Postextrasystolic Potentiation and Echocardiography

The Effect of Varying Basic Heart Rate, Extrasystolic Coupling Interval and Postextrasystolic Interval

M. WAYNE COOPER, M.D., LORENZ O. LUTHERER, M.D., PH.D., AND ROBERT M. LUST, PH.D.

SUMMARY The purpose of this study was to determine whether echocardiography can be used to monitor postextrasystolic potentiation (PESP) and, if so, which of the echocardiographic variables are valid indicators of PESP and under what conditions. An implantable M-mode echocardiographic transducer was sewn to the right ventricular outflow tract of the dog heart to record continuously across the minor diameter of the left ventricle. The sinus node pacemaking region was excised and a pacing protocol was used to vary the basic heart rate, the extrasystolic coupling interval and the postextrasystolic interval. The decreases in ejection time and diastolic dimension as well as the increases in the mean rate of circumferential fiber shortening (Vcf) and fractional shortening (%FS) that occur with increasing heart rate were detected by echocardiography. There were also increases in posterior wall maximal velocity and excursion and an increase in the rate of diastolic relaxation. Shortening the coupling interval of the extrasystole resulted in the expected potentiation of Vcf, %FS and the excursion, maximal velocity and rate of diastolic relaxation of the posterior wall. No correlation was observed for percent thickening of the posterior wall or interventricular septum, either because the technique was too insensitive or because wall thickening does not reflect the rapid-phase force-frequency perturbation of PESP. Allowing a full compensatory pause for the postextrasystolic interval resulted in a greater potentiation of all variables than if the postextrasystolic interval was timed to occur when postextrasystolic diastolic pressure and dimension were identical to preextrasystolic diastolic pressure and dimension (isolength). However, only at isolength was potentiation highly predictable, and then only if the heart rate and the coupling interval were known. We conclude that most of the variables measured echocardiographically can be used to determine whether the PESP response is equivalent to a predicted value, provided all intervals are known or carefully controlled.

THE POTENTIATION of contractile state after a single closely coupled extrasystole has been proposed as an index of the progression of regional contraction abnormalities in acutely ischemic cardiac muscle. Cohn et al. proposed echocardiography as a noninvasive method of measuring the effects of externally induced postextrasystolic potentiation (PESP). We sought to determine whether echocardiography could be used to evaluate the PESP response experimentally and, if so, which echocardiographic variables are valid indicators of PESP and under what conditions.

Methods

Dog Preparation

Seven adult mongrel dogs that weighed 20-30 kg were anesthetized with i.v. pentobarbital, 30 mg/kg, and underwent a tracheotomy. Cannulas were placed so their tips were in the aorta, the vena cava and the left ventricular (LV) and right ventricular (RV) chambers. The chest was opened by a thoracotomy at the right fourth intercostal space, and the dog was placed on positive-pressure ventilation for the remainder of the experiment. The heart was supported temporarily in a pericardial cradle. The sinus node pacemaker region was excised by a modification of the technique described by Euler et al. An incision-resuture technique was applied to the entire sinoatrial nodal region to isolate the sinus pacemaker cells from the conduction system. Successful surgery was characterized by abolition of the p wave from the electrocardiographic recording and a junctional rhythm of 85–95 beats/min. Lead II of the ECG was monitored from limb leads with a Beckman R411 Dynagraph recorder. Stimuli were introduced by an electrode attached to the right atrium outside of the excised portion and connected to a Grass SD-9 stimulator coupled with a Grass S-88 stimulator. The pericardium was closed and an implantable echocardiographic transducer was sewn to its surface. The dogs were then placed in the prone position, and the respiration was adjusted to maintain arterial oxygen tension at 82.5 ± 2.4 mm Hg, arterial carbon dioxide tension at 41.6 ± 2.2 mm Hg and pH at 7.38 ± 0.08. Blood gases were measured on a radiometer blood gas analyzer (Copenhagen model PHM72MK2).

Pacing Protocol

The stimulators were set up to program the basic drive cycle (S, S), the extrasystolic coupling interval (S, S) and the postextrasystolic interval (S, S). The basic heart rate was increased in increments of 10 beats/min from 110 to 150 beats/min; at least 5 minutes were allowed for equilibration after each increase. Thus, S, S ranged from 550 to 400 msec. S, S was increased in 50-msec increments from 200 to 350 msec. S, S corresponding to each set of S, S intervals and each set of S, S intervals was programmed to occur at two different S, S intervals. The first S, S was computed from an empirical formula to occur when the LV end-diastolic dimension and pressure were identical to the dimension and pressure in the basic beats. This S, S interval, or “isotension,” permitted assessment of the effect of different S, S intervals without

From the Departments of Internal Medicine and Physiology, Texas Tech University Health Sciences Center, Lubbock, Texas. Address for correspondence: M. Wayne Cooper, M.D., Division of Cardiology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas 79430.

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changes in initial muscle length (preload). The actual equivalence of the dimension was confirmed by echocardiography. The second S,S interval, or "complete pause," was a full compensatory pause (i.e., S was timed to occur when S,S,S was twice S,S). We chose this interval because a full compensatory pause occurs when PESP is used clinically. The compensatory pause S,S varied from 475 to 683 msec (mean 541 ± 4.2 msec), and the isovelocity S,S varied from 320 to 340 msec (mean 331 ± 0.5 msec).

Echocardiography

Echocardiograms were obtained as follows: An implantable 5-mm, 5.0 MHz echocardiographic transducer (K.B. Aerotech) was sutured to the pericardium so that the echo beam passed through the RV wall, the RV cavity, the interventricular septum and the LV posterior wall just below the tips of the mitral valve leaflets. This scan plane closely approximates the LV minor-axis diameter. The endocardial surfaces of the interventricular septum and posterior wall were delineated by rapid injection of saline into the RV and LV cavities during echocardiographic recording. The following measurements were made from the echocardiograms, using standard methods.8

Ejection time (ET) was measured from the posterior wall echocardiogram, counting from end-diastole to the point of maximal anterior endocardial motion and subtracting 50 msec to compensate for isovolumic systole. The LV end-diastolic dimension (EDD) was measured at the onset of the QRS complex. The LV endsystolic dimension was measured at the nadir of systolic motion, (i.e., when the ventricular septum was farthest from the anterior chest wall) or, if the septum moved paradoxically, at the point of peak anterior motion of the posterior wall. From these measurements, fractional shortening (%FS) was calculated as

\[
\frac{\text{EDD} - \text{ESD}}{\text{EDD}} \times 100.
\]

Vcf was calculated as

\[
\frac{\text{EDD} - \text{ESD}}{\text{EDD} \times \text{ET}}
\]

The diastolic thickness of interventricular septum (D th IVS), the diastolic thickness of posterior wall (D th PW), the systolic thickness of interventricular system (S th IVS) and the systolic thickness of posterior wall (S th PW) were measured and used to calculate

\[
\% \ \text{th IVS} = \frac{\text{S th} - \text{D th}}{\text{D th}} \times 100
\]

\[
\% \ \text{th PW} = \frac{\text{S th} - \text{D th}}{\text{D th}} \times 100
\]

The thicknesses of the interventricular septum and the posterior wall were measured in the same portion of the record used to measure the LV internal dimensions. The maximal velocity of the posterior wall was taken from a tangent drawn to the steepest portion of the posterior wall endocardium in systole. The excursion of posterior wall (Ex) was the maximal distance moved from end-diastole to end-systole. The mean velocity of the posterior wall was calculated as Ex/ET. The maximal diastolic velocity of the posterior wall was taken by drawing a tangent to the steepest portion of the posterior endocardial motion in diastole.

Data Analysis

The average of three measurements of each variable was taken for each interval combination for every dog. The mean of these averages was then obtained to provide a single value for each variable at each interval combination for the group. Mean values were compared by t test. Ratios of potentiation for the group at each interval combination were obtained in similar fashion using the postextrasystolic value/preextrasystolic value to determine the desired ratio. The relationship between changes in any variable and changes in any of the intervals was investigated by regression analysis. Regression coefficients for the relationship were derived and converted to t values on standard statistical formulas. The significance of r values was determined from the t value. The r values were compared by converting them to z values and examining the relationship with the standard test for homogeneity of regression coefficients. Differences were considered significant at the p < 0.05 level.

Results

Accuracy and Reproducibility of Echocardiographic Measurements

We compared the thickness of the interventricular septum and posterior wall measured from the echocardiogram with direct measurements of the same segments of ventricular wall at the time of sacrifice. Before use, the echocardiograph was calibrated with a standard 100-mm test object (American Institute of Ultrasound in Medicine). After the echo transducer was sutured to the epicardial surface of the right ventricular outflow tract, the near-gain, time-gain compensation ramp and depth compensation were adjusted to delineate the endocardial surfaces, which were further defined by rapid injection of saline into the RV and LV cavities during echocardiographic recording. Calibration dots were printed out on the echo paper and the machine knobs were taped in position so the settings could not change during the experiment. One-centimeter calibration dots were divided into 0.1-cm divisions using the leading edge of each printed centimeter dot as a reference point.

After the experiment, the echocardiographic transducer was lifted from the epicardial surface, and while the heart was still beating, a 21-gauge needle was plunged through the heart in the direction of the echo beam. The dog was then killed and the heart removed rapidly. The heart was dissected away from around the needle track, and the thicknesses of the interventricular
TABLE 1. Effect of Varying \( S_1 S_2 \)

<table>
<thead>
<tr>
<th>( S_1 S_2 ) (msec)</th>
<th>HR (beats/min)</th>
<th>%Th PW</th>
<th>%Th IVS</th>
<th>EDD (cm)</th>
<th>PW Ex (cm)</th>
<th>PW max vel (cm/sec)</th>
<th>PW mean vel (cm/sec)</th>
<th>ET (msec)</th>
<th>%FS</th>
<th>Vcf (circ/sec)</th>
<th>D vel PW (cm/sec)</th>
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</thead>
<tbody>
<tr>
<td>550</td>
<td>110</td>
<td>27.20</td>
<td>13.10</td>
<td>3.89</td>
<td>0.96</td>
<td>7.03</td>
<td>5.92</td>
<td>162.00</td>
<td>27.50</td>
<td>1.72</td>
<td>8.20</td>
</tr>
<tr>
<td>( \pm 2.17 )</td>
<td>( \pm 1.07 )</td>
<td>( \pm 0.04 )</td>
<td>( \pm 0.03 )</td>
<td>( \pm 0.14 )</td>
<td>( \pm 0.25 )</td>
<td>( \pm 2.89 )</td>
<td>( \pm 0.90 )</td>
<td>( \pm 0.08 )</td>
<td>( \pm 0.28 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>500</td>
<td>120</td>
<td>24.10</td>
<td>16.80</td>
<td>3.54</td>
<td>0.87</td>
<td>7.08</td>
<td>5.54</td>
<td>157.00</td>
<td>26.80</td>
<td>1.71</td>
<td>7.70</td>
</tr>
<tr>
<td>( \pm 2.21 )</td>
<td>( \pm 1.01 )</td>
<td>( \pm 0.04 )</td>
<td>( \pm 0.02 )</td>
<td>( \pm 0.14 )</td>
<td>( \pm 0.16 )</td>
<td>( \pm 2.22 )</td>
<td>( \pm 0.84 )</td>
<td>( \pm 0.02 )</td>
<td>( \pm 0.48 )</td>
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<tr>
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<td>16.10</td>
<td>18.00</td>
<td>3.34</td>
<td>1.04</td>
<td>9.51</td>
<td>6.69</td>
<td>155.50</td>
<td>30.60</td>
<td>1.98</td>
<td>11.80</td>
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<td>( \pm 1.91 )</td>
<td>( \pm 1.51 )</td>
<td>( \pm 0.05 )</td>
<td>( \pm 0.05 )</td>
<td>( \pm 0.77 )</td>
<td>( \pm 0.54 )</td>
<td>( \pm 1.90 )</td>
<td>( \pm 1.47 )</td>
<td>( \pm 0.09 )</td>
<td>( \pm 0.78 )</td>
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<td></td>
</tr>
<tr>
<td>400</td>
<td>140</td>
<td>15.90</td>
<td>17.80</td>
<td>3.36</td>
<td>1.17</td>
<td>12.20</td>
<td>8.36</td>
<td>139.60</td>
<td>36.00</td>
<td>2.65</td>
<td>14.50</td>
</tr>
<tr>
<td>( \pm 3.18 )</td>
<td>( \pm 3.53 )</td>
<td>( \pm 0.02 )</td>
<td>( \pm 0.02 )</td>
<td>( \pm 0.51 )</td>
<td>( \pm 0.20 )</td>
<td>( \pm 2.58 )</td>
<td>( \pm 0.76 )</td>
<td>( \pm 0.08 )</td>
<td>( \pm 0.73 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( r )</td>
<td>0.55</td>
<td>0.01</td>
<td>0.94*</td>
<td>0.80*</td>
<td>0.88*</td>
<td>0.83*</td>
<td>0.89*</td>
<td>0.84*</td>
<td>0.85*</td>
<td>0.92*</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SEM for control beats only.

* \( p < 0.001 \).

Abbreviations: \%Th PW = percent change in thickness in systole of posterior wall; \%Th IVS = percent change in thickness in systole of interventricular septum; EDD = diastolic dimension of the left ventricle; PW Ex = posterior wall excursion; PW max vel = maximal systolic posterior wall velocity; PW mean vel = mean posterior wall systolic velocity; ET = ejection time; \%FS = fractional shortening; Vcf = mean rate of circumferential fiber shortening; D vel PW = diastolic velocity of the posterior wall.

septum and the posterior wall immediately adjacent to the needle were measured to the nearest 0.01 cm by micrometer (Mitutoyo Mfg. Co.). The echocardiographic wall thickness measurements were taken from the leading edge of the mark for each endocardial wall and recorded independently by a second investigator who had no knowledge of the direct measurements of thickness at autopsy. The echocardiographic measurements were recorded to the nearest 0.1 cm, and the results of all measurements of a particular wall were averaged to the nearest 0.01 cm and compared with the autopsy results. The mean ± SEM of echocardiographic and direct measurements were 1.44 ± 0.07 vs 1.43 ± 0.07 cm for the interventricular septum and 1.19 ± 0.03 vs 1.17 ± 0.03 cm for the posterior wall, respectively.

The echocardiographic measurements were generally reproducible. Table 1 lists the mean ± SEM for all measurements at the different heart rates (S1S2). The standard error was low for all measurements; the wall thickness calculations were the most variable.

Varying S1S2

As heart rate was increased, the echocardiograms demonstrated progressive decreases in ejection time and diastolic dimension and increases in Vcf and fractional shortening (fig. 1, table 1). Evaluation of segmental variables showed that as heart rate increased, the posterior wall velocity and excursion and the rate of diastolic relaxation of the posterior wall also increased. The degree of systolic thickening did not change with increasing heart rate (table 1).

Varying S1S2

Table 2 shows the results of varying the coupling interval of the extrasystole (S1S2) on the degree of potentiation (expressed as the ratio of the postextrasystolic and the preextrasystolic value) at a heart rate of 140 beats/min (S1S2 = 430 msec) measured after an isoleth length pause. The echocardiogram reflected an inverse relationship between coupling interval and degree of potentiation in both global and segmental measurements, including Vcf, fractional shortening, excursion and maximal and mean velocity of the posterior wall, as well as diastolic velocity of the posterior wall. The coupling interval (S1S2) did not correlate with potentiation of interventricular septal and posterior wall thickening.

Table 3 shows the results of varying the coupling interval of the extrasystole (S1S2) on the degree of potentiation, again at a heart rate of 140 beats/min, but measured after a complete compensatory pause (S1S2). The coupling interval correlated significantly with all echocardiographic variables except posterior wall per-

TABLE 2. Effect of Varying \( S_1 S_2 \) on Ratio Potentiation (Postextrasystolic/Preextrasystolic) Measured at Isoleth \( S_1 S_2 \)

<table>
<thead>
<tr>
<th>( S_1 S_2 ) (msec)</th>
<th>%Th PW</th>
<th>%Th IVS</th>
<th>PW Ex</th>
<th>PW max vel</th>
<th>PW mean vel</th>
<th>%FS</th>
<th>Vcf</th>
<th>D vel PW</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td>1.80</td>
<td>0.88</td>
<td>2.71</td>
<td>2.24</td>
<td>2.44</td>
<td>1.67</td>
<td>1.51</td>
<td>1.85</td>
</tr>
<tr>
<td>250</td>
<td>1.52</td>
<td>1.34</td>
<td>1.58</td>
<td>1.62</td>
<td>1.50</td>
<td>1.33</td>
<td>1.26</td>
<td>1.35</td>
</tr>
<tr>
<td>300</td>
<td>1.20</td>
<td>1.96</td>
<td>1.37</td>
<td>1.26</td>
<td>1.33</td>
<td>1.11</td>
<td>1.08</td>
<td>1.26</td>
</tr>
<tr>
<td>350</td>
<td>2.35</td>
<td>0.94</td>
<td>1.17</td>
<td>1.34</td>
<td>1.25</td>
<td>1.07</td>
<td>1.11</td>
<td>1.26</td>
</tr>
<tr>
<td>( r )</td>
<td>0.35</td>
<td>0.21</td>
<td>-0.91*</td>
<td>-0.89*</td>
<td>-0.88*</td>
<td>-0.95*</td>
<td>-0.91*</td>
<td>-0.85*</td>
</tr>
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</table>

All values are for a heart rate of 140 beats/min using the isoleth length pause and are expressed as the ratio of the postextrasystolic value and the control value. \( S_1 S_2 = 430 \) msec.

* \( p < 0.001 \).

Abbreviations: See table 1.
compensatory pause (3.22 ± 0.04 cm, p < 0.001). At any heart rate and coupling interval, increasing S,S3 to a full compensatory pause resulted in greater potentiation of all echocardiographic variables. Table 4 shows the effect of varying heart rate and postextrasystolic interval on the ratio of potentiation of Vcf at an S,S3 of 300 msec. The ratio of potentiation correlated significantly (p < 0.001) with both the isoolength and complete S,S3 (r = 0.95 and 0.77, respectively). Further tests revealed that although both correlations were significant, they were also significantly different from each other (p < 0.0001). Additional analyses were therefore performed to compare the effects of isoolength S,S3 with those of complete S,S3, on the ratio of potentiation. Table 5 lists the mean ± SEM for the ratio of potentiation for dP/dt max at each coupling interval (S,S3) and heart rate (S,S3) for the isoolength and complete S,S3. Heart rate and coupling interval correlated with this ratio (r > 0.85, p < 0.001 in all cases), but only when the isoolength S,S3 was used. No significant correlations could be determined for this ratio at complete S,S3. Figure 2 compares the degree of potentiation at each coupling interval (S,S3) at isoolength S,S3 and full pause S,S3. As S,S3 was lengthened, the degree of potentiation of the postextrasystolic beat was decreased in both isoolength and full compensatory pause. Allowing a full compensatory pause always resulted in greater potentiation, although a statistical difference between the means at any S,S3 could not be demonstrated for Vcf. When this relationship was examined based on dP/dt max (table 5), a statistical difference between isoolength and complete S,S3 was observed for all means except an S,S3 of 250 msec at an S,S3 of 120 msec. The data in tables 4 and 5 indicate that potentiation at isoolength S,S3 was at least 60% of the potentiation at complete S,S3, and that the percentage increase in potentiation from isoolength to compensatory pause increased as S,S3 was lengthened. In every experiment, more than 60% and up to 85% of postextrasystolic potentiation at complete S,S3 can be accounted for apart from any demonstrable loading-dependent changes.

Discussion

The rapid-phase force-frequency response known as PESP has been proposed as a method of detecting contractile reserve in ischemic myocardial segments.1,2 The increased wall motion after an externally induced extrasystole can be detected by echocardiography,3 and single-plane echocardiography accurately reflects global left ventricular volume and function in the normal left ventricle.4 Two-dimensional echocardiography, by providing a multiplane view of all segments of the myocardium, may be useful for detecting segmental wall motion abnormalities in coronary heart disease.9,10 Therefore, if the echocardiogram can accurately and reproducibly show subtle beat-to-beat changes in segmental wall function in response to induced postextrasystolic potentiation, it could be a valuable technique for detecting potentially salvagable myocardium.

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** (A) Representative echocardiograms taken at heart rates (HR) of 110 and 140 beats/min. IVS = interventricular septum; PW = posterior wall; EDD = end-diastolic dimension; ESD = end-systolic dimension. (B) Representative echocardiogram with induced extrasystole. Postextrasystole was induced after a complete pause.

Varying S2S3

To analyze the effect of varying S2S3, the ratio of potentiation of each echocardiographic variable at isoolength S2S3 was compared with the same variable at a full compensatory pause. The isoolength interval was correctly programmed, as the end-diastolic dimension of the postextrasystolic beat was not different from that of the control (2.96 ± 0.04 vs 3.01 ± 0.04 cm). In contrast, there was a significant increase at the full
TABLE 3. Effect of Varying \( S_1/S_2 \) on Ratio Potentiation (Postextrasystolic/Preextrasystolic) Measured at Complete Compensatory Pause \( S_1/S_3 \)

<table>
<thead>
<tr>
<th>( S_1/S_2 ) (msec)</th>
<th>%PW</th>
<th>%Th IVS</th>
<th>PW Ex</th>
<th>PW max vel</th>
<th>PW mean vel</th>
<th>%FS</th>
<th>Vcf</th>
<th>D vel PW</th>
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<td>200</td>
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<td>2.88</td>
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<td>350</td>
<td>2.40</td>
<td>3.22</td>
<td>1.65</td>
<td>0.87</td>
<td>1.70</td>
<td>1.38</td>
<td>1.24</td>
<td>1.43</td>
</tr>
</tbody>
</table>

\[ r = 0.05 + 0.99^* - 0.85^* - 0.18 - 0.84^* - 0.91^* - 0.92^* - 0.65^* \]

All values are for a heart rate of 140 beats/min using the complete compensatory pause and are expressed as the ratio of the postextrasystolic value and the control value. \( S_1/S_1 = 430 \) msec.

*\( p < 0.001 \).
Abbreviations: See table 1.

TABLE 4. Effect of Varying Heart Rate and Postextrasystolic Interval on the Potentiation Ratio (Postextrasystolic/Preextrasystolic) of the Mean Rate of Circumferential Fiber Shortening at an \( S_1/S_2 \) of 300 Msec

<table>
<thead>
<tr>
<th>Heart rate (beats/min)</th>
<th>Isolength ( S_1/S_2 )</th>
<th>Complete ( S_1/S_3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>110</td>
<td>1.47*</td>
<td>1.93</td>
</tr>
<tr>
<td>120</td>
<td>1.39</td>
<td>1.54</td>
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<tr>
<td>130</td>
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<td>140</td>
<td>1.04</td>
<td>1.48</td>
</tr>
<tr>
<td>150</td>
<td>0.98</td>
<td>1.40</td>
</tr>
</tbody>
</table>

\[ r^+ = -0.95 < 0.001 \]

*Mean ratio (\( n = 28-30 \) for all values).
\(^+\)Correlation coefficient between ratio of potentiation and heart rate.

In our experimental model, the echocardiogram detected changes in LV dimensions and wall motion in response to increasing heart rate (decreasing \( S_1/S_2 \)), increasing coupling intervals for an extrasystole (increasing \( S_1/S_3 \)), and varying \( S_1/S_3 \). As expected, increasing heart rate resulted in a decrease in end-diastolic dimension and increase in ejection phase indexes, posterior excursion, velocity and diastolic velocity of the posterior wall.\(^{11-13}\) We could not detect an increase in systolic thickening with increasing heart rate.

A fundamental property of the PESP response is the inverse relationship between the extrasystolic coupling interval and the degree of potentiation.\(^4\) Numerous studies in several experimental models have affirmed that the shorter the coupling interval the greater the PESP response. We detected such a relationship between coupling interval and Vcf, fractional shortening, and systolic excursion and velocity and diastolic velocity of the posterior wall. Again, we could not detect such an association between extrasystolic coupling interval and systolic thickening of the interventricular septum and posterior wall.

We also found that the degree of PESP is determined by the length of the postextrasystolic interval and that the correlation between extrasystolic coupling interval and potentiation is more significant if the postextrasystolic beat is timed to occur at isolength (i.e., when postextrasystolic diastolic dimension and pressure are the same as preextrasystolic dimension and pressure). The echocardiographic measurement of end-diastolic dimensions confirmed that the postextrasystolic beat was delivered at isolength. In a previous study confirmation had also been made on the basis of end-diastolic pressures. These results are in agreement with other

TABLE 5. The Effect of Varying \( S_1/S_1, S_1/S_2 \) and \( S_1/S_3 \) on the Potentiation of \( dP/dt \) max

| Isolength \( S_1/S_1, S_1/S_2 \) and \( S_1/S_3 \) on the Potentiation of \( dP/dt \) max |
|------------------------------------------|------------------------|------------------------|------------------------|------------------------|
| \( S_1/S_2 \) (msec) | 250 | 300 | 350 | \( r^* \) | 250 | 300 | 350 | \( r^* \) |
| Heart rate (beats/min) |      |      |      |      |      |      |      |      |
| 110                    | 2.13 | 1.79 | 1.51 | -0.893\( \ddagger \) | 2.00 | 1.91 | 1.65 | -0.233 |
| \( \pm 0.06 \) | \( \pm 0.05 \) | \( \pm 0.01 \) |      | \( \pm 0.06 \) | \( \pm 0.03 \) | \( \pm 0.05 \) |      |
| 120                    | 2.05 | 1.67 | 1.41 | -0.900\( \ddagger \) | 2.12 | 1.89 | 1.73 | -0.187 |
| \( \pm 0.01 \) | \( \pm 0.06 \) | \( \pm 0.03 \) |      | \( \pm 0.07 \) | \( \pm 0.05 \) | \( \pm 0.05 \) |      |
| 130                    | 1.74 | 1.44 | 0.99 | -0.911\( \ddagger \) | 1.83 | 1.65 | 1.46 | -0.319 |
| \( \pm 0.03 \) | \( \pm 0.03 \) | \( \pm 0.03 \) |      | \( \pm 0.05 \) | \( \pm 0.05 \) | \( \pm 0.04 \) |      |
| 140                    | 1.58 | 1.14 | 0.89 | -0.858\( \ddagger \) | 1.75 | 1.58 | 1.35 | -0.273 |
| \( \pm 0.03 \) | \( \pm 0.02 \) | \( \pm 0.04 \) |      | \( \pm 0.07 \) | \( \pm 0.07 \) | \( \pm 0.05 \) |      |
| 150                    | 1.51 | 1.10 | 0.74 | -0.925\( \ddagger \) | 1.96 | 1.72 | 1.34 | -0.162 |
| \( \pm 0.02 \) | \( \pm 0.01 \) | \( \pm 0.03 \) |      | \( \pm 0.05 \) | \( \pm 0.05 \) | \( \pm 0.07 \) |      |

\( r^+ = -0.975\( \ddagger \) - 0.979\( \ddagger \) - 0.972\( \ddagger \) - 0.201 - 0.239 - 0.377\)

\(^*\)Correlation coefficient between ratio potentiation and extrasystolic coupling interval (\( S_1/S_2 \)).
\(^\ddagger\)Correlation coefficient between ratio potentiation and heart rate.
\( \ddagger \)Correlation coefficient between ratio potentiation and heart rate.
\( p < 0.001 \), all other values not significant.
reports on the PESP response. These results suggest that to use the PESP response to detect contractile reserve, all intervals, including heart rate, extrasystolic coupling and postextrasystolic interval, must be known or controlled. This is in agreement with what we showed with hemodynamic measurements using a high-fidelity micromanometer in the left ventricle.

Most of our measured echocardiographic variables of LV function reflected the changes detected hemodynamically. LV dp/dt max is an accurate measure of the rapid-phase force-frequency response of PESP if the postextrasystolic beat is programmed to occur when preextrasystolic and postextrasystolic dimensions are identical. We found similar results in the echocardiogram. Our failure to demonstrate a significant correlation between extrasystolic coupling interval and postextrasystolic thickening is an interesting finding. We consistently found that systolic thickening was potentiated after an extrasystole, but the degree of potentiation did not appear to reflect the degree of prematurity of the extrasystole, a fundamental property of the PESP response. Perhaps our methods were too insensitive to detect the subtle beat-to-beat changes in thickening. We made a special effort to detect the anterior and posterior borders of the interventricular septum by rapid saline injections. However, specular reflectors exist within the RV cavity and within the interventricular septum and may lead to a false appearance of border-forming echoes. It is also possible that systolic thickening represents a distinct inotropy not responsive to rapid-phase frequency perturbations.

The implications of this study are that the echocardiogram can demonstrate changes in wall motion associated with frequency perturbations and accurately detect the PESP response. To detect the subtle rapid-phase force-frequency effects of an extrasystole predictably and reproducibly, one must know or control all intervals, including heart rate, extrasystolic coupling interval and postextrasystolic interval. This requirement makes noninvasive reproduction of the PESP response difficult, but not impossible. If several studies at multiple heart rates and extrasystolic intervals were performed, it might be possible to derive correlations similar to those produced for systolic time intervals and to compare individual responses with these norms.

Or results suggest that echocardiography is valuable for detecting changes in LV function associated with the force-frequency response.

References

Postextrasystolic potentiation and echocardiography: the effect of varying basic heart rate, extrasystolic coupling interval and postextrasystolic interval.
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