Observations on Patients with Primary Ventricular Fibrillation Complicating Acute Myocardial Infarction

By K. I. Lie, M.D., Hein J. J. Wellens, M.D., Eugene Downar, M.D., and Dirk Dubber, M.D.

SUMMARY

In order to evaluate the events preceding primary ventricular fibrillation (PVF), continuous tape recording was performed in 262 patients consecutively admitted to the hospital within six hours of infarction in whom antiarrhythmic therapy was withheld. Warning arrhythmias (defined as ventricular ectopic beats occurring with a frequency of more than five beats per minute, in runs, falling in the vulnerable phase of the cardiac cycle or being multiformed) were registered in an equal percentage in patients who did or did not develop PVF. Immediately prior to PVF seven patients showed sinus tachycardia, 10 a sinus rate ranging from 60 to 100 beats per minute and two bradycardia due to complete atrioventricular block. The ventricular ectopic beat initiating PVF had a late coupling interval (QR'/QT ≥ 0.85) in 11 patients and a left bundle branch block configuration as frequent as a right bundle branch block.

Conclusions: 1) Warning arrhythmias are not considered good criteria for institution of antiarrhythmic therapy in order to prevent PVF. 2) In patients with sinus rhythm there may be an association between heart rate and onset of PVF. 3) The malignancy of a ventricular ectopic beat is not determined by its coupling interval or its configuration.

THE SIGNIFICANCE of so-called predisposing factors of primary ventricular fibrillation (PVF) following acute myocardial infarction has recently been challenged. However, antiarrhythmic intervention may have influenced the natural course of mechanism of PVF in these studies. The purpose of our study therefore was to evaluate the events preceding PVF during continuous tape recording of 262 patients, consecutively admitted within six hours of onset of infarction, in whom antiarrhythmic therapy was withheld on purpose.

Material and Methods

The study was carried out on patients admitted to the hospital within six hours of the onset of typical chest pain suggestive of acute myocardial infarction. The diagnosis of acute myocardial infarction was based on a typical history of chest pain correlated with the appearance of diagnostic Q waves and characteristic serial changes in serum enzymes. Excluded from the study were patients with congestive heart failure, cardiogenic shock, persistent ventricular tachycardia or ventricular fibrillation (VF) on admission. The diagnosis of congestive heart failure was made in the presence of basal crepitations not cleared by coughing and a third heart sound. Also excluded were patients who received digitalis or antiarrhythmic therapy prior to admission.

From November 1972 to June 1973, antiarrhythmic intervention was withheld from all patients who met our criteria. Informed consent was given by all patients. From June 1973 to September 1974, a double-blind randomized study with lidocaine was performed. Only the control patients of the double-blind randomized study were included in the present study.

Continuous electrocardiographic monitoring was performed in all patients with continuous tape recording during the first 12 hours. Leads I, II, III, with either aVR, aVL, aVF or V₅ and V₆ were recorded simultaneously during all tape recordings. The tape recordings were analyzed and the following data were obtained:

1) The presence or absence of so-called warning arrhythmias (WA). These were defined as ventricular ectopic beats (VEBs) fulfilling one of the following criteria: occurring within a frequency of more than five beats per minute; having a short coupling interval (this was expressed as a prematurity index [QR'/Q-T] of less than 0.85 and was determined by dividing the coupling interval of the VEB (QR') by the Q-T interval of the preceding sinus beat); being multiformed or being coupled or occurring in runs.

2) The development of a sustained ventricular tachycardia.

3) The development of PVF, defined as VF occurring in the absence of heart failure.

4) The ventricular rate immediately prior to onset of PVF.

5) The prematurity index of the VEB initiating PVF.

6) The QRS morphology of the VEB initiating PVF.

7) The QRS morphology of the successive VEBs initiating PVF.

Results

According to the previously listed criteria, 262 patients with acute myocardial infarction entered the study. Fifty percent of patients were admitted within two and half hours after onset of infarction. The over-
Incidence of Ventricular Arrhythmias in the 262 Patients Studied

<table>
<thead>
<tr>
<th>Type of arrhythmia</th>
<th>No. of patients</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ventricular extrasystole</td>
<td>42</td>
<td>16%</td>
</tr>
<tr>
<td>Occasional ventr. extrasystole*</td>
<td>65</td>
<td>25%</td>
</tr>
<tr>
<td>Premontitory ventr. extrasystole</td>
<td>155</td>
<td>59%</td>
</tr>
<tr>
<td>multifomed</td>
<td>63</td>
<td>24%</td>
</tr>
<tr>
<td>R on T</td>
<td>27</td>
<td>10%</td>
</tr>
<tr>
<td>bigeminy</td>
<td>35</td>
<td>13%</td>
</tr>
<tr>
<td>run</td>
<td>95</td>
<td>36%</td>
</tr>
<tr>
<td>&gt;5/min</td>
<td>97</td>
<td>37%</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>13</td>
<td>5%</td>
</tr>
<tr>
<td>Primary ventricular fibrillation</td>
<td>20</td>
<td>7%</td>
</tr>
</tbody>
</table>

* <5/min.

all incidence of ventricular arrhythmias is presented in table 1. Although 19 patients with PVF could be successfully defibrillated, one patient died from recurrent attacks of VF, the attacks being unresponsive to antiarrhythmic therapy, cardiac pacing or repeated defibrillation. Table 2 shows the electrocardiographic data of the 20 patients with PVF obtained during continuous tape recording. The 12 patients in whom so-called WA were registered prior to PVF included three with bigeminy, two with bigeminy and short coupling intervals of their VEBs and seven with runs of VEBs. In four of the latter seven patients the sequence of VEBs initiating PVF was identical to the runs of VEBs, which were registered prior to PVF (fig. 1). Seven patients showed a sinus rate of 100 or more beats per minute prior to onset of PVF, while in the two patients in whom a bradycardia was registered prior to onset of PVF the slow heart rate was due to complete atrioventricular block. Three patterns of initiation were noted. The first pattern was the initiation by a closely coupled VEB (QR'/Q-T < 0.85) and was seen in nine patients; the second was initiation of PVF by a late coupled VEB (QR'/Q-T ≥ 0.85) and was observed in seven patients. Finally, four patients developed PVF subsequent to the onset of a ventricular tachycardia. In all four patients ventricular tachycardia was initiated by a late coupled VEB that was well clear of the preceding T wave (fig. 2) and deteriorated into PVF within one minute.

A left bundle branch block pattern was present in the PVF initiating VE in six patients. All had inferior myocardial infarction. Six patients showed a right bundle branch block pattern. In eight patients the PVF initiating VEB could not be classified as showing either left or right bundle branch block configuration.

Discussion

Significance of Warning Arrhythmias

The occurrence of WA in the setting of acute myocardial infarction is generally considered a criterion for institution of antiarrhythmic therapy. 3

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Infarction</th>
<th>No.</th>
<th>Site</th>
<th>WA</th>
<th>Rhythm prior to PVF Type</th>
<th>Rate</th>
<th>VES initiating PVF QR/Q-T Config</th>
<th>Initiation PVF</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>m</td>
<td>I</td>
<td>1</td>
<td>I</td>
<td>no</td>
<td>SR+AVB</td>
<td>45</td>
<td>0.80</td>
<td>unclass</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>m</td>
<td>I</td>
<td>1</td>
<td>I</td>
<td>no</td>
<td>SR</td>
<td>80</td>
<td>0.75</td>
<td>LBBB</td>
</tr>
<tr>
<td>3</td>
<td>62</td>
<td>m</td>
<td>I</td>
<td>2</td>
<td>I</td>
<td>run</td>
<td>SR</td>
<td>120</td>
<td>1.20</td>
<td>LBBB</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>m</td>
<td>I</td>
<td>2</td>
<td>I</td>
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<td>SR</td>
<td>95</td>
<td>0.75</td>
<td>LBBB</td>
</tr>
<tr>
<td>5</td>
<td>59</td>
<td>m</td>
<td>I</td>
<td>1</td>
<td>I</td>
<td>big</td>
<td>SR</td>
<td>65</td>
<td>0.80</td>
<td>unclass</td>
</tr>
<tr>
<td>6</td>
<td>35</td>
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<td>A</td>
<td>1</td>
<td>A</td>
<td>no</td>
<td>SR</td>
<td>100</td>
<td>1.35</td>
<td>RBBB</td>
</tr>
<tr>
<td>7</td>
<td>61</td>
<td>m</td>
<td>I</td>
<td>1</td>
<td>I</td>
<td>run</td>
<td>AF+AVB</td>
<td>40</td>
<td>1.35</td>
<td>RBBB</td>
</tr>
<tr>
<td>8</td>
<td>56</td>
<td>m</td>
<td>A</td>
<td>2</td>
<td>A</td>
<td>no</td>
<td>SR</td>
<td>90</td>
<td>0.80</td>
<td>unclass</td>
</tr>
<tr>
<td>9</td>
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<td>m</td>
<td>I</td>
<td>1</td>
<td>I</td>
<td>no</td>
<td>SR</td>
<td>75</td>
<td>1.15</td>
<td>LBBB</td>
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<tr>
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<td>65</td>
<td>f</td>
<td>A</td>
<td>1</td>
<td>A</td>
<td>no</td>
<td>SR</td>
<td>80</td>
<td>0.75</td>
<td>unclass</td>
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<tr>
<td>11</td>
<td>69</td>
<td>m</td>
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<td>A</td>
<td>big</td>
<td>SR</td>
<td>120</td>
<td>1.65</td>
<td>RBBB</td>
<td>flutter</td>
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<tr>
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<td>1</td>
<td>I</td>
<td>run</td>
<td></td>
<td>SR</td>
<td>130</td>
<td>1.25</td>
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<tr>
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<td>66</td>
<td>m</td>
<td>1</td>
<td>A</td>
<td>run</td>
<td></td>
<td>AVR</td>
<td>95</td>
<td>0.65</td>
<td>RBBB</td>
</tr>
<tr>
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<td>1</td>
<td>I</td>
<td>run</td>
<td></td>
<td>SR</td>
<td>100</td>
<td>0.90</td>
<td>RBBB</td>
</tr>
<tr>
<td>15</td>
<td>60</td>
<td>m</td>
<td>2</td>
<td>I</td>
<td>big</td>
<td></td>
<td>SR</td>
<td>110</td>
<td>0.85</td>
<td>LBBB</td>
</tr>
<tr>
<td>16</td>
<td>63</td>
<td>m</td>
<td>1</td>
<td>I</td>
<td>no</td>
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<td>90</td>
<td>1.30</td>
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</tr>
<tr>
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<td>m</td>
<td>2</td>
<td>A</td>
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<td>SR</td>
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<td>0.70</td>
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</tr>
<tr>
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<td>m</td>
<td>1</td>
<td>A</td>
<td>big</td>
<td></td>
<td>SR</td>
<td>80</td>
<td>0.80</td>
<td>RBBB</td>
</tr>
<tr>
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<td>m</td>
<td>1</td>
<td>I</td>
<td>run</td>
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<td>SR</td>
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<td>1.65</td>
<td>LBBB</td>
</tr>
<tr>
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<td>m</td>
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<td>I</td>
<td>big</td>
<td></td>
<td>SR</td>
<td>95</td>
<td>1.40</td>
<td>unclass</td>
</tr>
</tbody>
</table>

Abbreviations: WA = warning arrhythmias; PVF = primary ventricular fibrillation; VEB = ventricular extrasystole; I = inferior; A = anterior; big = bigeminy; SR = sinus rhythm; AF = atrial fibrillation; AVB = atrioventricular block; AVR = accelerated ventricular rhythm; unclass = unclassifiable; LBBB = left bundle branch block; RBBB = right bundle branch block; VT = ventricular tachycardia.
Recently, however, Dhurandhar et al. reported that during continuous tape recording of patients with acute myocardial infarction five of 20 patients with PVF showed no WA prior to onset of PVF. The lower incidence of WA (60%) prior to PVF found in the present study may be due to the disparity in mean admission time between Dhurandhar's patients (9 hours) and ours (2½ hours), since Julian et al. and Lawrie et al. mentioned that PVF of early onset was frequently not preceded by WA. The over-all incidence of WA of 59% found in the present study during continuous tape recording was also reported previously by Mogensen who performed continuous electrocardiographic recording during 24 hours in patients with

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**Figure 1**

Primary ventricular fibrillation preceded by sinus tachycardia and initiated by a late ectopic beat. Note that the sequence of ventricular ectopic beats initiating ventricular fibrillation is identical to the preceding sequence of ventricular ectopic beats that do not end in ventricular fibrillation. Leads I, II, III, aVR, aVL, aVF were simultaneously recorded.

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**Figure 2**

Primary ventricular fibrillation initiated by a ventricular ectopic beat with a prematurity index of 1.35. In this patient a sinus tachycardia and no warning arrhythmias were registered prior to primary ventricular fibrillation. Leads I, II, III, V₁, V₆ were simultaneously recorded.

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**Figure 3**

Primary ventricular fibrillation initiated by a ventricular ectopic beat of diminishing coupling interval with a left bundle branch block pattern. Leads I, II, III, V₁, V₆ were simultaneously recorded.
acute myocardial infarction. These data revealed that WA are not helpful in deciding whether or not antiarrhythmic therapy should be instituted in order to prevent PVF. The high incidence of these WA suggests that they can be considered a common phenomenon in acute myocardial infarction rather than a warning signal.

Since the incidence of PVF falls exponentially with time after onset of infarction, the time lapse after onset of infarction is in our view a better criterion for institution of antiarrhythmic therapy than the presence or absence of WA.

Heart Rate and PVF

Experimental evidence on the relation of ventricular arrhythmias to heart rate is controversial. It was initially observed\(^\text{10}\) that at slow heart rates temporal disparity in recovery times was increased and the VF threshold decreased. However, these observations were made on nonischemic myocardium. Recent experimental studies on ischemic myocardium have shown that slow heart rates may decrease ventricular ectopic activity\(^\text{11,12}\) and rapid heart rates may increase ventricular ectopic activity, nonhomogeneity of refractory periods in contiguous areas of myocardium and vulnerability to VF.\(^\text{13-15}\)

Chadda et al.\(^\text{14}\) found that following coronary occlusion both slow and rapid heart rates were associated with increased ventricular ectopic activity including ventricular tachycardia and VF. The present observations in man suggest that in patients with sinus rhythm there may be an association between heart rate and onset of PVF.

It should be noted that the slow heart rates in our two patients with bradycardia prior to onset of PVF were not due to sinus bradycardia but to complete atrioventricular block. Similar observations were made previously by Meltzer and Kitchell\(^\text{17}\) and Lawrie et al.\(^\text{15}\) Moreover other studies\(^\text{15,16}\) have revealed that sinus bradycardia was not registered in any of the patients immediately prior to PVF.

A recent experimental study\(^\text{15}\) demonstrated that apart from slowing heart rate vagal stimulation per se increased VF threshold. Although we do not know whether ventricular fibrillation threshold as studied in animals has any relevance to the clinical situation, our data in man suggest that patients with complete atrioventricular block may differ from those with sinus bradycardia at equivalent heart rates as far as their susceptibility to developing PVF is concerned. In atrioventricular block vagal activity may play a less important role or may be counterbalanced by an increase in sympathetic drive so that patients with atrioventricular block may be more susceptible to PVF than patients with sinus bradycardia.

QRS Configuration of VEB Initiating PVF

It has been reported\(^\text{19}\) that there is a highly significant difference in QRS configuration between VEBs occurring in coronary artery disease and those in normal hearts. Patients with coronary artery disease tended to have VEBs with a right bundle branch block configuration suggesting a left ventricular origin. In contrast VEBs in normal hearts tended to have a left bundle branch block configuration. This was compatible with a right ventricular origin and was considered to have no clinical significance.

Our present and previous\(^\text{20}\) observations do not find this to be valid in the setting of acute myocardial infarction, since both PVF and ventricular tachycardia were initiated as frequently by a VEB with left bundle branch block morphology as they were by right bundle branch block.

Coupling Interval of VEB Initiating PVF and Pattern of Initiation of PVF

The classical initiation of PVF by a close coupled VEB was an instance of the R on T phenomenon\(^\text{21}\) and traditionally would be explained by invoking considerations of a vulnerable period and disparity in recovery times.\(^\text{22}\) In 11 of our patients, late coupled VEBs (QR'/Q-T \(\geq 0.85\)) initiated runs of VEBs or ventricular tachycardias that ended in PVF. Recent experimental work\(^\text{12,23}\) also has shown that ventricular tachycardia and VF can be repeatedly initiated by late coupled VEBs. Evidence is mounting that slow fragmented activation of ischemic myocardium is a major determinant of malignant ventricular arrhythmias.\(^\text{12,23-26}\) Williams et al.\(^\text{25}\) observed that runs of VEBs that end in VF are associated with increasing delays in activation in certain ischemic regions, whereas runs that do not end in VF have decreasing delays in activation. In addition they observed that the coupling interval of VEBs and the onset of ventricular tachycardia are related not only to delayed activation but also to delay in exit of activation from ischemic regions.

Figure 3 illustrates initiation of PVF associated with a diminishing ectopic coupling interval. Such instances should perhaps be regarded in the light of recent experimental work as examples of a critical degree of delay in activation being associated with maximal fragmentation of activation. According to prevailing conditions this may occur at close coupled or late coupled ectopic intervals.

In four of our patients PVF was initiated by a run of VEBs which was identical to earlier runs that did not end in PVF. This sequence of events could be explained by the experimental studies of Waldo and Kaiser,\(^\text{28}\) in which the duration of localized fibrillation determined the onset of either VEBs or VF. These authors observed that continuous electrical activity or
localized fibrillation may occur within infarcted myocardium. When this continuous electrical activity persisted beyond the T wave of the preceding beat, it was always associated with VEBs. Sustained episodes of continuous electrical activity or localized fibrillation did provoke ventricular tachycardia or ventricular fibrillation. In the latter situation continuous electrical activity was first recorded from one or more electrodes within the area of infarct, then spread to all electrodes within the infarcted region before involving the non-infarcted myocardium.

From the experimental studies mentioned above it can be concluded that in ischemic myocardium factors other than a vulnerable period may also be responsible for initiation of VF. Our data in man indicate that the malignancy of a VEB is not only related to its coupling interval. This suggests that the same factors responsible for initiation of VF in the experimental situation may account for the malignancy of certain VEBs in man.

References
Observations on patients with primary ventricular fibrillation complicating acute myocardial infarction.
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