Diastolic “Locking” of the Mitral Valve: The Importance of Atrial Systole and Intraventricular Volume

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SUMMARY Diastolic mitral valve “locking,” defined as sustained diastolic closure of the mitral valve after atrial systole, was investigated by simultaneous hemodynamic and echocardiographic recordings during a protocol of programmed pacing in six dogs with surgically induced atrioventricular block. Atrial extrasystoles were introduced at progressively increasing coupling intervals during programmed prolonged pauses in ventricular pacing. As the coupling interval of the atrial extrasystole was increased, both the mitral reopening time (MRT) and the calculated left ventricular volume (LVV) at the end of the MRT increased proportionally. These interrelations could be best expressed by a general logarithmic function of the form \( y = a + b \ln(x) \), where \( x \) = the coupling interval of the atrial extrasystole and \( y \) = the MRT or the LVV. Correlations between the measured data and the predicted data were excellent \( (r \geq 0.95) \). In each dog, a specific LVV had to be attained to allow a diastolic “locking” of the mitral valve. Atrial standstill and atrial fibrillation were also induced in each dog to study the relative role of atrial systole in locking of the mitral valve. During either atrial standstill or atrial fibrillation, the mitral valve closed transiently, but did not lock, despite the accumulation of a LVV larger than the LVV necessary to lock the valve during sinus rhythm. Thus, diastolic locking of the mitral valve has several determinants, including the presence of active atrial systole and the accumulation of a sufficient intraventricular volume.

THE MECHANISMS of mitral valve closure have been studied, but not completely elucidated. In 1843, Baumgarten\(^1\) postulated that atrial contraction was an important element in the presystolic closure of the mitral leaflets. Others have shown that the abrupt cessation of rapid forward flow through the mitral valve at the end of atrial systole and the vortex formation or eddy currents behind the mitral leaflets may be important in the initiation of mitral valve closure.\(^2\)\(^-\)\(^4\) Evidence for these hypotheses has been obtained in both experimental and human studies.\(^2\)\(^-\)\(^9\) However, Dean\(^6\) observed that in the absence of a subsequent, properly timed ventricular systole, the mitral valve, previously closed by atrial systole, tended to reopen and assume a “midstream” position. It was apparent, therefore, that the contribution of atrial systole to mitral valve motion could only initiate a closing motion of the mitral valve, but was insufficient to “lock” the valve in the closed position for the duration of diastole. The mechanisms that sustain diastolic mitral valve “locking” have never been demonstrated. In this study, we correlated echocardiographic and hemodynamic data obtained during various patterns of atrioventricular (AV) pacing in an experimental canine model.

Material and Methods

The study was performed in six healthy mongrel dogs, mean weight 17.3 ± 1.8 kg. The dogs were anesthetized with i.v. sodium pentobarbital (30 mg/kg), intubated and ventilated with room air by a Harvard respirator. The heart was exposed by mid sternotomy, and pairs of 0.1-mm-diameter bipolar plunge electrodes that were Teflon-coated except at the tips were placed intramurally in the left atrium and left ventricle for cardiac pacing. AV block was induced by electrocoagulation of the AV node through a right atrial approach.\(^20\) The heart was paced with a custom-designed programmable stimulator (Bloom Associates, S6) as detailed below. The sinus node was mechanically crushed to slow the spontaneous sinus rate. Surface ECG lead L, as well as left ventricular and left atrial pressures (Millar micromanometer catheters models 350 and PC 370) were recorded continuously throughout each experiment. Both pressure catheters were balanced and calibrated for common baseline and sensitivity. Each catheter was calibrated with a mercury manometer before insertion. Once the catheters were placed in the respective cardiac chambers, both pressures were equilibrated during a diastolic period prolonged by temporary cessation of ventricular pacing. This procedure was repeated throughout the experiment. M-mode echocardiography of the left ventricle was performed with a Smith Kline echocardiograph (model 20A) connected to an Irex multichannel recorder (Continue Trace, model 101). The echocardiographic transducer was attached to a rigid bar fixed to the surgical table.\(^21\) The 2.25-MHz M-mode echocardiographic transducer was placed on the right ventricular surface at an angle that enabled visualization of both the lower part of the anterior and posterior mitral valve leaflets as well as the interventricular septum and left ventricular posterior wall.

Experimental Protocol

Echocardiographic, hemodynamic and echocardiographic data were recorded simultaneously in each
dog during the programmed pacing protocol. The heart was paced in an AV-synchronous mode. The left atrium and left ventricle were simultaneously paced with 2-msec pulses at twice diastolic threshold. The basic pacing rate was kept at a cycle length of 450 msec (heart rate approximately 133 beats/min) to allow consistent atrial capture and overdrive suppression of sinus beats. After every sixth AV paced beat, a programmed atrial extrasystole was introduced at progressively increasing coupling intervals of 200--1000 msec in steps of 50 msec. Each atrial extrasystole was followed by a prolonged programmed pause (1.5--2.0 seconds) in the AV pacing. After the programmed atrial extrasystole and throughout the prolonged pause, spontaneous sinus rhythm was allowed to resume. Typically, after a drive of six paced beats at a cycle length of 450 msec, there was a 600--1000-msec pause before resumption of a spontaneous sinus beat.

After these studies, transient atrial fibrillation was created by rapidly stimulating the atria at a cycle length of 70--100 msec. At the same time, the ventricles were paced regularly at a cycle length of 450 msec for six consecutive beats, followed by a prolonged programmed pause (2 seconds). Normal sinus rhythm spontaneously resumed immediately after cessation of rapid atrial pacing. In four dogs, i.v. verapamil was administered in a dose of 0.1 mg/kg. This dose was sufficient to cause transient atrial standstill for approximately 3 minutes, but had no significant effect on ventricular mechanical function or systemic blood pressure.

**Definitions and Measurements**

The time intervals and ventricular dimensional measurements used in this study are shown in figure 1. The independent variable in these experiments was the coupling interval (CI) of the atrial extrasystole, measured from S1 of the last of the regularly paced atrioventricular beats to S2 of the atrial extrasystole. At each coupling interval, the "mitral reopening time" (MRT) in msec was measured from the point of initial mitral valve closure, induced by active atrial systole, to the point of passive diastolic mitral leaflet reopening on the echocardiogram. The left ventricular volume (LVV) at the mitral reopening point was calculated from the echocardiographically determined left ventricular diameter at that point. LVV was calculated for each left ventricular diameter (D) using the formula advocated by Teichholz et al.

\[ \text{LVV} = \frac{\pi D^3}{6(0.075D + 0.18)} \]

This formula is sufficiently accurate \((r = 0.92)\) in hearts with diameters of 2--8 cm. Left ventricular and left atrial pressures were measured after the Millar catheters were balanced and calibrated as detailed above.

**Statistical Analysis**

For each dog, a logarithmic function, \(y = a + b \ln(x)\), was derived to model the dependence of mitral valve reopening time (\(y\)) on coupling interval (\(x\)) (i.e., MRT = \(a + b \ln\ CI\)). A least-squares regression method was used to estimate and test the model parameters. The same method was used to model and test the dependence of left ventricular diameter (as well as the derived LVV) (\(y\)) on coupling interval (\(x\)) i.e., \(D = a + b \ln\ CI\). Linear functions for MRT, left ventricular diameter and LVV vs coupling interval were also determined for each dog using the function \(y = a + bx\). Correlation coefficients were considered significant at the \(p < 0.05\) level.

**Results**

**Effect of Coupling Interval on Mitral Reopening Time**

Mitral valve closure was consistently initiated after the premature atrial systole. However, at short coupling intervals (300--500 msec), the mitral valve reopened shortly after the initial closing motion and assumed a midstream position (MRT = 50 msec; fig. 2A). Incremental prolongation of the coupling interval of the atrial premature beat resulted in a progressive

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**Figure 1.** A typical combined recording of the ECG, left ventricular pressure (LVP) and left atrial pressure (LAP), as well as the M-mode echocardiogram of the left ventricle depicting the interventricular septum (IVS), the mitral valve (MV) and the left ventricular posterior wall (PW). The coupling interval (CI) is measured from the last atrioventricular paced beat (S1) to the atrial extrasystole (S2). The mitral reopening time (MRT) is the distance between the atrial systole–induced mitral valve closure (CL) and the spontaneous reopening point (RE). The left ventricular volume (LVV) is calculated from the left ventricular diameter (D) at the point of mitral valve reopening (RE).
prolongation of the MRT (MRT = 190 msec; fig. 2B). This relationship of MRT and coupling interval was characterized by the general logarithmic function of the form \( y = a + b \ln(x) \). In this case, \( y = \) MRT and \( x = \) coupling interval (fig. 3). In each dog, the predicted values for MRT correlated closely with the actual measurements \( (r = 0.95-0.98, p < 0.001) \) (fig. 3). Alternatively, these \( r \) values also represent the regression correlation coefficient of the measured MRT values vs \( \ln(x) \), where \( x = \) the coupling interval. Using the linear function \( y = a + bx \), correlation coefficients were also excellent \( (r = 0.97-0.99, p < 0.001) \).

Notably, at a critically long coupling interval specific for each dog, the mitral valve locked and did not passively reopen (fig. 2C). Once locked, the mitral valve reopened only in response to a subsequent atrial systole or after ventricular emptying caused by the next ventricular systole. The duration of the MRT was closely related to the duration of the transiently maintained ventriculoatrial pressure gradient. At short coupling intervals and with progressive atrial filling, this gradient was dissipated and the mitral valve reopened (figs. 2A and 2B). In contrast, locking of the mitral valve was associated with a gradient across the AV valve that was maintained until the next ventricular systole (fig. 2C). Left atrial and left ventricular pressures continued to rise gradually during diastole after locking of the mitral valve.

Effect of Coupling Interval on Left Ventricular Diameter and Volume
The effect of the coupling interval of atrial extrasystoles on intraventricular diameter and LVV at the MRT for each dog is shown in figure 2. Prolongation of the
Interrelation between Left Ventricular Volume and Mitral Reopening Time

The interrelation between LVV and the MRT was derived from the previously described functions (MRT = a₁ + b₁ ln CI, D = a₂ + b₂ ln CI and LVV = π D²/6(0.075D + 0.18)) and therefore, by definition, was expected to be linear. The relationship found experimentally was consistent with this expectation and the coefficient of correlation was 0.89–0.98 (p < 0.01) in individual dogs. Increases in LVV resulted in a progressive prolongation in MRT (fig. 2). A "critical" ventricular volume, designated the "locking volume" specific for each dog, was required to prevent passive reopening of the mitral valve after the atrial extrasystole, and thus to lock the mitral valve for the remainder of the diastolic pause (fig. 2C).

Mitral Valve Mechanics During Atrial Fibrillation and Standstill

To further define the relative roles of atrial systole and LVV in the locking mechanism of the mitral valve, active atrial systole was abolished by simulating atrial fibrillation with rapid atrial pacing and by inducing atrial standstill pharmacologically with verapamil. During either atrial fibrillation or atrial standstill, the mitral valve assumed a diastolic midstream position and remained there throughout the entire pause in ventricular pacing despite a progressive passive increase in LVV (fig. 4). Even though the calculated end-diastolic LVV during atrial standstill was markedly larger than the locking volume during sinus rhythm (51 vs 41 ml, figs. 2C and 4), locking of the mitral valve did not occur when atrial systole was absent. In each dog, the calculated LVV at the end of the prolonged diastolic pause during atrial fibrillation or atrial standstill was equal to or greater than the critical volume that had successfully locked the mitral valve during sinus rhythm. However, in the absence of an effective atrial systole, diastolic mitral valve locking did not occur and no pressure gradient developed across the mitral valve (fig. 4).

Discussion

The role of atrial systole in the initiation of mitral valve closure was postulated by Baumgarten as early as 1843. Further theoretical emphasis on the role of the atrium in the closure of the mitral valve was expressed by Kreiß. Straub was the first to postulate that turbulence created by atrial contraction played a role in the mechanism of mitral valve closure. Later, Henderson and Johnson demonstrated experimentally the importance of the "breaking of the jet" phenomenon at the end of atrial systole, as well as the occurrence of eddies, or vortex formation, behind the AV valves, to the initiation of mitral valve closure. Subsequent researchers provided further evidence that atrial systole was important to mitral valve closure using model studies of the left heart and mitral valve, mechanical tracing of the motion of the mitral leaflets in an isolated heart, radiographic tracing of markers attached to the mitral leaflets, analysis of atrioventricular pressure...
Thus, early of these conditions has resulted in an initial closing motion of the mitral valve, the leaflets floated open and assumed a midstream position for the remainder of the diastolic period (arrows). The left ventricular volume (LVV) was 10 ml larger than the locking LVV in figure 2C (51 ml vs 41 ml). Despite the larger LVV, the mitral valve remained open and no atrioventricular pressure gradient was apparent. The ventricular systole terminating the prolonged diastolic pause closed the mitral valve from a fully open position, allowing some degree of mitral regurgitation.

The Importance of Intraventricular Volume in the Locking of the Mitral Valve

By progressively prolonging the coupling interval \((S_2-S_1)\) of the atrial extrasystole, we have gained insight into the mechanisms that are important to diastolic locking of the mitral valve. In addition to active atrial systole, the accumulation of a critical LVV is necessary to ensure diastolic locking of the mitral valve. Atrial extrasystoles with short coupling intervals allow for a short period of ventricular filling. The mitral valve closed by an early atrial systole reopens immediately due to the lack of sufficient intraventricular volume and the nearly instantaneous equalization of atrial and ventricular pressures (fig. 2A). However, with progressive prolongation of the coupling interval and increasing intraventricular volume, a longer time is necessary for passive atrial filling to overcome left ventricular pressure and open the mitral valve (fig. 2B). When the LVV exceeds a critical value after an atrial systole, the mitral valve locks. This phenomenon can be explained by the fact that the accumulated LVV creates an intraventricular pressure that exceeds atrial pressure for the remainder of the diastolic phase (fig. 2C). Even after the mitral valve locks, pressure continues to rise in both the left atrium and the left ventricle. This pressure increase was observed consistently and requires further elucidation. Conversely, the accumulation of LVV in itself was not sufficient to lock the mitral valve in the absence of active atrial systole. This was demonstrated by our findings during atrial fibrillation and atrial standstill. During each of these conditions, a prolonged pause in ventricular pacing was introduced to allow a prolonged period of passive left ventricular filling. In each dog, the passively accumulated LVV equaled even exceeded the critical locking volume, but the mitral valve remained open for the duration of the diastolic pause (fig. 4).

The relationships between coupling intervals, MRT, and LVV were remarkably consistent in each dog (fig. 3). However, the minor but progressive increase in left ventricular diastolic pressure, even during periods of

![Diagram](https://i.imgur.com/9Q5Q5Q.png)
mitral valve locking (figs. 1 and 2), and variability between dogs suggest that additional factors may play a role in the locking mechanism of the mitral valve. These factors include respiratory influences on ventricular filling as well as various autonomic and neurohumoral factors that may affect myocardial contractility or relaxation and atrial contractility.

Clinical Implications
The occurrence of a ventricular systole when the mitral valve is not locked may result in reflux of blood into the atrium. The volume of the regurgitant fraction depends on the extent of mitral leaflet opening and the amount of blood entrapped in the AV funnel when ventricular systole occurs. In any clinical situation in which one of the described mitral valve locking conditions is absent or only incompletely satisfied, the mitral valve may reopen during diastole, and mitral regurgitation may follow during the subsequent ventricular systole. This is especially true in the presence of atrial fibrillation and AV dissociation. During atrial fibrillation with relatively slow ventricular rates, the mitral valves reopen after the rapid-filling phase and subsequently, because of loss of active atrial contraction, does not lock during the remainder of the diastolic pause, thereby creating the conditions necessary for mitral regurgitation. The occurrence of mitral regurgitation during atrial fibrillation has been demonstrated by other investigators. During AV dissociation, the asynchrony of atrial and ventricular contraction may lead intermittently to inadequate ventricular filling, resulting in the failure of the mitral valve to lock, and thereby lead to mitral regurgitation. The ability to initiate closure, but not to lock the mitral valve in the closed position for the duration of diastole, may further explain some of the deleterious hemodynamic consequences of rhythms characterized by AV dissociation, including ventricular premature complexes and ventricular tachyarrhythmias, as well as complete AV block. In addition, this phenomenon may also occur in patients in whom ventricular rather than AV pacemakers are implanted and may further contribute to the so-called pacemaker syndrome.

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