Transseptal pressure gradient and diastolic ventricular septal motion in patients with mitral stenosis

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ABSTRACT Previous studies from our laboratory have shown that the position of the ventricular septum relative to the two ventricles at end-diastole is determined by the instantaneous transseptal pressure gradient (TSG) defined as left ventricular minus simultaneous right ventricular pressure. Since patients with mitral stenosis often have exaggerated leftward (paradoxic) motion of the ventricular septum during early diastole, we studied seven patients with mitral stenosis undergoing cardiac catheterization to determine if position (and therefore motion) of the ventricular septum was determined by TSG throughout diastole. Mode echocardiograms derived from a two-dimensional parasternal short-axis view were recorded with simultaneous micromanometer measurements of left ventricular and right ventricular pressures. Six of seven patients demonstrated abnormal early diastolic leftward motion of the ventricular septum in at least one cardiac cycle. TSG measured at intervals throughout diastole ranged from −2.5 to +20 mm Hg, with abnormal TSG observed in most of the 40 cardiac cycles selected for analysis. The intracardiac position of the ventricular septum, defined as the distance from the right ventricular epicardium (RVEpi) to the left surface of the ventricular septum normalized for total cardiac dimension (RVEpi-VS), was plotted against left ventricular pressure, right ventricular pressure, and TSG. Linear regression of pooled data from all patients (164 observations) demonstrated a highly significant correlation between the instantaneous TSG and the relative intracardiac position of the ventricular septum (RVEpi-VS = 1.52 TSG + 42.7; r = .79, p < .0001). The position of the ventricular septum was significantly better correlated (p < .0001) with instantaneous TSG than with left ventricular intracavitary pressure (r = .51) or right ventricular intracavitary pressure (r = .28). We conclude that, in patients with mitral stenosis, septal position throughout diastole is determined by the instantaneous TSG. An abnormal TSG in early diastole, probably reflecting the increased impedance to left ventricular filling, results in the exaggerated leftward diastolic septal movement. These data further clarify the complex interplay between active and passive motion of the ventricular septum throughout the cardiac cycle.


THE PRESENCE of “paradoxical” or anterior (rightward) motion of the ventricular septum during systole has been recognized in a number of clinical conditions, including right ventricular volume,1–8 or pressure overload,3, 8–12 left bundle branch block,13, 14 Wolff-Parkinson-White syndrome,15 and transposition of the great arteries,16 as well as after cardiac surgery.17, 18 The abnormal septal motion observed in these various conditions has been ascribed to a number of mechanisms. For example, in patients with previous cardiac surgery it has been attributed to excessive anterior motion of the entire heart, presumably related to pericardiectomy17 or to fixation of the heart anteriorly by sternal adhesions.18 However, many studies have demonstrated that the abnormal systolic motion in right ventricular volume or pressure overload is associated with abnormal shape5–11, 19, 20 or position7, 11 of the septum at end-diastole.

Recently we have shown in both open-chest and conscious dogs that the position (shape) of the septum between the ventricles at end-diastole is directly related to the instantaneous transseptal pressure gradient during right ventricular volume overload (produced by
opening a pulmonary artery-to-right atrial shunt), pressure overload (produced by pulmonary artery constriction), and simulated left bundle branch block (produced by right ventricular pacing).21 22 More recently, we have demonstrated that the same relationship exists in man; when the septum was shifted markedly leftward at end-diastole (by the development of an abnormal transseptal gradient) paradoxic (anterior) motion occurred during the subsequent systole.23 Thus, systolic motion of the septum is a function of the position of the septum at end-diastole; the position in turn directly reflects the instantaneous transseptal pressure gradient.

In contrast to these abnormalities of systolic septal motion, patients with mitral stenosis often have abnormal leftward motion of the ventricular septum in early diastole. This has been termed paradoxic diastolic septal motion, although it actually reflects an exaggeration of the normal slight posterior septal movement during this phase of the cardiac cycle. Some patients with mitral stenosis and atrial fibrillation have marked variability in diastolic filling periods. Since right ventricular filling is unimpeded while the stenotic mitral valve restricts left ventricular filling, long diastolic intervals result in marked variation in the diastolic transseptal pressure gradient. Based on our previous observations, we postulated that septal position throughout diastole would be determined by the instantaneous transseptal pressure gradient. We expected, therefore, that the exaggerated early diastolic septal motion observed in mitral stenosis would result from an abnormal early diastolic transseptal pressure gradient. The wide range of transseptal pressure gradients throughout diastole, which could uniquely be obtained without intervention in this group of patients, prompted us to explore the relationship between instantaneous diastolic transseptal pressure gradient and septal position.

Methods

Subjects. The study population was selected from patients scheduled for diagnostic right and left heart catheterization with a diagnosis of mitral stenosis and a supine echocardiogram of good quality. The group was comprised of seven such patients, several of whom also had mild or moderate mitral regurgitation. There were three men and four women ranging in age from 31 to 61 (mean = 47) years. Mitral stenosis was considered to be mild (mitral valve orifice greater than 1.5 cm² by the Gorlin formula) in four patients and moderate (1 to 1.5 cm²) in three patients. No patient had evidence of significant coronary artery disease (greater than 70% luminal diameter reduction) and none had previous cardiac surgery. Chronic atrial fibrillation was present in four patients.

Protocol. All patients gave written informed consent to participate in the study, which had prior approval of the institutional Ethics Committee. Each was studied supine in the postabsorptive state after the administration of 2.5 to 10 mg diazepam orally or intravenously. Micromanometer-tip catheters (Models PC-470, PC-484A, Millar Instruments Inc., Houston, TX) were positioned in the left ventricle from a femoral artery and in the right ventricle from a femoral or brachial vein. Accuracy of the pressures was ensured by comparing the output of each micromanometer to that of an equisensitive external manometer (Bell and Howell 4-327-1, Pasadena, CA) connected to the fluid lumen of the high-fidelity catheter. This was reassessed immediately before and after each measurement and the data were discarded unless the difference between the two systems was less than 1 mm Hg. The pressures were recorded on paper with the use of a multichannel recorder (Electronics for Medicine VR16, Honeywell Medical Electronics, White Plains, NY). For the assessment of septal position and motion, simultaneous echocardiography was performed with a 2.25 MHz phased-array transducer and a commercially available imaging system (CV-3400R, Diasonics Cardio/Imaging, Salt Lake City, UT). The transducer was positioned in the left parasternal area and oriented to obtain a short-axis image of the left ventricle at the tips of the papillary muscles. Images were stored on videotape and a derived M mode was recorded on paper. With the auxiliary input channels on this instrument, left and right ventricular pressures were superimposed on the echocardiographic recordings. Pressures and echocardiograms were recorded simultaneously for several minutes during quiet respiration.

Data analysis. Measurements were obtained from 4 to 8 (average = 5.7) cardiac cycles per patient, selected to produce the greatest possible range in transseptal pressure gradients (left ventricular minus simultaneous right ventricular pressure). Measurements were obtained throughout diastole, defined as the interval from the nadir to the beginning of the rapid upstroke of left ventricular pressure. The onset of this interval was selected to ensure nearly complete ventricular relaxation since the stiffness characteristics of the septum would be expected to vary during contraction and relaxation. Two to six measurements (average = 4.1) were obtained during diastole, as dictated by the total duration of diastole. In all diastoles demonstrating abnormal early septal movement, the first measurement was made before the peak of the abnormal leftward motion.

To relate the transseptal pressure gradient to the instantaneous septal position, we analyzed the derived M mode echocardiographic tracing using a method similar to that previously described by Pearlman et al.24 This technique is illustrated in figure 1. The right ventricular epicardium at end-diastole was defined and a line was constructed through this point, parallel to the transducer face. The distance from this line to the endocardial echo of the left ventricular surface of the ventricular septum (RVEpi- VS) was expressed as a percentage of the distance from the right ventricular epicardial line to the posterior left ventricular epicardium (total cardiac dimension). The RVEpi- VS values were then plotted against the instantaneous transseptal pressure gradient, thereby defining a septal diastolic “compliance” curve for each patient.

Statistical analysis. Correlations between septal position and instantaneous left and right ventricular pressures and the transseptal pressure gradient were analyzed by linear regression using the forced entry method (SPSS Inc., Chicago). The significance of the differences between correlation coefficients was tested by the sample estimate test.

Results

Satisfactory pressure and echocardiographic recordings were obtained in all patients. Figures 1 and 2 show M mode echocardiograms of patients with mitral stenosis. These recordings demonstrate the characteristic
FIGURE 1. M mode echocardiogram with superimposed pressure tracings demonstrating the method of measurement. The right ventricular epicardium (RVEpi) was defined at end-diastole and a line was constructed through this point parallel to the transducer face. The distance from this line to the left surface of the ventricular septum (VS) was measured (RVEpi-VS). This distance was normalized by dividing by the total cardiac dimension. Note that at the end of the first diastole the septum is positioned markedly rightward (straight arrow), associated with a large transseptal pressure gradient, but that early in the subsequent diastole, the septum shifts abruptly leftward (curved arrow) in response to a markedly reduced transseptal gradient.

FIGURE 2. M mode echocardiogram below the tips of the mitral leaflets of a patient with mitral stenosis. This echocardiogram demonstrates the exaggerated leftward motion of the ventricular septum in early diastole (arrows).

exaggerated (paradoxic) motion of the ventricular septum in early diastole. This abnormal diastolic motion was present in 21 of 40 cardiac cycles analyzed. Only one patient did not demonstrate this motion pattern at least one cardiac cycle. The variation in transseptal pressure gradient during two consecutive diastolic intervals of different duration in a patient with atrial fibrillation is shown in figure 3. An abnormal diastolic transseptal pressure gradient was present in some cardiac cycles in all patients.

In each patient there was a significant correlation between transseptal pressure gradient and instantaneous septal position, with r values ranging from .41 to .91 (table 1). Figure 4 shows the results of this analysis in each patient. The regression equation for the pooled data from all patients (figure 5) was RVEpi-VS = 1.52 TSG + 42.7 (r = .79, p < .0001, SEE = 4.3).

Although we have used linear regression to define the relationship, we knew intuitively that it would become curvilinear at the extremes of transseptal pressure gradient. This would occur given the obvious physical limits of the maximum excursion of the ventricular septum in either direction.
filling secondary to the mitral stenosis. With continued filling of the left ventricle, the normal (left ventricle > right ventricle) transseptal gradient is reestablished and the septum moves progressively rightward. In the presence of atrial fibrillation and long diastolic pauses, the left ventricular pressure continues to increase after the right ventricular pressure has reached a plateau. This may result in a markedly increased transseptal gradient at end-diastole (complex B, figure 3). In such instances, the septum becomes markedly displaced into the right ventricle (complex 2, figure 1), thereby explaining the large range of septal positions evident in figure 5. Thus, during diastole, the septum acts as a compliant membrane between the two ventricles; that is, the position of the septum is responsive to even small alterations in transseptal gradient. Moreover, the results of this study clearly indicate that septal position is most closely related to transseptal gradient and is much less strongly correlated with the absolute pressures in either ventricle.

The current data do not directly address the mechanism of the early diastolic leftward motion of the septum normally observed, but rather only the magnitude of the exaggerated motion occurring in patients with mitral stenosis. The onset of the leftward motion occurs at a time when pressure in the left ventricle is still declining, although right ventricular pressure has usually reached its nadir and begun to increase. Thus, leftward motion is initiated at a time when the transseptal gradient, although decreasing, is still substantially positive (left ventricle > right ventricle). Data shown in figures 4 and 5 were collected only from the nadir of the left ventricular pressure to the onset of ventricular contraction. Septal position before this time was not linearly correlated with the instantaneous transseptal gradient; this is not surprising since during this period, the relaxation process is still incomplete. The responsiveness of septal position to transseptal gradient at this time would be expected to be modulated by the altered stiffness of the contracted (or incompletely relaxed) myocardium. In all patients, however, the nadir or the left ventricular diastolic pressure occurred before the maximum leftward early diastolic septal motion. Quite clearly therefore, the data in figure 5 demonstrate that the extent of the leftward motion is directly related to the degree of alteration in transseptal pressure gradient. Most of the data points at or to the left of the zero transseptal pressure gradient line represent transseptal pressure-position coordinates at or near the peak of leftward septal motion. That is, the marked degree of early diastolic leftward motion characteristic of patients with mitral stenosis reflects an

**FIGURE 3.** Pressure tracings from a patient with atrial fibrillation with high-gain left ventricular pressure (PLV) and right ventricular pressure (PRV) above and low-gain PLV below. PRV exceeds PLV throughout the first diastole (A), but during the subsequent, longer, diastole (B), PRV rapidly plateaus whereas PLV continues to increase until end-diastole. This results in marked variation in transseptal pressure gradient throughout diastole.

By the sample estimate test, the correlations between septal position and left ventricular intracavitary pressure \(r = .51\) (figure 6) and right ventricular intracavitary pressure \(r = .28\) (figure 7) were significantly weaker than that \(r = .79\) for transseptal pressure gradient \(p < .0001\).

**Discussion**

The results of this study demonstrate that, at least in patients with mitral stenosis, the position of the septum throughout diastole is highly correlated with the instantaneous transseptal pressure gradient. The accentuated leftward early diastolic septal movement observed in such patients therefore reflects an abnormal early diastolic transseptal pressure gradient that in turn almost certainly occurs because of delayed left ventricular

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**TABLE 1**

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LV = left ventricular; RV = right ventricular; TSG = transseptal pressure gradient (PLV-PRV).
FIGURE 4. Data from each patient demonstrating that as transseptal pressure gradient (horizontal axis) decreases, the septum moves leftward (RVEpi-VS increases).

FIGURE 5. Pooled data from all patients demonstrating the highly significant correlation between transseptal pressure gradient and septal position.

FIGURE 6. Pooled data from all patients demonstrating the poor correlation between intracavitary left ventricular (LV) pressure and septal position.
FIGURE 7. Pooled data from all patients demonstrating the weak correlation between intracavitary right ventricular (RV) pressure and septal position.

Abnormal transseptal gradient — often with reversal of the normal gradient.

To our knowledge, this represents the first demonstration of the close linear relationship between transseptal pressure gradients throughout diastole and the diastolic motion of the ventricular septum in patients with mitral stenosis. However, our data are in general agreement with the observations of others. Weyman et al. noted a correlation between the magnitude of the early diastolic septal motion abnormality and the severity of mitral stenosis. These authors suggested that the change in diastolic shape of the left ventricle caused by the abnormal septal movement might reflect inequality of the initial diastolic filling rates of the two ventricles. They noted that the ratio of left ventricular to right ventricular end-diastolic pressure was not significantly different between the patients with mild compared with those with marked abnormalities of early diastolic septal motion. This finding is not inconsistent with our data, however, since pressures in the study of Weyman were measured at end-diastolic and not at the time of the abnormal septal motion. Our patient group is too small to attempt a correlation between severity of the mitral orifice narrowing and the magnitude of the abnormal early diastolic transseptal pressure gradient.

However, our findings, both in this study and in our prior animal experiments, indicate that the greater the alteration in the normal transseptal gradient, the greater the septal displacement. In this regard, it is worth emphasizing that the septum moves in response to the magnitude of the (net) pressure difference across the septum rather than the ratio of the pressures in the two chambers.

Although this study addresses the relationship between transseptal pressure gradient and septal position during diastole, it contributes to the elucidation of the transseptal pressure-position relationship throughout the cardiac cycle. There now are data documenting that septal position at end-systole is also responsive to the instantaneous transseptal pressure gradient. In a closed-chest conscious dog preparation, we have demonstrated a tight linear correlation between septal position and transseptal gradient both at end-diastole and at end-systole. The slopes of the relationships were very different, however, with the systolic transseptal pressure-position relationship being much steeper than that during diastole. This is not unexpected and would be in keeping with the increased stiffness of the contracted myocardium during systole. These animal data are consistent with clinical observations. King et al. demonstrated leftward displacement of the ventricular septum during systole to be a useful predictor of right ventricular systolic hypertension. Nichol et al. showed an association between the severity of the systolic flattening of the ventricular septum and the degree of elevation of the pulmonary arterial pressure in patients with mitral stenosis. Ryan et al. used an eccentricity index to quantitate the degree of septal flattening and showed that end-diastolic septal flattening occurred in patients with right ventricular volume overload while those with right ventricular systolic pressures greater than 45 mm Hg (pressure overload) also had septal flattening at end-systole.

Shimada et al. using a similar approach, were able to identify those patients with atrial septal defect who had developed pulmonary hypertension. Furthermore, they demonstrated a correlation between the severity of the pulmonary hypertension and the magnitude of the shift in systolic septal position. The subjects of the present study were selected because the expected wide range of diastolic transseptal pressure gradients would allow us to explore the relationship between diastolic septal position and ventricular pressures. However, this population had a very limited range of systolic transseptal gradients, obviating any opportunity to explore the systolic transseptal pressure-position relationship.

Although abnormal motion of the ventricular septum during diastole (as observed in mitral stenosis) is relatively uncommon and has attracted little attention, abnormal systolic motion of the septum is very frequently encountered clinically and has been the subject of considerable interest. Results of both experimental and clinical studies are consistent with the observation that systolic motion abnormalities (in the absence of ischemia or infarction) are related to abnormal transseptal pressure gradients at end-diastole. Thus, when the normal transseptal pressure gradient
at end-diastole is reduced or reversed, the septum is displaced leftward and may even invert and become concave to the right ventricle.21 Depending on the degree of leftward septal displacement, septal motion during the subsequent systole may be reduced leftward, flat or reversed (paradoxic). Experimental studies have also demonstrated that the abnormal early systolic leftward motion of the septum observed in left bundle branch block reflects an abnormal (reversed) transseptal gradient during left ventricular isovolumetric contraction.21, 26 Conversely, when the diastolic transseptal gradient is increased, such as occurs with aortic regurgitation, the septum is displaced toward the right ventricle and demonstrates exaggerated leftward motion during the subsequent systole. Thus, abnormal transseptal pressure gradients result in septal displacement during both diastole and systole, whereas the end-diastolic gradient influences septal motion during the subsequent systole.

In conclusion, this study provides a hemodynamic explanation for exaggerated early diastolic leftward motion of the ventricular septum observed in patients with mitral stenosis. The results indicate that changes in the septal position (and therefore motion) throughout diastole reflect changes in the transseptal pressure gradient. Although we have chosen to demonstrate this in patients with mitral stenosis, we do not believe that septal mechanics are intrinsically different in these patients compared with other patient groups. This information, combined with data from other studies dealing with abnormalities of systolic septal motion, is important in the assessment of ventricular performance. In particular, this improved understanding of septal mechanics highlights the potential pitfalls associated with the use of septal motion as an index of myocardial function. Thus, septal motion throughout the cardiac cycle is responsive to hemodynamic factors (transseptal pressure gradient) and, under some conditions, this “passive” motion may play a more important role in determining net movement than contraction or relaxation of the myocardium.

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