Relationships between beat-to-beat interval and the strength of contraction in the healthy and diseased human heart


ABSTRACT Twenty-six adult patients, classified by clinical and catheter criteria into groups of those with normal and abnormal left ventricular function, were studied during cardiac catheterization. Right heart pacing was established, and left ventricular dP/dt was measured with end-catheter manometers. By varying the interval preceding a test beat after periods of steady pacing it was confirmed that recovery of left ventricular mechanical function (maximum dP/dt) occurs approximately 800 msec (optimum interval) after a beat. The augmentation of maximum dP/dt of the first 2 beats after an extrasystole, each spaced at the optimum interval, was also studied; the amount of potentiation was varied by alterations in extrasystolic interval. Potentiation decayed from the first to the second postextrasystolic beat with a ratio that was fixed in each individual patient. The ratio (recirculation fraction) was higher in patients with normal than in those with abnormal left ventricular function (mean ± SD 0.52 ± 0.10 vs 0.37 ± 0.11, p < .005). There was an inverse relationship between this ratio and the degree of potentiation of the first postextrasystolic beat (r = .80, p < .001). We postulate a disturbance of excitation-contraction coupling mechanisms to explain these effects.


Our first objective in this study was to measure the recirculation fraction in man. Since a disturbance of excitation-contraction coupling, and thus of intracellular calcium handling, might underlie malfunction of cardiac muscle, our second objective was to compare this recirculation fraction in patients with normal and abnormal myocardial function.

Methods

Patients. Twenty-six subjects were studied during the course of diagnostic cardiac catheterization. The indications for catheterization included breathlessness, chest pain, and arrhythmias. Informed consent was obtained from the subjects before the study, which had been approved by the ethical committees of the respective institutions. Patients were studied while supine and after an overnight fast.

The patients were divided into three groups on the basis of the information presented in table 1 and figure 1. The first group (A, nine patients) were classified as having “normal” hearts based on the following criteria: pulmonary arterial chest x-ray cardiothoracic ratio less than 0.5, left ventricular end-diastolic pressure less than 12 mm Hg,4 maximum rate of rise in left ventricular pressure greater than 1000 mm Hg/sec,2 and a cineangiographic ejection fraction between 0.56 and 0.78,4 or, in the absence of cineangiographic studies, normal ventricular function on an M mode echocardiogram. A final criterion was the absence of significant (>60%) coronary arterial narrowing.

In the second group (B) 11 of 12 patients were classified as having abnormal left ventricular function on the basis of abnor-
### TABLE 1
Clinical characteristics of patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>ECG</th>
<th>CT ratio (cm)</th>
<th>BP (mm Hg)</th>
<th>Treatment</th>
<th>Echo</th>
<th>LV cine angiography</th>
<th>EF (%)</th>
<th>Coronary angiography</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>J. N.</td>
<td>55</td>
<td>M</td>
<td>Normal</td>
<td>14/33</td>
<td>120/70</td>
<td>$\beta B$</td>
<td>Not done</td>
<td>Normal</td>
<td>73</td>
<td>Normal</td>
<td>NAD</td>
</tr>
<tr>
<td>R. P.</td>
<td>53</td>
<td>M</td>
<td>Normal</td>
<td>15/31</td>
<td>150/85</td>
<td>$\beta B$</td>
<td>Not done</td>
<td>Normal</td>
<td>76</td>
<td>Normal</td>
<td>NAD</td>
</tr>
<tr>
<td>D. C.</td>
<td>49</td>
<td>M</td>
<td>$\Delta T$ N/S</td>
<td>120/60</td>
<td>None</td>
<td>Not done</td>
<td>Normal</td>
<td>63</td>
<td>Normal</td>
<td>NAD</td>
<td></td>
</tr>
<tr>
<td>L. F.</td>
<td>40</td>
<td>F</td>
<td>Normal</td>
<td>11/30</td>
<td>110/70</td>
<td>$\beta B + D + T4$</td>
<td>Not done</td>
<td>Normal (not digitized)</td>
<td>Normal</td>
<td>NAD</td>
<td></td>
</tr>
<tr>
<td>L. E.</td>
<td>51</td>
<td>M</td>
<td>Normal</td>
<td>12/30</td>
<td>130/80</td>
<td>None</td>
<td>Not done</td>
<td>Normal</td>
<td>67</td>
<td>Normal</td>
<td>NAD</td>
</tr>
<tr>
<td>L. S.</td>
<td>36</td>
<td>M</td>
<td>Normal</td>
<td>12/30</td>
<td>130/80</td>
<td>None</td>
<td>Normal</td>
<td>Normal</td>
<td>76</td>
<td>Normal</td>
<td>NAD</td>
</tr>
<tr>
<td>J. F.</td>
<td>41</td>
<td>F</td>
<td>Normal</td>
<td>14/33</td>
<td>135/90</td>
<td>$\beta B$</td>
<td>Normal</td>
<td>72</td>
<td>Normal</td>
<td>NAD</td>
<td></td>
</tr>
<tr>
<td>W. M.</td>
<td>54</td>
<td>M</td>
<td>Partial RBBB</td>
<td>14/31</td>
<td>100/65</td>
<td>$\beta B$</td>
<td>Not done</td>
<td>Mild apical dyskinesia</td>
<td>67</td>
<td>Normal</td>
<td>NAD</td>
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<td>K. B.</td>
<td>40</td>
<td>F</td>
<td>—</td>
<td>Normal</td>
<td>145/90</td>
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<td>Not done</td>
<td>Normal</td>
<td>64</td>
<td>Normal</td>
<td>NAD</td>
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<tr>
<td>Mean</td>
<td>47</td>
<td></td>
<td></td>
<td>13/31</td>
<td>127/77</td>
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<td>70</td>
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<td>SD</td>
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<td></td>
<td>1.5/1.3</td>
<td>16.0/10.9</td>
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#### Group B

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<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>ECG</th>
<th>CT ratio (cm)</th>
<th>BP (mm Hg)</th>
<th>Treatment</th>
<th>Echo</th>
<th>LV cine angiography</th>
<th>EF (%)</th>
<th>Coronary angiography</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. K.</td>
<td>59</td>
<td>F</td>
<td>Nodal bradycardia</td>
<td>22/32</td>
<td>105/65</td>
<td>D</td>
<td>Dilated LV</td>
<td>Not done</td>
<td>—</td>
<td>Not done</td>
<td>COCM</td>
</tr>
<tr>
<td>H. C.</td>
<td>52</td>
<td>M</td>
<td>LVH</td>
<td>18/31</td>
<td>130/80</td>
<td>CG</td>
<td>Dilated LV</td>
<td>Dilated LV; global hypok.</td>
<td>32</td>
<td>Not done</td>
<td>COCM</td>
</tr>
<tr>
<td>J. F.</td>
<td>65</td>
<td>M</td>
<td>$\Delta T$ N/S</td>
<td>15/31</td>
<td>125/70</td>
<td>D</td>
<td>Generalised dyskinesia</td>
<td>Dilated LV; global hypok.</td>
<td>27</td>
<td>CAD × 3</td>
<td>COCM + CAD</td>
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<tr>
<td>W. R.</td>
<td>44</td>
<td>M</td>
<td>LAD</td>
<td>15/31</td>
<td>110/90</td>
<td>CG</td>
<td>Dilated LV</td>
<td>Not done</td>
<td>—</td>
<td>Not done</td>
<td>COCM</td>
</tr>
<tr>
<td>E. S.</td>
<td>60</td>
<td>M</td>
<td>$1^{st}$HB $\Delta S$</td>
<td>17/32</td>
<td>140/80</td>
<td>N + CG</td>
<td>Dilated LV</td>
<td>Not done</td>
<td>—</td>
<td>Not done</td>
<td>COCM + CAD</td>
</tr>
<tr>
<td>D. I.</td>
<td>38</td>
<td>M</td>
<td>$1^{st}$HB</td>
<td>17/32</td>
<td>125/85</td>
<td>N</td>
<td>Septal hypertrophy</td>
<td>No cavity obliteration</td>
<td>80</td>
<td>Not done</td>
<td>HCM</td>
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<tr>
<td>L. K.</td>
<td>40</td>
<td>M</td>
<td>Old inf. MI</td>
<td>17/34</td>
<td>120/60</td>
<td>$\beta B$</td>
<td>Not done</td>
<td>Dilated LV; mild hypok.</td>
<td>53</td>
<td>CAD × 3</td>
<td>CAD</td>
</tr>
<tr>
<td>D. H.</td>
<td>51</td>
<td>M</td>
<td>Old inf. MI</td>
<td>15/32</td>
<td>100/60</td>
<td>$\beta B + N$</td>
<td>Not done</td>
<td>Inf. akinesia; ant. hypok.</td>
<td>41</td>
<td>CAD × 3</td>
<td>CAD</td>
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<tr>
<td>S. M.</td>
<td>65</td>
<td>M</td>
<td>$QV_{1-3}$ $\Delta T$ inf.</td>
<td>16/35</td>
<td>190/100</td>
<td>None</td>
<td>Dilated LV; EF reduced</td>
<td>Dilated LV; EF reduced</td>
<td>51</td>
<td>CAD × 3 + CAD</td>
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<tr>
<td>A. J.</td>
<td>67</td>
<td>M</td>
<td>$\Delta T$ ant.</td>
<td>17/31</td>
<td>110/60</td>
<td>$D + \beta B + V$</td>
<td>Not done</td>
<td>Dilated LV; global hypok.</td>
<td>26</td>
<td>CAD × 2</td>
<td>COCM</td>
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<tr>
<td>J. S.</td>
<td>62</td>
<td>M</td>
<td>LBBB</td>
<td>17/31</td>
<td>90/55</td>
<td>None</td>
<td>Dilated LV; EF reduced</td>
<td>Dilated LV; global hypok.</td>
<td>25</td>
<td>Normal</td>
<td>COCM</td>
</tr>
<tr>
<td>B. M.</td>
<td>57</td>
<td>M</td>
<td>$\Delta T$-T; N/S</td>
<td>20/30</td>
<td>130/75</td>
<td>$D + \beta B$</td>
<td>Not done</td>
<td>Relaxation abnormality</td>
<td>60</td>
<td>Normal</td>
<td>COCM (re-mission)</td>
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<td>Mean</td>
<td>55</td>
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<td></td>
<td>17.2/32.1</td>
<td>123/73</td>
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<td>SD</td>
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<td>2.1/1.3</td>
<td>25.7/14</td>
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</table>

#### Group C

<table>
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<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>ECG</th>
<th>CT ratio (cm)</th>
<th>BP (mm Hg)</th>
<th>Treatment</th>
<th>Echo</th>
<th>LV cine angiography</th>
<th>EF (%)</th>
<th>Coronary angiography</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>R. K.</td>
<td>57</td>
<td>M</td>
<td>$\Delta T$ N/S</td>
<td>13/30</td>
<td>135/70</td>
<td>None</td>
<td>Not done</td>
<td>Minor inf. dyskinesia</td>
<td>64</td>
<td>CAD × 2</td>
<td>CAD</td>
</tr>
<tr>
<td>C. K.</td>
<td>46</td>
<td>F</td>
<td>Normal</td>
<td>13/27</td>
<td>140/80</td>
<td>None</td>
<td>Not done</td>
<td>Normal</td>
<td>75</td>
<td>Not done</td>
<td>? CAD</td>
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<tr>
<td>W. S.</td>
<td>40</td>
<td>M</td>
<td>Normal</td>
<td>14/31</td>
<td>130/100</td>
<td>None</td>
<td>Normal</td>
<td>Not done</td>
<td>—</td>
<td>Not done</td>
<td>? CAD</td>
</tr>
<tr>
<td>L. T.</td>
<td>57</td>
<td>M</td>
<td>$\Delta T$ inf.</td>
<td>14/34</td>
<td>130/75</td>
<td>$\beta B + N + V$</td>
<td>Not done</td>
<td>Normal</td>
<td>58</td>
<td>CAD × 2</td>
<td>CAD</td>
</tr>
<tr>
<td>E. W.</td>
<td>59</td>
<td>M</td>
<td>$\Delta T$ N/S</td>
<td>14/31</td>
<td>160/95</td>
<td>$\beta B + D$</td>
<td>Not done</td>
<td>Normal</td>
<td>61</td>
<td>CAD × 1</td>
<td>CAD</td>
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<tr>
<td>Mean</td>
<td>52</td>
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<td>14/30</td>
<td>139/84</td>
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<td></td>
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<tr>
<td>SD</td>
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<td>0.6/2.5</td>
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<td></td>
<td></td>
<td></td>
<td>7.4</td>
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<td></td>
</tr>
</tbody>
</table>

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CT ratio = chest x-ray cardiothoracic ratio; BP = arterial blood pressure; EF = LV ejection fraction. ECG column: $\Delta T$ N/S = nonspecific T wave changes; RBBB = right bundle branch block; LVH = left ventricular hypertrophy; LAD = left-axis deviation; $1^{st}$HB = first degree heart block; $\Delta T$ = ST segment changes; MI = myocardial infarction; $\Delta T$ = T wave inversion. Treatment column: $\beta B$ = oral $\beta$-blocker; D = diuretic; T4 = thyroxine; CG = cardiac glycoside; N = nifedipine; V = vasodilator. LA = left atrium; LV = left ventricle; hypok. = hypokinesia; CAD = coronary artery disease (no. of vessels indicated); COCM = congestive cardiomyopathy; HCM = hypertrophic cardiomyopathy.

* $p < .01$ (A vs B, B vs C).
normal angiographic ejection fraction or left ventricular dysfunction evident on a M mode echocardiogram. The other patient in this group (B. M.) had clinically well-documented alcoholic cardiomyopathy but a normal left ventricular angiogram at the time of the study; he died suddenly 6 weeks later and at autopsy the presence of biventricular dilatation without evidence of ischemia was revealed. The third group of subjects (C, five patients) met all the criteria for normality except that their coronary angiograms were abnormal or they did not undergo angiographic examination.

Procedures. A catheter-tipped manometer was passed into the left ventricle via the right femoral or right brachial artery of each patient. A bipolar pacing catheter was inserted via the right femoral or right brachial vein and positioned with its tip on the lateral wall of the right atrium (seven patients) or at the apex of the right ventricle (19 patients). Pacing was performed with a 1 to 2 msec square-wave stimulus of 2.5 to 4.5 V.

Equipment and measurements. The characteristics of the pacing and recording systems and the calibration procedure have been described in detail previously.3 Left ventricular pressure was measured with end-catheter manometers and differentiated electronically to obtain the rate of change in ventricular pressure. An example of the records obtained is shown in figure 2.

Protocols

Determination of optimum test pulse interval. The interval at which the largest mechanical response occurred (optimum test pulse interval) was examined in detail in a previous study.3 This interval was determined in 17 of the patients in the present study. Steady-state pacing was established with use of an interval of approximately 800 msec. A test beat was then introduced at varying intervals, and the shortest interval at which a maximal mechanical response was obtained was identified as the optimum test pulse interval.

Determination of recirculation fraction. Steady pacing was established at an interval as near the optimum as was technically feasible. In those patients in whom the optimum interval was not measured, it was assumed to be within the normal range found in our previous study. A premature beat (extrastyle) was then introduced and followed by two test stimuli (DP1 and DP2) (figure 2). Test beat DP1 followed the premature beat at the optimum interval and DP2 followed DP1, also at the optimum interval. The potentiation of contractility of the first test beat was varied by adjusting the interval preceding the extrastyle. This stimulation arrangement also ensured that the filling time for each of the beats examined would be equal, minimizing any potential influence of preload on maximum left ventricular dP/dt. In a previous study the influence of left ventricular end-diastolic pressure on maximum left ventricular dP/dt of the steady-state priming beats was shown to be very small.3 The data were normalized by dividing maximum left ventricular dP/dt of beats DP1 and DP2 by the mean of many steady-state beats (SS). A beat was accepted as potentiated when it was greater than SS by more than 1.645 multiplied by the SD of SS; this limits the probability that the potentiation is due to chance to less than 5%. The amount of potentiation in DP1 and DP2 was expressed as the fractional potentiation of DP1 (ΔDP1) and of DP2 (ΔDP2) from

\[
\Delta DP = (DP/SS) - 1
\]

At least four values of ΔDP2 and ΔDP1 were obtained in each patient, and were fitted to the equation

\[
\Delta DP_2 = B \times \Delta DP_1
\]

by a modified linear regression analysis in which the intercept was forced through zero.7 This requires the assumption that

![FIGURE 1. Mean hemodynamic and study data in the three groups of patients. LV = left ventricular; LVEDP = LV end-diastolic pressure. Bracketed and starred values are significantly different: *p < .05; **p < .02; ***p < .005.](http://circ.ahajournals.org/doi/abs/10.1161/01.CIR.70.5.801? curing=v/Images/1575/1575f1.jpg)
when there is no potentiation of \( \text{DP}_1 \), there is no potentiation of \( \text{DP}_2 \), but this was reasonable under the circumstances of our experiment since the steady-state intervals and the intervals preceding \( \text{DP}_1 \) and \( \text{DP}_2 \) were all equal. The recirculation fraction, representing the proportion of activator recirculated from beat \( \text{DP}_1 \) to beat \( \text{DP}_2 \), was given by \( B \), the slope of the line relating \( \Delta \text{DP}_2 \) to \( \Delta \text{DP}_1 \).

Quantification of postextrasystolic potentiation. To compare the degree of postextrasystolic potentiation in different subjects, the potentiation of \( \text{DP} \), obtained in the above protocol by a premature beat (extrasystole) at 400 m sec was analyzed. This extrasystolic interval was chosen since it was obtained in the majority of subjects and produced considerable potentiation in most of them.

Statistical analysis. Comparisons between groups were made by Student’s \( t \) test for unpaired samples. Relationship between parameters were investigated by linear regression with use of the method of least squares.7

Results

The criteria used in separating the patients into the three groups were listed in Methods. From the data presented in table 1 and figure 1 we can be confident that the patients in group A had normal left ventricular function. This was also true of group C patients, who were initially separated out on the basis of abnormal or undefined coronary anatomy. When the data in table 1 and figure 1 were examined statistically, however, no parameter showed a significant difference between groups A and C.

All but one patient in group B (D. H.) had at some time been found to have radiologically evident cardiomegaly, even though at the time of catheterization this abnormality had resolved in four (J. F., W. R., S. M., and L. K.). Nevertheless, mean cardiac diameter on chest x-rays was higher in group B than in group A or C patients and the left ventricular end-diastolic pressure was significantly higher in group B than in group A. The mean maximum \( \text{dP} / \text{dt} \) was significantly lower in group B than in group A. No other clinical parameters differed among patient groups.

Optimum test pulse interval. The time course of the recovery of left ventricular mechanical function after the last in a train of steady-state beats was 815 ± 85 (SD) msec. This was very close to that found previously (825 ± 10 msec).3

Recirculation fraction. A record illustrating the beats from which the recirculation fraction was calculated is shown in figure 2. The potentiation of \( \text{DP}_1 \) was inversely proportional to the interval preceding the extrasystole (figure 3), and varying this interval provided a means of exploring the relationship between this beat and the subsequent one (\( \text{DP}_2 \)). A plot of this relationship for one patient is shown in figure 4. In most of the other patients, comparable numbers of data points could not be obtained, but in 14 of the 15 patients in whom more than 6 points were obtained, significant linear correlations were observed (mean ± SD \( r = .72 ± .17 \)). In those patients from whom fewer than 6 data points were obtained, the ratio of \( \Delta \text{DP}_2 \) to \( \Delta \text{DP}_1 \) was also calculated for individual data pairs. The mean of these values did not differ appreciably from the slope calculated assuming a linear relationship, and the latter result is used for each patient in calculating the data for figure 1. This slope, which expresses the ratio of \( \Delta \text{DP}_2 \) to \( \Delta \text{DP}_1 \), we call the recirculation fraction. In the patients in group B this fraction was 0.37 ± 0.11 (SD), significantly lower than the mean value in group A (0.52 ± 0.10, \( p < .005 \)) and also lower than the value for the patients in group C (0.59 ± 0.11, \( p < .005 \)).

Quantification of postextrasystolic potentiation. The de-
degree of potentiation produced when the interval preceding the extrasystole was fixed (as near 400 msec as possible) was significantly higher in the patients with abnormal compared with those with normal left ventricular function (1.43 ± 0.19 vs 1.25 ± 0.06, p < .02).

The relationship between the amount of potentiation (DP1/SS) and the recirculation fraction (RF) in individual patients is illustrated in figure 5. This plot suggests an inverse linear relationship between these parameters such that

\[
RF = -0.68 (DP1/SS) + 1.39 \quad (r = -0.80, p < .001)
\]

Discussion

The results of this study are compatible with the model for excitation-contraction coupling that has been developed in isolated rabbit myocardium\(^3\) and intact dogs.\(^2\),\(^9\),\(^10\) In a previous study in man\(^1\) we showed that contractility, as indicated by the maximum left ventricular dP/dt, increased with test pulse interval to reach an optimum at approximately 800 msec. This process, described in the earlier literature on isolated cardiac muscle preparations as "restitution" of contractile function,\(^11\) and considered to represent either the recovery of the contractile potential of the muscle\(^11\) or the decay of a negative inotropic influence of the previous contraction,\(^12\) is now interpreted as a delay in the handling of calcium ions sequestered during an excitation-contraction-relaxation cycle. Immediately after relaxation, calcium is not in a form in which it can be fully released to produce another full contraction; the recirculation process takes a finite time for completion. In the present study we confirmed our previous observation,\(^3\) and that of others,\(^13\) that in man this time is approximately 800 msec.

That contractility recovers to a plateau after approximately 800 msec carries implications for studies of changes in contractility of individual heart beats. The intervals preceding test beats have to be at or near the plateau, as in the present study, if the effects of the recovery process are not to mask changes in contractility.
After extrasystolic intervals shorter than the steady-state pacing interval potentiation of the first postextrasystolic beat (DP1) was invariably produced (figure 3), the degree of potentiation being an inverse function of the interval before the extrasystole and decaying with subsequent beats. This behavior has been observed and interpreted many times in the past.11, 12, 14 Our current theories concerning postextrasystolic potentiation and its decay are based on the theory elaborated in many recent studies15-20 of recirculation of activator calcium from one beat to the next. According to this model of cellular calcium handling, the magnitude of a beat is dependent on the amount of calcium released during the excitation-contraction process. The potentiation of a postextrasystolic beat (DP1) is therefore equated to the presence of an extra “bolus” of activator calcium, which is made available by the extrasystole. A fraction of this bolus reappears in beat DP2, accounting for the potentiation also observed in this beat. When the relationship between the potentiation of DP1 and DP1 was examined by varying the interval before the extrasystole, it appeared to be linear (figure 4), implying that the fraction of extra activator recirculated from DP1 to DP2 is constant — a result similar to that reported in isolated rabbit papillary muscle20 and intact dog ventricle.2 We call this the recirculation fraction.

We calculated the recirculation fraction from the slope of the linear regression equation of ∆DP2 against ∆DP1 for a number of reasons. Continuity of the line through the steady-state data (i.e., zero intercept) was maintained, linearity of the relationship could be confirmed, and estimates of the error of the slope could be calculated. The recirculation fraction has no dimensions; this circumvents factors that influence the absolute value of maximum dP/dt such as dyskinesia, global contractility, and asynchrony. The effect of changes in ventricular filling are eliminated when the constant intervals preceding DP1 and DP2 are used.

Our results suggest a significant reduction in the recirculation fraction in the patients with abnormal left ventricular function (group B). This group included patients with abnormal function resulting from several different causes and of varying severities. No statement concerning the cause of the lower recirculation fraction in these patients can be made, particularly since therapy was not uniform. No consistent trends in the recirculation fraction were noted with particular drugs, but in this initial study we did not feel justified in withdrawing treatment before catheterization.

Our observations on the potentiating effect of an extrasystole have some relevance to the clinical application of postextrasystolic potentiation, which has been used in the assessment of myocardial contractile function.21-25 In patients with impaired left ventricular function the rate of rise in left ventricular pressure has been reported to be both augmented21 and depressed22 after an extrasystole, while ejection fraction, initially lower than normal in such patients, may show a greater rise23 or respond variably24 after an extrasystole. Such inconsistencies may in part be due to a failure to appreciate the importance of the time course of mechanical recovery, which demands a postectopic interval of approximately 800 msec. This interval does not appear to have been controlled in any of the studies cited. Moreover, since the ectopic interval controls the degree of potentiation14 and may affect other hemodynamic variables,26 interindividual comparisons can only be made if this interval is also fixed, as in the present study. Finally, it is important to avoid use of the second postextrasystolic beat as a control, as has been done in some studies.23 Potentiation in the normal heart takes 6 or more beats to decay,2, 14 and our experience in abnormal hearts is that although the decay is more rapid than in normal hearts, it varies between patients.

Figure 5 shows a negative association between the amount of postextrasystolic potentiation and the recirculation fraction. In other words, a more rapid decay of potentiation is associated with greater initial potentiation. In terms of our model, the implication of this is that some hearts acquire a proportionately larger bolus of activator after an extrasystole but retain less of it from beat to beat. Such behavior might be an indicator of myocardial cell dysfunction.

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