Changes in the Radius of Curvature of the Ventricular Septum at End Diastole During Pulmonary Arterial and Aortic Constrictions in the Dog

Sheng-Jing Dong, MD, PhD; Eldon R. Smith, MD; and John V. Tyberg, MD, PhD

**Background.** At end diastole, the position and shape of the ventricular septum depend on the transseptal pressure gradient. It is not clear, however, how the septal radius of curvature changes in response to the gradual change in transseptal pressure gradient during progressive pulmonary arterial constriction (PAC) and aortic constriction (AC).

**Methods and Results.** In 11 anesthetized open-chest dogs, the septal radius of curvature was measured from the short-axis two-dimensional echocardiogram, and the transseptal pressure gradient (left ventricular [LV] pressure minus right ventricular [RV] pressure) was calculated from ventricular pressures measured with micromanometers. Seven dogs were studied with both PAC and AC (group 1) and four dogs only with PAC, which was initiated before and after volume loading (group 2). The transseptal pressure gradient decreased during PAC. As the transseptal pressure gradient decreased, the septum shifted continuously leftward with decreases in the LV septum-free wall diameter and in LV cross-sectional area. The septal radius of curvature (R) increased until the septum became flat. The flat septum (i.e., R = ∞) occurred at a relatively constant value of transseptal pressure gradient (-4.6±1.4 mm Hg) independently of the absolute values of LV pressures when between 2 and 9 mm Hg, although necessarily a greater RV pressure was needed to make the septum flat when LV pressure was higher. After inversion, the septum again became curved, with a decrease in the absolute value of septal radius of curvature as the transseptal pressure gradient became increasingly negative. The septum was still concave to the LV cavity at zero transseptal pressure gradient, and its curvature decreased (i.e., its radius of curvature increased) with increases in ventricular pressures. During AC, the septal radius of curvature also increased, but with an increase in transseptal pressure gradient accompanied by increases in LV septum–free wall diameter and in LV area. In group 2 animals, at zero transseptal pressure gradient, the normalized septal radius of curvature was greater (p < 0.005) at high LV pressure than at low LV pressure. The transseptal pressure gradient required to make the septum flat was not significantly different between low and high LV pressure, which confirmed the results of group 1.

**Conclusions.** The results of the present study show that the shape and position of the ventricular septum are determined by the transseptal pressure gradient but that the shape of the septum is also affected by the ventricular pressures. The septum was not flat but rather still concave to the LV cavity at zero transseptal pressure gradient. Approximately 5 mm Hg of negative transseptal pressure gradient was required to displace the septum farther leftward and make it flat. The septal radius of curvature increased during both PAC (which decreased transseptal pressure gradient) and AC (which increased transseptal pressure gradient), indicating that the mechanisms involved in changing septal radius of curvature are different during PAC and AC. *(Circulation* 1992;86:1280–1290)

**Key Words** • pressure, transseptal • ventricular septal position • septal segment length • echocardiography

From the perspective of ventricular mechanics, the ventricular septum is a complicated structure that has been difficult to study directly. In the intact heart, studies of septal mechanical properties have used only echocardiographic techniques.1–4 These studies have suggested that, at end diastole, the ventricular septum behaves like a passive compliant membrane between two liquid-filled chambers and that its position is a continuous monotonous function of the transseptal pressure difference or gradient between left ventricular (LV) and right ventricular (RV) pressures.1–4 In the normal working heart, which has a positive end-diastolic transseptal pressure gradient of about 5 mm Hg, the...

Address for correspondence: Dr. J.V. Tyberg, Departments of Medicine and Medical Physiology, University of Calgary, Health Science Center, 3330 Hospital Drive N.W., Calgary, Alberta, Canada T2N 4N1.

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septum is concave to the LV cavity, with a radius of curvature similar to that of the LV free wall.\textsuperscript{3,5-7} Septal flattening and/or inversion have been observed in patients\textsuperscript{1,4-8} and in experimental animals\textsuperscript{1,2} with RV volume and pressure overloading. None of these studies, however, provided direct, continuous measurements of septal radius of curvature related to the transseptal pressure gradient or an integrated description of how changes in septal position correspond to changes in septal curvature. Furthermore, because none of these studies provided measurements of septal segment strain, it has not been possible to relate septal position to septal strain. In the present study, we continuously and simultaneously measured the septal minor axis radius of curvature (by two-dimensional echocardiography) and septal midwall segment length (by sonomicrometry) and related these measurements to the pressures in the LV and RV (micromanometers) and to measurements of LV diameters (two-dimensional echocardiography) during alternate pulmonary arterial constriction (PAC) and aortic constriction (AC). Our objectives were 1) to determine how the end-diastolic septal radius of curvature varies as a function of transseptal pressure gradient and in relation to changes in septal position; 2) to determine the level of transseptal pressure gradient at which the septum becomes flat and to see whether this septum-flattening transseptal pressure gradient is a function of LV pressure; and 3) to describe the influence of the ventricular pressures on the curvature of the septum at constant transseptal pressure gradient.

**Methods**

**Experimental Preparation**

Eleven adult mongrel dogs of either sex (weight 21–28 kg) were anesthetized, initially with sodium thiopental (25 mg/kg i.v.) and subsequently with an infusion of fentanyl citrate (25 mg · kg\(^{-1}\) · hr\(^{-1}\)). After intubation, the animals were placed in the right lateral position and ventilated with a 70% nitrous oxide–30% oxygen mixture by use of a constant-volume respirator (model 607, Harvard Apparatus, Millis, Mass.). A large-bore cannula was introduced into the external jugular vein for liquid administration. A thoracotomy was performed through the left fifth intercostal space, and inflatable silicone occluders were placed around the main pulmonary artery and aorta.

The ventrolateral surface of the pericardium was incised transversely (length, \(\approx 5\) cm) along the base of the heart and widely retracted for the insertion of a pair of sonomicrometer crystals (Triton Technology, San Diego, Calif.) into the midportion of the septum to measure the septal segment length. The crystals were advanced by use of long plastic sleeves, the interventricular groove having been penetrated beside the distal left anterior descending coronary artery. Two crystals were placed approximately 1 cm apart, circumferentially half-way between the anterior and posterior insertions and midway between the apex and base in the midlayer of the septum (mid 50% of the septal wall), and therefore were parallel to the direction of the midwall circumferential myocardial fibers.\textsuperscript{9} The crystals were placed such that septal midwall segment length changed in proper phase with LV pressure (i.e., the septal midwall segment length was longest at end diastole\textsuperscript{10}) and the LV pressure–septal midwall segment length loop was positive (i.e., it moved in a counterclockwise direction). The heart was then repositioned into the pericardium, and the pericardial margins were reapproximated with several individual sutures, taking care to avoid decreasing the pericardial volume. Two 8F micromanometer-tipped catheters with reference luminas (model PR 279, Millar Instruments, Houston, Tex.) were introduced through a carotid artery and internal jugular vein into the LV and RV, respectively. A liquid-filled catheter was inserted into the aorta via a femoral artery to monitor pressure. The liquid-filled catheters were attached to transducers (P23Ib, Gould, Inc., Oxnard, Calif.) and referenced to the level of the right atrium. Pressures measured by the micromanometers were matched to those measured from the liquid-filled catheters before each data collection to correct any baseline drift. After surgical preparation, the animals were allowed to stabilize. Throughout the experiment, body temperature was maintained by a heating pad, and a limb lead ECG (lead II) was recorded to monitor the heart rhythm and rate. After each experiment, the heart was dissected and the position of the crystals was examined. Septal midwall segment length data from one dog were excluded because the crystal position was not appropriate.

All conditioned hemodynamic signals were amplified (model VR16, Electronics for Medicine/Honeywell, White Plains, N.Y.) and recorded on paper (Gould, Inc., Cleveland, Ohio); they were also passed through an antialiasing low-pass filter with a cutoff frequency of 100 Hz and digitized (model 5170, IBM, Armonk, N.Y.) at a sampling frequency of 200 Hz. The digital data were subsequently analyzed with specially developed software (CVSOFT, Odessa Computer Systems, Ltd., Calgary, Canada) on a VAX 11/750 computer (Digital Equipment Corp., Maynard, Mass.).

Two-dimensional echocardiography was performed with a 2.5-MHz transducer (Diasonics V3400, Salt Lake City, Utah) to evaluate the geometric changes in the septum and LV. The transducer was placed in the right fourth or fifth intercostal space parasternally to record a short-axis cross-sectional image of LV at the level of the tips of the papillary muscles.\textsuperscript{11} Because the dogs lay in the right lateral position and because of the shape of the canine chest, we could usually obtain clear images, even with the chest open. If the image was unsatisfactory because of poor acoustic coupling, we put a little saline into the chest, which enabled us to obtain high-quality images. The two-dimensional echocardiogram was recorded on 1/2-in. videotape at 30 frames per second for later stop-frame analysis. Gain controls were carefully adjusted to define the endocardial surface optimally.

**Experimental Protocol**

Hemodynamic and echocardiographic data were obtained simultaneously and continuously for 1–1.5 minutes during each intervention, which was preceded by a 10-second control period. Between interventions, 10–20 minutes was allowed to elapse for hemodynamic stabilization.

To describe a large range of transseptal pressure gradient, PAC and AC were performed alternately in seven dogs (group 1). In another four dogs (group 2),
only PAC was performed. In group 2, PAC was performed first at baseline volume state and then repeated after volume loading (sufficient to increase LV pressure from 7.3±0.7 to 13.9±0.4 mm Hg, p<0.005) with warmed, heparinized Ringer's lactate solution.

Data Analysis

Only data collected at end diastole and end expiration were analyzed. End diastole was defined by the peak of the R wave, and end expiration was indicated by a voltage pulse from a switch installed on the respirator. Transseptal pressure gradient was defined as the instantaneous end-diastolic difference between LV pressure and RV pressure.

Echocardiographic Analysis

The method used to analyze the echocardiographic images was similar to that reported in our previous studies.12,13 The appropriate end-diastolic frames were digitized with a Gould IP8500 image processor and frame grabber (Gould, Inc., Fremont, Calif.) attached to a Digital VAX 11/750 computer. However, before digitization, the video signal was sent from the video-cassette recorder (model AG6300, Panasonic) through a Hotronic Time Base Corrector (AD51, Hotronic, Inc., Burlingame, Calif.) to synchronize the video with the image processor. The digitized images were then analyzed with software developed in our laboratory. The system was calibrated by the internally generated markers displayed on the echocardiogram. Because the hemodynamic and echocardiographic data were obtained with two different recording systems, they were synchronized by recording a signal corresponding to each echocardiographic frame on the computer.

The LV endocardial border was traced to eliminate the irregularities of trabeculation, cut through the papillary muscle insertions, and identify the septal insertion points. The following parameters were measured from this tracing. The LV cross-sectional cavity area was calculated as the area within the tracing. The septal radius of curvature was measured over the middle 60% of length of the septal perimeter, which was determined by standard geometrical techniques considering 30% of the septal perimeter on each side of the midpoint between the septal insertions. The radius of the LV free wall was measured by the same standard techniques, considering the entire free wall perimeter between the septal insertions. Normally, the septum was concave toward the LV cavity, in which case the radius of curvature was defined as positive. Accordingly, when the septum was convex toward the LV cavity, the radius of curvature was said to be negative, and when the septum was flat, the radius of curvature was deemed to be infinite. The LV septum–to–free wall diameter was measured as the distance between the midpoint of the septal surface and the midpoint of the LV free wall perimeter. The LV anteroposterior diameter was measured as the longest anteroposterior diameter perpendicular to the LV septum–to–free wall diameter.

To express changes in septal radius of curvature (R_s) as independently as possible from changes in LV cavity area, we used a normalized parameter. First, the idealized radius (R_i) was calculated from the measured LV cross-sectional cavity area (A_v) assuming that the area was perfectly circular; thus, R_i=\(A_v/\pi\). Then, the normalized septal radius of curvature (R_s*) was defined as the ratio of septal radius of curvature to idealized radius (i.e., R_s*=R_s/R_i). The greater the absolute value of normalized septal radius of curvature, the flatter the septum. When the septum became flat, septal radius of curvature and normalized septal radius of curvature became infinite, and when the LV cross-sectional cavity area became nearly circular, normalized septal radius of curvature approached unity. Similarly, negative values of normalized septal radius of curvature represented the reversal of the septal curvature with the septum convex toward the LV cavity.

Statistical Analysis

The results are expressed as mean±SD. Repeated-measures ANOVA was performed with Student-Newman-Keuls correction for multiple comparisons. Student's t test was used for the paired observations. Statistical testing was performed using spssx statistical software (SPSS Inc., Chicago) on a VAX 11/750 computer. A probability of less than 0.05 was considered to be statistically significant.

Results

Group 1

The average values of the pressure measurements from seven group 1 dogs under control conditions and at the peak effect of PAC and AC are listed in Table 1. During PAC, RV pressure increased, and LV pressure decreased; the resultant end-diastolic transseptal pressure gradient decreased and became negative (2.0±1.5 versus −6.5±1.2 mm Hg, p<0.001). During AC, LV pressure increased dramatically, but RV pressure did not change significantly; this resulted in a large increase in transseptal pressure gradient (from 1.7±1.6 to 15.0±4.5 mm Hg at end diastole, p<0.001).

Figure 1 presents typical end-diastolic two-dimensional echocardiographic images obtained at the level of the papillary muscles under control conditions and during the interventional. Average values of the geometric measurements are listed in Table 1. Under control conditions, the septum was normally concave toward the LV. During PAC, the septum shifted leftward, gradually flattening and inverting and changing the septal radius of curvature from a positive value of 2.21±0.51 cm to a negative value of 5.13±1.93 cm (p<0.001). LV cross-sectional cavity area, radius of the LV free wall, and LV diameters all decreased. During AC, LV cross-sectional cavity area increased symmetrically, accompanied by increases in the radii of curvature of the septum and LV free wall and in the LV septum–to–free wall and anterior–to–posterior wall diameters.

The relation between transseptal pressure gradient and the septal radius of curvature is shown by an example in Figure 2. During AC, the increase in transseptal pressure gradient resulted in an increase in septal radius of curvature, whereas there was a slight, nonsignificant decrease in normalized septal radius of curvature; this indicates that the increase in septal radius of curvature was caused by the increase in LV cross-sectional cavity area. During PAC, which decreased transseptal pressure gradient, both septal radius of curvature and normalized septal radius of curvature were positive and increased until the septum became...
TABLE 1. Effect of Pulmonary Arterial and Aortic Constrictions on Pressures and LV Geometry*

<table>
<thead>
<tr>
<th></th>
<th>Pulmonary arterial constriction</th>
<th>Aortic constriction</th>
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<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Peak effect</td>
</tr>
<tr>
<td>Hemodynamics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P_LVPS (mm Hg)</td>
<td>103±9</td>
<td>71±30</td>
</tr>
<tr>
<td>P_RVPS (mm Hg)</td>
<td>27.1±4.1</td>
<td>59.0±12.6</td>
</tr>
<tr>
<td>P_o (mm Hg)</td>
<td>8.9±3.4</td>
<td>3.8±2.2</td>
</tr>
<tr>
<td>P_n (mm Hg)</td>
<td>6.9±2.4</td>
<td>12.4±2.1</td>
</tr>
<tr>
<td>P_s (mm Hg)</td>
<td>2.0±1.5</td>
<td>−8.6±1.2</td>
</tr>
<tr>
<td>Two-dimensional echocardiographic measurements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A_s (cm²)</td>
<td>9.68±3.24</td>
<td>4.30±1.95</td>
</tr>
<tr>
<td>D_s-fw (cm)</td>
<td>3.13±0.47</td>
<td>1.49±0.35</td>
</tr>
<tr>
<td>D_s-ap (cm)</td>
<td>3.88±0.71</td>
<td>2.98±0.68</td>
</tr>
<tr>
<td>R_s (cm)</td>
<td>2.21±0.51</td>
<td>−5.13±1.93</td>
</tr>
<tr>
<td>R_s* (cm)</td>
<td>1.27±0.11</td>
<td>−4.48±1.42</td>
</tr>
<tr>
<td>R_t (cm)</td>
<td>1.94±0.37</td>
<td>1.49±0.35</td>
</tr>
</tbody>
</table>

P_LVPS, left ventricular (LV) peak systolic pressure; P_RVPS, right ventricular (RV) peak systolic pressure. The following values are end-diastolic: P_o, LV pressure; P_n, RV pressure; P_s, transseptal pressure gradient; A_s, LV cross-sectional area; D_s-fw, LV septum–to–free wall diameter; D_s-ap, LV anteroposterior diameter; R_s, measured septal radius of curvature; R_s*, normalized septal radius of curvature; R_t, LV free wall radius of curvature.

*Group 1, n=7.

flat (i.e., septal radius of curvature and normalized septal radius of curvature equaled infinity) at a transseptal pressure gradient of −4.4 mm Hg in this example; then the septum inverted (i.e., septal radius of curvature and normalized septal radius of curvature became negative), and its curvature became less negative with further increases in the negative transseptal pressure gradient. The parallel responses of septal

FIGURE 1. Two-dimensional, short-axis, stop-frame echocardiographic images at the level of the papillary muscles at end diastole during control and during gradual pulmonary arterial constriction (PAC, top panel) and during aortic constriction (AC, bottom panel). At control (A), the cross-sectional outline of the left ventricular (LV) cavity was nearly circular. AC enlarged the LV symmetrically (B, C), leading to an increase in the radius of curvature both of the septum and the LV free wall. PAC shifted the septum leftward continuously, flattening (C) and inverting (D) the septum. At zero transseptal pressure gradient (B), the curvature of the septum was still concave toward the LV cavity.
radius of curvature and normalized septal radius of curvature to the decreased transseptal pressure gradient during PAC indicate that the leftward septal shift resulted in a true change in the septal radius of curvature. In order to relate transseptal pressure gradient to normalized septal radius of curvature continuously, we plotted the reciprocal of normalized septal radius of curvature (1/R*_s) against transseptal pressure gradient (Figure 3; data were obtained during PAC only). There was a linear relation between transseptal pressure gradient (P_n) and 1/R*_s. Mean R^2 of the linear regression was 0.95±0.01 (range, 0.92–0.97) from seven group 1 dogs; the regression equation of pooled data was 1/R*_s=0.525+0.094·P_n (p<0.001). It should be noted that, when P_n=0, the values of 1/R*_s were positive, which meant that the curvature of the septum remained concave toward the LV cavity. At 1/R*_s=0, which represented the truly flat septum, the transseptal pressure gradient was negative. These results indicate that the septum did not become flat at P_n=0 but rather required greater forces on the right side of the septum.

To determine what pressure on the right side was needed to make the septum flat and whether greater RV pressure was needed if the LV pressure was higher, we selected pressure data from each dog at the point when the septum was flat (Table 2) and plotted RV pressure and transseptal pressure gradient against LV pressure (Figure 4). For the septum to be flat, higher RV pressure than LV pressure was needed, and greater RV pressure was needed with a greater LV pressure.

However, the value of transseptal pressure gradient when the septum became flat was nearly constant in that there was no relation between transseptal pressure gradient and LV pressure. We called this the “septum-flattening transseptal pressure gradient,” which was −4.6±1.4 mm Hg (Table 2) in the present study.

As demonstrated above, at zero transseptal pressure gradient, the septum was concave toward the LV. Figure 5 shows the relation between LV pressure and normalized septal radius of curvature at approximately zero transseptal pressure gradient (0.1±0.3 mm Hg, n=7). Normalized septal radius of curvature increased with the increase in LV pressure, indicating that, at zero transseptal pressure gradient, the shape of the septum depends on the distending pressure of the LV. In other words, the radius of curvature increases as the LV cavity gets bigger secondary to the increased ventricular pressure.

![Figure 2](image1.png)

**Figure 2.** Plot showing relations between the measured (R_s, closed symbols) and normalized septal radius of curvature (R*_s, open symbols) and the end-diastolic transseptal pressure gradient (P_n) in a representative dog. During aortic constriction (circles), R_s (closed circles) increased with the increase in P_n (2.71 cm at control vs. 3.11 cm at peak effect of constriction), whereas R*_s (open circles) did not change (1.35 at control vs. 1.31 at peak effect of constriction). During pulmonary arterial constriction (squares), the septum shifted leftward with the decrease in P_n; R_s (closed squares) and R*_s (open squares) increased until the septum became truly flat (i.e., R_s and R*_s=0) at P_n=−4.4 mm Hg (dashed line) and then became negative after septal inversion. R_s and R*_s became less negative as P_n became increasingly negative. At P_n=0, the septum was still concave toward the left ventricular cavity with R_s=4.13 cm and R*_s=2.34.

![Figure 3](image2.png)

**Figure 3.** Plot showing relation between the reciprocal of normalized, end-diastolic septal radius of curvature (1/R*_s) and the transseptal pressure gradient (P_n) during pulmonary arterial constriction (data from seven dogs, group 1). There was a linear relation between P_n and 1/R*_s. Mean R^2 of the linear regression was 0.95±0.01 (range, 0.92–0.97), and the regression equation of pooled data was 1/R*_s=0.525+0.094·P_n, indicated by the dashed line (p<0.001). Note that at P_n=0, the values of 1/R*_s were positive and at 1/R*_s=0, P_n had negative values, indicating that the flat septum did not occur at P_n=0 but required more force on the right side of the septum.

**Table 2.** End-Diastolic Pressures (mm Hg) When R_s=0

<table>
<thead>
<tr>
<th>Dog</th>
<th>P_LV</th>
<th>P_RV</th>
<th>P_n</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.3</td>
<td>11.8</td>
<td>−3.5</td>
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<tr>
<td>2</td>
<td>4.7</td>
<td>9.3</td>
<td>−4.6</td>
</tr>
<tr>
<td>3</td>
<td>8.7</td>
<td>13.1</td>
<td>−4.4</td>
</tr>
<tr>
<td>4</td>
<td>4.5</td>
<td>11.7</td>
<td>−7.2</td>
</tr>
<tr>
<td>5</td>
<td>2.0</td>
<td>7.1</td>
<td>−5.1</td>
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<tr>
<td>6</td>
<td>3.6</td>
<td>8.5</td>
<td>−5.0</td>
</tr>
<tr>
<td>7</td>
<td>7.5</td>
<td>10.1</td>
<td>−2.7</td>
</tr>
<tr>
<td>Mean</td>
<td>5.6</td>
<td>10.2</td>
<td>−4.6</td>
</tr>
<tr>
<td>SD</td>
<td>2.6</td>
<td>2.1</td>
<td>1.4</td>
</tr>
</tbody>
</table>

R_s, septal radius of curvature (R_s=0 when septum is flat); P_LV, left ventricular pressure; P_RV, right ventricular pressure; P_n, transseptal pressure gradient.
Relations Between Septal Segment Length and LV Diameters

Figure 6 shows the effects of changes in transseptal pressure gradient on LV septum–to–free wall diameter and septal midwall segment length during PAC and AC from a representative dog. Both LV septum–to–free wall diameter and septal midwall segment length decreased gradually and continuously as a function of decreasing transseptal pressure gradient.

Figure 6 also shows that there was a close linear relation between changes in septal midwall segment length and changes in LV septum–to–free wall diameter. For this relation, the average $R^2$ value from six dogs for which septal midwall segment length data were available was $0.88\pm0.11$ (range, 0.72–0.99). As the septum shifted to the left, septal midwall segment length decreased correspondingly, indicating that the septum was less stretched. There was also a close linear relation between septal midwall segment length and LV anteroposterior diameter. The $R^2$ value was $0.90\pm0.06$.

FIGURE 4. Plot showing right ventricular end-diastolic pressure ($P_{rv}$, squares) and end-diastolic transseptal pressure gradient ($P_{ts}$, circles) plotted against left ventricular end-diastolic pressure ($P_{lv}$) with the data selected at the point at which the septum was flat (data from seven dogs, group 1). $P_{rv}$ and $P_{ts}$ were positively and significantly correlated ($R^2=0.69$, $p<0.05$), but there was no correlation between $P_{rv}$ and $P_{ts}$, indicating that, for the septum to be flat, greater $P_{rv}$ is needed as $P_{ts}$ increases but that the value of $P_{ts}$ required to make the septum flat is relatively constant.

FIGURE 5. Plot of normalized septal radius of curvature ($R^*_s$) against left ventricular end-diastolic pressure ($P_{lv}$) at zero end-diastolic transseptal pressure gradient ($P_{ts}$) (data selected from seven dogs, group 1). When $P_{ts}=0$ mmHg, $R^*_s$ was positive and increased as $P_{ts}$ increased ($R^2=0.56$, $p=0.05$).

FIGURE 5. Plot showing right ventricular end-diastolic pressure ($P_{rv}$, squares) and end-diastolic transseptal pressure gradient ($P_{ts}$, circles) plotted against left ventricular end-diastolic pressure ($P_{lv}$) with the data selected at the point at which the septum was flat (data from seven dogs, group 1). $P_{rv}$ and $P_{ts}$ were positively and significantly correlated ($R^2=0.69$, $p<0.05$), but there was no correlation between $P_{rv}$ and $P_{ts}$, indicating that, for the septum to be flat, greater $P_{rv}$ is needed as $P_{ts}$ increases but that the value of $P_{ts}$ required to make the septum flat is relatively constant.

FIGURE 6. Plots showing the effects of transseptal pressure gradient ($P_{ts}$) on left ventricular septum–to–free wall diameter ($D_{s-fw}$) (panel A), septal segment length ($L_s$) (panel B), and the correlation between $D_{s-fw}$ and $L_s$ (panel C) at end diastole in a representative dog. $D_{s-fw}$ and $L_s$ are represented as percentages of end-diastolic $D_{s-fw}$ and $L_s$ at $P_{ts}=0$, respectively. Note that both $D_{s-fw}$ and $L_s$ decreased gradually and continuously as a function of decreasing $P_{ts}$. Panel C shows that there was an excellent linear correlation between $D_{s-fw}$ and $L_s$ ($R^2=0.989$, $p<0.001$). Circles indicate the data from aortic constriction; squares indicate those from pulmonary arterial constriction.
TABLE 3. Effect of Volume Loading*

<table>
<thead>
<tr>
<th>Pressure (mm Hg)</th>
<th>Control A</th>
<th>Control B</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pbs (mm Hg)</td>
<td>7.3±0.7</td>
<td>13.9±0.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pir (mm Hg)</td>
<td>5.0±1.5</td>
<td>10.4±1.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pir (mm Hg)</td>
<td>2.3±0.9</td>
<td>3.4±1.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

Control A was the condition at baseline volume state, and Control B was the condition after volume loading. Pbs, left ventricular pressure; Pir, right ventricular pressure; Pir, transseptal pressure gradient.

*Group 2, n=4.

The good correlation between septal midwall segment length and LV anteroposterior diameter suggests that the distension of the LV will also stretch the septum and, therefore, increase the septal preload. The slope of the septal midwall segment length–LV septum–to–free wall diameter relation tended to be steeper than that of the septal midwall segment length–LV anteroposterior diameter relation in every dog (average value, 4.70±4.06 versus 2.55±2.78). This implies that the deformation of the septum was greater than that of the LV free wall during these interventions.

Group 2

PAC was initiated at two different levels of LV pressure, one at baseline volume state and the other after volume loading. The changes in end-diastolic transseptal pressure gradient and LV pressure caused by the PAC and volume loading are shown in Figure 7. During PAC, both end-diastolic transseptal pressure gradient and LV pressure decreased as in the group 1 dogs. However, volume loading increased end-diastolic LV pressure and RV pressure but only slightly increased transseptal pressure gradient (average values are listed in Table 3), moving the control points from A to B (see Figure 7) and shifting the transseptal pressure gradient–LV pressure relation to the right. Therefore, two different levels of LV pressure existed at a single level of transseptal pressure gradient, and the effect of ventricular pressures on the septal radius of curvature can be compared at constant transseptal pressure gradient.

Figure 8 shows that after volume loading, a greater RV pressure (13.4±1.7 versus 8.3±0.7 mm Hg, p<0.01) was needed to make the septum flat because of the increased LV pressure (7.8±1.6 versus 4.1±1.0 mm Hg, p<0.05), although the septum-flattening transseptal pressure gradient was not significantly different (-5.6±3.1 versus -4.2±0.6 mm Hg). Figure 9 shows that, at zero transseptal pressure gradient, normalized septal radius of curvature was greater (2.73±0.25 versus 1.86±0.22, p<0.005) at high than at low LV pressure (11.6±0.9 versus 6.2±1.0 mm Hg, p<0.001). These results confirmed those observed in group 1 animals.

Discussion

The results of the present study demonstrate a close relation between the transseptal pressure gradient and the shape and position of the ventricular septum at end diastole, consistent with our previous results and those of others. The normal shape of the septum (concave toward the LV cavity) depends on the presence of a positive transseptal pressure gradient. The reduction or reversal of such a gradient causes a progressive leftward shift, flattening and eventually inverting the septum; as we previously demonstrated, the leftward septal shift was continuous as a function of transseptal pressure gradient rather than an all-or-none phenomenon.
zero transseptal pressure gradient, the septum retained a curvature concave toward the LV cavity. This zero-transseptal pressure gradient radius of curvature of the septum was dependent on LV pressure and increased with increasing LV pressure. For the septum to be flat (i.e., the radius of curvature was infinite), RV pressure needed to exceed LV pressure. The magnitude of this negative transseptal pressure gradient was relatively constant and was approximately equal to −5 mm Hg in the present study, in which values of LV pressure ranged from 2 to 9 mm Hg.

The present study was performed in open-chest anesthetized dogs with intact circulations while septal shape and position were manipulated by controlled PAC and AC. The responses of the pressures to these constrictions were quite different. As shown in Table 1, during PAC, RV pressure increased, whereas LV pressure decreased, presumably because of the reduced pulmonary venous return. As a result, diastolic transseptal pressure gradient gradually decreased and became negative. During AC, LV pressure increased dramatically, but RV pressure did not change, resulting in a great increase in transseptal pressure gradient both in systole and diastole. In group 2, repeated PAC initiated from two different levels of LV pressure provided two different levels of LV pressure at any level of transseptal pressure gradient in the same animal, because volume loading increased LV pressure at any level of transseptal pressure gradient and shifted the transseptal pressure gradient—LV pressure relation to the right in a parallel fashion (Figure 7). Thus, the method is advantageous in that it allows relatively independent control of transseptal pressure gradient and of LV pressure, thereby allowing observations of their individual effects on the shape and position of the ventricular septum.

The mechanisms by which the septal radius of curvature changed in response to the changes in transseptal pressure gradient were different in PAC and AC. In AC, the increase in the septal radius that occurred with the increase in transseptal pressure gradient was caused mainly by the symmetrical enlargement of the LV cavity, because the radii of both the septum and the LV free wall increased by a similar amount (0.46 cm for the septal radius and 0.41 cm for LV free wall radius) and because normalized septal radius of curvature, the septal radius normalized by the LV cross-sectional area, did not change (1.25±0.07 versus 1.20±0.07; p=NS). During PAC, the septal radius also increased, but in this instance, the increase was associated with a decreasing transseptal pressure gradient. In this case, the decrease in transseptal pressure gradient caused a leftward shift of the septum and, in turn, an increase in radius until the septum became flat. With further decrease in transseptal pressure gradient below −5 mm Hg, the septum shifted farther to the left and inverted, with its curvature becoming negative and convex toward the LV cavity.

In the normal situation, the shape of the ventricular septum at end diastole was concave to the LV cavity and, as previously described,6 “although the left ventricle appeared qualitatively round in short axis image it was not perfectly circular.” The septal radius of curvature is slightly greater than that of LV free wall. Table 4 lists the results from the current study and from other echocardiographic studies.3,7,8,12–15 Note that the results vary, even among the studies from the same laboratory.3,7,14 The results of our dog study are close to those from the human studies.7,8,13,15 Note that the configuration of the septum in the normal human and dog is actually a deformed state, i.e., shifted rightward because of the positive transseptal pressure gradient.

What is the shape of the septum when the transseptal pressure gradient is zero? Consistent with the results of other studies,3,8 the present data showed that the septum became flattened when transseptal pressure gradient decreased to zero, but rather than being truly flat, it still maintained its positive curvature concave toward the LV cavity. In a study of children with congenital heart disease, Agata et al9 used a linear regression of the radius ratio (the ratio of the septal radius to the LV free wall radius) versus the pressure ratio (the ratio of RV pressure to LV pressure) to analyze the correlation between the septal radius of curvature and the transseptal pressure gradient. They found that the regression equation was radius ratio equals 1.75 times pressure ratio plus 0.26 at end diastole. According to this equation, at zero transseptal pressure gradient (i.e., when the pressure ratio is 1), the radius ratio was 2, which means that the septal radius is twice that of the LV free wall, indicating that the septum was not truly flat but rather concave toward the LV cavity. In a study of patients who were undergoing open-heart surgery for coronary heart disease and who had normal global and regional LV function, Lima et al10 showed that, when the heart was arrested, the transseptal pressure gradient estimated by subtracting right atrial pressure from pulmonary capillary wedge pressure was 0.5±0.4 mm Hg and that the radius ratio (2.9±1.0 versus 1.1±0.4 cm, respectively) was 2.6. Expressed in the same way, our results showed that at zero transseptal pressure gradient (0.0±0.4 mm Hg, pooled data from both groups 1 and 2), the radius ratio (3.1±0.9 versus 1.9±0.4 cm) was
1.7±0.4, close to the values cited above. However, this zero transseptal pressure gradient position of the septum was not unique but rather changed with changes in the absolute ventricular intracavitary pressures. As demonstrated in both group 1 and group 2 of the present study (Figures 5 and 9), when transseptal pressure gradient is 0 mm Hg, the septal radius of curvature increased (or the septal curvature decreased) with increases in LV pressure; therefore, it seems likely that the increased ventricular pressures circumferentially and longitudinally stretched the septum from its junctions with the ventricular free walls, even though the forces acting on the septum in the radial direction were relatively constant. This was also supported by the good correlation of septal midwall segment length and LV anteroposterior diameter. Therefore, the zero transseptal pressure gradient state is not the unstressed state for the septum if the ventricular pressures are not zero. The unstressed state or, more accurately, the no-external-load state should be the situation in which both transseptal pressure gradient and ventricular pressures are zero.

That the zero transseptal pressure gradient position of the septum is concave toward the LV cavity implies that RV pressure needs to be higher than LV pressure to push the septum farther to the left, making it flat or inverted. Our results did, indeed, demonstrate that RV pressure had to be higher than LV pressure to make the septum flat (i.e., to eliminate all curvature), and this value of transseptal pressure gradient was relatively constant (about −5 mm Hg) under different conditions, although, as shown in Figures 4 and 7, higher RV pressure was required at higher LV pressure. Three considerations are relevant to the requirement of a significantly negative transseptal pressure gradient to make the septum flat. The first is the observation that the natural shape of the septum is concave toward the LV cavity. (An excised septum suspended in isodensity liquid continues to be concave toward the LV endocardium.) To deform the septum either to the left or to the right requires extra external forces. This is consistent with the observation that RV pressure must exceed LV pressure to push the septum leftward and make it flat. The second consideration is that the septum is a thick, complex structure, and it should not be expected that thin-wall theory should prove to be completely sufficient to describe its behavior, for example, the bending moment that occurs with deformation of a thick-walled structure. The third consideration is that residual stress of the LV myocardium exists, especially the circumferential compressive residual stress in the endocardium. This endocardial compressive residual stress can exert potential forces on the midwall myocardium and epicardium, tending to maintain a more circular LV.

In the present study, excellent correlations existed between the end-diastolic septal segment length and LV dimensions. The reason for the excellent septal midwall segment length−LV septum−to−free wall diameter correlation appears to be that both the septal segment length and LV septum−to−free wall diameter are determined by both the transseptal pressure gradient and LV transmural pressure. The increase in the transseptal pressure gradient displaces the septum rightward, increasing the LV septum−to−free wall diameter as well as the septal segment length. The increase in LV transmural pressure distends the LV free walls, increasing the LV septum−to−free wall diameter, and stretches the septum at its junction with the LV free walls, elongating the septal segment length. The good correlation between septal midwall segment length and LV anteroposterior diameter suggests that septal midwall segment length is also affected by the LV distension. However, such a septal midwall segment length−LV anteroposterior diameter relation might not have existed if the RV pressure overload had been performed while LV volume was kept constant; in that case, the leftward shift of the septum would have increased LV pressure and LV anteroposterior diameter.
portance of these observations is that changes in the preload of the ventricular septum (i.e., the end-diastolic septal segment length) can be estimated clinically by changes in the LV dimensions by use of echocardiography. Thus, we confirm our earlier conclusion\(^2\) — that, in response to changes in transseptal pressure gradient, the septum moves continuously and monotonically — and extend it in that the present data demonstrate that septal displacement assessed in terms of ventricular diameters corresponds exactly and precisely to septal elongation.

Although this close relation between septal segment length and LV diameters was demonstrated under conditions in which one of the ventricles was loaded, it may also be true under conditions in which the ventricle is unloaded, because the parallel changes between septal segment length and LV diameters have been observed during vena caval constriction (i.e., both septal segment length\(^20\) and LV diameters\(^21\) decreased). However, as with the results of any study, extrapolation beyond the experimental conditions we used must be done with caution.

The present study extends the observations of others\(^1\)–\(^3\),\(^8\) by demonstrating the change in the septal radius of curvature in response to the gradual change in transseptal pressure gradient over a large range. In the study of Tanaka et al.,\(^1\) the end-diastolic leftward septal shift and inversion were observed in patients with pulmonary hypertension and in dogs during PAC, but this was a qualitative study in which there was no quantitative measurement of the septal radius. Kingma et al.\(^2\) found a positive linear relation between transseptal pressure gradient and LV septum-to-free wall diameter. However, this diameter not only reflects the change in the septal position but also includes changes in the position of the LV free wall. As transseptal pressure gradient decreased during PAC, this diameter decreases because of the combined effects of the leftward septal shift and a smaller LV cavity resulting from the reduced pulmonary venous return. Agata et al.\(^8\) and Lima et al.\(^3\) did have the quantitative measurements of the septal radius of curvature and related them to the pressures. Agata et al used pooled data, however: one data point from each of 32 children with congenital heart disease, whereas Lima et al recorded intermittently during four different states: control, open pericardium, cardiopulmonary bypass, and cardiac arrest in patients who were undergoing cardiac surgery.

Another advantage of the present study is that the septal position was measured simultaneously with the septal curvature and strain. Thus, we were able to describe how changes in septal position corresponded to changes in the septal curvature and the septal strain.

To date, we have studied only the end-diastolic circumferential radius of curvature of the septum on short-axis, two-dimensional echocardiographic images. The results showed that, at a transseptal pressure gradient of approximately \(-5\) mm Hg, the septum inverts, with its curvature becoming convex to the LV cavity. If the septal inversion does not occur simultaneously in both the long- and the short-axis planes, however, a catenoidal or saddle-shaped septum might result; this configuration has been observed in patients with myocardial infarction\(^22\) and hypertrophic cardiomyopathy.\(^23\)

At end diastole, the shape and position of the septum is determined by the external forces on the septum, because the myocardium is completely relaxed. At end systole, the transseptal pressure gradient is also the main determinant of the septal position.\(^2\),\(^24\),\(^25\) The end-systolic position of the septum shifted leftward with a decrease in the LV septal–to–free wall diameter as the end-systolic transseptal pressure gradient decreased. However, other factors may also play a role. In a study of normal children, King et al.\(^2\) found that, during systole, there was a progressive leftward shift in the septal position, with a resultant septal flattening and a decrease in septal curvature. They postulated that this systolic flattening of the septum resulted from the active effect of muscular contraction, which was independent of the ventricular pressures and tended to pull the septum toward a midline position, because this septal shift occurs in the opposite direction to the increasing transseptal pressure gradient. In two other studies,\(^7\),\(^14\) it was noted that the septum, flattened during diastole in response to the Mueller maneuver, did not increase its curvature during systole, despite the increased transseptal pressure gradient. The possible mechanism suggested\(^3\) was that the systolic increase in stiffness was sufficient to counterbalance the increase in transseptal pressure gradient, which tended to push the septum toward the right ventricle. Further work is obviously needed to define the changes in the long-axis septal radius of curvature in relation to the transseptal pressure gradient and the determinants of the systolic septal shape and position.

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