Frequency Domain Measures of Heart Rate Variability Before the Onset of Nonsustained and Sustained Ventricular Tachycardia in Patients With Coronary Artery Disease

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Background. Low heart rate variability (HRV) is associated with an increased risk of arrhythmic death and ventricular tachycardia (VT). The purpose of this study was to examine whether there is a temporal relation between changes in HRV and the onset of spontaneous episodes of VT in patients at high risk of life-threatening arrhythmias.

Methods and Results. Components of HRV in the frequency domain were analyzed before the onset of 28 episodes of nonsustained VT (more than four impulses; duration <30 seconds) and 12 episodes of sustained VT (>30 seconds or requiring defibrillation) in 18 patients with coronary artery disease. Seven patients had survived cardiac arrest not associated with acute myocardial infarction, and 11 had a history of sustained VT. All frequency domain measures of HRV, i.e., total power (p<0.001), high-frequency power (p<0.05), low-frequency power (p<0.01), very-low-frequency power (p<0.01), and ultralow-frequency power (p<0.05), were significantly lower before the onset of sustained VT than before nonsustained VT. Total power of HRV was also lower during the 1-hour period before the onset of sustained VT than the average 24-hour HRV (p<0.05). An indirect correlation existed between the length of VT and the total power of HRV analyzed during the 15 minutes before the onset of VT (r=0.54, p<0.01). HRV had a trend toward increasing values before the onset of nonsustained VT (p<0.01) but not before the sustained VT episodes. The ratio between low-frequency and high-frequency powers increased substantially before both nonsustained and sustained VT episodes (p=0.06 and p=0.05, respectively). The rate of VT or the coupling interval initiating the VT did not differ significantly between the nonsustained and sustained VT.

Conclusions. Spontaneous episodes of VT are preceded by changes in HRV in the frequency domain. Divergent dynamics of HRV before the onset of nonsustained and sustained VT episodes may reflect differences in factors that can facilitate the perpetuation of these arrhythmias. (Circulation 1993;87:1220–1228)

Key Words • heart rate variability • tachyarrhythmias

Ambulatory ECG recordings have been used to study the factors that may serve as triggers or contribute to initiation of spontaneously occurring malignant ventricular arrhythmias.4–6 Previous studies have focused on the characteristics of premature ventricular beats initiating ventricular tachycardias (VT) and changes in basic heart rate preceding the spontaneous episodes of VT.4–6

By analyzing the power spectral components of the heart rate variability (HRV), however, it is possible to estimate neural, hormonal, and other influences on the heart,7–9 reflecting modulation of the electrophysiological substrate by functional influences.10 Recent studies have revealed that low total HRV and low measures of various frequency domain components of HRV can identify patients who are at increased risk of arrhythmic events after myocardial infarction.11–13 However, the mechanisms by which the pathophysiological changes reflected by impaired HRV predispose to the occurrence of malignant arrhythmias are largely unknown. The purpose of the present study was 1) to examine temporal changes in the HRV before spontaneous episodes of VT and 2) to test the hypothesis that quantitative differences in various frequency domain measures of HRV exist before the onset of nonsustained and sustained episodes of VT.

Methods

Patients

The patient population consisted of 18 consecutive patients who were admitted to electrophysiological test-
ing because of cardiac arrest or VT (16 at Oulu University Central Hospital and two at the University of Miami Medical Center). Each patient had spontaneous episodes of VT (more than four consecutive beats) on Holter recording performed 1–2 days before electrophysiological studies. Antiarrhythmic drugs and β-blocking drugs had been withdrawn at least 4 half-lives before the studies. Seven patients were receiving digitalis, nine diuretics, six calcium channel blocking therapy, five angiotensin converting enzyme inhibitors, and 14 nitrate therapy. Other clinical data on the patients are presented in Table 1. The patients gave their informed consent for the studies.

Electrophysiological and Angiographic Studies

Electrophysiological testing included incremental ventricular pacing and programmed ventricular stimulation using up to three extrastimuli and two basic drive cycle lengths (600 and 400 msec) from the right ventricular apex and outflow tract. Left ventricular cineangiography and coronary angiograms were performed in 14 patients. All 14 patients had angiographically verified coronary artery disease. In four patients with previous myocardial infarction, the ejection fraction was measured by echocardiography. Ejection fraction and inducibility of ventricular tachyarrhythmias on electrophysiological testing are presented in Table 1.

Analysis of Holter Recordings

Two-channel 24-hour ECG recordings were analyzed on a Delmar Avionics scanner. Average heart rate, number of ventricular premature beats, episodes of repetitive beats (two to four consecutive beats), and episodes of VT (more than four beats; rate, >100 beats per minute) were analyzed from the tape recordings. The analysis of each tape recording also included existence of a pause (defined as an RR interval exceeding 125% of the average cycle length over the five preceding beats) before the onset of VT, prematurity index defined as the ratio of the coupling interval and the immediately preceding RR cycle, and the length, rate, and morphology of the VT.

VT was defined as nonsustained if it lasted more than four beats but <30 seconds and as sustained when its duration was >30 seconds or if defibrillation was required for termination of VT. Polymorphic VTs and VTs that were preceded by a pause were not included in the analysis.

Analysis of HRV

The ECG data were digitally sampled and transferred from the Delmar Avionics scanner to a microcomputer for analysis of HRV. A linear detrend was applied to the RR interval data segments of 512

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Prior MI</th>
<th>EF (%)</th>
<th>Arhythmic history</th>
<th>VT episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>66</td>
<td>M</td>
<td>Ant</td>
<td>36</td>
<td>Sustained VT</td>
<td>1 2</td>
</tr>
<tr>
<td>2</td>
<td>49</td>
<td>M</td>
<td>Inf</td>
<td>45</td>
<td>Sustained VT</td>
<td>2 1</td>
</tr>
<tr>
<td>3</td>
<td>73</td>
<td>M</td>
<td>Ant+inf</td>
<td>40</td>
<td>Sustained VT</td>
<td>3 1</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>F</td>
<td>Inf</td>
<td>38</td>
<td>Sustained VT</td>
<td>1 2</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>M</td>
<td>Ant</td>
<td>42</td>
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<td>3 1</td>
</tr>
<tr>
<td>6</td>
<td>66</td>
<td>M</td>
<td>Ant+inf</td>
<td>32</td>
<td>Cardiac arrest</td>
<td>1 2</td>
</tr>
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<td>7</td>
<td>77</td>
<td>M</td>
<td>Ant</td>
<td>35</td>
<td>Sustained VT</td>
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</tr>
<tr>
<td>8</td>
<td>61</td>
<td>M</td>
<td>Ant</td>
<td>30</td>
<td>Sustained VT</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>37</td>
<td>F</td>
<td>Ant</td>
<td>48</td>
<td>Cardiac arrest</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>70</td>
<td>F</td>
<td>Inf+ant</td>
<td>34</td>
<td>Cardiac arrest</td>
<td>2</td>
</tr>
<tr>
<td>11</td>
<td>50</td>
<td>M</td>
<td>None</td>
<td>65</td>
<td>Cardiac arrest</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>63</td>
<td>M</td>
<td>Ant</td>
<td>36</td>
<td>Cardiac arrest</td>
<td>3</td>
</tr>
<tr>
<td>13</td>
<td>61</td>
<td>M</td>
<td>Ant</td>
<td>51</td>
<td>Sustained VT</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>71</td>
<td>M</td>
<td>None</td>
<td>55</td>
<td>Sustained VT</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>65</td>
<td>M</td>
<td>Ant</td>
<td>42</td>
<td>Sustained VT</td>
<td>1</td>
</tr>
<tr>
<td>16</td>
<td>65</td>
<td>F</td>
<td>Ant</td>
<td>52</td>
<td>Cardiac arrest</td>
<td>1</td>
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<tr>
<td>17</td>
<td>62</td>
<td>M</td>
<td>Ant</td>
<td>45</td>
<td>Sustained VT</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>64</td>
<td>M</td>
<td>Ant</td>
<td>42</td>
<td>Sustained VT</td>
<td>2</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; EF, ejection fraction; VT, ventricular tachycardia; nonsust, nonsustained; sust, sustained; EPS, electrophysiological study; ant, anterior; inf, inferior; VF, ventricular fibrillation; NI, noninducible.
samples to make the data more stationary. This was implemented by first fitting a straight line to a segment by a standard least-squares method and then subtracting it from the sample values. The RR interval series was passed through a filter that eliminates unwanted premature beats and noise and fills the resulting gaps with an average value computed in the local neighborhood. An RR interval is interpreted as a premature beat if it deviates from the previous qualified interval value by more than a given tolerance (e.g., 30%), which is a programmable parameter depending on the prematurity index of ectopic beats in each patient. With this filtering technique, abrupt temporary changes in RR interval sequence, representing noise or ectopic beats, were removed and more stationary data were achieved for analysis. In addition, the RR intervals were reviewed on the computer display by an experienced observer, and the questionable portions were compared with the printouts of Holter ECG recordings. Only those RR intervals related to normal sinus beats in a stationary state were included in the final analysis. In our experiments, by eliminating randomly different numbers of RR intervals and filling the gaps by average RR intervals, reliable measurements of spectral components of HRV have been achieved by this technique (<5% error) if <15% of impulses are excluded from the analysis. Therefore, only those segments with >85% of qualified beats were included in the analysis.

An autoregressive model was used to estimate the power spectral densities of the RR interval variability. The size of 10 was used for the model order in the analysis of the RR data. The computer program automatically calculates the autoregressive coefficients to define the power spectral density. Power spectra were quantified by measuring the area in five frequency bands: total power, very low frequency (very low frequency), very low-frequency (very low frequency), low-frequency (very low-frequency), low-frequency (very low-frequency), high frequency, very low frequency, ultralow frequency, and tachycardia.

**TABLE 3. Heart Rate and Heart Rate Variability in Relation to the Onset of Ventricular Tachycardia**

<table>
<thead>
<tr>
<th></th>
<th>24-Hour average (n=18)</th>
<th>1 Hour before the onset of nonsustained VT (n=28)</th>
<th>1 Hour before the onset of sustained VT (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average RR interval (msec)</td>
<td>900±20</td>
<td>915±171</td>
<td>895±163</td>
</tr>
<tr>
<td>Total power of HRV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>msec²×10</td>
<td>133±104</td>
<td>209±128</td>
<td>77±58</td>
</tr>
<tr>
<td>ln</td>
<td>6.9±0.7</td>
<td>7.2±0.7</td>
<td>5.9±0.8*</td>
</tr>
<tr>
<td>HF power of HRV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>msec²×10</td>
<td>26±34</td>
<td>38±41</td>
<td>16±18</td>
</tr>
<tr>
<td>ln</td>
<td>5.1±0.8</td>
<td>5.5±0.9</td>
<td>4.8±0.8**</td>
</tr>
<tr>
<td>NU</td>
<td>52±70</td>
<td>54±52</td>
<td>60±63</td>
</tr>
<tr>
<td>LF power of HRV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>msec²×10</td>
<td>23±27</td>
<td>39±38</td>
<td>12±19</td>
</tr>
<tr>
<td>ln</td>
<td>5.0±0.8</td>
<td>5.5±1.0</td>
<td>4.4±0.9***</td>
</tr>
<tr>
<td>NU</td>
<td>53±52</td>
<td>53±52</td>
<td>42±60</td>
</tr>
<tr>
<td>VLF power of HRV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>msec²×10</td>
<td>70±63</td>
<td>105±87</td>
<td>39±34</td>
</tr>
<tr>
<td>ln</td>
<td>6.2±0.8</td>
<td>6.6±0.9</td>
<td>5.6±1.0***</td>
</tr>
<tr>
<td>NU</td>
<td>53±52</td>
<td>53±52</td>
<td>42±60</td>
</tr>
<tr>
<td>ULF power of HRV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>msec²×10</td>
<td>14±11</td>
<td>27±13</td>
<td>10±10</td>
</tr>
<tr>
<td>ln</td>
<td>4.6±0.8</td>
<td>5.1±1.0</td>
<td>4.3±1.0**</td>
</tr>
</tbody>
</table>

VT, ventricular tachycardia; HRV, heart rate variability; HF, high frequency; NU, normalized units; LF, low frequency; VLF, very low frequency; ULF, ultralow frequency.

*p<0.001, **p<0.05, ***p<0.01 between nonsustained and sustained ventricular tachycardia. p<0.05 with paired t test between 24-hour average power and 1-hour power before the onset of sustained VT.

**FIGURE 1.** Graph showing 24-hour total power of heart rate variability (HRV) and 1-hour power before the onset of nonsustained and sustained ventricular tachycardia (VT) in patients who had both nonsustained and sustained tachycardias during the same ECG recording.
The table below shows the heart rate variability in patients who had both nonsustained and sustained episodes of ventricular tachycardia during the same 24-hour recording.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time</th>
<th>Average RR interval (msec)</th>
<th>Total power of HRV (msec&lt;sup&gt;2&lt;/sup&gt;×10&lt;sup&gt;7&lt;/sup&gt;)</th>
<th>HF power of HRV (msec&lt;sup&gt;2&lt;/sup&gt;×10&lt;sup&gt;7&lt;/sup&gt;)</th>
<th>LF power of HRV (msec&lt;sup&gt;2&lt;/sup&gt;×10&lt;sup&gt;7&lt;/sup&gt;)</th>
<th>VLF power of HRV (msec&lt;sup&gt;2&lt;/sup&gt;×10&lt;sup&gt;7&lt;/sup&gt;)</th>
<th>ULF power of HRV (msec&lt;sup&gt;2&lt;/sup&gt;×10&lt;sup&gt;7&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24-Hour average</td>
<td>913</td>
<td>61</td>
<td>6.4</td>
<td>15.0</td>
<td>5.0</td>
<td>6.4</td>
</tr>
<tr>
<td></td>
<td>1 Hour before VT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonsust (6 beats)</td>
<td>740</td>
<td>93</td>
<td>6.8</td>
<td>19.0</td>
<td>5.2</td>
<td>19.0</td>
</tr>
<tr>
<td></td>
<td>Sust (106 beats)</td>
<td>906</td>
<td>59</td>
<td>6.4</td>
<td>17.0</td>
<td>5.1</td>
<td>6.4</td>
</tr>
<tr>
<td>2</td>
<td>24-Hour average</td>
<td>785</td>
<td>92</td>
<td>6.8</td>
<td>9.0</td>
<td>4.5</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td>1 Hour before VT</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonsust (9 beats)</td>
<td>748</td>
<td>89</td>
<td>6.8</td>
<td>12.0</td>
<td>4.7</td>
<td>9.4</td>
</tr>
<tr>
<td></td>
<td>Nonsust (10 beats)</td>
<td>844</td>
<td>86</td>
<td>6.8</td>
<td>7.0</td>
<td>4.3</td>
<td>10.4</td>
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<tr>
<td></td>
<td>Sust (250 beats)</td>
<td>813</td>
<td>28</td>
<td>5.6</td>
<td>8.0</td>
<td>4.4</td>
<td>10.4</td>
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<tr>
<td>3</td>
<td>24-Hour average</td>
<td>1,135</td>
<td>530</td>
<td>8.6</td>
<td>162.0</td>
<td>7.4</td>
<td>124.0</td>
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<td></td>
<td>1 Hour before VT</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Nonsust (7 beats)</td>
<td>1,146</td>
<td>384</td>
<td>8.3</td>
<td>83.0</td>
<td>6.7</td>
<td>83.6</td>
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<td>Nonsust (9 beats)</td>
<td>1,144</td>
<td>468</td>
<td>8.5</td>
<td>110.0</td>
<td>7.0</td>
<td>101.0</td>
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<tr>
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<td>Nonsust (19 beats)</td>
<td>1,132</td>
<td>614</td>
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<td>108.0</td>
<td>7.0</td>
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<td>Sust (75 beats)</td>
<td>1,110</td>
<td>232</td>
<td>7.7</td>
<td>68.0</td>
<td>6.5</td>
<td>66.0</td>
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<td>4</td>
<td>24-Hour average</td>
<td>808</td>
<td>67</td>
<td>6.5</td>
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<td></td>
<td>Nonsust (5 beats)</td>
<td>820</td>
<td>340</td>
<td>8.1</td>
<td>160.0</td>
<td>7.4</td>
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<td></td>
<td>Sust (212 beats)</td>
<td>809</td>
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<td>6.7</td>
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<td>7.0</td>
<td>4.2</td>
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<td>6.2</td>
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<td>Nonsust (5 beats)</td>
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<td>26.0</td>
<td>5.6</td>
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<td>102</td>
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<td>23.0</td>
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<td></td>
<td>Nonsust (5 beats)</td>
<td>1,148</td>
<td>70</td>
<td>6.6</td>
<td>15.0</td>
<td>5.0</td>
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<td>Sust (76 beats)</td>
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<td>9.0</td>
<td>4.5</td>
<td>6.0</td>
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<td>5.4</td>
<td>9.5</td>
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<td>1 Hour before VT</td>
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<td></td>
<td></td>
</tr>
<tr>
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<td>Nonsust (25 beats)</td>
<td>779</td>
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<td>6.0</td>
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<td>Sust (84 beats)</td>
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<td>3.0</td>
<td>3.4</td>
<td>1.0</td>
</tr>
<tr>
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<td>Sust (78 beats)</td>
<td>781</td>
<td>13</td>
<td>4.9</td>
<td>7.0</td>
<td>4.3</td>
<td>2.3</td>
</tr>
</tbody>
</table>

HRV, heart rate variability; HF, high frequency; LF, low frequency; VLF, very low frequency; ULF, ultralow frequency; VT, ventricular tachycardia; nonsust, nonsustained VT; sust, sustained VT.

*Corresponds to the number of the patient in Table 1.

The power of a given component by the total power, from which the power <0.04 Hz has been subtracted, and multiplying by 100.15 The average heart rate and power spectral components of HRV were calculated in 1-hour segments for the 24-hour period and in four 15-minute and three 5-minute periods before the onset of VT.

**Statistics**

The significance of changes in spectral areas, average heart rate, and number of premature ventricular beats before the onset of VT was analyzed by ANOVA for repeated measurements. Differences in data before the onset of nonsustained and sustained VT were compared by unpaired Student's t test and by paired t test in patients who had both nonsustained and sustained episodes of VT during the same 24-hour recording. The 24-hour HRV and the HRV before the onset of nonsustained and sustained VT, respectively, were compared by paired t test. In cases with several episodes of VT during the same recording, an average value of HRV was used for comparisons. Linear regression analysis was used to estimate the correlations. Because of the skewness of the data, log transformation of the components of HRV and number of ventricular premature beats was performed before statistical analyses. A value of \( p < 0.05 \) was considered significant.

**Results**

**Characteristics of VT**

A total of 40 episodes of VT were analyzed. Twenty-eight episodes were nonsustained and 12 were sustained. Nine sustained VT episodes terminated spontaneously, and three were terminated by defibrillation. One VT degenerated to ventricular fibrillation before its termination. Other characteristics of VT episodes are summarized in Table 2.
FIGURE 2. Tracings of Holter recordings in a patient who had two episodes of nonsustained ventricular tachycardia (upper and middle tracings) and one sustained episode of ventricular tachycardia requiring defibrillation (lowest tracing).

Comparisons Between Nonsustained and Sustained Episodes of VT

The average heart rate and number of ventricular premature beats were not significantly different before the onset of nonsustained and sustained VT episodes. The prematurity index of the initiating beat and the rate of VT did not differ between the nonsustained and sustained VT (Table 2). Total power of HRV analyzed in 1-hour, 15-minute, and 5-minute segments was significantly lower before the onset of sustained than nonsustained VT ($p<0.001$ for all). An indirect correlation existed between the length of VT and the total power of HRV estimated from the 15-minute period before the onset of VT ($r=-0.54$, $p<0.01$). No correlation existed between the total power of HRV and the number of ventricular premature beats before the onset of VT ($r=0.12$, NS). Power spectral analysis showed that all frequency components of HRV were significantly lower before the onset of sustained VT compared with nonsustained VT (Table 3). Total power of HRV was also significantly lower during the 1-hour period before the onset of sustained VT than the average 24-hour HRV ($p<0.05$, see Table 3). In addition, all measures showed nonsignificant trends to higher values before nonsustained VT than were found during the total 24-hour period. The normalized units of LF and HF power did not differ significantly before the onset of nonsustained and sustained VT episodes.

Six patients had both nonsustained and sustained VT episodes with similar morphology during the same recording period. Total power of HRV analyzed for the 1-hour period before the onset of sustained VT was lower than the 24-hour average HRV or the HRV analyzed before the onset of nonsustained VT ($p<0.05$) (Figure 1). Table 4 shows the frequency domain measures of 24-hour HRV and 1-hour HRV before the onset of nonsustained and sustained VT, respectively. All four frequency domain components of HRV were reduced compared with 24-hour average measures before the onset of sustained VT episodes in these patients. Figure 2 shows the spontaneous episodes of VT in a patient who had two nonsustained VT runs and one sustained VT requiring defibrillation during the same recording period. Figure 3 shows the spectral analysis of HRV in the 15-minute periods before these VT episodes.

Changes in HRV Before the Onset of VT

Average heart rate did not change significantly before the onset of nonsustained VT but demonstrated a tendency to increase during the 15-minute period before the onset of sustained VT ($p<0.05$). The number
of ventricular premature beats had an increasing trend before both nonsustained and sustained VT episodes ($p<0.01$ and $p<0.05$, respectively).

Total power of HRV increased significantly during the 1-hour period before the onset of nonsustained VT but not before the onset of sustained VT (Figure 4).
Power spectral analysis revealed that the absolute units of LF and HF power had an increasing trend before the onset of nonsustained VT runs (p<0.05 for both), and the LF power analyzed in normalized units also increased before the onset of nonsustained VT (Figure 5). The HF power analyzed in normalized units did not change before the onset of VT episodes (Figure 5). The LF/HF ratio increased substantially during the 1-hour period before both nonsustained and sustained VT (Figure 6) and also during the 15-minute periods before the onset of both nonsustained and sustained VT (p=0.06 and p=0.05, respectively).

Discussion

Differences Between Nonsustained and Sustained VT

There has been little information about the possible differences between spontaneously occurring nonsustained and sustained VT episodes, although these two arrhythmias may be mechanistically different and have different prognostic significance. Kim et al found that sustained VTs tend to be faster than spontaneously occurring nonsustained VT runs. Swerdlow et al reported that faster basic heart rate before the VT would protect against its extended duration. In this study, no significant differences were found between the rate of VT, heart rate before the VT, or the coupling interval initiating the nonsustained and sustained VT. Concurring with previous results, most of the VT episodes were initiated with a rather long coupling interval.3,16,17

A major finding of this study is that all power spectral components of HRV were significantly lower before the onset of sustained VT episodes than before the nonsustained VT runs. This difference was also evident in patients who had both nonsustained and sustained VT.
runs during the same 24-hour recording. Total power of HRV was also reduced before the onset of sustained VT episodes compared with the 24-hour average HRV, demonstrating the temporal relation between the impaired HRV and sustained VT. On the contrary, HRV tended to increase before the onset of nonsustained VT runs compared with the 24-hour average HRV.

**Potential Mechanisms of the Association Between HRV and Onset of VT**

Several potential mechanisms may explain the association between changes in HRV and onset of VT. Goldberger et al.\(^7\) reported that patients at high risk of sudden death show abrupt spectral changes (bifurcations) in the heart rate. Similar fluctuations were observed in the spectral components of HRV in this study, and these had a temporal relation with the onset of VT episodes. These fluctuations in the dynamics of HRV may reflect changes in factors that can lead to electrical instability and facilitate the initiation or perpetuation of arrhythmias. For instance, the presence of low HRV at the time of onset of an arrhythmia may favor its persistence, whereas higher HRV may favor (or participate in) its termination. Under such circumstances, low HRV may be more than a predictive marker; it may actively participate in the pathophysiological process.

All four frequency domain components of HRV were reduced before the onset of sustained VT. The physiology of this type of concomitant reduction of all spectral components of HRV is not completely understood. It is possible that reduction of total variance of HRV reflects a change in target organ responsiveness to neural modulatory activities, because no significant changes were observed in normalized spectral components of HRV. HF power reflects primarily vagal activity, and LF power reflects combined sympathetic and vagal tone, modulated by baroreflex activity.\(^7,9\) but the precise physiologies of VLF and ULF power are not known. These components are thought to reflect changes in the activity of the renin–angiotensin system or thermoregulation.\(^7,19\) There has been some concern about the adequacy of spectral analysis to estimate VLF oscillations from the time series of a few hundred beats.\(^20\) Therefore, the pathophysiological significance of analyzing these components remains uncertain.

A change in the hemodynamic state results in reflex-mediated changes in cardiac autonomic tone. Transient ischemia may also result in reduction of cardiac vagal activity and consequently in a decrease in at least some components of HRV.\(^21\) The normalized unit of LF power and LF/HF ratio increased before the onset of nonsustained VT, suggesting adrenergic activation before these arrhythmia episodes. Acceleration of heart rate and a substantial increase in LF/HF ratio before the onset of sustained VT episodes is also suggestive of decreased vagal tone or altered sympathovagal interaction as a contributory factor for genesis of sustained arrhythmias.

Previous studies have shown that a circadian rhythm of HRV exists so that the lowest HRV is observed in the morning, corresponding to the time period of highest incidence of sustained VT and sudden death.\(^22–24\) Most of the sustained VT episodes in this study occurred during waking hours. Thus, circadian fluctuation of HRV may partly explain the association between the low HRV and occurrence of sustained VT episodes.

Ventricular premature beat frequency tended to increase before the onset of VT episodes, reflecting changes in electrical stability before the occurrence of repetitive ectopic activity. Premature beats were carefully excluded from analysis of HRV and replaced by an average of neighborhood RR intervals, and no correlation existed between the number of premature beats and HRV. Therefore, it is evident that the changes in spectral components of HRV preceding the VT episodes represent changes in sinus beat intervals.

**Significance of Temporal Changes of HRV in the Genesis of Life-Threatening Arrhythmias**

All patients in this study had a history of potentially fatal ventricular arrhythmia, and the majority of patients were inducible into a sustained ventricular tachyarrhythmia during the electrophysiological testing. Previous studies have shown the association between the low HRV and arrhythmic events after myocardial infarction.\(^11–13\) The present findings demonstrate that a temporal relation exists between the decrease of all frequency domain components of HRV and the onset of sustained VT. However, the causal relation between the onset of life-threatening arrhythmias and low HRV needs to be confirmed in larger populations with different risks of arrhythmic deaths before these data can be generalized. Furthermore, studies must be designed to establish the physiology of concomitant temporal changes in all frequency domain measures of HRV and their significance in arrhythmogenesis.

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