Left Atrial Transport in Mitral Stenosis

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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 (LVPSP). 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, LVPSP 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 recent excellent 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

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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-

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Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Calculated mitral valve area (cm²)</th>
<th>Associated valvular 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.

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 a 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.

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 sinus rhythm, thus producing near isorhythmic dissociation. 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 ventricular 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. Diastolic 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:

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

(1)

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

(2)

Equation 2 was then altered to solve for diastolic flow:

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

(3)

where

- MVA = mitral valve area (cm²) calculated from measurements made during sinus rhythm;
- CO = cardiac output (ml/min);
- DFP = diastolic filling period (sec/beat);
- HR = heart rate (beats/min);
- LA - LV = mean diastolic pressure gradient across the mitral valve (mm Hg);
- DF = diastolic flow (ml/beat).

Similar calculations for beat-to-beat stroke volume in aortic stenosis as a fixed orifice have been previously reported from this laboratory by Kroetz and associates,\textsuperscript{30} 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 demonstrated 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 complex, a prominent a wave develops in the LA pressure contour, the early diastolic LA pressure 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) increase 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 complexes 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 increase in diastolic flow and LVET as P-R interval changes from zero to optimal length in patient E.O. A regression equation for this line is:

\[
LVET = 0.0795 + 0.0034 DF.
\]

Cumulative Effects

The tendency for the diastolic flow and the parameters of LV output to lag behind the
Figure 3

The cumulative effect of a series of well-placed atrial systoles can better be appreciated when recorded at a slower paper speed. The pressure contours shown are the same as in figures 1 and 2 except that the paper speed is slower (25 mm/sec). The mean LA pressure rises as the P wave moves out in front of the QRS and an a wave develops. LVPSP increases as the gradient increases. This cyclic change occurred repeatedly.

Change in P-R interval is shown in figure 8. Detailed graphing of LVPSP 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, LVPSP, 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 LVPSP increases. As several additional beats occur at optimal P-R interval, there is progressive increase in LVPSP. Then, as P-R begins to shorten, the LVPSP briefly maintains the increases. The LVPSPs 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 LVPSP 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
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.

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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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 ($P < 0.005$).

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 contraction (complex 7). The important point is, however, that these are two different situations 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 systole 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 might be required to maintain the same flow. The observed data do not conflict with Call and Frahm's concept of the relationship of MLAP to left ventricular end-diastolic pressure (LVEDP). They emphasized the importance of the LVEDP in determining the characteristics of ventricular contraction and MLAP in determining the symptoms of heart failure.

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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. over the range of P-R intervals shown.

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 LVPSP 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 LVPSP 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 LVPSP 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 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.

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