Left Atrial Transport in Mitral Stenosis

By Fred P. Heidenreich, M.D., Mark E. Thompson, M.D., James A. Shaver, M.D., and James J. Leonard, M.D.

SUMMARY

Active left atrial transport was examined acutely in five patients with mitral stenosis and sinus rhythm. To observe the effect of active left atrial contraction on subsequent left ventricular output, the timing of atrial contraction with respect to ventricular contraction was varied. Atrioventricular (A-V) dissociation produced by right ventricular pacing was used to change continually the relationship of left atrial (LA) to left ventricular (LV) contraction. Measurements of each beat included mitral valve gradient, left ventricular ejection time (LVET), and left ventricular peak-systolic pressure (LVSP). The diastolic gradient was used to calculate diastolic flow per beat after the area of the stenotic mitral orifice had been previously determined. Calculated diastolic flow increased significantly (24%) as did the parameters of left ventricular output, LVSP and LVET (P < 0.005 for both), when atrial contraction was optimally timed. Cumulative effects were observed when a series of well-placed or poorly placed atrial contractions occurred. The method documents change in LV output which depends on appropriate timing of LA contraction that may not have been seen with a steady-state approach.

Additional Indexing Words:
A-V dissociation Pacing Atrial function

EXTENSIVE experimental evidence demonstrates active atrial transport in animal preparations\(^1\)\^-\(^8\); in man, however, the role of atrial function is more difficult to evaluate.\(^9\)\^-\(^10\)
Several excellent recent studies are available in which atrial transport was evaluated by changes in cardiac output measured before and after cardioversion from atrial fibrillation to sinus rhythm.\(^11\)\^-\(^17\) In these studies, changes in cardiac output varied. Unfortunately, due to the complex nature of cardiac output regulation, little insight is gained as to the importance of atrial contraction by these studies. It has been shown in animal work that atrial asystole\(^6\) or acute atrial fibrillation\(^18\) promptly evokes compensatory changes by homeostatic mechanisms such as carotid baroreceptor afferents and presumed myocardial and peripheral vascular adrenergic efferents.\(^18\) To eliminate such compensatory mechanisms and unmask the effect of atrial contraction, A-V dissociation was produced by right ventricular pacing in the present series. With a continually changing temporal relationship of atrial to ventricular contraction, it was possible to study the effect of atrial contraction alone, free of homeostatic mechanisms inherent in steady-state observations. Patients with mitral stenosis were chosen for this study because the hydraulics of a fixed orifice obstruction, serving as a flowmeter, permits direct calculation of diastolic flow if the gradient is known. The diastolic flows resulting from a properly timed and from a poorly timed atrial contraction were then compared. It must be emphasized that the right ventricular (RV) pacing technique also resulted in improperly timed atrial...

From the Cardiac Diagnostic Laboratories, Presbyterian-University Hospital, and the Department of Medicine (Division of Cardiology), University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.

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contractions. These improperly timed atrial contractions may represent disadvantageous rather than indifferent atrial contractions.

Methods

Five patients with valvular mitral stenosis were studied during diagnostic transseptal left heart catheterization. Normal sinus rhythm was present in all. Hemodynamic findings and surgical description of the valve are presented in table 1. All patients were studied in the postabsorptive state. They were premedicated with meperidine (50 to 75 mg) and promethazine hydrochloride (25 mg) intramuscularly. Lidocaine was used as the local anesthetic for percutaneous cannulation or exposure of vessels. All pressures were measured with equisensitive P23Db Statham transducers. Left atrial pressure was recorded through a no. 9 Ross catheter placed transseptally into the left atrium. Left ventricular pressure was measured through a small-bore polyethylene catheter (PE-90; 0.023 ID)* threaded through the Ross catheter into the left ventricle, or by retrograde arterial catheterization. A 15-cm polyethylene catheter (PE-160; 0.045 ID)* was introduced percutaneously into the left brachial artery to monitor arterial pressure and sample the blood. The indirect carotid pulse was recorded with a standard funnel-shaped pick-up connected to a P23Db transducer placed over the point of maximal pulsation of the carotid artery. Left ventricular ejection time was measured as the interval from the beginning of the upstroke to the trough of the incisural notch. A no. 5 or 6 bipolar pacing catheter was placed into the apex of the right ventricle through a right antecubital venotomy. The electrocardiogram was obtained by using the lead which most clearly demonstrated P waves. All events were recorded on a multichannel photorecorder at a paper speed of 100 mm/sec with lines indicating 20-msec intervals.

With the patient in normal sinus rhythm, simultaneous left ventricular and left atrial pressures were recorded on equisensitive gauges, and the mitral diastolic gradient was obtained by planimetry of the diastolic portions of 10 consecutive complexes. Cardiac output was determined by the Fick method in all patients except W.P., on whom the indicator-dilution method was used. The mitral valve area was calculated by the method of Gorlin and Gorlin.19

Right ventricular pacing was then instituted and produced A-V dissociation with a fixed R-R interval and a randomly changing temporal rela-

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Calculated mitral valve area (cm²)</th>
<th>Associated valvar lesions</th>
<th>Resting RV pressure (mm Hg)</th>
<th>Resting cardiac index (L/min/m²)*</th>
<th>Description of valve at operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.C.</td>
<td>40</td>
<td>M</td>
<td>3.3</td>
<td>AI mild</td>
<td>29/4</td>
<td>3.32</td>
<td>Not operated</td>
</tr>
<tr>
<td>A.H.</td>
<td>39</td>
<td>F</td>
<td>0.9</td>
<td>MI minimal</td>
<td>50/4</td>
<td>2.08</td>
<td>Valve orifice approximately 0.75 cm². Leaflets flexible but each commissure was fused and thickened</td>
</tr>
<tr>
<td>W.P.</td>
<td>61</td>
<td>M</td>
<td>1.6</td>
<td>MI minimal</td>
<td>35/5</td>
<td>2.27</td>
<td>Tightly stenotic without regurgitation</td>
</tr>
<tr>
<td>E.D.</td>
<td>33</td>
<td>M</td>
<td>1.0</td>
<td>MI mild</td>
<td>44/3</td>
<td>2.17</td>
<td>The mitral valve was heavily calcified around its annulus with calcium extending along the free edge of the aortic cusp. The mitral cusp was entirely replaced by calcium, was quite short, rigid and immobile with approximately 2+ regurgitation. Both commissures fused</td>
</tr>
<tr>
<td>M.J.</td>
<td>60</td>
<td>F</td>
<td>0.7</td>
<td>TI mild</td>
<td>50/7</td>
<td>1.92</td>
<td>Fairly flat valve with moderately mobile aortic leaflet, thick plaque in its mid-portion with a firm sharp edge suggesting calcification. Commisures were fused and stiff but seemingly less calcified. The orifice seemed unusually tight, about 0.7 cm in diameter</td>
</tr>
</tbody>
</table>

* Normal in our laboratory is 2.9 ± 0.3.

Abbreviations: AI = aortic insufficiency; MI = mitral insufficiency; TI = tricuspid insufficiency.
Figure 1
Simultaneous recording of left ventricular and left atrial pressure during pacing-induced A-V dissociation. The mean mitral gradient is indicated for each complex in the area of the gradient. Values for left ventricular peak-systolic pressure (PSP) and left ventricular ejection time (ET) are shown for each complex. The left atrial contour shows a prominent wave in the first complex when the P-R interval is 0.20 secs. The last complex on the right shows a P-R of zero and no a wave preceding ventricular systole. As the a wave is lost, the mitral gradient decreases and PSP and ET decline.

Figure 2
A representative sequence of pacing-induced A-V dissociation. As P-R lengthens, a progressive increase in the size of the a wave, results in progressive increase in the mean mitral gradient. Note progressive improvement in parameters of LV output as atrial systole is more appropriately placed.
tionship of atrial to ventricular contraction. In
three patients the right ventricular pacing rate
was only slightly faster than the spontaneous sinu
rhythm, thus producing near isorhythmic disso
ciation. Multiple sequences were recorded in
which the P wave gradually marched out in
front of the QRS and then gradually receded back
into it. A typical recorded series is shown in figure
1. In each study between 32 and 151 (average
86) individual cardiac cycles were analyzed for:
(a) P-R interval, (b) diastolic filling period, (c)
mean mitral diastolic gradient, (d) left ventricu
lar peak-systolic pressure, and (e) left ventricular
ejection time.
Assuming that the stenotic mitral valve is a
fixed orifice obstruction, the formula of Gorlin
and Gorlin relating pressure gradient, valve area,
and flow was transposed to solve for flow. Di
astolic flow for each cardiac cycle was determined
by using the mitral valve area calculated from
measurements during sinus rhythm; the diastolic
filling period and mitral gradient were measured
directly on each cardiac complex. Transposition
of the formula of Gorlin and Gorlin was as follows:

\[ \text{MVA} = \frac{\text{CO/DFP} \times \text{HR}}{31 \sqrt{\text{LA-LV}}} \]  

(1)

\[ \frac{\text{CO}}{\text{HR}} = \text{MVA} \times \text{DFP} \times 31 \sqrt{\text{LA-LV}} \]  

(2)

Equation 2 was then altered to solve for diastolic
flow:

\[ \text{DF} = \text{MVA} \times \text{DFP} \times 31 \sqrt{\text{LA-LV}} \]  

(3)

where

- \( \text{MVA} \) = mitral valve area (cm\(^2\)) calculated from measurements made during sinus rhythm;
- \( \text{CO} \) = cardiac output (ml/min);
- \( \text{DFP} \) = diastolic filling period (sec/beat);
- \( \text{HR} \) = heart rate (beats/min);
- \( \text{LA-LV} \) = mean diastolic pressure gradient across the mitral valve (mm Hg);
- \( \text{DF} \) = diastolic flow (ml/beat).

Similar calculations for beat-to-beat stroke vol
ume in aortic stenosis as a fixed orifice have been
previously reported from this laboratory by Kroetz and associates,\(^{20}\) and the validity of these
calculations are presented in detail. The minimal
degree of associated valvular regurgitation as
specified in table 1 was not of sufficient magnitude
appreciably to alter the results of the study.

**Results**

Representative hemodynamic data recorded
are shown in figure 2 for subject A.H. A
marked change in LA pressure contour is dem
onstrated as the P wave moves out in front of
the QRS complex. In the initial complex shown
in the sequence, with a P-R interval of zero, the
atrium is presumably contracting against a closed
mitral valve. The early diastolic pressure in the
atrium is low (12 mm Hg), with no \( a \) wave preceding ventricular contraction and near zero left ventricular end
-diastolic pressure (LVEDP). As the P wave
moves progressively in front of the QRS com
plex, a prominent \( a \) wave develops in the LA
pressure contour, the early diastolic LA pres
sure rises to 22 mm Hg, the \( a \) wave rises to 32
mm Hg, and during this transition the LVEDP
increases to 4 mm Hg. At the same time, left
ventricular ejection time (LVET) and left
ventricular peak-systolic pressure (LVSP) in
crease strikingly. The cumulative effect of
this sequence is better appreciated at a slow
paper speed (fig. 3).

**Diastolic Flow Versus P-R Interval**

In figure 4, the calculated diastolic flow was
correlated with the P-R interval for all com
plexes analyzed for all five patients. There
was a mean increase of 10 cc (24%) in diastolic
blood flow from inappropriate to optimal P-R
interval (\( P < 0.05 \)).

**Left Ventricular Ejection Time and Peak
Pressure Versus P-R Interval**

The mean increase in LVSP as the optimal
P-R interval occurs is shown in figure 5. The
mean LVSP increased for all four patients
(not recorded in W.P.). The mean absolute
increase was 27 mm Hg (\( P < 0.005 \)) or 24%.

Figure 6 shows the mean increase in LVET
as the optimal P-R interval occurs. The mean
increase in LVET for all five patients was 31
msec (\( P < 0.005 \)) or 13%.

Figure 7 shows a regular progressive in
crease in diastolic flow and LVET as P-R in
terval changes from zero to optimal length in
patient E.O. A regression equation for this
line is:

\[ \text{LVET} = 0.0795 + 0.0034 \text{DF}. \]

**Cumulative Effects**

The tendency for the diastolic flow and the
parameters of LV output to lag behind the

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change in P-R interval is shown in figure 8. Detailed graphing of LVPSs against P-R interval as shown for patient A.H., in whom this was most prominent, demonstrates cumulative change at the optimal and zero P-R intervals. As can be seen, for a given P-R interval (for example, 0.12 sec), the parameter of LV function, LVPS, was different depending on whether the P-R interval was in a sequence of lengthening (approaching a more optimal level) or whether the P-R had been at the optimal level for some beats and was now returning toward a P-R interval of zero (a detrimental P-R interval). Figure 8 incorporates the direction of change of the P-R of the sequence from which the given complex is taken and better depicts this hysteresis. As the P-R interval lengthens and arrives at the patient's normal P-R interval, the LVPS increases. As several additional beats occur at optimal P-R interval, there is progressive increase in LVPS. Then, as P-R begins to shorten, the LVPS briefly maintains the increase. The LVPSs are different for a given P-R between an inappropriate P-R and an optimal P-R, depending upon whether the P-R has been poor for some time and now is moving toward optimum, or whether the P-R has been at optimal level with high LVPS and is now moving toward a less advantageous P-R interval. Similar cumulative changes occurred with diastolic flow and LVET.

Discussion

This study focuses for the first time on acute changes in the mitral diastolic gradient during alteration of the P-R interval in patients with mitral stenosis. Atrioventricular dissociation produced by right ventricular pacing in this study documents a marked increase in the mitral diastolic gradient when atrial contraction is well placed. There is a subsequent increase in transportation of blood from the left atrium to the left ventricle, calculated on a beat-to-beat basis and manifested by a corresponding improvement in simultaneously...
recorded parameters of left ventricular output. The left atrium, therefore, is a potential booster pump that can improve left ventricular output in mitral stenosis.

Figure 2 shows a mean diastolic gradient of 10.7 mm Hg preceding the first ventricular contraction shown (P-R of zero). The mean diastolic gradient in the next to the last complex shown (P-R optimal) is 17.8 mm Hg, or nearly double. Braunwald and co-workers have shown that in pure mitral stenosis and atrial fibrillation the characteristics of the subsequent ventricular contraction are dependent on the left ventricular end-diastolic segment length and left ventricular end-diastolic pressure which is affected by the preceding filling time. In this study cycle length is constant. The increased gradient causes increased filling of the left ventricle. The cumulative effects seen in this study may be due in part to the gradual increase in the degree of filling of the left ventricle from a series of well-placed atrial contractions. Ventricular filling is better after three or four well-placed atrial beats than after one. Similarly, when the atrial contraction is no longer well placed, progressive emptying of the left ventricle occurs over the next few contractions. Thus, the performance of the first few beats after loss of atrial contraction may be good because of the transiently maintained end-diastolic ventricular volume and increased central blood volume.

The marked changes in left atrial pressure and mitral gradient in the present study may be partly explained by other factors. Grant's group emphasized the different roles of the

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Figure 4

The calculated diastolic flow (see text) for each cycle analyzed is plotted against P-R interval in each patient. The calculated diastolic flow increased in all patients as optimal P-R was reached.
LEFT ATRIAL TRANSPORT IN MITRAL STENOSIS

Figure 5
Mean LVSP is compared at zero P-R interval with mean LVSP at optimal P-R interval. LVSP increased as optimal P-R occurred for each patient (P < 0.005).

Figure 6
Mean left ventricular ejection time (LVET) is compared at zero P-R interval and at optimal P-R interval for all five patients. LVET increased in each patient as the optimal P-R occurred (P < 0.005).

Atrium depending on the phase of the cardiac cycle. The atrium behaves as a distensible reservoir during ventricular systole, as a conduit during ventricular diastole, and as an active booster pump in presystole. Atrioventricular dissociation, as produced here, with inappropriate P-R interval, substitutes atrial systole in that phase of the cardiac cycle when the atrial chamber should be passively dilating and storing venous return. The positive effect of a well-placed atrial systole should be separated from the potentially deleterious effect of interference with reservoir functions.

At first thought, the lower mean left atrial pressure (MLAP) shown in figure 2 (complex 1) with a disadvantageously placed atrial contraction may seem desirable compared with the increased MLAP with well-placed atrial contraction (complex 7). The important is, however, that these are two different and that much less flow occurs at the zero P-R interval and much greater flow at the optimal P-R interval. At either state of flow, the presence or the absence of an optimally placed atrial contraction could alter the MLAP. That is, at the low level of flow shown in complex 1 of figure 2, if a well-placed atrial contraction had been present, an even lower early diastolic pressure might have been able to maintain the same flow. Similarly, at the higher flow seen at complex 7 in figure 2, if a mechanical atrial systole had been absent, even higher MLAP would be required to maintain the same flow.

The observed data do not conflict with Gold and Frahm's concept of the response of MLAP to left ventricular end-diastolic pressure (LVEDP). They emphasized the importance of the LVEDP in determining characteristics of ventricular contraction and MLAP in determining the symptoms of heart failure.

The aim of this study is such that in four out of five patients, the P-R interval lengthened to the
The relationship of left ventricular ejection time and diastolic flow grouped according to the P-R interval labeled above each point. A regression equation was obtained for this relationship in patient E. O.

The patient's spontaneous P-R interval, because of normal A-V node function, orthoconduction replaced the ectopic right ventricular focus of depolarization. One has to consider what role the change in conduction plays in contributing to the changes seen with variation in P-R interval. The strongest evidence that atrial transport was the predominant factor in producing the changes in LVSP and LVET is the simultaneously determined mitral valve gradient proving the difference in driving pressure across the mitral valve. Change in ventricular activation would be a systolic event and would not contribute to the change in previous diastolic gradient. Ectopic activation, if anything, should lengthen the duration of systole, hence the observed changes; in other words shortening of LVET with poorly timed atrial systole and ectopic ventricular activation are all the more meaningful. It is acknowledged, however, that ventricular activation is normal with the well-placed atrial contraction, and this may be partly responsible for increased LVSP due to more synchronous ventricular systole. Patient W.P. demonstrated A-V nodal disease with spontaneous Wenkebach rhythm at the time of catheterization. During pacing-induced A-V dissociation in that patient, there was very little orthoconduction; yet LVET and LVSP changes occurred to essentially the same degree as in the other cases in which ventricular activation did change, suggesting that they were primarily due to variation in P-R interval.

The potential contribution of atrial systole to left ventricular filling was evaluated by constantly changing the temporal relationship of atrial to ventricular contraction. In this way, the beat-to-beat effect of atrial contraction was observed allowing little time for compensatory mechanisms to operate. It is interesting that in steady-state conditions utilizing sequential A-V pacing, Carleton and Graettinger\textsuperscript{24} showed no change in systolic ejection time, blood pressure, and cardiac output when recorded 3 to 19 min after creation of ineffective atrial systole. The most likely explanations for these differences are twofold: (1) Cardiac
output is an insensitive indicator of hemodynamic change, and its regulation is complex, involving the interplay of many factors. This is particularly true in mitral stenosis. An intervention changing the timing of atrial systole is probably not a prime determinant of integrated cardiac output. This study was directed at uncovering atrial function acutely. Whether the intact patient at rest tends to utilize the potential function or not cannot be determined by his study.

References
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FRED P. HEIDENREICH, MARK E. THOMPSON, JAMES A. SHAVER and JAMES J. LEONARD

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