

# Recurrence of Ventricular Fibrillation in Acute Ischemic Heart Disease

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**SUMMARY** We assessed factors during an initial episode of ventricular fibrillation that may be predictive of recurrence. Of 141 consecutive patients with acute ischemic heart disease who survived an initial episode of ventricular fibrillation, 41 (29%) had recurrent ventricular fibrillation during hospitalization. The incidence of recurrent ventricular fibrillation was lower among those with an acute myocardial infarction than among those with an acute ischemic episode. Recurrent ventricular fibrillation occurred more frequently among patients with secondary ventricular fibrillation complicating an acute myocardial infarction than among those with primary ventricular fibrillation. Primary ventricular fibrillation that occurred within 2 hours of the onset of symptoms was no more likely to be recurrent than when it occurred later. Age, sex, site of infarction, place of arrest, adequacy of initial resuscitation, interval onset of symptoms to the initial episode of ventricular fibrillation, onset of symptoms to intensive care and delay before initial attempted defibrillation were not significantly related to the recurrence of ventricular fibrillation.

VENTRICULAR FIBRILLATION is the major cause of death within the early hours of the acute heart attack.<sup>1, 2</sup> The major objective in both out-of-hospital and in-hospital coronary care is the prevention and treatment of ventricular fibrillation. Although successful correction of ventricular fibrillation both outside and inside the hospital has been reported,<sup>1-3</sup> little information is available on its recurrence during hospitalization. This study was designed to assess factors present at the initial episode of ventricular fibrillation that suggest that recurrence may be likely during hospitalization.

## Patients and Methods

A retrospective study was made of 270 consecutive patients with ventricular fibrillation who were managed during 1973-1974. Ventricular fibrillation was determined at the time of the arrest by the continuous recording of the ECG in 265 patients and by observation of a monitoring oscilloscope in five patients. Two patients had ventricular fibrillation on each of two admissions to hospital at 4 months and 10 months, respectively, after the first arrest, and were counted as four patients. Of the 154 survivors of the initial arrest, four were excluded from analysis because insufficient details were available.

In 121 of the 150 survivors, ventricular fibrillation complicated an acute myocardial infarction. The diagnosis of myocardial infarction was made when at least two of the following were present: typical chest pain, clinically significant rise in cardiac enzymes (CPK > 210 IU/l; LDH > 600 IU/l; AST > 80 IU/l [upper limits of normal 140, 270 and 40 IU/l, respectively]), or characteristic evolving ECG changes. Myocardial infarction was also diagnosed at autopsy. In 20 patients, ventricular fibrillation complicated an

acute ischemic episode. An acute ischemic episode was defined as prolonged chest pain at rest due to acute myocardial ischemia without evidence of infarction. In nine patients other etiologies were present, e.g., electrolyte disturbance, digoxin toxicity, or malfunctioning permanent pacemaker.

This investigation deals with the 141 patients in whom the initial episode of ventricular fibrillation complicated acute myocardial infarction or an acute ischemic episode.

The initial arrest occurred outside the hospital in 36 patients, in the accident and emergency department in 16, the coronary care unit in 62, and elsewhere in the hospital in 27. From the clinical records, we assessed the adequacy of initial resuscitation, the interval from the onset of symptoms (usually chest pain or sudden collapse) to the first episode of ventricular fibrillation, onset of symptoms to intensive care (arrival of the mobile coronary/coronary care team), and the delay before the initial attempted defibrillation.

One hundred five patients were male (mean age 59 years) and 36 were female (mean age 61 years). Of the 121 patients with acute myocardial infarction, 61 had had an anterior infarction, 40 an inferior infarction, seven a subendocardial infarction, and 13 either anterior and inferior infarction, lateral infarction or bundle branch block. Hemodynamic disturbance was recorded when the patient was first seen, when there was clinical evidence of significant left ventricular failure (dyspnea at rest with third heart sound at apex and extensive bilateral fine crepitations in the lung fields) or cardiogenic shock (systolic blood pressure  $\leq$  80 mm Hg in the presence of cold, clammy, sweating and cyanosed extremities). No patient with hemodynamic disturbances had transient hypotension. When ventricular fibrillation was the presenting feature, the assessment was made within 24 hours of resuscitation. The initial episode of ventricular fibrillation in 31 patients was secondary ventricular fibrillation, i.e., ventricular fibrillation in the presence of cardiogenic shock (six patients) or significant left heart failure (25 patients). Among patients in whom the initial episode was primary ventricular fibrillation, in all but one patient the initial recurrence was also

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primary ventricular fibrillation. In those with an initial episode of secondary ventricular fibrillation, the initial recurrence was associated with shock or significant left-heart failure in all but two patients. At the time of recurrence of ventricular fibrillation, all patients were under our care. If the recurrence took place within 4 days of the initial arrest, when the patient was in the coronary care unit, then, with frequent observation of the blood pressure and the hemodynamics, clinical reassessment was performed within a very short time of the recurrence of ventricular fibrillation. If ventricular fibrillation recurred many days after the initial event, such close observation was not possible in the intermediate coronary care unit.

Recurrent ventricular fibrillation is defined as the recurrence of this dysrhythmia half an hour or more after its correction and restoration of a satisfactory circulation. The number of DC shocks (unsynchronized, 200 or 400 J) used in each episode of cardiac arrest was also noted. No patient had a further immediate infarction either before the initial episode or at the time of recurrence of ventricular fibrillation. Two patients had further pain approximately 1 hour before the recurrence of ventricular fibrillation, but showed no electrocardiographic evidence of further infarction. Neither patient had evidence of heart failure or shock at that time.

The management of ventricular fibrillation has been documented previously.<sup>1</sup> After successful resuscitation, the care of all patients was continued in the cardiac department. Intravenous antiarrhythmic agents were continued for 12–24 hours from the time of the initial arrest. Oral antiarrhythmic therapy was started or i.v. infusions were recommenced if there was evidence of ventricular irritability. The period of hospitalization ranged from 1–73 days (mean 23 days). Among patients with an acute ischemic episode, the hospital mortality rate was 30% (six of 20); among those with a myocardial infarction in whom the initial episode was primary ventricular fibrillation, it was 22% (21 of 94); and among patients with secondary ventricular fibrillation at the initial episode complicating an acute myocardial infarction, it was 85% (23 of 27). Ninety-one patients survived the hospitalization.

Statistical analyses were performed with a chi-square test; when cell expectation fell below 5, Yates' correction was applied.

### Results

Of the 141 patients, 41 (29%) had recurrent ventricular fibrillation (table 1). Thirty-one (26%) of the 121 patients with acute myocardial infarction had recurrent ventricular fibrillation, and of the 20 patients with an acute ischemic episode, 10 (50%) had recurrent ventricular fibrillation. Recurrence among those with an acute ischemic episode was significantly greater than among those with an acute myocardial infarction ( $p < 0.05$ ) (table 1). Of the 94 patients with primary ventricular fibrillation complicating an acute myocardial infarction, 19 (20%) had recurrent ven-

TABLE 1. *Recurrence of Ventricular Fibrillation, Primary and Secondary Ventricular Fibrillation Complicating Acute Myocardial Infarction or an Acute Ischemic Episode*

	No. of pts	RVF
Total	141	41 (29%)
MI	121	31 (26%)*
PVF	94	19 (20%)*
SVF	27	12 (44%)*
AIE	20	10 (50%)*
PVF	16	8 (50%)
SVF	4	2 (50%)

\* $p < 0.05$ .

Abbreviations: MI = myocardial infarction; PVF = primary ventricular fibrillation; SVF = secondary ventricular fibrillation; AIE = acute ischemic episode; RVF = recurrent ventricular fibrillation.

tricular fibrillation; of the 27 with secondary ventricular fibrillation, 12 (44%) had recurrent ventricular fibrillation (table 1). Recurrence among those with secondary ventricular fibrillation complicating an acute myocardial infarction was significantly more frequent than among those with primary ventricular fibrillation ( $p < 0.05$ ) (table 1). Patients with primary or secondary ventricular fibrillation complicating an acute ischemic episode, had a similarly high incidence of recurrence (50%) (table 1).

Nonsignificant factors in the recurrence of ventricular fibrillation were age, sex, site of infarction, adequacy of initial resuscitation, place of arrest, interval between onset of symptoms to initial ventricular fibrillation (table 2), onset of symptoms to intensive care (table 3), and delay before initial attempted defibrillation (table 4).

Twenty patients were receiving antiarrhythmic drugs at the time of recurrence of ventricular fibrillation. Six were on a lidocaine infusion, 2 mg/min; eight had a Mexiletine infusion and six were taking Kinidin (quinidine) durules, 500 mg orally twice daily. Nineteen were not taking antiarrhythmic agents, nine because ventricular fibrillation was secondary to hypotension or left-heart failure and eight because there was a long interval between the initial episode of ventricular fibrillation and its recurrence. In two patients, the status of antiarrhythmic therapy was unknown at the time of the recurrence.

Of the 141 patients, the initial episode in 110 was primary ventricular fibrillation. The time from the onset of symptoms to the initial episode is shown in

TABLE 2. *Recurrence of Ventricular Fibrillation and Onset of Symptoms to Initial Episode of Ventricular Fibrillation*

Onset to VF (hours)	No. of pts	RVF
< 1	32	7
1–6	47	10
> 6	62	24

Abbreviations: VF = ventricular fibrillation; RVF = recurrent ventricular fibrillation.

TABLE 3. *Recurrence of Ventricular Fibrillation and Interval Onset of Symptoms to Intensive Care*

Onset to intensive care (hours)	No. of pts	RVF
0-3	94	22
>3-6	17	5
>6	30	14

Abbreviation: RVF = recurrent ventricular fibrillation.

figure 1. Fifteen patients collapsed in ventricular fibrillation. Twenty-seven of the 110 (25%) had a recurrence (table 5). The first recurrence occurred 38 minutes to 17 days (mean, 4 days) from the initial episode of ventricular fibrillation.

In 73 of the 110, primary ventricular fibrillation occurred within 12 hours of the onset of symptoms (fig. 1). Direct-current shocks and thump versions required for the correction of ventricular fibrillation at the time of the initial arrest are shown in figure 2. One to 12 shocks (mean, two shocks) were required. Three patients had 10 or more shocks. Thirty-six of the 73 had a single arrest with a single episode of ventricular fibrillation. Twenty-six had a single arrest with two to 10 episodes (mean, three episodes) of ventricular fibrillation. Eleven patients had several arrests: from two to three arrests (mean, two arrests) with two to seven episodes (mean, two episodes) of ventricular fibrillation for each arrest.

In 41 of the 110 patients, primary ventricular fibrillation occurred within the first 2 hours after the onset of symptoms (table 5). One to six episodes (mean, two episodes) of ventricular fibrillation occurred during this initial arrest. In six of the 41 (15%), ventricular fibrillation was recurrent. The first recurrence occurred 40 minutes to 6 days (mean, 2 days) after the initial arrest. In 69 of the 110, primary ventricular fibrillation occurred more than 2 hours after the onset of symptoms. In 21 (30%), ventricular fibrillation was recurrent. The recurrence among those with primary ventricular fibrillation less than 2 hours after the onset of symptoms and among those with a later episode was not statistically significantly different (table 5).

### Discussion

Lie et al.<sup>4</sup> reported that of 400 consecutive patients with acute myocardial infarction, 18 developed pri-

TABLE 4. *Recurrence of Ventricular Fibrillation and Delay Before Initial Attempted Defibrillation*

Initial VF to DC shock (min)	No. of pts	RVF
<1	55	17
1-2	25	6
>2-4	38	12
>4	23*	6

\*Twelve patients were in VF for 10-36 minutes.

Abbreviation: VF = ventricular fibrillation; RVF = recurrent VF.

TABLE 5. *Primary Ventricular Fibrillation and Recurrence*

VF (hours)	No. of pts	RVF
<2	41	6 (15%)*
>2	69	21 (30%)*
Total	110	27 (25%)

\* $p > 0.05$ .

Abbreviations: RVF = recurrent ventricular fibrillation.

mary ventricular fibrillation in hospital. Twelve of the 18 had recurrent attacks of ventricular fibrillation during hospitalization. Lie and Durrer<sup>5</sup> reported 30 patients with primary ventricular fibrillation complicating acute myocardial infarction. Eight (27%) of the 30 had recurrent attacks of primary ventricular fibrillation during hospitalization. All were refractory to antiarrhythmic intervention and to cardiac pacing. El-Sherif et al.<sup>6</sup> reported that of 450 consecutive patients with acute myocardial infarction, 20 developed primary ventricular fibrillation during hospitalization. Six of the 20 (30%) had recurrent episodes during this period. These data compare favorably with our results: Of 94 patients with primary ventricular fibrillation complicating an acute myocardial infarction, 19 (20%) had recurrent ventricular fibrillation.

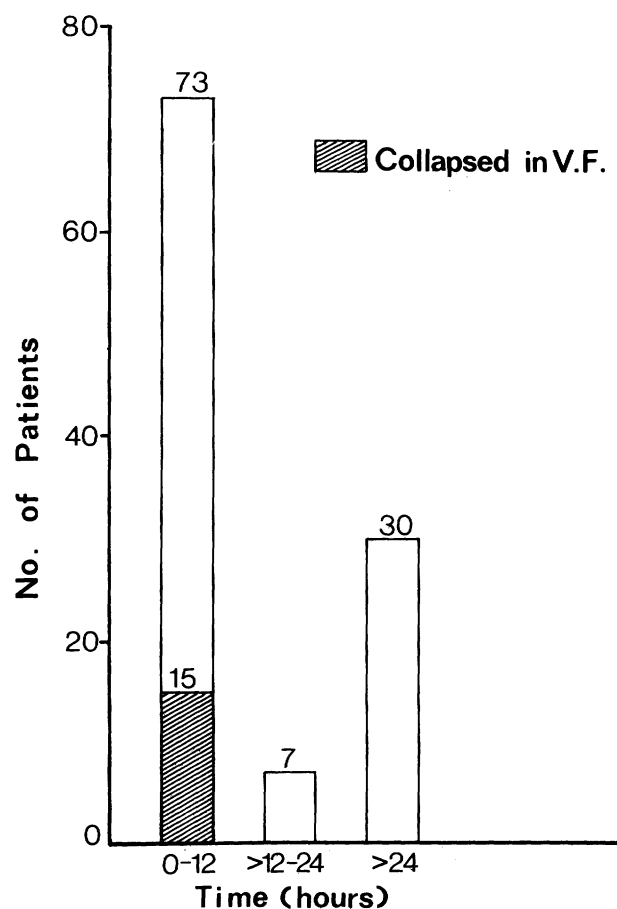


FIGURE 1. Interval between onset of symptoms and initial primary ventricular fibrillation (VF) in 110 patients with an acute myocardial infarction or an acute ischemic episode.



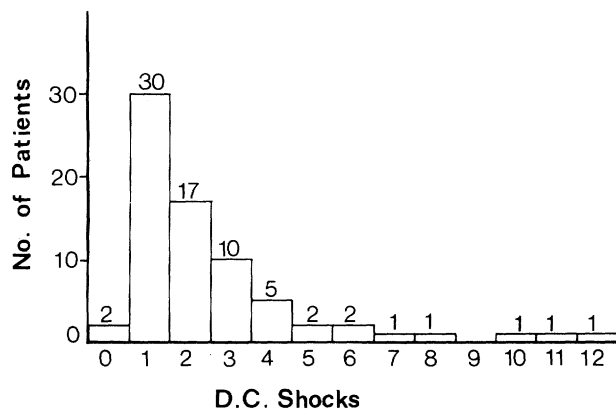


FIGURE 2. Seventy-three patients with primary ventricular fibrillation within 12 hours of the onset of symptoms. 0 = thump version.

Among patients resuscitated from ventricular fibrillation outside the hospital and discharged home, the incidence of recurrent out-of-hospital ventricular fibrillation is significantly greater when the initial episode of ventricular fibrillation complicates ischemic heart disease rather than acute myocardial infarction.<sup>7, 8</sup> Our findings indicate that during hospitalization, the incidence of recurrent ventricular fibrillation among those with an acute ischemic episode is almost twice that of patients who have had an acute myocardial infarction. This increased risk of recurrence among those with an acute ischemic episode may reflect continuing myocardial electrical instability. Haynes et al.<sup>9</sup> compared the 12-lead ECGs of survivors from out-of-hospital ventricular fibrillation complicating ischemic heart disease with those from patients who were ambulatory and had had a myocardial infarction without ventricular fibrillation. They found that survivors of out-of-hospital ventricular fibrillation had a higher incidence of ventricular ectopic beats, greater prevalence of ST-segment depression, T-wave flattening and QTc prolongation. These differences between the two groups were independent of drug therapy.

When ventricular fibrillation complicates hypotension or heart failure, it is likely to be recurrent. In this study, among those with an initial episode of secondary ventricular fibrillation complicating acute myocardial infarction, the recurrence rate was twice that of those with primary ventricular fibrillation. Weaver et al.<sup>10</sup> found that a history of congestive heart failure was common in patients with out-of-hospital recurrent ventricular fibrillation and sudden death. They also found that patients with recurrent ventricular fibrillation and sudden death had more three-vessel coronary artery disease, lower ejection fractions and more severe abnormalities of left ventricular contraction compared with those who had a single episode of ventricular fibrillation and survived follow-up.

Age, sex, site of infarction, adequacy of initial resuscitation, place of arrest, interval onset of symptoms to initial ventricular fibrillation, onset of symp-

toms to intensive care, and delay before attempted defibrillation were of no significance in the recurrence of ventricular fibrillation. Of the 41 patients with recurrent ventricular fibrillation, 19 were not receiving antiarrhythmic therapy at the time of recurrence of ventricular fibrillation. The major reasons were the presence of hypotension or heart failure or the delay between the initial episode and its recurrence.

Lie et al.<sup>4</sup> and Lie and Durrer<sup>5</sup> reported that in patients with recurrent primary ventricular fibrillation, no recurrence took place 12 hours or more after the onset of infarction. Their observations suggested that in patients with recurrent primary ventricular fibrillation, electrophysiologic changes that cause recurrent primary ventricular fibrillation disappear after myocardial infarction has reached a certain age. However, our results show that of eight patients with recurrent primary ventricular fibrillation within 12 hours of the onset of infarction, six had a recurrence more than 12 hours after the onset of symptoms. None of these six had a further infarction before the recurrence.

Meltzer and Cohen<sup>11</sup> reported that approximately 30% of all episodes of primary ventricular fibrillation occur after 24 hours from onset of infarction. Lie and Durrer<sup>5</sup> and Lie et al.<sup>12</sup> found that among patients who developed their first episode of primary ventricular fibrillation more than 24 hours after infarction, almost all had another infarct within 1-6 hours before the onset of the ventricular fibrillation. They suggested that primary ventricular fibrillation of late onset may be secondary to a recurrent infarction or to an extension of infarction occurring shortly before the onset of primary ventricular fibrillation. In this study, 23 had primary ventricular fibrillation more than 24 hours after the onset of an acute myocardial infarction. In none did a reinfarction precede this initial episode of late ventricular fibrillation. Nine of the 23 had a recurrence. The time of the recurrence varied from 7-49 days (mean 20 days) from onset of symptoms.

Our findings indicate that early primary ventricular fibrillation was no more likely to be recurrent than that occurring later (table 5). In 41 patients with primary ventricular fibrillation within 2 hours of an acute myocardial infarction or an acute ischemic episode, six (15%) had recurrent ventricular fibrillation and of 69 similar patients with ventricular fibrillation later, 21 (30%) had recurrent ventricular fibrillation.

Of the 73 patients in this study with primary ventricular fibrillation within 12 hours of the onset of symptoms, 36 had a single arrest and a single episode of ventricular fibrillation. Twenty-six had a single arrest with several episodes of ventricular fibrillation and 11 had several arrests with several episodes. At the initial arrest in these 73 patients, an average of two shocks was required to correct ventricular fibrillation, although three patients required 10 or more shocks. Perhaps these factors should be considered in the development of defibrillators; portable defibrillators do not have an unlimited power supply.

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## Etiology, Warning Signs and Therapy of Torsade de Pointes

### A Study of 10 Patients

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**SUMMARY** Torsade de pointes, also called atypical ventricular tachycardia (AVT), was diagnosed in 10 patients, nine on antiarrhythmic therapy and one with acute central nervous system damage. Four patients received quinidine and five disopyramide, either alone or in combination with amiodarone. AVT was dose-dependent in some, but in others, it started shortly after initiation of drug therapy (idiosyncrasy). All patients had QT prolongation longer than 0.60 second immediately before the onset of AVT. This measurement appeared to be a more sensitive predictor of the development of AVT than QTc prolongation or QRS widening. All patients also showed bradycardia before AVT onset. After therapy, the QT immediately decreased, while QTc and QRS remained prolonged for longer periods. Isoproterenol was effective in five of seven patients, but was contraindicated in two others. Ventricular pacing was used in four patients, including the two who did not respond to isoproterenol, and this abolished AVT promptly. Isoproterenol or pacing appear to be the therapy of choice for AVT, while the conventional drugs used to treat the usual form of ventricular tachycardia are not only ineffective, but even contraindicated.

QUINIDINE SYNCOPE due to paroxysmal ventricular fibrillation was first described by Selzer and Wray in 1964,<sup>1</sup> but the distinctive features of this life-threatening arrhythmia were characterized somewhat later by Dessertenne<sup>2</sup> and other French authors.<sup>3-7</sup> The name "torsade de pointes" seems to describe satisfactorily the unique trait of changing QRS axis during

the episodes of this arrhythmia, but in the English-language literature, atypical ventricular tachycardia (AVT) is becoming an accepted name. AVT was found to be induced mainly by quinidine<sup>1, 8-13</sup> and by other antiarrhythmic and cardiac drugs such as procainamide,<sup>11, 14</sup> disopyramide,<sup>15, 16</sup> lidocaine<sup>11</sup> and prenylamine.<sup>11</sup> Occasionally, other drugs such as phenothiazines,<sup>17</sup> as well as hypokalemia,<sup>4, 7</sup> hypomagnesemia,<sup>4, 18</sup> electrical ventricular stimulation,<sup>19</sup> congenital QT prolongation syndrome,<sup>20</sup> or acute central nervous system damage<sup>21</sup> may precipitate AVT. The accepted warning sign for an impending AVT is a widening of the QRS complex<sup>22-25</sup> which, if drug-induced, mandates interruption of therapy.

We describe 10 patients who developed AVT within

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