PATHOPHYSIOLOGY AND NATURAL HISTORY
VENTRICULAR PERFORMANCE

Septal geometry in the unloaded living human heart

JOAO A. C. LIMA, M.D., PABLO A. GUZMAN, M.D., FRANK C. P. YIN, M.D., PH.D.,
ROBERT K. BRAWLEY, M.D., LINDA HUMPHREY, M.D., THOMAS A. TRAILL, M.R.C.P.,
SANDRA D. LIMA, PAOLO MARINO, M.D., MYRON L. WEISFELDT, M.D.,
AND JAMES L. WEISS, M.D.

ABSTRACT Right ventricular loading leads to diastolic septal flattening in man without necessarily requiring right ventricular pressure to exceed left ventricular pressure. This observation suggested that the unstressed septal configuration is flat and that its normal concave shape is due to the left-to-right transseptal pressure gradient. To examine this hypothesis, we studied septal configuration by two-dimensional echocardiography in nine patients with normal global and regional left ventricular function during surgery for coronary artery disease. The transseptal pressure gradient was obtained from pulmonary capillary wedge pressure minus right atrial pressure. Measurements were obtained at control (open chest, intact pericardium [C]), with the pericardium open (OP), on cardiopulmonary bypass (CPB), and after cardiac arrest (CA). There were no changes in any measurements between C and OP or between CPB and CA. Left ventricular end-diastolic cavity area decreased from 16.5 ± 2.1 cm² at C to 11.1 ± 4.5 cm² after CPB, and further decreased to 8.9 ± 3.5 cm² after CA (p < .001), yet the septum flattened, as shown by an increase in its radius of curvature from 1.7 ± 0.5 cm during C to 2.5 ± 0.7 cm after CPB, and to 2.9 ± 1.0 cm after CA (p < .001), or from 0.4 ± 0.1 to 0.8 ± 0.4 to 1.1 ± 0.5 U (p < .001) when normalized for cavity area. Diastolic transseptal pressure gradient was reduced from 4.1 ± 2.3 mm Hg during C to 1.1 ± 1.8 mm Hg after CPB, and to 0.5 ± 1.4 mm Hg after CA (p < .01). Thus, in the unloaded human heart, the interventricular septum is more flat and occupies a neutral position between the left and right ventricle. Septal flattening due to a reduced but not reversed transseptal left-to-right gradient results from assumption of this unstressed shape as the right ventricular end-diastolic pressure approaches the left ventricular end-diastolic pressure.


OWING TO its anatomic position, the interventricular septum is postulated to be a mediator of ventricular interaction. However, the mechanisms underlying the changes in septal position are still unclear. Previous work from our laboratory demonstrated leftward displacement of the interventricular septum with acute right ventricular loading during a Mueller maneuver in humans (a forced inspiration against a closed airway). In an effort to determine whether these shifts occurred as a result of right ventricular diastolic pressure exceeding left ventricular diastolic pressures, we then measured the diastolic transseptal pressure gradient during the Mueller maneuver, and correlated these changes with alterations in septal geometry. This study (again in humans) showed that the septal flattening that occurs with acute right ventricular loading is accompanied by a decrease in the diastolic left-to-right transseptal pressure gradient, without requiring a reversal of this gradient. This raised the possibility that the reason why the interventricular septum shifts leftward during acute right ventricular loading is that the normal septal configuration in the unloaded heart is flat, and that in the working heart it is held in its usual position concave to the left ventricular cavity by the normal and persistent left-to-right positive transseptal pressure gradient. The goal of the current study was to determine the position and configuration of the interventricular septum in the living human heart when the heart is arrested and the transseptal pressure approaches zero.

Methods

Study protocol. We studied nine patients with phased-array two-dimensional echocardiography who were undergoing open heart surgery for coronary artery disease (table 1). All patients had normal global and segmental left ventricular func-

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From the Cardiology Division, Department of Medicine, and the Department of Surgery, The Johns Hopkins Medical Institutions, Baltimore.

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Address for correspondence: James L. Weiss, M.D., 591 Carnegie Building, The Johns Hopkins Hospital, 600 N. Wolfe St., Baltimore, MD 21205.

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TABLE 1
Patient characteristics

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age/sex</th>
<th>EF (%)</th>
<th>Coronary angiographic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>52/M</td>
<td>57</td>
<td>99% proximal LAD occlusion</td>
</tr>
<tr>
<td>2</td>
<td>58/M</td>
<td>72</td>
<td>90% LAD, right and left circumflex marginal branch occlusion</td>
</tr>
<tr>
<td>3</td>
<td>59/M</td>
<td>54</td>
<td>50% to 70% proximal LAD and 70% left circumflex marginal branch occlusion</td>
</tr>
<tr>
<td>4</td>
<td>56/M</td>
<td>53</td>
<td>70% to 90% proximal LAD and 70% to 90% mid right coronary artery occlusion</td>
</tr>
<tr>
<td>5</td>
<td>52/F</td>
<td>59</td>
<td>Total proximal LAD occlusion</td>
</tr>
<tr>
<td>6</td>
<td>42/M</td>
<td>65</td>
<td>99% proximal LAD occlusion</td>
</tr>
<tr>
<td>7</td>
<td>54/M</td>
<td>50</td>
<td>70% to 90% proximal LAD occlusion</td>
</tr>
<tr>
<td>8</td>
<td>56/M</td>
<td>62</td>
<td>99% proximal LAD and distal right occlusions</td>
</tr>
<tr>
<td>9</td>
<td>45/M</td>
<td>57</td>
<td>50% to 70% mid LAD and 50% to 70% mid right coronary artery occlusion</td>
</tr>
</tbody>
</table>

EF = ejection fraction; LAD = left anterior descending coronary artery.

Inclusion as previously determined by left ventriculography. Mean ejection fraction by this technique was 59 ± 7% (range 50% to 72%, table I). None had a history or evidence of a previous myocardial infarction. All patients gave written informed consent for the research protocol.

Two-dimensional echocardiograms (Varian V3400) were recorded in cross-sectional views (at the level of the papillary muscles) on 1/2 inch magnetic videotape (Sony-Betamax) with a modified transducer described previously. Briefly, a castor oil–filled standoff device was attached to the transducer head to offset the transducer from the right ventricular epicardial surface and minimize mechanical interference with cardiac motion. This transducer was inserted into a long, sterile plastic sheath filled previously with ultrasonic gel and placed directly on the heart. The echocardiograms were recorded during four stages: stage I, open-chest, intact pericardium control; stage II, open pericardium, after it had been reflected; stage III, during cardiopulmonary bypass before arrest; stage IV, immediately after cardiac arrest was induced by cold potassium cardioplegia.

Right atrial and pulmonary capillary wedge pressures were recorded as indirect measures of right and left ventricular end-diastolic pressures with a Swan-Ganz thermodilution catheter (Edwards Laboratories) inserted transvenously into the pulmonary artery.

Data analysis

Echocardiographic data. Two-dimensional echocardiographic frames corresponding in time to end-diastole (defined by the onset of the QRS) and end-systole (defined as the smallest cross-sectional cavity area throughout the cardiac cycle) were selected from each of the four above-described stages (end-systolic measurements were obtained from the first three stages only). The endocardial contours and left ventricular cavity areas were obtained directly from a commercially available system for echocardiographic image processing and quantification (Microsonics, Inc.). All contouring was done manually. The left ventricular septal and free wall radii of curvature were calculated independently by two investigators, as described previously. Because the radius of curvature of a circle varies with the square root of the area of that circle, a normalized radius of curvature was also calculated by methods described previously, to minimize the possibility that a change in the radius of a myocardial segment was a result of a change in ventricular cavity area. This was done by dividing the radius of curvature of a particular segment by the square root of the ventricular cavity area, and expressing the resultant value in arbitrary units. We verified the appropriateness of use of the radius of curvature as an index of shape change for both the septum and free wall endocardial contour by calculating the variation in measurements obtained at 10 equally spaced points throughout both septal and free wall segments, both during the control period and after cardiac arrest. There was no significant variation in the values for the radius of curvature of either the septum or free wall during these two periods.

To minimize the effects of local pressures on the heart by the transducer, the echocardiogram was recorded continuously during all four stages as the transducer was lifted slowly off the heart until all echocardiographic images were lost. The frames used were those obtained immediately before the loss of the echocardiographic image.

Intracardiac pressures. Right atrial and pulmonary capillary wedge pressure were recorded on a strip-chart recorder (Hewlett Packard) and measured directly from the analog tracings. The pressure data were synchronized to the echocardiographic data by superimposing a square-wave artifact on an electrocardiogram recorded simultaneously with both the recorded pressure and the echocardiographic videotape. The transseptal pressure gradient was then derived by subtracting the right atrial pressure from the pulmonary capillary wedge pressure.

Statistical analysis. The statistical significance of differences in pressures, cross-sectional cavity areas, and radii of curvature from the different sequential stages of the protocol was calculated by analysis of variance (ANOVA) with repeated measures. The Student-Newman-Keuls (SNK) test was used to test for the significance of differences between two individual stages of the protocol, isolated from the repeated-measures analysis of variance.

Results

The size of the left ventricle (figure I), indexed by the end-diastolic cross-sectional cavity area, decreased from 16.5 ± 2.1 cm² during control and 15.6 ± 3.2 cm² after the pericardial sac was opened to 11.1 ± 4.5 cm² during cardiopulmonary bypass, and further to 8.9 ± 3.5 cm² after cardioplegia and arrest (ANOVA, p < .001, and SNK test, p < .05, from opened pericardium to bypass and from bypass to arrest). The end-systolic cavity areas were also reduced from 9.0 ± 3.2 and 9.3 ± 3 cm² with intact and opened pericardium, respectively, to 6.5 ± 2.1 cm² during cardiopulmonary bypass (ANOVA, p < .005; figure I). As the heart approached and achieved total arrest, the transseptal pressure gradient (figure 2) decreased from 4.1 ± 2.3 and 3.9 ± 2.3 mm Hg with intact and opened pericardium, respectively, to 1.1 ± 1.8 mm Hg during cardiopulmonary bypass, and further to 0.5 ± 1.4 mm Hg during arrest (overall ANOVA, p < .01). Both cardiac size and transseptal pressure gradient remained unchanged after the pericardial sac was opened but before cardiopulmonary bypass (SNK, p = NS). Similarly, the transseptal pressure gradient did not
FIGURE 1. End-diastolic (open bars) and end-systolic (hatched bars) left ventricular (LV) cross-sectional cavity area during cardiopulmonary bypass (CPB) and cardiac arrest (CA). Both decreased during CPB, and end-diastolic area decreased further during CA (SNK, p < .05 from OP to CPB and from CPB to CA; overall ANOVA, p < .001 for both). Between control (C) and open pericardium (OP), there were no changes in cavity area (SNK test, p = NS).

change from cardiopulmonary bypass to cardiac arrest (SNK, p = NS). Results for right atrial and pulmonary capillary wedge pressure were directionally and statistically similar to those for transseptal pressure.

The cross-sectional shape of the left ventricle changed markedly after cardiopulmonary bypass and cardioplegic arrest (figure 3). The interventricular septum flattened, as indexed by an increase in its radius of curvature, from $1.7 \pm 0.5$ and $1.6 \pm 0.6$ cm with intact and opened pericardium, respectively, to $2.5 \pm 0.7$ cm during bypass and $2.9 \pm 1.0$ cm after cardiac arrest (overall ANOVA, p < .001; SNK test, p = NS from bypass to complete arrest; figure 4). The changes in the septal radius of curvature, normalized to changes in end-diastolic cross-sectional area, were similar (from $0.4 \pm 0.1$ and $0.4 \pm 0.2$ U with intact and opened pericardium to $0.8 \pm 0.4$ U during bypass and $1.1 \pm 0.5$ U during arrest; overall ANOVA, p < .001; SNK test, p = NS from bypass to arrest; figure 4). By contrast, the free wall radius of curvature (diametrically opposite the interventricular septum) measured at end-diastole (figure 5) was unchanged throughout the entire experiment (from $1.4 \pm 0.4$ cm with intact pericardium to $1.1 \pm 0.4$ cm during arrest; ANOVA, p = NS). The free wall radius of curvature adjusted for changes in end-diastolic area also remained unchanged (from $0.3 \pm 0.1$ to $0.4 \pm 0.2$ U during arrest; ANOVA, p = NS; figure 5).

The changes in the normalized septal radius of curvature measured at end-systole (figure 6) during cardiopulmonary bypass were in the same direction as those measured at end-diastole (from $0.4 \pm 0.2$ and $0.4 \pm 0.1$ U during intact and opened pericardium, respectively, to $0.5 \pm 0.1$ U during bypass; ANOVA, p < .05). However, the absolute septal radius of curvature did not change significantly (from $1.2 \pm 0.5$ cm with intact pericardium to $1.3 \pm 0.2$ cm during cardiopulmonary bypass; ANOVA, p = NS). Conversely, the absolute end-systolic free wall radius of curvature (figure 7) decreased from $1.0 \pm 0.2$ cm with intact pericardium and $0.9 \pm 0.2$ cm with opened pericardium to $0.7 \pm 0.3$ cm during bypass (ANOVA, p < .05), while the normalized free wall radius of curvature remained unchanged (from $0.3 \pm 0.1$ to $0.3 \pm 0.2$ U, p = NS). There were no cross-sectional shape changes in the left ventricle after the pericardial sac was opened and reflected before cardiopulmonary bypass (figures 3 to 7).

Discussion

This study verifies the hypothesis that septal configuration is relatively flat in the unloaded human heart. That is, as the heart approaches a totally unloaded state and the positive left-to-right transseptal gradient approaches zero, the septum flattens from its normal configuration concave to the left ventricle.

The effects of the diastolic transseptal pressure gradient on interventricular septal position have been the subject of recent interest and investigation. Data from our institution,1, 2 and other laboratories3-5 have shown that the position and shape of the septum at end-diastole is determined by the transseptal pressure gradient and that a reduction or reversal of such a gradient shifts the septum toward the left ventricle. While it is not difficult to understand leftward septal shifts in the presence of a reversed (negative with respect to the left ventricle) transseptal gradient, it is not as easy to conceptualize why there is a leftward shift in the presence of a reduction in the left-to-right gradient only. Our data suggest one possible mechanism for such a phenomenon: in the living but nonbeating human heart.

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the interventricular septum is relatively flat and occupies a neutral position between the two ventricles. Therefore, the more familiar round configuration of the septum, with its concavity toward the left ventricle, is a result of the positive diastolic left-to-right transseptal pressure gradient. As this pressure gradient is reduced and approaches zero, the septum shifts toward its neutral position.

There is an alternative mechanism that could explain why the septum flattens in the presence of a reduced but not reversed transseptal gradient. If the septal surface exposed to right ventricular pressure exceeded that exposed to left ventricular pressure, the net force on the septum could be directed toward the left ventricle despite the pressure in the left ventricle being slightly higher than that in the right ventricle. This possibility, however, can only be confirmed with simultaneous measurements of right and left septal areas in situ — a very difficult undertaking.

In addition to the end-diastolic septal flattening as the heart was unloaded, we found a small increase in end-systolic radius of curvature. These changes were
Why the septum maintains its flat configuration during systole when the left ventricular cavity pressure greatly exceeds right ventricular pressure is not known. As ventricular contraction proceeds, the stiffness of the muscle increases above the level present during diastole, when it is more flaccid. Thus, one possible explanation for the persistent systolic flattening is that the increase in stiffness in the initially flattened septum is enough to counterbalance the increase in left-to-right forces tending to push the septum toward the right ventricle. If this hypothesis is correct, then both the timing and relative extent of diastolic septal flattening are critical determinants of the systolic septal configuration. If too little diastolic flattening occurs, or if it occurs too late, the increase in septal stiffness would not be sufficient to prevent the net systolic forces from pushing the septum toward the right ventricle and persistent systolic flattening or displacement would not be observed. This could be the reason that no end-systolic shape change was observed in the dog by Kingma et al. during right ventricular volume or pressure overload. That group, however, did note a decrease in septal-to-free wall diameter during those interventions as well as a simultaneous decrease in left-to-right transseptal pressure gradient. Stool et al. also noted a decrease in the septal-to-lateral wall dimension during pulmonary hypertension in the dog. Clearly, further work is needed to clarify the mechanism of the behavior of the interventricular septum during systole.

Our study was designed to test the hypothesis that septal configuration is flat in the unloaded human liv-

far less striking than the end-diastolic flattening seen during bypass or cardiac arrest, but are consistent with findings of previous studies that indicated persistent septal flattening throughout several cardiac cycles. Why the septum maintains its flat configuration during systole when the left ventricular cavity pressure greatly exceeds right ventricular pressure is not known. As ventricular contraction proceeds, the stiffness of the muscle increases above the level present during diastole, when it is more flaccid. Thus, one possible explanation for the persistent systolic flattening is that the increase in stiffness in the initially flattened septum is enough to counterbalance the increase in left-to-right forces tending to push the septum toward the right ventricle. If this hypothesis is correct, then both the timing and relative extent of diastolic septal flattening are critical determinants of the systolic septal configuration. If too little diastolic flattening occurs, or if it occurs too late, the increase in septal stiffness would not be sufficient to prevent the net systolic forces from pushing the septum toward the right ventricle and persistent systolic flattening or displacement would not be observed. This could be the reason that no end-systolic shape change was observed in the dog by Kingma et al. during right ventricular volume or pressure overload. That group, however, did note a decrease in septal-to-free wall diameter during those interventions as well as a simultaneous decrease in left-to-right transseptal pressure gradient. Stool et al. also noted a decrease in the septal-to-lateral wall dimension during pulmonary hypertension in the dog. Clearly, further work is needed to clarify the mechanism of the behavior of the interventricular septum during systole.

Our study was designed to test the hypothesis that septal configuration is flat in the unloaded human liv-
volume of the intracardiac chambers diminished. On the other hand, great care was taken to minimize these effects by use of the transducer of modified design, maintenance of internal landmarks in this image (papillary muscles), and by recording echocardiographic frames immediately before the loss of the image (see Methods). We have previously validated this approach using the same transducer stand-off device in the open-chest dog by documenting a lack of significant change in cross-sectional left ventricular shape as the stand-off device was lifted from the heart.11

Our data showed no difference in left ventricular cross-sectional configuration or in any of the other measured parameters before and after the pericardial sac was opened and reflected during surgery. It has been reported that the pericardium mediates or potentiates ventricular interaction by restraining overall cardiac distensibility.12-15 Such evidence has been obtained by assessing the effects of selective loading or unloading of one or more cardiac chambers in the presence or absence of the pericardium. In our study, there were no changes in cross-sectional left ventricular cavity area after the pericardium was reflected before cardiopulmonary bypass. In addition, our patients had normal angiographic left ventricular cavity size and function before surgery, and none developed dysfunction during the surgical procedure. Thus, although we detected no changes in left ventricular shape attributable to the absence of the pericardium in our patients, right or left ventricular overload was not likely present before pericardiotomy, and distensibility may not have been limited by the pericardium for this reason.

In summary, we have documented that in patients undergoing cardiac surgery the interventricular septum flattens as the heart approaches and then achieves a totally unloaded state, and that under the conditions of this study in the living human heart, the position of the interventricular septum is not affected by the presence of the pericardium. Our results are further evidence in man that the diastolic position of the interventricular septum is a reflection of the left-to-right transseptal pressure gradient, and that it is through changes in this gradient that the interventricular septum, by altering its shape and/or position, may mediate diastolic ventricular interaction.

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Septal geometry in the unloaded living human heart.
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