Nonsustained Ventricular Tachycardia in the Setting of Acute Myocardial Infarction
Tachycardia Characteristics and Their Prognostic Implications
Asim N. Cheema, MD; Kathleen Sheu, MD; Michele Parker, MS; Alan H. Kadish, MD; Jeffrey J. Goldberger, MD

Background—Nonsustained ventricular tachycardia (NSVT) has significant prognostic implications in the setting of healing and healed myocardial infarction (MI), but only limited information is available on its importance in the setting of acute MI. We evaluated the prognostic significance of NSVT characteristics in the setting of acute MI.

Methods and Results—A prospective database was used to identify 112 patients with NSVT within 72 hours of acute MI. A control group was identified matched for age, sex, type of MI, and thrombolytic treatment. Mean age was 64 to 65 years in the 2 groups with 71% to 72% men. Q-wave MI was noted in 52% to 53%, and thrombolytic therapy was administered to 31% to 32% of patients in each group. In-hospital ventricular fibrillation occurred more frequently in the NSVT group (9% versus 0% in the control group; \( P < 0.001 \)), but total in-hospital (10% versus 4%) and follow-up mortality (10% versus 17%) did not differ between the 2 groups. With a Cox regression model, specific NSVT characteristics were predictive of mortality. The strongest predictor was time from presentation to occurrence of NSVT. Shortest RR interval during NSVT was also a univariate predictor of mortality. Multivariate analysis identified time from presentation to occurrence of NSVT as the strongest predictor of mortality (\( P = 0.0001 \)). The increased relative risk of NSVT was first significant when it occurred 13 hours from presentation and continued to increase as the time from presentation to occurrence of NSVT increased, plateauing at \( \approx 24 \) hours with a relative risk of 7.5.

Conclusions—Contrary to prevailing clinical opinion, NSVT that occurs in the setting of acute MI does have important prognostic significance. Specifically, the currently accepted notion that NSVT that occurs within 48 hours of acute MI has no prognostic significance needs to be adjusted. Although NSVT that occurs within the first several hours of presentation does not have an associated adverse prognosis, NSVT that occurs beyond the first several hours after presentation is associated with significant increases in relative risk. (Circulation. 1998;98:2030-2036.)

Key Words: myocardial infarction ■ tachycardia ■ risk factors ■ prognosis

During acute myocardial infarction (MI), a variety of ventricular arrhythmias may be observed, including premature ventricular complexes, nonsustained ventricular tachycardia (NSVT), sustained ventricular tachycardia, and ventricular fibrillation. Premature ventricular complexes are seen in the majority of cases of acute MI and do not appear to adversely affect short-term prognosis.\(^1\)\(^2\) The incidence of sustained monomorphic ventricular tachycardia within 48 hours of acute MI is reported as 0.3% to 1.9%.\(^3\)\(^4\) Its presence may be a sign of extensive myocardial damage and may serve as an independent predictor of mortality.\(^4\) Polymorphic ventricular tachycardia is also an uncommon arrhythmia in acute MI, occurring in 0.3% to 2% of patients.\(^3\)\(^5\) This arrhythmia may be a marker of ongoing myocardial ischemia and can be effectively managed by anti-ischemic interventions.\(^5\) Ventricular fibrillation has been reported somewhat more commonly during acute MI in \( \approx 3 \)% of cases,\(^6\) with a peak incidence within the first 4 hours.\(^7\) Although there is evidence of increased in-hospital mortality related to the occurrence of ventricular fibrillation in acute MI,\(^8\)\(^9\) most studies show that long-term prognosis is not affected.\(^8\)\(^9\)

The incidence of nonsustained (monomorphic) ventricular tachycardia in the setting of acute MI has generally been reported to be in a similar range, from 1% to 7%.\(^3\)\(^7\)\(^11\) but has been reported to be as high as 75%.\(^12\) Very limited data are available regarding the prognostic significance of NSVT in acute MI. Eldar et al\(^1\) noted no adverse effect on either in-hospital or 1-year survival of primary NSVT in 49 patients. This limited information suggests that the prognostic significance of NSVT in acute MI is more similar to the presence of premature ventricular complexes than to the occurrence of sustained ventricular tachycardia. In contrast to the acute MI setting, NSVT that occurs in the setting of a healing MI does have an adverse prognosis.\(^13\)\(^15\) We therefore hypothesized...
that NSVT in the setting of acute MI may have prognostic implications, particularly when its rate, duration, timing, and the presence of a healed, previous MI are taken into consideration.

Methods

Patient Population

From July 1990 to February 1993, a prospective database was kept of all patients who presented with acute MI to Northwestern Memorial Hospital in Chicago, Ill (~900 patients). Patients with acute MI underwent continuous ECG monitoring throughout their stay in the coronary care unit (typically 3 days during the study period). The monitoring system in the coronary care unit (Marquette series 7010) detects arrhythmias automatically and is generally set to trigger detection for rates >100 to 120 bpm. The presence of NSVT within 72 hours of presentation was monitored, and a separate log was kept of these patients. NSVT was defined as ≥3 consecutive ventricular complexes at a mean rate >120 bpm so that accelerated idioventricular rhythms were excluded. To evaluate the prognostic significance of NSVT in this group of patients, a case-control methodology was used. For each case (NSVT) patient, a control patient was selected from the database matched for age, sex, type of infarction (anterior Q wave, inferior Q wave, or non-Q wave), and treatment with thrombolytics. One hundred twenty-eight patients with acute MI and NSVT were identified. While attempting to identify matched control patients, we identified an additional 12 patients with NSVT; these patients were also included in the case group. Appropriate matches could not be identified for 28 patients in the NSVT group. Twenty-seven of these cases were patients with Q-wave MIs who had received thrombolytic therapy. The excluded patients did not otherwise differ from the study group in any of the clinical characteristics or mortality, except for a slightly lower mean age (58.9 ± 12.5 vs 64.6 ± 12.7 years; P < 0.04). Thus, only 112 patients were included in the case-control analysis in each group. Charts of all NSVT patients and control subjects were reviewed for retrieval of clinical data. MI was confirmed in all patients by elevation of cardiac enzymes (creatine phosphokinase [CPK] and CPK-MB fraction). Patients presenting with sustained ventricular tachycardia as the initial arrhythmia were excluded from the study.

Data Collection

Baseline patient characteristics recorded in all subjects were presence or absence of hypertension, diabetes mellitus, hypercholesterolemia, angina pectoris, prior MI, prior coronary angioplasty, and prior CABG surgery. Ejection fractions were determined from technically adequate echocardiographic studies, gated blood pool scans, or left ventriculograms, which were available in 59 pairs of patients (the index case and the matched control). A history of prior MI was confirmed by either previous ECG or cardiac enzyme documentation, previously identified wall motion abnormalities, or the presence of a wall motion abnormality in a noninfarct-related artery vascular territory on an imaging study obtained after the index MI. Follow-up information was obtained from the patient’s primary physician, review of hospital and clinic records, or personal interview of the patient by telephone. Follow-up data were available for all but 1 patient for a mean duration of 34 months.

Tracings of NSVT were routinely kept in the patient’s hospital record. Each episode of NSVT was characterized according to the number of beats, time period from presentation to the emergency room to the occurrence of NSVT, the mean RR interval, and the shortest RR interval in each episode. In case an individual patient had >1 episode of NSVT, the longest and fastest episodes of NSVT were identified and characterized. The presence of congestive heart failure (CHF) or electrolyte imbalance (hypokalemia or hypomagnesemia) at the time of the arrhythmia was identified. Administration of antiarrhythmic agents before NSVT and any antiarrhythmic intervention related to the presence of NSVT were also noted.

Statistical Analysis

Data for the 112 case-control pairs were compared by use of a paired t test for continuous data or the McNemar test for categorical data. A case-control paired analysis was done for comparison of postdischarge events. Ninety-five pairs were available for comparison of postdischarge events. A total of 16 pairs were excluded because 1 of the members had experienced in-hospital death. One additional pair was excluded because no discharge follow-up was available for 1 member. All comparisons were 2-sided, and P < 0.05 was regarded as statistically significant.

Because several studies have suggested that classification of the mechanism of death may be inaccurate,14,15 the primary end point of the present study was total mortality. To determine the prognostic significance of NSVT, life table analysis with the product-limit method was used to estimate rates of freedom from death. Comparisons between the case and control groups, the case subgroups, and the case subgroups and control group were made by use of the Cox-Mantel statistic. The effect of clinical and NSVT characteristics on time to death was initially assessed by univariate Cox regression analysis. Variables with a significance level < 0.2 were considered for inclusion in a multivariate Cox regression model. Only variables with a significance level < 0.05 were retained in the final models.

Results

Baseline Characteristics

Baseline patient characteristics are shown in Table 1. A history of diabetes mellitus was more common in the control group (P < 0.01). Intravenous lidocaine was administered in 30% of patients in the case group (1 patient had received intravenous procainamide) before the detection of NSVT and 17% of patients in the control group (P < 0.02). The incidence of resuscitated cardiac arrest (ventricular fibrillation) during hospitalization was significantly higher in the NSVT group than in the control group (9% versus 0%; P < 0.001). At discharge, 5% of the case group and 2% of the controls were treated with antiarrhythmic agents (P = NS), and 68% of patients in each group were treated with β-blockers.

Among the 112 patients in the NSVT group, 54 (48%) had multiple episodes of NSVT during the first 72 hours of presentation. Twenty-eight patients (25%) had clinical or radiographic signs of CHF at the time of occurrence of NSVT. Four patients (4%) were found to have hypokalemia, and 4 had hypomagnesemia at the time of tachycardia. Lidocaine and procainamide were administered because of the arrhythmia in 78 (70%) and 7 (6%) patients, respectively.

Figure 1 shows the Kaplan-Meier survival curves for the NSVT and control groups. In-hospital mortality for the NSVT group was 10% versus 4% for the control group (P = NS). There were no significant differences in sudden death or cardiac mortality. Total mortality during the follow-up period also did not differ (10% for the NSVT group versus 17% for the control group).

Effect of NSVT Characteristics and Prior MI on Mortality

The effect of NSVT characteristics on mortality was evaluated only in the case group. Table 2 shows the NSVT characteristics for the patients who died and for survivors. The time from presentation to occurrence of NSVT was significantly longer in those who died versus those who survived (P < 0.002 and P < 0.01 for the fastest and longest episodes, respectively). There were no significant differences
between those who died and survivors in the number of NSVT beats or in the mean RR interval (for either the fastest or longest episode of NSVT). However, the shortest RR interval during NSVT was significantly shorter in the patients who died than in the survivors (for both the fastest and longest episodes of NSVT).

There were 41 case patients with NSVT and prior MI and 30 control patients with prior MI. Baseline clinical characteristics, in-hospital events, and postdischarge events for these subgroups did not differ. Total mortality for the case group with prior MI was 32%; for the control group with prior MI, it was 17% (P<0.15). Among the case group only, 62% of patients who died had NSVT and prior MI versus 31% of those who survived (P<0.01).

### Predictors of Mortality

Univariate predictors of all-cause mortality for the 2 groups combined and for the NSVT group are shown in Table 3.
β-Blocker usage at hospital discharge was also a significant ($P<0.0001$) predictor of survival. However, many of the patients who died did so in the hospital; when β-blocker usage was evaluated in only the subgroup of patients who were discharged, a trend remained for β-blockers to be predictive of survival ($P<0.13$). β-Blocker use was not further incorporated into the multivariate analysis. In a multivariate analysis, age ($P=0.001$), history of angina ($P=0.004$), revascularization during the hospitalization ($P=0.01$), and history of hypercholesterolemia ($P=0.03$) were independent predictors of all-cause mortality.

In a multivariate analysis for the NSVT group, time from presentation to the occurrence of NSVT ($P<0.0001$), CHF in association with NSVT ($P<0.006$), and history of hypercholesterolemia ($P<0.04$) were independent predictors of subsequent mortality. The relative risk increases 5.5% for every hour increment in time from presentation to NSVT (relative risk ratio, 1.055; 95% CIs, 1.030 to 1.080). Time from presentation to NSVT occurrence is an important predictor of mortality, even when the usual clinical variables are considered.

To more precisely define the effect of time from presentation on mortality, we used a Cox regression model to compare the relative mortality risk for different time cutoffs after presentation. As shown in Figure 2, the relative risk for increased mortality was first significant at a cutoff of 13 hours and progressively increased until it plateaued at $\approx 24$ hours. Figure 3 shows Kaplan-Meier survival curves for patients with NSVT that occurred within 24 hours of presentation versus those with NSVT that occurred beyond 24 hours, as well as the survival curve of the control group. There was no significant difference between the survival curve of the control group and that for patients with NSVT within 24 hours of presentation. However, the survival curve for patients with NSVT that occurred $>24$ hours after presentation significantly differed ($P<0.001$) from the survival curves for patients with NSVT within 24 hours of presentation and for the controls.

### Discussion

This study explored the prognostic significance of NSVT and NSVT characteristics in the setting of acute MI. These data were obtained in a group of patients who were eligible for thrombolytic therapy, which makes the results applicable to current approaches in acute MI. We found that NSVT in the setting of acute MI identifies patients at risk for in-hospital cardiac arrest. Importantly, contrary to prevailing clinical opinion, NSVT that occurs within 48 hours of acute MI does have important prognostic significance. Specifically, the 48-hour cutoff needs to be adjusted. NSVT that occurs within the first several hours of presentation does not have an associated adverse prognosis. However, NSVT that occurs beyond the first several hours after presentation is associated with substantial increases in relative risk. Finally, there does appear to be an interaction between NSVT and previous MI, with a resultant increase in mortality.

Our understanding of the mechanisms of ventricular arrhythmias that occur in the acute MI setting are based on animal models of acute infarction. Peri-infarct ventricular arrhythmias have been classified into several phases.18 Phase 1a arrhythmias occur from 2 to 10 minutes after occlusion. Although many potential mechanisms are possible to explain these arrhythmias, the pathophysiology is likely related to acute alterations in cellular electrophysiology due to ischemia. Phase 1b arrhythmias occur 10 to 30 minutes after acute coronary occlusion. During this time, many parameters of conduction and refractoriness have returned to near-normal values. Arrhythmias in this phase may be related to local accumulation of catecholamines. Given the time delay inherent in the arrival of patients at the emergency department after clinical coronary occlusions, it is unlikely that the arrhythmias observed in the present study are related to either of these mechanisms. A second or delayed phase of ventricular arrhythmias has been described to occur between 6 and 72 hours after coronary artery occlusion, with a peak incidence between 12 and 24 hours. Arrhythmias in this phase may be

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**TABLE 2. NSVT Characteristics and Total Mortality**

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>90</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Prior MI</td>
<td>28 (31%)</td>
<td>13 (62%)</td>
<td>$&lt;0.008$</td>
</tr>
<tr>
<td>Multiple NSVT runs</td>
<td>45 (50%)</td>
<td>13 (59%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

#### Fastest NSVT episode

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
<th>Median ± SD</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from presentation, h</td>
<td>13.2 ± 10.3</td>
<td>29.6 ± 21.4</td>
<td>$&lt;0.002$</td>
<td></td>
</tr>
<tr>
<td>Number of beats</td>
<td>6.4 ± 4.3</td>
<td>7.2 ± 4.4</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Mean RR interval, ms</td>
<td>429 ± 78</td>
<td>396 ± 64</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Shortest RR interval, ms</td>
<td>388 ± 67</td>
<td>352 ± 52</td>
<td>$&lt;0.01$</td>
<td></td>
</tr>
</tbody>
</table>

#### Longest NSVT episode

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
<th>Median ± SD</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from presentation, h</td>
<td>13.4 ± 10.0</td>
<td>25.1 ± 19.1</td>
<td>$&lt;0.01$</td>
<td></td>
</tr>
<tr>
<td>Number of beats</td>
<td>7.5 ± 5.0</td>
<td>7.8 ± 4.3</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Mean RR interval, ms</td>
<td>449 ± 84</td>
<td>419 ± 85</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Shortest RR interval, ms</td>
<td>400 ± 71</td>
<td>366 ± 65</td>
<td>$&lt;0.05$</td>
<td></td>
</tr>
</tbody>
</table>
due to abnormal automaticity within surviving Purkinje fibers, triggered activity arising from Purkinje fibers, or reentry involving either the Purkinje fibers or within the ischemic myocardium. Given the acute nature of the pathophysiological abnormalities responsible for these arrhythmias, one would expect that these arrhythmias would not have long-lasting prognostic importance.

Although animal models have provided substantial insights regarding ventricular arrhythmias associated with...
coronary occlusion, there are several clinical factors that may contribute to the importance of these arrhythmias in the human, clinical setting. First, NSVT in the setting of healing MI (7 to 10 days after MI) has been demonstrated to have negative prognostic implications.\textsuperscript{13–15} There are no data that pinpoint at what point after the acute infarction NSVT begins to have prognostic importance. Next, an important interaction between the presence of a previous MI and NSVT during an acute MI may be present; this may be especially important given the prognostic significance of NSVT in the setting of a healed MI.\textsuperscript{19} These issues prompted the current evaluation of the prognostic significance of NSVT in acute MI.

When analyzed as a dichotomous variable (ie, presence or absence), NSVT that occurred within 72 hours of acute MI was not found to have an adverse prognosis. This is consistent with the reports by Eldar et al\textsuperscript{11} and de Soyza et al.\textsuperscript{11} However, the present study suggests that a 48- to 72-hour cutoff is incorrect. Coincident with the peak incidence of phase 2 arrhythmias in animal models, there is a cutoff between 12 and 24 hours after coronary occlusion beyond which the occurrence of NSVT does have important prognostic implications. Thus, it is likely that in the early hours after coronary occlusion, NSVT is due to acute pathophysiological derangements such as those identified as underlying phase 2 arrhythmias in animal models. However, beyond several hours after presentation (in the present study, 13 hours), the proportion of these arrhythmias that are due to these acute changes declines and the presence of NSVT becomes more likely due to other mechanisms that are associated with a poor prognosis. Although the exact reason for the adverse prognosis of NSVT beyond this time is not known, it should be noted that most of the mortality in the present study was early mortality. Thus, NSVT that occurs beyond 13 hours may be a harbinger of persistent ischemia, left ventricular dysfunction, or electrophysiological instability. Additional studies are therefore warranted to understand the pathophysiology of ventricular arrhythmias that occur in this time period to understand whether specific interventions are warranted and may result in improvement in prognosis.

Limitations

Although a prospective log was kept of patients with NSVT during acute MI, review of the control patient charts did identify some patients with NSVT who were not listed in the NSVT log. This accounted for <10% of the cases. In addition, it is possible that some episodes of NSVT were missed by the monitors. Given the large number of patients studied and the use of case-control methodology, it is not likely that this would result in a systematic bias. The timing of NSVT that occurred in the setting of acute MI in the present study was based on the time of presentation to the emergency department. Although this does not truly represent the time from the onset of coronary occlusion, this could not be objectively assessed in all patients in the study. Given the large number of patients and the increased relative risk related to time from presentation over a wide range of time, this should not represent a significant bias.

Clinical Implications

Several recent management guidelines\textsuperscript{20–22} have discussed the management of ventricular arrhythmias that occur during acute MI. These reports note that arrhythmias that occur in the first 48 hours have no prognostic significance. In light of the current data, these guidelines should be reconsidered. Although the presence of NSVT that occurs within the first several hours of presentation should be considered to have no important prognostic significance, NSVT that occurs beyond the first several hours after presentation does have important implications, particularly for early mortality. These findings are particularly relevant because there are few data on the significance of NSVT that occurs within the first several days of an acute MI; most studies that have assessed the significance of NSVT after acute MI have evaluated the predischarge Holter monitor study performed ≥5 days after the MI. Additional studies are needed to evaluate the mechanisms responsible for the adverse prognosis associated with early NSVT and potential therapeutic approaches.

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References


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