**Diminished Short-Term Heart Rate Variability Predicts Inducible Ventricular Tachycardia**

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**Purpose:** The purpose of this study is to determine whether short-term heart rate variability (HRV) can be used successfully to predict inducible ventricular tachycardia (VT).

**Methods:** A high-speed (300 mm/s) electrocardiographic recording was obtained in 32 patients in the supine position prior to programmed ventricular stimulation. Beat-to-beat RR intervals (in milliseconds) were derived from an 11-beat strip (10 RR intervals). Logistic regression was used to study the relationship between several variables and a dichotomous dependent variable (inducible, clinical, or electrocardiographic evidence of VT).

**Results:** Of 32 patients, 12 had inducible VT (inducible VT group) and 20 had no clinical or electrocardiographic evidence of VT (control group). Mean short-term HRV values were significantly lower in those with inducible VT than in the control group in all patients (25±15 ms, n=12 vs 67±22 ms, n=20; p<0.0001) and in patients with coronary artery disease or congestive heart failure or both (22±13 ms, n=11 vs 63±23 ms, n=11; p<0.0001). For the group as a whole, short-term HRV was ≤50 ms in 11 of 12 patients (92%) with inducible VT, but was ≤50 ms in only 3 of 20 control subjects (15%; p<0.001). As a result of a stepwise selection procedure conducted within the logistic regression, only the short-term HRV was found to be predictive of inducible VT (p<0.0001).

**Conclusion:** Short-term HRV is significantly lower in subjects with inducible VT than in those without clinical or electrocardiographic evidence of VT. The probability of developing sudden death increases substantially when short-term HRV decreases below 50 ms.

*(CHEST 1998; 113:312-16)*

**Key words:** congestive heart failure; coronary artery disease; inducible ventricular tachycardia; short-term heart rate variability

**Abbreviations:** HRV=heart rate variability; VT=ventricular tachycardia

Prior studies have shown that diminished heart rate variability (HRV) in patients who have suffered myocardial infarction may predict sudden cardiac death independent of other risk factors.1-5 Most clinical studies that have explored the role of HRV in sudden cardiac death have employed 24-h ambulatory electrocardiographic monitoring with associated computer analysis as a diagnostic probe.1-9 Heart rate may be influenced by such factors as breathing, blood pressure alterations, changes in body temperature, posture, and physical activity.6-13 All of these factors are likely to influence HRV during a 24-h period of monitoring. For this reason, short-term HRV may provide an assessment of sympathetic-parasympathetic balance that is less likely to be influenced by physiologic stimuli than HRV obtained over a 24-h period. This study determines whether short-term HRV can be used successfully to predict the presence or absence of inducible sustained ventricular tachycardia (VT).

**METHODS AND MATERIALS**

**Patient Selection**

Patients with histories of unexplained syncope, resuscitated sudden cardiac death, or documented spontaneous sustained VT were considered for the experimental arm of the study. Those with inducible VT during programmed ventricular stimulation were entered into the experimental arm (inducible VT group). A group of patients with similar age and gender distribution, but no

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history of syncope, of resuscitated sudden death, or of spontaneous VT, was selected as a control group. The control group did not undergo programmed ventricular stimulation. All patients were required to be in normal sinus rhythm at the time of study and were required to be free from administration of any drug that could affect cardiac rhythm or repolarization at least five half-lives prior to programmed ventricular stimulation. Subjects with frequent ectopic beats (which precluded obtaining an 11-beat high-speed continuous electrocardiographic recording) were excluded, as were subjects with second- or third-degree atrioventricular block.

Protocol

A high-speed (300 mm/s) electrocardiographic recording free from supraventricular or ventricular ectopy was obtained on each patient after 15 min of complete rest just prior to programmed ventricular stimulation. Beat-to-beat RR intervals were measured in milliseconds from an 11-beat strip (10 RR intervals) using an electrophysiology recording system (Labsystem 24; Bard, Inc; Murray Hill, NJ). HRV was defined as the difference between maximum and minimum RR intervals. This value was corrected to a mean heart rate of 75 beats per minute as follows: corrected HRV=500 (ms)/measured HRV (ms)/mean of 10 RR intervals (ms). This method of HRV was developed by the investigators specifically for the purposes of this study. Maximum beat-to-beat variability was defined as the largest increment in consecutive RR intervals on the 10-beat rhythm strip. Correction for heart rate was accomplished in a manner similar to that used for HRV.

Programmed ventricular stimulation was performed from two right ventricular sites with the use of two cycle lengths and up to three extrastimuli. The intensity and duration of the extrastimuli were ≤0.9 mA and 2 ms, respectively. Inducible VT was defined as VT >30 s in duration or VT associated with syncope. All patients underwent coronary angiography. Coronary artery disease was defined as >60% stenosis of one or more of the major coronary arteries. Left ventricular ejection fraction was determined using contrast left ventriculography in all cases. Congestive heart failure was diagnosed in accordance with criteria of McKee et al in the Framingham study.14

Statistical Methods

All of the statistical analyses were performed using the Statistical Analysis System Software (SAS, Inc; Cary, NC). The two-sample t test was used to compare mean age and HRV in the subgroups of patients with and without inducible VT. The χ² test with a Yates correction was used for the comparison of proportions between groups. Logistic regression was used to study the relationship between several descriptors and a dichotomous dependent variable (inducible, no clinical or electrocardiographic evidence of VT). A stepwise selection procedure was used to determine which variable would be included in the model. A mathematical model was developed to estimate the probability of inducible VT.

RESULTS

Patient Characteristics

A total of 20 patients were originally screened for entry into the inducible VT group. Six were excluded due to the presence of frequent ventricular or atrial ectopic beats,2 atrial fibrillation, flutter, or the presence of complete atrioventricular block.1 Also excluded were two patients with documented sudden death due to VT or ventricular fibrillation who were not inducible during programmed ventricular stimulation. Twenty consecutive patients without unexplained syncope, resuscitated sudden death, or spontaneous VT with similar demographic features comprised the control group. Table 1 shows patient characteristics in the subgroups with and without inducible VT. Coronary artery disease and congestive heart failure were significantly more prevalent in subjects with inducible VT than in the control group.

Short-Term HRV and Maximum Beat-to-Beat Variability in Subjects With and Without Inducible VT

Table 2 shows the incidence of short-term HRV ≤50 ms and >50 ms in subjects with inducible VT and in the control group. The incidence of short-term HRV ≤50 ms was significantly higher in subjects with inducible VT than in the control group (p<0.001). Mean short-term HRV was significantly lower in subjects with inducible VT (25±15 ms) than in the control group (67±21 ms; p<0.0001). HRV ≥50 ms as a mark of inducible VT was associated with a sensitivity of 79%, a specificity of 94%, a positive predictive accuracy of 92%, and a negative predictive value of 85%. Maximum beat-to-beat variability was significantly lower in patients with inducible VT (27±16 ms) than in the control group (37±17 ms; p<0.04).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Inducible VT Group (n=12)</th>
<th>Control Group (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, yr, ±SD</td>
<td>59.5±9.5</td>
<td>52±16</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>8 (67)</td>
<td>14 (70)</td>
</tr>
<tr>
<td>F</td>
<td>4 (33)</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>10 (84)</td>
<td>14 (70)</td>
</tr>
<tr>
<td>Black</td>
<td>1 (8)</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (84)</td>
<td>11 (55)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5 (42)</td>
<td>5 (25)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>11 (92)</td>
<td>10 (50)*</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>8 (67)</td>
<td>5 (25)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>9 (75)</td>
<td>5 (25)*</td>
</tr>
<tr>
<td>Left ventricular ejection fraction ≤40</td>
<td>7 (58)</td>
<td>5 (25)</td>
</tr>
<tr>
<td>Coronary artery bypass surgery</td>
<td>6 (50)</td>
<td>4 (20)</td>
</tr>
</tbody>
</table>

*p<0.05 compared to inducible VT group.
Table 2—Frequency of Subjects With High and Low HRV*

<table>
<thead>
<tr>
<th>Subjects</th>
<th>HRV, ms</th>
<th>Inducible VT Group, No. (%)</th>
<th>Control Group, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>≤50</td>
<td>11/12 (91.6)</td>
<td>3/20 (15)</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>1/12 (8.4)</td>
<td>17/20 (85)</td>
</tr>
<tr>
<td>Those with coronary artery disease and/or congestive heart failure</td>
<td>≤50</td>
<td>11/11 (100)</td>
<td>2/11 (18)</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>0/11 (0)</td>
<td>9/11 (82)</td>
</tr>
</tbody>
</table>

*p<0.001, χ² test of independence.

Table 3—Measured HRV*

<table>
<thead>
<tr>
<th>Group</th>
<th>Inducible VT Group</th>
<th>Control Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>25.1±15.2 (n=12)</td>
<td>66.8±21.9 (n=20)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>22.4±12.6 (n=11)</td>
<td>63.6±24.4 (n=10)</td>
<td>&lt;0.0004</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>18.6±9.7 (n=10)</td>
<td>55.1±19.6 (n=5)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Coronary artery disease or congestive heart failure</td>
<td>22.4±12.6 (n=11)</td>
<td>63±23.2 (n=11)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Values are expressed as mean ms values±1 SD.

Short-Term HRV in Subjects With and Without Coronary Artery Disease or Congestive Heart Failure or Both

Table 3 shows mean short-term HRV values in subjects with inducible VT and the control group in subgroups with coronary artery disease, congestive heart failure, and both. Mean short-term HRV was significantly lower in subjects with inducible VT than in the control group in the coronary artery disease (p<0.0004), congestive heart failure (p<0.0005), and combined coronary artery disease and congestive heart failure (p<0.0001) subgroups.

Interrelation of Short-Term HRV, Inducible VT, and Left Ventricular Ejection Fraction

The interrelation of short-term HRV, inducible VT, and left ventricular ejection fraction is shown in Figure 1. The majority of subjects with inducible VT had short-term HRV values of ≤50 ms regardless of left ventricular ejection fraction status.

Probability of Inducible VT Based on Short-Term HRV

As a result of stepwise selection procedure conducted within the logistic regression, only the short-term HRV was found to be predictive of the inducible VT (p<0.0001). In the presence of HRV, no other variable was selected for entry into the model. The computed index of rank correlation between the observed responses and predicted probabilities is concordance=0.940, which indicates high predictive ability of the developed logistic model. The probability (P) of inducible VT for a given short-term HRV can be derived by using the following mathematical formula:

\[ P = \frac{\exp(3.7693 - 0.0966xHRV)}{1 + \exp(3.7693 - 0.0966xHRV)} \]

Figure 2 shows the predicted probability of inducible VT and the 95% confidence limits for the probability. Subjects whose short-term HRV was ≥50 ms had a low probability of developing inducible VT. When short-term HRV decreased below 50 ms, the probability of inducible VT rose substantially.

DISCUSSION

This study shows that short-term HRV is significantly lower in subjects with inducible VT than in the controls without unexplained syncope, resuscitated sudden death, or spontaneous VT, particularly in patients with coronary artery disease, in patients with
congestive heart failure, and in patients whose left ventricular ejection fraction was ≤40%. Even maximum beat-to-beat variability was significantly lower in those with inducible VT than in the control group.

Short-term HRV has been assessed previously in the setting of acute myocardial infarction. Wolf et al3 analyzed 30 consecutive beats of a 50-s electrocardiographic recording for HRV and noted increased in-hospital mortality in patients whose HRV values were <32 ms. Several other studies1,2,4,5 assessing HRV by computer analysis with use of 24-h ambulatory electrocardiographic monitoring have reported an association between decreased HRV and both total mortality and sudden death in patients with acute myocardial infarction. HRV calculated over a 24-h period may be influenced not only by changes in breathing, blood pressure, and body temperature, but also by variation induced by changes in posture, physical activity, and diurnal rhythm.8,9 By eliminating the influence of these variables, short-term HRV may be a better predictor of sympathovagal balance and therefore a better tool for assessing the risk for development of malignant ventricular arrhythmias and sudden death.8,9 Maximum beat-to-beat variability is heavily influenced by heart rate and may be a less effective marker of autonomic tone than HRV.

The fibrillation threshold of the ventricle decreases with sympathetic activity and increases with vagal activity. Thus, increased sympathetic activity increases the likelihood of developing malignant ventricular tachyarrhythmias, and increased vagal activity decreases the likelihood of developing such rhythm disturbances.10-12 Sympathetic activity has been reported to be enhanced and parasympathetic activity reduced in patients with acute myocardial infarction.13 Previous studies have demonstrated that patients with acute myocardial infarction and diminished HRV have a greater propensity for developing ventricular fibrillation.4,5,15 Several studies have demonstrated diminished HRV in patients with chronic coronary artery disease.1,4,5 An increase in the frequency of ventricular tachyarrhythmias and mortality has been reported in patients with coronary artery disease whose HRV was <50 ms.1 Our results support and extend these observations by showing that patients with chronic coronary artery disease and inducible VT have significantly lower short-term HRV than coronary artery disease patients without clinical or electrocardiographic evidence of VT.

The reported incidence of ventricular tachyarrhythmias and sudden death is disproportionately high in patients with clinical congestive heart failure and in those whose left ventricular ejection fraction is ≤40%.15 Patients with congestive heart failure have enhanced sympathetic tone and depressed parasympathetic tone.16-19 This autonomic imbalance may produce a decrease in HRV.16-18,20 For this reason, short-term HRV was analyzed in subjects with clinical evidence of congestive heart failure and in those whose left ventricular ejection fraction was ≤40%. In patients with congestive heart failure and in those with a left ventricular ejection fraction ≤40%, subjects with inducible VT had significantly lower mean short-term HRV values than those in the control group. Among the subjects with a left ventricular ejection fraction ≤40%, inducible VT was noted mainly in those whose short-term HRV was ≤50 ms (Fig 1), suggesting that short-term HRV may have more power than low left ventricular ejection fraction in predicting inducible VT. After adjusting for age, diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, and left ventricular ejection fraction ≤40% (factors that may influence HRV), diminished HRV remained a strong predictor of inducible VT. Figure 2 shows that the probability of inducible VT rises dramatically when short-term HRV decreases below 50 ms.
The major limitation of this study was the small sample size. In addition, breathing may have produced minor alterations in HRV. However, short-term HRV analysis was conducted under identical conditions on all subjects; thus, any alterations induced by breathing would be expected to affect both groups equally. Only one patient with inducible VT did not have coronary artery disease. Thus, the findings of this study cannot be generalized to subjects without coronary artery disease and inducible VT. Another limitation is the lack of programmed ventricular stimulation studies in the control groups.

In conclusion, short-term HRV is significantly lower in subjects with inducible VT than in those without clinical or electrocardiographic evidence of VT. This observation holds for all patients studied, those with coronary artery disease and those with congestive heart failure or a left ventricular ejection fraction ≤40%, or both. The probability of developing sudden cardiac death increases substantially when HRV decreases below 50 ms.

REFERENCES