diastolic pressure (7%), and aortic flow (13%); left atrial

TABLE IA. Hemodynamic Changes During Variable Mitral Regurgitation in Dogs with "Normal" Contractility.

	HR	LVSysP (mm Hg)	LVEDP (mm Hg)	LAVw (mm Hg)	AoSysP (mm Hg)	AoDiasP (mm Hg)	AoFl (cc/min)	Ratio Regurg. Fl/ Forward El
Small cylinder (7 mm i.d.) (No. sequences)	(43)	(43)	(43)	(43)	(25)	(25)	(25)	(25)
Cont. ± SEM	145 ± 5	123 ± 2	5 ± 0.3	5 ± 0.3	133 ± 2	92 ± 2	1900 ± 60	1.26 ± 0.1
MR ± SEM	145 ± 5	112 ± 3	7.0 ± 4	11 ± 1	125 ± 2	85 ± 2	1670 ± 70	
Δ% SEM	—	−9 ± 1	+50 ± 7	120 ± 9	−6 ± 0.1	−7 ± 1	−13 ± 2	
P	NS	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	
Medium cylinder (11 mm i.d.) (No. sequences)	(16)	(16)	(16)	(16)	(9)	(9)	(9)	(9)
Cont. ± SEM	137 ± 9	127 ± 3	5 ± 0.5	6.4 ± 0.5	129 ± 1	94 ± 2	1680 ± 120	
MR ± SEM	137 ± 9	93 ± 3	11.5 ± 1	23.7 ± 2	103 ± 2	75 ± 3	1180 ± 100	4.7 ± 0.3
Δ% ± SEM	—	−27 ± 2	+166 ± 33	274 ± 17	−20 ± 2	−20 ± 3	−30 ± 3	
P	NS	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	
Large cylinder (16 mm i.d.) (No. sequences)	(21)	(21)	(21)	(21)	(21)	(21)	(21)	(21)
Cont. ± SEM	145 ± 8	133 ± 2	4 ± 0.5	3.7 ± 1.3	134 ± 2	96 ± 2	1800 ± 100	
MR ± SEM	144 ± 8	93 ± 3	12 ± 0.5	27.5 ± 1	98 ± 2	66 ± 2	1100 ± 100	7.6 ± 0.5
Δ% ± SEM	—	−30 ± 2	+300 ± 40	650 ± 30	−27 ± 2	−30 ± 3	−35 ± 3	
P	NS	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	

V wave increased by 120% and left ventricular end-diastolic pressure by 50%. The estimated ratio of regurgitant flow/forward flow was 1.3. Minor, nonsignificant decreases were observed in peak *dp/dt*, peak V_{ce} and V_{max}.

When a "moderate" amount of mitral regurgitation was produced (11-mm cylinder), left ventricular systolic pressure decreased by 27%, aortic systolic pressure by 20%, aortic diastolic pressure by 20%, and aortic flow by 30%; left atrial V wave increased by 274% and left ventricular end-diastolic pressure by 166%. The estimated regurgitant flow/forward flow ratio increased to 4.7, left ventricular *dp/dt* decreased by 17%, V_{ce} by 20%, and V_{max} by 13%, all of these changes being statistically significant.

When the large cylinder was used to cause "massive" mitral regurgitation, changes in all parameters (except heart rate) were more pronounced. Left ventricular systolic pressure decreased by 30%, aortic systolic pressure by 27%, aortic diastolic pressure by 30%, and aortic flow by 35%. Left ventricular end-diastolic pressure increased by 300%, and left atrial V wave rose to 650% of the control value. The estimated regurgitant flow/forward flow increased to 7.6; contractile indices all showed a similar decrease of about 20% of their control values.

Influence of altered contractility on the effect of mitral regurgitation. In this group of experiments, the first sequence of mitral regurgitation was performed with the medium-sized cylinder (11 mm i.d.) and without changing the contractile state, and were used as a reference for the following sequences with altered contractility. Heart rate did not change significantly, left ventricular systolic pressure decreased by 28%, and aortic flow by 29%. Left ventricular end-diastolic pressure rose by 170% and left atrial V wave by 274%. Contractile indices showed significant decreases, *dp/dt* by 17%, V_{ce} by 12%, and V_{max} by 16%. These changes were similar to those obtained in the first group of experiments when the same sized cylinders were used.

Following the recording of these control sequences, norepinephrine was administered (4 μg/kg/min), when this produced a stable elevation of the left ventricular systolic pressure (approximately 25%) and *dp/dt* rose (approximately 100%). Mitral regurgitation was provoked while

TABLE IB. Changes in Contractility Indices in Dogs with Normal Contractility and Variable Mitral Regurgitation.

	dp/dt (mm Hg/sec)	V_{ce} M-L/sec	V_{max} M-L/sec
Small cylinder (7 mm i.d.) (No. sequences)	(43)	(43)	(43)
Cont. ± SEM	3480 ± 160	2.7 ± 0.1	3.6 ± 0.1
MR ± SEM	3400 ± 164	2.5 ± 0.1	3.5 ± 0.1
Δ% ± SEM	−3 ± 1	−6 ± 2	−2 ± 1
P	NS	NS	NS
Medium cylinder (11 mm i.d.) (No. sequences)	(16)	(16)	(16)
Cont. ± SEM	3280 ± 150	2.45 ± 0.1	3.26 ± 0.13
MR ± SEM	2660 ± 140	1.94 ± 0.1	2.80 ± 0.12
Δ% ± SEM	−17 ± 3.5	−20 ± 4	−13 ± 3
P	< 0.005	< 0.001	< 0.001
Large cylinder (16 mm i.d.) (No. sequences)	(21)	(21)	(21)
Cont. ± SEM	3830 ± 110	2.71 ± 0.1	3.97 ± 0.1
MR ± SEM	2960 ± 130	2.2 ± 0.1	3.18 ± 0.2
Δ% ± SEM	−20 ± 2	−19 ± 2	−20 ± 2
P	< 0.001	< 0.001	< 0.001

maintaining the norepinephrine drip at the same rate. Under these conditions, there was a small, nonsignificant increase in heart rate (7%), significant decreases in left ventricular systolic pressure (28%) and aortic flow (29%), and elevations of left ventricular end-diastolic pressure (182%) and left atrial V wave (500%). Relative to the control levels, there was a somewhat greater decrease in *dp/dt* (22%) and V_{ce} (16%). The percentage change in V_{max} was the same as control (16%).

After norepinephrine was discontinued and its effects dissipated, hemodynamic changes returned to control levels. Propranolol (2 mg/kg) was then given intravenously as a single bolus; after 20 min, average peak *dp/dt* had decreased to 70% of control. Similar mitral regurgitation sequences were obtained at this time, with the following results observed: heart rate did not change, left ventricular systolic pressure decreased by 31% and aortic flow by 30%, left ventricular end-diastolic pressure rose by 122% and left atrial V wave by 298%. Changes in contractile indices were: peak left ventricular *dp/dt*, −16%; peak V_{ce}, −18%, and V_{max}, −9%.

A further depression of contractility was obtained by giving an intravenous bolus of diabutal (20 mg/kg), reducing *dp/dt* to 60% of control. Routine sequences of mitral regurgitation were once more recorded, during which heart rate did not change, left ventricular systolic pressure was reduced by 30%, and aortic flow by 35%, left ventricular end-diastolic pressure rose 125%, and left ventricular V wave to 299%. V_{ce} showed a reduction of 17%; both *dp/dt* and V_{max} were reduced somewhat less than in control conditions (12 and 9%, respectively).

Discussion. Several hemodynamic studies have been carried out experimentally in animals (6–11) and clinically (12–15) during the past 20 years delineating the acute hemodynamic changes during mitral regurgitation. In general, they have found an initial decrease in forward output and pressures, with rapid restoration to normal or near-normal levels, coupled with an increase in the mechanical efficiency of the normal heart, reflected by an increased ejection fraction. The profound alteration in hemodynamics, brought about by changes in the

impedance to the ejection of the left ventricle, makes difficult the evaluation of the contractile state. The application of traditional indices in this condition gives frequently misleading results (16), and even a normal ejection fraction may be consistent with impaired contractility (7). In models of mitral regurgitation *in vitro*, a decrease has also been shown in the reserve of the Frank–Starling mechanism not accompanied by changes in contractile state (17).

The use of velocity indices of myocardial contraction, based upon the work of several investigators (1, 2, 18, 19), has been proposed for clinical evaluation of myocardial contractility, independent of pre- and afterload influences. The first derivative of the left ventricular pressures, *dp/dt*, has been shown to be an indicator of inotropic state (16, 19), but it is also somewhat affected by changes in heart rate (16). Many studies in isolated and intact canine heart have been undertaken to evaluate the effects of preload and afterload changes upon *dp/dt*; the results are somewhat contradictory; some studies found it to be affected by afterload but not by preload changes (10, 20), and others reported a significant effect on both preload and afterload (1, 5).

In the presence of mitral regurgitation, *dp/dt* has also been shown to be affected by these factors in both *in vitro* muscle preparations and in intact hearts (11, 17). Although preliminary studies of premature left ventricular unloading did not recommend the use of V_{ce} and V_{max}, due to the absence of a true isometric phase (1), studies *in vitro* indicated no changes in V_{max} in simulated mitral regurgitation (17, 21). The same results were also reported in intact dogs with left ventricular-left atrial shunt, with regurgitant flows of about the same magnitude as forward output (22, 23). However, the ventricular–atrial shunt method of producing mitral regurgitation is less satisfactory for determining the effect of mitral regurgitation on isometric systole because of the greater inertial mass of blood contained in the shunt, which tends to delay the movement of blood from ventricle to atrium (24). It was for this reason that we developed the method above for producing mitral regurgitation.

In our experimental model, using a high-frequency response system to record pressures and *dp/dt*, and observing the changes in contractile indices without controlling preload or afterload, there were no significant changes in *dp/dt*, V_{ce}, and V_{max} when mitral regurgitation was relatively mild. With more marked levels of mitral regurgitation, we observed decreases in all inotropic parameters, in the presence of a "normal" contractile state.

The degree of mitral regurgitation that we observed with the small cylinder (7 mm i.d.) is most probably similar to that obtained in previous studies using a left ventricular–left atrial shunt as a model for mitral regurgitation in the dog (6, 7, 9–11, 22). From previous studies (6), a volume of regurgitant flow at least equal to the forward flow was determined as the amount needed to cause these minimum changes in the hemodynamic parameters. The duration of the isometric phase was not changed nor was the contour of the left atrial pressure curve during this period. As previously described (8), most of the elevation of the left atrial pressure occurred in the ejection phase and in protodiastole, since a short period of time is still required to overcome the inertia of blood within the ventricles; and with small degrees of mitral regurgitation, a significant amount of blood is not set in backward motion until the aortic valve opens (8). Preload and afterload also change little, thus explaining the absence of change in contractile indices.

When mitral regurgitation was provoked by using the mid-sized cylinder (11 mm i.d.), a much more evident change in hemodynamics was observed. These hemodynamic changes were more pronounced than in previous studies using left ventricular–left atrial shunts, perhaps due to the limitation of flow in these shunts caused by internal diameter and length and the greater inertial mass of blood within the shunt. The approximate ratio of 4.7 for regurgitant forward flow ratio is in the range of the so-called "severe" clinical mitral regurgitation, as measured by several methods to be 3:1 – 4:1 (25–27), though these measurements were all made in chronic mitral regurgitation. In clinical acute mitral regurgitation (14), similar hemodynamic changes have been reported. Under these circumstances, a shortening of the isometric phase undoubtedly occurs, in part due to mitral regurgitation occurring during this phase and to elevated left ventricular end-diastolic pressure and decreased aortic diastolic pressure. This last factor might be expected to influence *dp/dt* more than the other contractile indices, due to the early opening of the aortic valve (20) since peak *dp/dt*

TABLE II. Hemodynamic and Contractility Indices of Changes in Dogs with Moderate Acute Mitral Regurgitation and Altered Myocardial Contractility.

	HR	LVSysP (mm Hg)	LVEDP (mm Hg)	AoFl (cc/min)	LAVw (mm Hg)	*dp/dt* (mm Hg/sec)	V_{ce} M-L/sec	V_{max} M-L/sec
Normals								
(No. sequences)	(21)	(21)	(21)	(9)	(21)	(21)	(21)	(21)
Cont. ± SEM	171 ± 8	120 ± 3	5 ± 0.4	1580 ± 180	8 ± 0.05	3131 ± 145	2 ± 0.05	3 ± 0.09
MR ± SEM	172 ± 9	87 ± 4	12 ± 0.9	1050 ± 120	29 ± 2	2580 ± 180	1.7 ± 0.08	2.5 ± 0.1
Δ% ± SEM	—	−28 ± 2	+170 ± 28	−29 ± 3	274 ± 31	−17 ± 4	−12 ± 4	−16 ± 3
P	NS	< 0.001	< 0.001	< 0.001	< 0.001	< 0.0025	< 0.01	< 0.001
Norepinephrine								
(No. sequences)	(10)	(10)	(10)	(6)	(10)	(10)	(10)	(10)
Cont. ± SEM	170 ± 9	154 ± 8	5 ± 0.07	1580 ± 280	7 ± 2	6110 ± 570	2.5 ± 0.08	3.4 ± 0.2
MR ± SEM	181 ± 10	110 ± 6	14 ± 2	1080 ± 145	35 ± 3	4510 ± 200	2.1 ± 0.1	2.8 ± 0.2
Δ% ± SEM	+7 ± 1	−28 ± 2	+182 ± 33	−29 ± 2	500 ± 80	−22 ± 6	−16 ± 4	−16 ± 3
P	NS	< 0.001	< 0.001	< 0.025	< 0.001	< 0.05	< 0.005	< 0.0025
Propranolol								
(No. sequences)	(14)	(14)	(14)	(6)	(14)	(14)	(14)	(14)
Cont. ± SEM	137 ± 6	111 ± 4	6 ± 0.3	1082 ± 150	7.5 ± 0.6	2020 ± 70	1.7 ± 0.06	2.5 ± 0.07
MR ± SEM	137 ± 6	77 ± 4	13 ± 1	676 ± 100	29 ± 3	1700 ± 100	1.4 ± 0.07	2.25 ± 0.08
Δ% ± SEM	—	−31 ± 3	+122 ± 14	−35 ± 6	+298 ± 38	−16 ± 3	−18 ± 3	−9 ± 3
P	NS	< 0.001	< 0.001	< 0.05	< 0.001	< 0.001	< 0.001	< 0.025
Diabutal								
(No. sequences)	(20)	(20)	(20)	(10)	(20)	(20)	(20)	(20)
Cont ± SEM	139 ± 4	86 ± 3	6 ± 0.4	1040 ± 140	7 ± 0.7	1535 ± 90	1.6 ± 0.09	2.25 ± 0.1
MR ± SEM	138 ± 4	60 ± 2	12 ± 0.8	445 ± 51	26 ± 2	1325 ± 80	127 ± 0.07	2 ± 0.1
Δ% ± SEM	—	−30 ± 2	125 ± 17	−55 ± 10	299 ± 35	−12 ± 2	−17 ± 3	−9 ± 3
P	NS	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

occurs later in isometric phase than does peak V_{ce} or V_{max}.

Changes in V_{ce} and V_{max} with mitral regurgitation are secondary to several factors. First, there is a decrease in duration of isometric systole. In fact, there may be no true "isometric" phase due to participation of the compliant left atrium as a common chamber with the left ventricle during contraction. Second, there are probably changes in the geometry of the ventricle during mitral regurgitation which may affect assumptions made in calculation of the velocity indices (5). Third, there is an elevation of preload, which has been demonstrated to affect peak V_{ce} and V_{max}, particularly when they are calculated from total rather than developed pressure (28–30).

The degree of mitral regurgitation caused by the large cylinder (16 mm i.d.) has been reported infrequently in previous studies; it may approximate the degree of mitral regurgitation caused by ruptured papillary muscle in a heart with relatively normal contractility and normal size, noncompliant left atrial cavity, resulting in tall, peaked V waves (12, 13). The changes in afterload, preload, and duration of the isometric phase are more pronounced, and there is a prominent effect on the contractile indices.

In Table II are shown the effects of changes in the contractile state on changes in contractility indices, caused by acute mitral regurgitation resulting from a given mitral defect. Although there was a tendency for the contractile indices to fall a greater percentage in the presence of heightened contractility and to fall a lesser percentage in the presence of depressed contractility, these differences were neither marked nor consistent. Therefore, it would appear that for a given mitral valve defect, the percentage fall in contractile indices attributable to mitral regurgitation is relatively independent of the basal level of myocardial contractility.

In comparing the overall value of these three contractile indices in mitral regurgitation, we note that although all responded to a given degree of mitral regurgitation with approximately the same percentage fall, peak *dp/dt* was much more sensitive to changes in inotropic state than was peak V_{ce} or V_{max}. One would therefore anticipate that peak *dp/dt* would be more useful in detecting the presence of significant myocardial depression in the presence of significant mitral regurgitation. Slight amounts of mitral regurgitation would be expected to have only minimal effects on any of the contractile indices.

In a clinical setting, current evaluation of contractile state is made by a combination of hemodynamic measurements (4, 12–16). The availability of manometer-tipped catheters makes possible the calculation of peak *dp/dt*, peak V_{ce}, and V_{max} in clinical mitral regurgitation. Although there is not such study reported to date, experimental results such as ours and others (31) suggest that peak V_{ce} and V_{max} will not offer any advantage over peak *dp/dt* in evaluating the importance of myocardial dysfunction in the presence of mitral regurgitation. Possibly, a combination of hemodynamic measurements at rest and during exercise, peak *dp/dt*, left ventricular angiogram and ejection fraction may offer satisfactory evaluation of myocardial function in the presence of mitral regurgitation.

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