Incomplete filling and incoordinate contraction as mechanisms of hypotension during ventricular tachycardia in man

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ABSTRACT We sought to determine mechanisms for decrease of cardiac output and for hypotension during ventricular tachycardia (VT) in man. Two-dimensional and M mode echocardiograms and left ventricular pressure from micromanometer-tipped catheters were obtained in 20 patients before, during, and at the end of induced hypotensive VT. Patients were divided into two groups according to left ventricular function in sinus rhythm as assessed by angiographic ejection fraction (EF) before electrophysiologic study. Group 1 (n = 8) had angiographic EF ≥50% in normal sinus rhythm, and group 2 (n = 12) had EF ≤40%. During VT, left ventricular cavity volume (as indexed by short- and long-axis two-dimensional end-diastolic cavity areas) was markedly reduced in group 1, from 19.7 ± 2 to 8.6 ± 2 cm³ (p < .001) and from 32.0 ± 8 to 22.5 ± 7 cm³ (p < .001), respectively, but was only slightly reduced in group 2, from 34.1 ± 6 to 31.5 ± 7 cm³ (p = .044) and from 45.0 ± 8 to 49.4 ± 7 cm³ (p = NS), respectively. Conversely, left ventricular systolic function during VT (as indexed by fractional reduction in two-dimensional short- and long-axis areas) was markedly depressed in group 2, from 25.6 ± 6% to 4.2 ± 4% (p = .005) and from 13.7 ± 3% to 1.8 ± 0.8% (p < .001), respectively, but remained at control levels in group 1. Left ventricular end-diastolic pressures increased in group 1, from 11.8 ± 2 to 27.7 ± 8 mm Hg (p = .005) and did not change in group 2 during VT. Pressure-dimension loops from left ventricular pressure and M mode echocardiographically determined cavity dimensions generated from the end of the VT episodes showed that diastolic pressure-dimension relationships returned to control levels with the first prolonged diastolic interval in group 1 patients, indicating that incomplete relaxation was the mechanism responsible for reduction of cardiac output during VT in these patients. Coordination of contraction and relaxation (indicated by the percent ratio of the pressure-dimension loop area to the area of the rectangle just enclosing the loop) decreased from 37 ± 11% to 16 ± 13% in group 2 patients during VT (p = .013) but remained at control levels in group 1 patients. Thus, during VT patients with impaired left ventricular function in sinus rhythm (group 2) developed severe discoordination, and patients with normal or near-normal function (group 1) developed incomplete relaxation to account for stroke volume deterioration and hypotension.

Circulation 68, No. 5, 928–938, 1983.

MANY PATIENTS with ventricular tachycardia (VT) lose consciousness and die within a short time.1-4 The need for prompt resuscitation generally makes it difficult to study the hemodynamic mechanisms involved, but with recent advances in therapy for and control of these arrhythmias, an understanding of the pathophysiologic characteristics of this condition is increasingly important. We assessed left ventricular function using combined echocardiographic and hemodynamic data obtained during VT in a controlled setting in the electrophysiology laboratory.

Two general mechanisms can cause cardiac output to fall abruptly during VT: reduced filling of the heart and reduced systolic emptying. Mechanisms that impair left ventricular filling include (1) shortened diastolic filling time due to rapid rates, (2) incomplete ventricular relaxation between beats, (3) increased diastolic ventricular stiffness or other external restraints to ventricular filling, and (4) reflex factors influencing
venous return. Mechanisms that may impair forward systolic emptying include (1) electrically or mechanically induced discoordinate contraction, (2) ischemic myocardial dysfunction, (3) mitral regurgitation, or (4) a negative rate effect at very rapid rates.

In this study we examined left ventricular function before, during, and at the end of induced VT using two-dimensional and M mode echocardiograms combined with simultaneous left ventricular pressure data. The studies principally implicate two of these potential mechanisms: in patients with normal or near-normal ventricular function during sinus rhythm, incomplete ventricular relaxation leads to impaired filling, and in patients with preexisting left ventricular damage, incoordinate contraction predominates.

Methods

Patients. We studied 20 patients who developed hypotensive VT during clinical electrophysiologic testing. Systolic arterial pressure fell to below 70 mm Hg until VT converted to sinus rhythm, and all patients had had at least one episode of syncope caused by spontaneous ventricular arrhythmia (table 1). All patients gave written informed consent for the research protocol and were selected only on the basis of high-quality echocardiograms before the electrophysiologic study. All patients underwent cardiac catheterization with coronary angiography before the electrophysiologic study and were divided into two groups according to left ventricular function in sinus rhythm.

Group 1 included eight patients with ejection fraction above 50% (61 ± 8%) and no regional left ventricular dysfunction as determined by angiography. Their mean age was 35 ± 13 years and three were men. Two patients had mitral valve prolapse, and three others had ejection fraction below 60% (52%, 53%, and 53%) as determined by angiography. Two of those three had mild mitral regurgitation. No abnormalities were found on angiographic study in the remaining three patients. One had had a previous diagnosis of sarcoidosis several years before the study. All patients were receiving antiarrhythmic drugs at the time of catheterization.

Group 2 consisted of 12 patients with ejection fraction below 40% (29 ± 6%). Four patients had primary cardiomyopathy, and the remaining eight had ischemic heart disease with at least two episodes of documented myocardial infarction in the past. They were all men and their mean age was 48 ± 16 years. Two had moderate to severe mitral regurgitation as determined by angiography.

We also studied five episodes of nonhypotensive VT. Three occurred in patients from group 1 and the other two in patients who also had normal left ventricular function in sinus rhythm, but in whom hypotensive VT was not induced. This group is referred to as group 1B.

Electrophysiologic studies. Two to four electrode catheters were passed percutaneously into the femoral veins and positioned at the right atrium, His bundle recording site, and right ventricular apex. Repetitive ventricular response and programmed electrical stimulation techniques were used to induce tachycardia from the right ventricle. A detailed description of the protocol used in the electrophysiologic studies in our laboratory has been published.3 Five patients had self-terminating episodes of VT; all other episodes were terminated by overdrive suppression or DC shock. Left ventricular pressure was measured with a micromanometer-tipped catheter (Millar model 471) inserted through a sheath (Cordis) in the femoral artery. To minimize baseline drift the catheter was soaked in saline solution at 37°C for 3 hr and was calibrated initially and at the completion of the study with an electrical calibration signal. Zero pressure was taken as the pressure in air. To check catheter drift, zero position was determined at the start of the study and at the instant of withdrawal of the catheters from the patient. This latter level was used as zero-pressure reference in the data analysis. Fluid-filled catheters inserted in the right or left femoral artery measured arterial pressure throughout the entire study. The intracardiac electrograms were displayed simultaneously with three surface electrocardiograms and pressure tracings on a multichannel oscilloscope (Electronics for Medicine VR-12) and were recorded on paper at 100 to 250 mm/sec.

Echocardiograms. Two-dimensional and M mode echocardiograms were recorded sequentially in every patient. Two-dimensional echocardiograms (Varian V-3400 phased-array Ul-

| Table 1 | Clinical characteristics
<table>
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<tr>
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<tbody>
<tr>
<td>Patient</td>
<td>Age (yr)</td>
<td>Sex</td>
<td>Underlying disease</td>
<td>Cath-EP⁺</td>
</tr>
<tr>
<td>----------</td>
<td>----------</td>
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<td>---------</td>
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<tr>
<td>Group 1</td>
<td></td>
<td></td>
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<tr>
<td>F. B.</td>
<td>44</td>
<td>F</td>
<td>Unknown</td>
<td>63</td>
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<tr>
<td>F. R.</td>
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<td>M</td>
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<td>70</td>
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<tr>
<td>S. G.</td>
<td>29</td>
<td>F</td>
<td>MVP</td>
<td>70</td>
</tr>
<tr>
<td>T. C.</td>
<td>34</td>
<td>M</td>
<td>Unknown</td>
<td>64</td>
</tr>
<tr>
<td>S. S.</td>
<td>32</td>
<td>F</td>
<td>Unknown</td>
<td>53</td>
</tr>
<tr>
<td>D. K.</td>
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<td>M</td>
<td>Unknown</td>
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</tr>
<tr>
<td>J. P.</td>
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<td>F</td>
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<td>E. S.</td>
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<td>D. K.</td>
<td>20</td>
<td>M</td>
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<td>52</td>
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<tr>
<td>J. P.</td>
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<td>F</td>
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<td>J. A.</td>
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<td>J. M.</td>
<td>64</td>
<td>M</td>
<td>CAHD</td>
<td>38</td>
</tr>
<tr>
<td>D. C.</td>
<td>49</td>
<td>M</td>
<td>CAHD + An</td>
<td>31</td>
</tr>
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<td>R. E.</td>
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<td>M</td>
<td>CM</td>
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<td>M. F.</td>
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<td>R. B.</td>
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<td>CM</td>
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<td>CM</td>
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<td>M</td>
<td>CAHD</td>
<td>33</td>
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<td>CAHD</td>
<td>30</td>
</tr>
<tr>
<td>C. S.</td>
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<td>M</td>
<td>CAHD + An</td>
<td>17</td>
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<tr>
<td>W. M.</td>
<td>52</td>
<td>M</td>
<td>CAHD</td>
<td>37</td>
</tr>
</tbody>
</table>

MVP = mitral valve prolapse; CAHD = coronary atherosclerotic heart disease; CAHD + An = CAHD with aneurysm; CM = primary cardiomyopathy; several = more than five syncopal episodes due to malignant arrhythmias before the electrophysiologic study.

⁺Ejection fraction at cardiac catheterization performed before the electrophysiologic studies.

⁻Presence and degree of mitral regurgitation at cardiac catheterization.

⁻Number of syncopal episodes prior to electrophysiologic studies due to documented malignant arrhythmias.

No. 471) inserted through a sheath (Cordis) in the femoral artery. To minimize baseline drift the catheter was soaked in saline solution at 37°C for 3 hr and was calibrated initially and at the completion of the study with an electrical calibration signal. Zero pressure was taken as the pressure in air. To check catheter drift, zero position was determined at the start of the study and at the instant of withdrawal of the catheters from the patient. This latter level was used as zero-pressure reference in the data analysis. Fluid-filled catheters inserted in the right or left femoral artery measured arterial pressure throughout the entire study. The intracardiac electrograms were displayed simultaneously with three surface electrocardiograms and pressure tracings on a multichannel oscilloscope (Electronics for Medicine VR-12) and were recorded on paper at 100 to 250 mm/ sec.
trasonograph) were recorded on videotape (Sony Betamax). Parasternal long-axis as well as short-axis views at the level of the papillary muscles were obtained before, during, and after VT. M mode echocardiograms were recorded (Irex System II Echocardiograph) below the level of the mitral valve before, during, and after VT, at a paper speed of 100 mm/sec. Left ventricular pressure tracings obtained by micromanometer were superimposed on the M mode echocardiograms (figure 1). Two-dimensional and M mode echocardiographic measurements were obtained after the initial pressure drop and when systolic arterial pressure had reached a plateau, usually after the initial 20 to 30 beats.

**Analysis of two-dimensional echocardiograms.** Cavity size and systolic function were assessed by measuring cavity areas with short-axis and long-axis two-dimensional echocardiography by use of a computer-assisted contouring system (see below). In sinus rhythm, end-diastolic cavity area (EDA) was measured at the first deflection of the QRS complex. End-systolic cavity area (ESA) was taken as the smallest cavity area as determined by short-axis or long-axis echocardiography in a given cycle. During VT, EDA and ESA were taken as the largest and smallest areas, respectively. Particularly when wall movement was incoordinate during VT, these frames could not be identified without measuring areas frame by frame throughout the cycle. Values used are means of 3 beats, and variation between beats never exceeded 6%.

Fractional change in area (FCA), an index of ejection fraction, was calculated for both short-axis and long-axis views as follows:

\[
FCA = \frac{EDA - ESA}{EDA}
\]

The contouring system used to analyze two-dimensional short-axis and long-axis echocardiograms has been described in detail elsewhere. With this system, successive video frames of the short-axis or long-axis image are projected on a high-resolution x,y,z oscilloscope with a video disc (VAS). The computer superimposes two sets of 16 points equally spaced in angle around the image, and the reader places the points to fit the endocardial and epicardial margins. A best-fit contour for each two sets of points is selected by the computer with a spline-fitting technique. Each of the endocardial and epicardial points is repositioned at successive fields every 16 or 32 msec from end-diastole to the next end-diastole, beginning and ending with the simultaneously recorded first deflection of the QRS complex.

**Pressure-dimension loops.** M mode echocardiograms and superimposed left ventricular pressure tracings (figure 1) were hand-digitized with an Altek digitizing tablet and software available from the United Kingdom Department of Health and Social Security. Plots of instantaneous cavity dimension measured from the endocardial echo of the posterior wall to the left side of the septum were obtained from the digitized data. Cavity dimension was plotted against pressure in the form of a loop for 3 representative beats in sinus rhythm and VT. In 12 patients (seven of group 1 and five of group 2) who converted from VT without DC countershock, we plotted loops for the moment of reversion to sinus rhythm.

The influence of incoordinate of contraction and relaxation on ventricular function was assessed by the area enclosed within the pressure-dimension loop, expressed as a percentage of the area of a rectangle defined by the maximal and minimal pressures and dimensions reached during that particular cardiac cycle. This approach has previously been described and its rationale is discussed below.

Although incoordinate can easily be demonstrated in two-dimensional echocardiograms, quantification of its influence on left ventricular function is not straightforward. We therefore used a technique that relates the function and timing of a small region of myocardium studied by M mode echocardiography to behavior of the ventricle as a whole, reflected in the left ventricular pressure tracing. The pressure-dimension relationship provides a means for assessing the extent to which work performed by a region of myocardium is translated into work performed by the ventricle on the circulation. The area enclosed within the

**FIGURE 1.** Representative M mode echocardiogram in a patient in sinus rhythm with superimposed left ventricular pressure tracing.
**TABLE 2**

Hemodynamics and two-dimensional echocardiographic left ventricular cavity area measurements (group comparisons)

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 1B</th>
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<tbody>
<tr>
<td></td>
<td>SR</td>
<td>VT</td>
<td>p value&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>70±13</td>
<td>235±26</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td>123±15</td>
<td>40±10</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LV end-diastolic pressure (mm Hg)</td>
<td>11.8±2</td>
<td>27.7±8</td>
<td>.005</td>
</tr>
<tr>
<td>Short-axis areas (cm&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic</td>
<td>19.7±2</td>
<td>8.6±2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>End-systolic</td>
<td>8.1±1</td>
<td>3.7±2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fractional change (%)</td>
<td>59.4±5</td>
<td>60.2±15 NS</td>
<td></td>
</tr>
<tr>
<td>Long-axis areas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic</td>
<td>32.0±8</td>
<td>22.5±7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>End-systolic</td>
<td>21.7±6</td>
<td>15.8±6</td>
<td>&lt;.008</td>
</tr>
<tr>
<td>Fractional change (%)</td>
<td>32.4±7</td>
<td>31.6±8</td>
<td>NS</td>
</tr>
<tr>
<td>Loop area ratio (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>81±5</td>
<td>73±16</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
SR = sinus rhythm; VT = ventricular tachycardia; LV = left ventricular.
<sup>a</sup>By paired t test.
<sup>b</sup>Ratio of loop area to area of enclosing rectangle.

loop is by definition net work performed on the circulation per unit area of endocardium studied by the echocardiographic beam. For a given range of pressure and dimension this area is maximal when the loop is rectangular. When the onset of contraction and relaxation are asynchronous, changes in cavity shape during the periods of pressure rise and fall are manifested as obliquity of the "sides" of the pressure-dimension plot. Provided that cardiac valves are competent, such deviations from the rectangular configuration imply reduction in net work for this region due to incoordination. Thus, rather than attempt a direct measure of incoordination, a concept that has no units, we can assess its resulting mechanical decrement by expressing the area enclosed within the pressure-dimension loop as a proportion of the maximum possible, i.e., the area of the rectangle that just encloses it. Values for this ratio were taken as means from 3 beats. Beat-to-beat variation never exceeded 5%.

**Statistical analysis.** All values are expressed as mean ± SD. Paired t tests were used to compare data from sinus rhythm with that from VT, and differences between group 1 and group 2 data were compared by means of unpaired t tests. We used an unpaired test to compare differences from sinus rhythm to VT between group 1 and group 1B. Although some of the data are paired, this will merely increase the apparent probability of the null hypothesis.

### Results

**Peak systolic arterial pressure** (tables 2 and 3). Mean values of systolic pressure did not differ between the two groups in sinus rhythm and VT. Both groups developed hypotension of similar degree. Patients in group 1 with normal left ventricular function in sinus rhythm as determined by angiography had peak systolic pressure of 123 ± 15 mm Hg in sinus rhythm and 40 ± 10 mm Hg during VT; in group 2 patients with impaired left ventricular function in sinus rhythm, systolic pressure fell from 118 ± 18 mm Hg in sinus rhythm to 38 ± 16 mm Hg in VT.

**Heart rate** (tables 2 and 3). Mean values of heart rate in group 1 were 70 ± 13 beats/min in sinus rhythm and 235 ± 25 beats/min in VT. In group 2, heart rate increased from 75 ± 12 to 193 ± 29 beats/min. Heart rate did not differ in sinus rhythm between groups 1 and 2, but was significantly higher during VT (p = .005) in group 1. Thus, although there was some overlap between the two groups, patients in group 2 had

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hypotensive VT at lower heart rates than patients in group 1.

Left ventricular cavity size and function

EDA. We used short-axis and long-axis EDA as an index of end-diastolic left ventricular cavity volume. In sinus rhythm, cavity areas were greater in group 2 than in group 1 (table 3). This is consonant with the angiographic criteria used in the selection of the two groups.

Group 1 patients had marked reductions in both short-axis (19.7 ± 2 to 8.6 ± 2 cm², p < .001) and long-axis (32.0 ± 8 to 22.5 ± 7 cm²; p < .001) EDA during VT. Group 2 had a slight reduction in short-axis EDA (34.1 ± 6 to 31.5 ± 7 cm²; p = .044) but no reduction in long-axis area (52.1 ± 8 to 50.6 ± 7 cm²; p = NS).

ESAs. Short- and long-axis ESAs were also larger in group 2 than in group 1 in sinus rhythm (table 3). During VT, group 1 patients again demonstrated a marked reduction in cavity areas (short-axis 8.1 ± 1 to 3.7 ± 2 cm², p < .001; long-axis 21.7 ± 6 to 15.8 ± 6 cm², p < .008), and group 2 had an increase in both short-axis (25.4 ± 6 to 29.4 ± 7 cm²; p = .022) and long-axis ESAs (45.0 ± 8 to 49.4 ± 7 cm², p = .005).

Fractional change in area. In sinus rhythm, both short- and long-axis fractional change in areas were greater in group 1 (short-axis 59.4 ± 5%; long-axis 32.4 ± 7%) than in group 2 (short-axis 25.6 ± 6%; long-axis 13.7 ± 3%, p < .001, p = .003, respectively, table 3). This again reflects the criterion used to select the two groups. However, both short- and long-axis fractional change in areas fell in group 2 during VT (short-axis 25.6 ± 6 to 4.2 ± 4%, p = .005; long-axis 13.7 ± 3 to 1.8 ± 0.8%, p < .001), and group 1 showed no change during VT (short-axis 59.4 ± 5 to 60.2 ± 15%, p = NS; long-axis 32.4 ± 7 to 31.6 ± 8, p = NS).

Left ventricular end-diastolic pressure. End-diastolic pressure was taken at the onset of the QRS in sinus rhythm and as minimum diastolic pressure during VT. End-diastolic pressure increased during VT in group 1 from 11.8 ± 2 to 27.7 ± 8 mm Hg, (p = .005). Group 2 did not show any significant changes in end-diastolic pressures during VT (18.7 ± 6 mm Hg before, 16.5 ± 9 mm Hg during VT; p = NS).

Incomplete relaxation. Thus in group 1 stroke volume fell because of reduced filling of the left ventricle. The reduction in diastolic left ventricular cavity size during VT was associated with a significant elevation of end-diastolic pressure. There are two possible mechanisms that could explain this association. First, interruption of active relaxation by the premature onset of the next systole would prevent the ventricle from reaching the fully relaxed state of passive diastole (incomplete relaxation). Second, increased stiffness due to ischemia or other unknown factors would impair left ventricular filling, shifting the left ventricular diastolic pressure-volume relationship up during VT, resulting also in a small cavity with high end-diastolic pressure.

To differentiate these two mechanisms, pressure-dimension loops of beats in sinus rhythm, VT, and immediately on return to sinus rhythm were analyzed. Figure 2 shows representative pressure-dimension loops from a patient of group 1. During VT the loop is displaced to the left and upward in relation to a control sinus beat, consistent with the finding of cavity-size reduction and high end-diastolic pressure shown above. However, at the end of VT, the prolonged initial diastolic period that preceded the first sinus beat (figure 3)

FIGURE 2. Pressure-dimension loops in sinus rhythm (right) and during VT (left) from a patient in group 1. Displacement of the VT loop to the left and upward in relation to the pressure-dimension loops in sinus rhythm indicates marked reduction in cavity size with high diastolic pressure.
showed an immediate return to the pre-VT pressure dimension relationship. This finding is incompatible with a change in passive myocardial properties and implies the existence of incomplete relaxation during VT. As left ventricular pressure fell after the last VT systole, the left ventricle proceeded to reach a fully relaxed state as evidenced by the superimposition of the last VT beat on the control sinus rhythm beat. This occurred in seven of the eight patients in group 1. In one patient, all episodes of hypotensive VT were ended by DC shock.

Group 2 showed no such elevation of end-diastolic pressure during VT, so that the effects on systolic function must be explained by a different mechanism (figure 4).

Incoordination of contraction/relaxation. Group 2, in contrast with group 1, suffered marked impairment of left ventricular systolic function associated with a slight reduction in left ventricular cavity volume (as indicated by changes in end-diastolic areas). To explain systolic function deterioration in these patients, we looked for evidence that VT caused incoordination of contraction and relaxation. Such incoordination was obvious from visual analysis of two-dimensional echocardiograms from group 2 patients during VT, but not of those from group 1. Furthermore, such a pattern of incoordinate contraction was present from the first ec-
topic beat of VT and thus was attributable to the abnormal sequence of electrical activation. To assess the effects of incoordination on left ventricular function during VT, we studied pressure-dimension loops from patients of group 1 and group 2 by quantifying the degree of distortion of the loop shape from sinus rhythm to VT in both groups (see Methods).

Figures 5 and 6 show representative pressure-dimension loops from patients of groups 1 and 2 during sinus rhythm and VT. The shape of the pressure-dimension loop is only slightly distorted during VT in the patient from group 1 with normal left ventricular function in sinus rhythm. In contrast, the group 2 patient with impaired left ventricular function during sinus rhythm showed a marked distortion of loop shape in VT. These results were typical for the two groups. In group 1 the ratio of the area within the loop to the maximum possible was 81 ± 5% in sinus rhythm and 73 ± 16% (p = NS) during VT. Group 2 started with a significantly lower ratio of 37 ± 11% in sinus rhythm (p < .001, table 3) and suffered further marked deterioration to 16 ± 13% (p = .013) during VT.

To summarize, some degree of incoordination already existed in patients of group 2 in sinus rhythm. During VT, incoordination was markedly accentuated and contributed to decreased stroke volume. In contrast, patients of group 1 did not exhibit significant degrees of incoordination during VT.

Nonhypotensive VT. Five episodes of VT were studied during which there was no significant change in systolic pressure (mean 116 ± 14 mm Hg in sinus rhythm, 100 ± 9 mm Hg in VT). In these patients (table 2) in whom left ventricular function is comparable to that in patients in group 1, heart rate during VT was relatively slower (148 ± 16 beats/min, p < .01) and there was no rise in left ventricular end-diastolic pressure (9.4 ± 0.9 mm Hg in sinus rhythm compared with 7.4 ± 1.9 mm Hg during VT, figure 7). In group 2, as in group 1, there was no demonstrable effect of incoordination. The area of the pressure-dimension loop was 80 ± 11% of maximum in sinus rhythm and 76 ± 14% during VT. A small reduction in cavity size occurred in four of the five episodes. These changes were much less than those associated with hypotension in group 1 (p < .01).

Discussion

Several physiologic changes occur during VT, any of which might be expected to interfere with cardiac function and lead to circulatory collapse. These changes include (1) the effects of rapid heart rate, which may limit diastolic filling time or cause primary
changes in contractility through a negative staircase effect, (2) effects of cardiac ischemia secondary to increased heart rate and shortened diastolic time, and (3) effects of an ectopic ventricular activation site that may lead to incoordination of contraction and relaxation, mitral regurgitation, and loss of atrial transport. The results of the present study imply that under circumstances of normal left ventricular function in sinus rhythm, the predominant effect is due to heart rate by limiting the normal processes of diastole. The evidence suggests that diastolic properties of the heart are not changed, but only that their normal expression is prevented as relaxation is interrupted. By contrast, in patients with impaired left ventricular function in sinus rhythm, any effect on filling due simply to heart rate was overshadowed by profound effects of incoordination on overall pump function. Before discussing these issues in detail it is appropriate to review the potential methodologic problems of this study.

**Methodology.** The use of echocardiography to estimate or index left ventricular volume has recognized limitations, particularly when overall architecture of the heart is disturbed as it was in many of the patients in group 2, or when left ventricular function is incoordinate. However, our conclusions regarding ejection fraction and cavity volume at end-diastole and end-systole are based exclusively on two-dimensional echocardiographic data that use pairs of orthogonal views. The changes in long- and short-axis cavity area were consonant throughout, and none of the patients had such extreme architectural abnormalities as to make us doubt that we could reliably assess the direction and relative magnitude of volume changes in the two groups under both conditions. M mode echocardiographic data were not used to index overall changes in volume.

The use of pressure-dimension plots as a means of assessing incoordination was reviewed by Gibson and colleagues. It should be recognized that the primary use of such plots is to provide information relating local wall function in an arbitrarily selected region to pressure changes within the cavity as a whole. Insofar as they differ from the rectangular pressure-volume relationship, these plots indicate the existence of regional inhomogeneity in wall dynamics. Thus the main use of the M mode echocardiographic data in this study was to provide a quantitative assessment of the effects of incoordinate contraction and relaxation on pump function. Only when the plot is normal, as was the case in group 1, can changes in its position be used secondarily to draw inferences concerning changes in position of the overall pressure-volume relationship.

A problem in interpreting the results of the study, insofar as they relate to mechanisms for hypotension, is the absence of a substantial control group with nonhypotensive VT. However, such patients rarely require electrophysiologic studies, and our only control observations (group 1B) were on five episodes of nonhypotensive VT. These were in patients with primary electrical disorders with normal left ventricular function and can only be compared with those of group 1 patients. We suspect that patients such as those in group 2 almost always become hypotensive with VT.

**Incomplete relaxation.** In patients with normal left ventricular function in sinus rhythm (group 1), impairment of stroke volume during VT was caused by interruption of diastolic filling, as reflected by a profound reduction of left ventricular cavity size. Other aspects of left ventricular function, in particular coordination and ejection fraction, remained unchanged. Filling of the left ventricle can be insufficient as a result of its starting late (for example because of de-
layed mitral valve opening), finishing prematurely (because of tachycardia), or because myocardial elasticity is abnormal. The pronounced rise in diastolic pressure that occurred in all patients in this group was contrary to the first of these but could be interpreted as evidence of a change in the passive diastolic properties of the myocardium. However, the immediate return of the pressure-dimension relationship to that observed before VT, which occurred with the very first prolonged diastole of sinus rhythm, indicates that myocardial properties are unaffected and implies that the rise in diastolic pressure during the tachyarrhythmia reflects incomplete relaxation. Left ventricular filling was interrupted during active relaxation by the premature onset of the next systole. The straight downward return of the pressure-dimension plot to normal at the end of VT in figure 3 was characteristic of this group. It implies that during VT, interruption of the pressure-volume cycle by the following beat occurs during the period of isovolumic pressure fall. During VT in these patients, left ventricular filling occurs during early systole. The properties of the myocardium during this period represent the interaction between forces of relaxation and contraction.

The present study represents an "experiment of nature" comparable to the conditions under which incomplete relaxation has been demonstrated during rapid ventricular pacing in the dog. In that study the course of relaxation was indexed by the time constant of pressure fall (T), and in most cases incomplete relaxation occurred when diastole was interrupted less than 3.5 T from the time of peak negative dP/dt. Arterial pressure and cardiac output were controlled in these studies of normal hearts, and cavity size changed little, but the subjects of the present report showed large changes in preload and afterload. More important, with a definite contribution of systolic performance to the pressure-dimension relation during filling, we would hesitate to use data from the present study to establish "criteria" for man expressed in terms of T for incomplete relaxation.

When patients comparable to this group developed nonhypotensive VT (group 1B), they did so at relatively slow heart rates and showed neither the striking reduction in cavity size nor the increase in diastolic pressure observed in group 1. Evidently the mere occurrence of ectopic activation, even in the presence of moderate tachycardia, does not of itself cause hypotension or impair filling in the normal heart. Only when the rate is fast enough to encroach on the period of pressure fall is filling so curtailed as to limit cardiac output.

**Incoordinate function.** Patients of group 2 with impaired left ventricular function in sinus rhythm represent the majority of individuals under the threat of malignant arrhythmias. During VT these patients showed pump function deterioration, as indicated by a marked reduction of both short-axis and long-axis fractional change in area in the face of a fall in afterload, and cavity size was only slightly reduced. The mean heart rate for group 2 patients during VT was significantly lower than that in patients of group 1, and end-diastolic pressure did not rise. Thus, in addition to any effect of heart rate on filling, there was a separate and severe change in left ventricular performance during VT.

Incoordination of contraction and relaxation, the result of the abnormal sequence of electrical activation, represented a likely potential mechanism of such left ventricular dysfunction during VT. We used pressure-dimension loops to quantify the effects of incoordinate wall dynamics in both groups in sinus rhythm and VT. We found that left ventricular function was severely disturbed by wall motion disorganization in patients of group 2 during VT; in patients in whom left ventricular function was normal in sinus rhythm (group 1), the mechanical effects of ectopic ventricular activation were much less important. These findings were consistent with our visual impression of the two-dimensional studies; hearts with normal contraction at rest had small ventricles with coordinated contraction pattern in VT, and those with abnormal function often developed grotesque worsening of incoordination.

Why the effects of ectopic activation on coordination are so slight in group 1 is unclear. However, the findings in group 1B and previous experience with ectopic activation of normal hearts by pacemakers are both consistent with the finding that an abnormal electrical activation sequence has minimal effect on overall function of otherwise normal ventricles. It might be anticipated that widening of the QRS by perhaps 100 msec should lead to corresponding delay in segmental wall dynamics, which would easily be detected by our technique. The late activated region may be small or so placed that it does not have a generalized effect. Alternatively, mechanisms may exist in the normal ventricle whereby a segment that is activated late catches up with neighboring regions.

**Alternative mechanisms.** Other potential mechanisms of left ventricular dysfunction during VT include the development of cardiac ischemia, mitral regurgitation, and a change in contractility due only to the increase in heart rate. Most of the patients from group 2 had severe ischemic heart disease and had multiple episodes of
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myocardial infarction in the past. Particularly in this group, ischemia could have contributed to incoordination of contraction and relaxation during prolonged episodes of VT.\textsuperscript{30–32} However, both incoordinate contraction and reduced fractional change in area were apparent in the very first beats of VT and, although ischemia may develop in patients in whom the arrhythmia persists sufficiently long, in our study the primary and immediate effect appears to be related to the abnormal sequence of electrical activation. Patients in group 1 had normal coronary arteries, normal left ventricular function in sinus rhythm, and showed no change in systolic function or passive myocardial properties during VT. Ischemia was not likely a major determinant of the fall in cardiac output.

Mitral regurgitation has been reported to occur during ventricular pacing\textsuperscript{33,34} and VT\textsuperscript{31} and has been attributed to the abnormal sequence of papillary muscle activation, wall motion incoordination, or atrioventricular dissociation. It has been shown to be more severe with abnormal ventricular function. Mitral regurgitation may have contributed to further impairment of cardiac output in group 2, particularly in the setting of profound incoordination. However, the simultaneous reduction in ejection fraction and cavity size during VT argues against the presence of a significant regurgitant fraction. In group 1 the striking reduction in cavity size indicates that the major limitation to cardiac output during VT was diastolic.

Finally, changes in myocardial contractility secondary to changes in heart rate per se should be considered.\textsuperscript{35} Changes in contractile state with varying intervals between beats, that is, the positive and negative staircase effects, are thought to be mediated by calcium movement inside the cardiac cell or across its membrane.\textsuperscript{36} Our study does not permit an assessment of myocardial contractility in the context of incoordination and a change in afterload. However in group 1, overall systolic function neither improved nor deteriorated, and any contribution of a change in contractility was likely to have been slight.

In conclusion, the functional state of the heart at rest determines its mode of performance during VT. We showed distinct mechanisms of hypotension during VT for the two extremes of the left ventricular functional spectrum in sinus rhythm. Patients with normal left ventricular function in sinus rhythm develop hypotension during VT because of incomplete relaxation. In patients with impaired left ventricular function in sinus rhythm, profound deterioration in pump function occurs during VT and is the result of incoordinate contraction.

We thank Willard Graves, Ph.D., for his help with the data processing, Sandra Dorsey and Betsy Walters for their technical assistance in obtaining echocardiograms, and Spring Metcalf for secretarial assistance and typing of the manuscript.

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Circulation. 1983;68:928-938
doi: 10.1161/01.CIR.68.5.928

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