Nonsustained Ventricular Tachycardia in Coronary Artery Disease

Relation to Inducible Sustained Ventricular Tachycardia

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Background: Many physicians believe that electrocardiographic characteristics of nonsustained ventricular tachycardia correlate with the risk for sudden death in survivors of myocardial infarction. Sustained ventricular tachycardia induced by programmed electrical stimulation has also been shown to predict sudden death.

*For a list of additional MUSTT investigators, see the Appendix.

Objective: To determine whether electrocardiographic characteristics of spontaneous nonsustained ventricular tachycardia can predict the inducibility of sustained ventricular tachycardia by programmed electrical stimulation in patients with coronary artery disease having abnormal ventricular function.

Design: Observational cohort study.

Setting: 70 clinical electrophysiology laboratories in the United States and Canada.

Patients: 1480 consecutive patients with coronary artery disease, left ventricular ejection fraction of 0.40 or less, and asymptomatic nonsustained ventricular tachycardia.

Intervention: Electrophysiologic study attempting to induce sustained monomorphic ventricular tachycardia.

Measurements: Daily frequency, duration, and cycle length of spontaneous episodes of nonsustained ventricular tachycardia, measured by standard electrocardiographic recordings.

Results: No statistically significant difference in the frequency or duration of spontaneous nonsustained ventricular tachycardia was seen between patients with and those without inducible sustained ventricular tachycardia. Rates of spontaneous tachycardia were slightly slower in patients with inducible ventricular tachycardia than in patients without inducible ventricular tachycardia (P equals 0.047), but the difference was not clinically significant.

Conclusion: Electrocardiographic characteristics of spontaneous nonsustained ventricular tachycardia do not predict which patients with coronary artery disease will have inducible sustained ventricular tachycardia.


Most sudden deaths in patients with previous myocardial infarction are initiated by ventricular tachycardia. Frequent and complex ventricular ectopy and nonsustained ventricular tachycardia have long been recognized as independent predictors of cardiac-related death after myocardial infarction [1-7]. The relation between ventricular arrhythmias and death has been shown in both the pre- and post-thrombolytic era [7]. Many physicians believe that patients with more frequent, longer, or faster episodes of nonsustained ventricular tachycardia have a higher risk for sudden death. However, earlier studies have not shown a relation between electrocardiographic...
characteristics of spontaneous nonsustained ventricular tachycardia episodes--such as rate, duration, or frequency--and the risk for sudden cardiac death in survivors of infarction [3,8].

Sustained ventricular tachycardia induced by programmed electrical stimulation has been shown to predict death--specifically sudden death--in myocardial infarction survivors who have reduced ventricular function and present with asymptomatic ventricular ectopy or nonsustained ventricular tachycardia [9-12]. We evaluated whether electrocardiographic characteristics of spontaneous nonsustained ventricular tachycardia could predict the inducibility of sustained ventricular tachycardia by programmed electrical stimulation in a large sample of patients with documented coronary artery disease, reduced ventricular function, and spontaneous asymptomatic nonsustained ventricular tachycardia.

Methods

Patients

We did an analysis of the first 1480 patients enrolled in the ongoing Multicenter Unsustained Tachycardia Trial (MUSTT), which is testing whether electrophysiologically guided anti-arrhythmic therapy can reduce the risk for sudden cardiac death in high-risk patients with coronary artery disease. The major criteria for trial entry are documented coronary artery disease, left ventricular ejection fraction of 0.40 or less, and asymptomatic spontaneous nonsustained ventricular tachycardia. The protocol is described elsewhere [13].

Nonsustained ventricular tachycardia is defined as three or more consecutive premature ventricular complexes that last no more than 30 seconds and terminate spontaneously. At least two consecutive cycles must last 550 milliseconds or less (equivalent to more than equals 110 beats/min), and the average rate of the entire episode must be more than 100 beats/min. The qualifying nonsustained ventricular tachycardia must have been documented within 6 months before entry into the trial. In addition, the qualifying tachycardia must have occurred at least 4 days after the most recent myocardial infarction, coronary bypass grafting, or percutaneous transluminal coronary angioplasty. The qualifying tachycardia must not have been attributable to transient metabolic abnormalities such as myocardial ischemia and must not have produced symptoms severe enough to warrant treatment. All patients have at least 18 hours of analyzable continuous electrocardiographic monitoring.

Electrophysiologic Studies

The protocol for programmed electrical stimulation, standardized at all participating centers, includes delivery of 1, 2, and 3 ventricular extrastimuli at two right ventricular sites at pacing cycle lengths of 600 and 400 milliseconds. In addition, bursts of 5 to 15 ventricular stimuli at cycle lengths of 350 to 250 milliseconds are delivered. The endpoint for the stimulation protocol is the reproducible induction of sustained ventricular tachycardia or fibrillation or completion of the protocol.

Data Abstraction

Patient data, including characteristics of the spontaneous nonsustained ventricular tachycardia, are reported to the data coordinating center. The electrocardiographic characteristics of nonsustained ventricular tachycardia episodes are assessed and reported by individual investigators. To assure that the qualifying nonsustained ventricular tachycardia meets the entry criteria, the recordings of every episode of qualifying nonsustained ventricular tachycardia are reviewed by executive committee members who are blinded to other patient characteristics.

For our study, accuracy of the nonsustained ventricular tachycardia characteristics recorded by the participating investigators was checked in several additional ways. Electrocardiograms in a subset of data from 222 patients...
were reviewed. We also reviewed 1) all electrocardiographic tracings of patients with inducible ventricular tachycardia submitted by the eight study sites enrolling the most patients with inducible sustained ventricular tachycardia and 2) data from a random sample of 3 patients without inducible sustained ventricular tachycardia from each study site. The rate and duration of ventricular tachycardia reported on the data forms were compared with the rate of ventricular tachycardia on the submitted electrocardiograms, as measured by one author.

**Statistical Analysis**

Characteristics of spontaneous nonsustained ventricular tachycardia were summarized in patients with and those without inducible monomorphic sustained ventricular tachycardia using the median and the 5th, 25th, 75th, and 95th percentiles. The distributions of each characteristic in these two groups (inducible and noninducible) were compared using the nonparametric Wilcoxon rank-sum test [14].

Further statistical assessment of the relation of characteristics of the spontaneous nonsustained ventricular tachycardia with inducibility was done using logistic regression analysis. Inducibility during programmed electrical stimulation was the outcome variable, and characteristics of the nonsustained ventricular tachycardia were predictor variables. The relation between each predictor variable and inducible ventricular tachycardia was considered individually and jointly. To accommodate possible nonlinear relations between these predictors and inducibility, a flexible model-fitting approach involving cubic splines (piecewise cubic polynomials) was used [15,16]. Characteristics of the nonsustained ventricular tachycardia examined in these regression analyses included mean duration of the episodes documented, duration of the longest episode, mean rate of the episodes, and mean number of episodes per day. The ability of these characteristics (individually or jointly) to accurately predict inducible sustained ventricular tachycardia or discriminate between patients who did and did not have inducible sustained ventricular tachycardia with programmed stimulation was quantitated using the area under the receiver-operating characteristic (ROC) curve [17]. An area under the ROC curve near 0.5 indicates that predictions of inducibility made using characteristics of the nonsustained ventricular tachycardia are essentially random with respect to actual inducibility. An area under the ROC curve near 1.0 indicates that the predictions correctly discriminate between patients who did and did not have inducible ventricular tachycardia.

**Results**

Data were analyzed from the first 1480 consecutive patients enrolled in the trial. Of these patients, 438 (30%) had inducible sustained monomorphic ventricular tachycardia, and 1042 (70%) did not.

When the electrocardiographic tracings in the subset of 222 patients were reviewed, the cycle length and duration of the recordings of qualifying nonsustained ventricular tachycardia compared with the values reported on the case report form showed a mean difference in cycle length of only 25 milliseconds. The median duration of episodes in the sample was five beats, the same as the entire population. Thus, the submitted sample data were very close to the data reported by individual investigators on the case report forms.

Spontaneous nonsustained ventricular tachycardia qualifying patients for study entry was discovered during in-hospital telemetric electrocardiography in 793 (53%) of the 1480 patients, by continuous ambulatory electrocardiographic (Holter) recording in 609 (41%), during exercise electrocardiography in 39 (3%), and in the course of recording a standard 12-lead electrocardiogram in 25 (2%). One episode was documented by a transtelephonic event recorder, and the source of the documentation could not be obtained in 13 patients.

The median duration of all recorded episodes of spontaneous nonsustained ventricular tachycardia was five complexes. The median value for the longest episode of documented nonsustained ventricular tachycardia was seven complexes. The median value for the mean cycle length of recorded episodes of spontaneous nonsustained ventricular tachycardia was 420 milliseconds (equivalent to a rate of 143 beats/min). The median
frequency of documented nonsustained ventricular tachycardia was two episodes per day (mode, 1 episode/d).

Morphologic data on the spontaneous nonsustained ventricular tachycardia are limited. Nonsustained monomorphic ventricular tachycardia was recorded in 86% of patients, and polymorphic nonsustained ventricular tachycardia was recorded in 34% of patients (some patients had both events). However, the accuracy of the morphologic classification is compromised by the fact that spontaneous nonsustained ventricular tachycardia was recorded on two electrocardiographic leads in 75% of patients (12-lead electrocardiograms of nonsustained ventricular tachycardia are rarely available).

No significant differences were seen between patients with and those without inducible sustained monomorphic ventricular tachycardia in the distributions of the electrocardiographic characteristics, except for a slightly higher rate of nonsustained ventricular tachycardia in patients without inducible sustained ventricular tachycardia Table 1. The magnitude of difference in rates is small, and there is such considerable overlap in the heart rate distributions in both patient groups that the difference is not clinically useful.

No relations between characteristics of spontaneous nonsustained ventricular tachycardia with inducibility were significant by logistic regression analysis, except for the mean rate variable Table 2. However, even for this characteristic, the relation does not provide the ability to accurately discriminate between patients who have inducible ventricular tachycardia and those who do not, as quantified by the area under the ROC curve Table 2. Even when all four characteristics of spontaneous nonsustained ventricular tachycardia were considered together in a regression model to predict inducibility, the area under the ROC curve was only 0.552, reflecting almost no predictive ability. When any inducible sustained ventricular tachycardia (monomorphic or polymorphic) was considered as the measure of inducibility, the results were similar.

Discussion

Counter to intuition, electrocardiographic characteristics of spontaneous nonsustained ventricular tachycardia in patients with coronary artery disease cannot differentiate between patients with and those without sustained ventricular tachycardia inducible by programmed stimulation in the electrophysiology laboratory. The importance of this finding lies in the fact that programmed stimulation is one of the best techniques for identifying patients with coronary artery disease who are at high risk for sudden cardiac death. Other tests, such as measurement of left ventricular ejection fraction and the ambulatory electrocardiogram, can predict overall cardiac-related death but not whether death will or will not occur suddenly. Thus, these other tests cannot identify patients likely to benefit from antiarrhythmic therapy. In contrast, previous studies [9-12] have associated the presence of sustained ventricular tachycardia with an excess of sudden, as opposed to nonsudden, deaths. The signal-averaged electrocardiogram has yet to be tested prospectively in a large sample of patients with the characteristics of our study participants.
The noted electrocardiographic characteristics of spontaneous nonsustained ventricular tachycardia are remarkably similar to those reported in the Cardiac Arrhythmia Suppression Trial (CAST) [8]. We have confirmed that most episodes of nonsustained ventricular tachycardia in patients with coronary artery disease who are at high risk for sudden cardiac death are brief and occur infrequently. An analysis of cardiac arrest in CAST showed no electrocardiographic characteristic of nonsustained ventricular tachycardia that distinguished patients who had cardiac arrest from those who had not. This result was similar to that of a previous analysis that did not control anti-arrhythmic therapy in survivors with acute infarction [3].

Limitations

We did not use a core laboratory to analyze the Holter tapes. Investigators at each study site reviewed the electrocardiographic data and reported it on forms for entry into the computer database. Although analysis of Holter tapes by a core laboratory might have increased data accuracy, our study funds were insufficient to pay for Holter recording or analysis. Various recording systems were used: The systems in use depended on the study site and its referral sources. Despite this limitation, our findings are remarkably similar to those of previous studies that did use core laboratories. One advantage of our methods is that our data reflect the results that are likely to occur in actual clinical practice. Thus, these results should be generalizable to the entire patient sample meeting the study's entry criteria.

A second limitation, noted previously, is that with current technology, most episodes of spontaneous nonsustained ventricular tachycardia can only be recorded on one or two electrocardiographic leads. This limits our ability to accurately describe the morphologic characteristics of such arrhythmias.

Conclusions

No electrocardiographic characteristic of spontaneous nonsustained ventricular tachycardia can accurately predict whether patients will have inducible sustained ventricular tachycardia. Thus, we conclude that the rate, duration, and frequency of spontaneous nonsustained ventricular tachycardia in patients with abnormal left ventricular function caused by coronary artery disease cannot be used to make clinical decisions about the use of electrophysiologic studies for risk stratification.

Appendix: MUSTT Trial Investigators

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References

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### Table 1. Distribution of Electrocardiographic Characteristics of Spontaneous Nonsustained Ventricular Tachycardia*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients with Sustained Ventricular Tachycardia</th>
<th>Patients without Ventricular Tachycardia</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean duration, number of complexes</td>
<td>5 (3.5, 8.0) [3, 15]</td>
<td>5 (3.4, 8.0) [3, 15]</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>Longest documented episode, number of complexes</td>
<td>7 (4, 13) [3, 26]</td>
<td>7 (4, 13) [3, 29]</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>Mean rate, beats/min</td>
<td>143 (125, 158) [109, 188]</td>
<td>143 (128, 164) [111, 214]</td>
<td>0.047</td>
</tr>
<tr>
<td>Mean frequency, episodes/d</td>
<td>2 (1, 6) [0.2, 177]</td>
<td>2 (1, 9) [0.1, 233]</td>
<td>&gt;0.2</td>
</tr>
</tbody>
</table>

* Data are presented as median (25th percentile, 75th percentile) [5th percentile, 95th percentile].
Table 2. Logistic Regression Analysis of the Relation between Electrocardiographic Characteristics of Spontaneous Nonsustained Ventricular Tachycardia and Inducible Sustained Ventricular Tachycardia*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Chi-square (Value)</th>
<th>P Value</th>
<th>Chi-square (Value)</th>
<th>P Value</th>
<th>Area Under the ROC Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean duration</td>
<td>0.18 (1 df)</td>
<td>&gt;0.2</td>
<td>2.44 (3 df)</td>
<td>&gt;0.2</td>
<td>0.522</td>
</tr>
<tr>
<td>Longest documented episode</td>
<td>0.73 (1 df)</td>
<td>&gt;0.2</td>
<td>0.74 (3 df)</td>
<td>&gt;0.2</td>
<td>0.508</td>
</tr>
<tr>
<td>Mean rate</td>
<td>4.06 (1 df)</td>
<td>0.044</td>
<td>4.16 (3 df)</td>
<td>&gt;0.2</td>
<td>0.532</td>
</tr>
<tr>
<td>Mean frequency</td>
<td>0.62 (1 df)</td>
<td>&gt;0.2</td>
<td>0.96 (3 df)</td>
<td>&gt;0.2</td>
<td>0.521</td>
</tr>
<tr>
<td>All factors</td>
<td>3.66 (4 df)</td>
<td>&gt;0.2</td>
<td>10.25 (12 df)</td>
<td>&gt;0.2</td>
<td>0.552</td>
</tr>
</tbody>
</table>

* Results in the first four rows are based on a consideration of the designated variable by itself. In the final row, all four factors are considered together. ROC = receiver operating characteristic; df = degrees of freedom.
† Assuming that each variable's relation with inducibility is linear on the logit (log odds) scale.
‡ Values are likelihood ratio chi-square statistics with the designated degrees of freedom.
§ Based on the characterization of each variable's relation with inducibility using a restricted cubic spline fit with four knots, or join points (16).
¶ Based on the model in which cubic spline functions were used.
¶¶ This value is slightly less than the chi-square value for mean rate because when all four factors were considered together, a few patients were excluded because of missing data.