Diurnal Distribution of ST-segment Elevation and Related Arrhythmias in Patients with Variant Angina: A Study by Ambulatory ECG Monitoring

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SUMMARY Twenty-four-hour ambulatory ECG recording was performed in 26 patients with variant angina to evaluate the diurnal distribution of ST-segment elevation in relation to chest pain and the incidence of arrhythmias during the episodes. During a recording period of 52 days, 364 ST-segment elevations of 1 mm or greater were observed and 79% were asymptomatic. ST-segment elevation frequently occurred between 0:00 and 9:00 hours (72%) and most frequently between 5:00 and 6:00 hours (13%). Only a few episodes occurred between 10:00 and 18:00 hours. Premature atrial contractions, premature ventricular contractions (PVCs), ventricular tachycardia (VT) and complete atrioventricular block occurred during 12% of the episodes and were more common during painful episodes (32%) than during painless ones (6%). However, VT and severe forms of PVCs (couplets and bigeminy) appeared eight times during painless episodes and nine times during painful ones. Arrhythmias occurred more frequently when the elevated ST segment started to return or was returning to the control level (n = 38) than when the ST segment was rising (n = 8). The incidence of arrhythmias was lower when the daily frequency of ischemic episodes was high. This study shows that episodes of asymptomatic coronary artery spasm predominantly occur early in the morning as asymptomatic episodes; complex dysrhythmias appear during the asymptomatic episodes; arrhythmias occur predominantly during a "reperfusion period;" and more arrhythmias accompany infrequent daily episodes of ischemia than frequent ones.

IN PATIENTS with variant angina, anginal attacks occur more frequently at midnight or early in the morning, and arrhythmias, including life-threatening ones, are common during the attack.1-3 To our knowledge, however, no quantitative data have been reported on the diurnal distribution of ischemic episodes, such as chest pain and ECG changes, in variant angina except for a preliminary report by Kuroiwa4 which showed a higher frequency of recurrent ST-segment elevations early in the morning. It is important to clarify the diurnal distribution of the episodes for the evaluation of pathophysiology of variant angina as well as for treatment.

ST-segment elevation without pain has been observed in variant angina and recently proved to be due to coronary vascular spasm resulting, like painful ST-segment elevations, in myocardial ischemia.5-7 Twenty-four-hour ambulatory ECG monitoring is a good tool for evaluating ST-segment elevation in variant angina, especially that without chest pain,2, 8, 9 and can also be used to evaluate arrhythmias during the episodes.

In the present study, we studied the diurnal distribution of ischemic episodes with or without chest pain and the incidence of arrhythmias during the episodes using 24-hour ambulatory ECG recordings.

Materials and Methods

Twenty-six consecutive patients with variant angina admitted to our clinic from June 1976 to December 1981 were studied. Twenty-five were males and one was female, ages 44–72 years old. None of these patients had a history of myocardial infarction. Because all patients complained of chest pain at rest and transient ST-segment elevation had been confirmed by a standard 12-lead ECG, variant angina was diagnosed before 24-hour ambulatory ECG monitoring. ST-segment elevation was observed in the anterior leads in 15 patients and in the inferior leads in eight. Two patients showed ST-segment elevation in inferolateral leads and one in anterolateral leads. Coronary angiography was done in 19 patients. Five patients had no or minimal coronary lesions (0–24% stenosis) and eight showed stenosis of 25–49%. Six patients had a significant coronary lesion of a major coronary artery (50–74% in five and 75–89% in one). Eight patients also had angina on exertion.

Recording and Playback Analysis of the Ambulatory ECG

A precordial bipolar ECG was recorded continuously for 24 hours on a calibrated magnetic tape system (Avionics, Model 445-B or 446). One of the two leads was selected to mimic the lead that showed the highest ST-segment elevation observed on a 12-lead ECG during an anginal attack (i.e., CM<sub>4</sub> for V<sub>5</sub>); another lead was placed on the opposite site to record reciprocal ST-segment depression. The electrodes were placed firmly to avoid motion artifacts. In all patients, postural changes (supine, sitting and standing) were done initially to check the ST-segment displacement. All patient activities and symptoms, including the time of
ST-segment elevation, were entered in detail in the diary. Prophylactic agents such as calcium antagonists or long-acting oral nitrates were not used; sublingual nitroglycerin was used for chest pain. Twenty-four-hour ambulatory ECG recording was performed once in eight patients, twice in 12, three times in four and four times in two (mean, twice per patient).

Analysis of the recorded magnetic tapes was done using an Avionics Dynamic Electrocardioscanner (model 660A). Trendgrams of the ST segment and heart rate, averaging 15 beats, were obtained from both channels, where ST-segment deviations were measured 0.08 second from the nadir of the S wave. Meanwhile, an oscilloscope displaying the two ECG channels was monitored to detect ST-segment elevations and arrhythmias. All portions showing ST-segment elevation were then analyzed in real-time to evaluate the degree of ST-segment elevation and the appearance of arrhythmias.

ST-segment elevation was considered to be ischemic when the ST-segment shift was transient, smooth and did not accompany an abrupt change in the QRS complex, and thus resembled the pattern of ST-segment elevation on a 12-lead ECG during angina. All such ST-segment displacements of 1 mm or greater were counted. Postural ST-segment changes were excluded. Arrhythmias during ST-segment elevations were analyzed from the real-time tracing and the relationship between the phase of ST-segment elevation (rising or returning to the control level) and the appearance of arrhythmias were also studied. Arrhythmias analyzed were premature atrial contractions (PACs), premature ventricular contractions (PVCs), ventricular tachycardia (VT) and complete atrioventricular block (CAVB). Cases in which the same kinds of arrhythmias were observed even without ST-segment elevation were excluded from the analysis of arrhythmias. Actually, such cases were observed only in one tape. Furthermore, the 24-hour ECG was displayed on photosillographic paper using an Avionics Electrocardiovalidator (model 9300). This approach was used for all tapes to double check the incidence of ST-segment elevations and arrhythmias.

To evaluate the specificity with which ST-segment elevation was detected by the ambulatory ECG system, 24-hour ECG recording was performed in 57 patients without variant angina. These patients had valvular heart disease, arrhythmias or cardiomyopathy. Playback analysis of recorded tapes was done by the same method applied to patients with variant angina.

**Statistical Analysis**

Statistical analysis was done using the chi-square test.

**Results**

During 52 days of ambulatory ECG recording, ST-segment elevations of 1 mm or greater were observed 364 times in 26 patients. The amplitude of ST-segment elevations was 1–12 mm. Some patients had only one ST-segment elevation per day, while some others had as many as 68 episodes per day (fig. 1). Figure 2 is a

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**FIGURE 1.** Trendgrams of ST segment and heart rate from two patients, one who had a single episode (A) and one who had frequent episodes (B). Real-time tracings of ECG during control period and ST-segment elevation are shown on the right. Recurrent ST-segment elevation is observed in case B.
Most of the early particular physical occurrence only. However, more than 30 ST-segment elevations per day were observed only in three tapes. ST-segment elevations recurring 3 times/hour or more were observed in 19 tapes in 10 patients.

ST-segment elevation was not associated with particular physical or mental activities and usually occurred at rest. In cases of chest pain at midnight or early in the morning, the patients woke up after the occurrence of chest pain, and in cases with painless ST-segment elevation, patients were usually asleep. ST-segment elevation was not preceded by changes in heart rate in most cases. Heart rate changed slightly after the ST-segment elevation in many cases. In some cases, the heart rate increased during the ST segment elevation, whereas in some others it decreased.

**Diurnal Distribution of ST-segment Elevations With and Without Chest Pain**

The top panel of figure 3 shows the diurnal distribution of ST-segment elevations with or without chest pain. Most of the ST-segment elevations occurred from 0:00 to 10:00 hours (72%) and most frequently between 5:00 and 6:00 hours (48 episodes/hour [13%]). A few episodes of ST-segment elevations were observed between 10:00 and 18:00 hours. As shown in the lower two panels of figure 3, the same distribution pattern was found when ambulatory ECG tapes showing fewer than 6 episodes/day and those showing more than 30 episodes/day were analyzed separately. There were more ST-segment elevations without pain than with pain (287 vs 77). Furthermore, in tapes showing frequent episodes, fewer painful ST-segment elevations were observed.

**Arrhythmias Accompanying ST-Segment Elevation**

Seventeen of 26 patients had PACs, PVCs, VT or CAVB at least once during ST-segment elevation. However, only 42 of 364 episodes of ST elevation exhibited arrhythmias (12%). Arrhythmias were more frequent during episodes associated with chest pain (25 of 77 episodes, 32%) than during episodes without chest pain (17 of 287, 6%) ($p < 0.005$). However, even in cases without chest pain, more severe forms of PVCs, such as couplets and bigeminy, were observed in seven events and VT occurred in three (table 1). Most arrhythmias and all episodes of VT occurred when the elevated ST segment was returning to the control level or had just started to return. Arrhythmias were less frequent when the ST segments were still rising.

Figure 4 shows a case in which couplets and three consecutive PVCs (VT) occurred during a painless episode of ST-segment elevation. No arrhythmias occurred when the ST segment was rising, but couplets of PVCs and VT appeared when the ST segment was returning to its control level.

The incidence of arrhythmias during ST-segment elevation was higher when the daily number of episodes was small (1–5 times/day) than when the episodes were more frequent (6–19 times/day) (table 2). When the episodes were very frequent ($\geq 31$ times/day), no arrhythmias were observed.

Figure 5 shows relationship between the number of ST-segment elevations per day and the incidence of arrhythmias during the episodes. An inverse, curvilinear (logarithmic) relationship was found ($p < 0.01$).
TABLE 1. Arrhythmias During ST-segment Elevations and Their Time of Occurrence in Relation to the ST-segment Shift

<table>
<thead>
<tr>
<th></th>
<th>With pain</th>
<th></th>
<th>Without pain</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rising</td>
<td>Return-</td>
<td>Both</td>
<td>Total</td>
</tr>
<tr>
<td>VT</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>PVCs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Couplets</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Bigeminy</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>PACs</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>CAVB</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>20</td>
<td>5</td>
<td>31</td>
</tr>
</tbody>
</table>

Some of the ST-segment elevations accompanied more than one kind of arrhythmia. Abbreviations: VT = ventricular tachycardia; PVCs = premature ventricular contractions; PACs = premature atrial contractions; CAVB = complete atrioventricular block.

ST-segment Elevation Due to Postural Change

In 24 of 57 ambulatory ECG tapes obtained from 57 patients without variant angina, ST-segment elevation of 1 mm or greater was observed 41 times on trend-grams of the ST segment. These shifts were abrupt, usually lasted several minutes to a few hours, and then abruptly returned to the control level. Observation of

the oscilloscope or real-time ECG tracing during the ST-segment elevation revealed that the shift of ST segment occurred within one or two beats of abrupt changes in the QRS complex. Such changes in the QRS complex and the ST segment were considered to be caused by postural change or to be artifactual. There were no episodes of smooth ST-segment shifts without

FIGURE 4. Ventricular arrhythmias during painless ST-segment elevation. All strips are continuous recordings. Ventricular tachycardia (three consecutive premature ventricular contractions) occurred while the elevated ST segment was returning to its control level.
A significant inverse correlation was found.

**Table 2. Incidence of Arrhythmias During ST-segment Elevations With and Without Chest Pain and Its Relation to Daily Frequency of Episodes**

<table>
<thead>
<tr>
<th>No. of episodes per day</th>
<th>Incidence of arrhythmias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With pain (%)</td>
</tr>
<tr>
<td>1–5</td>
<td>19/32 (59)</td>
</tr>
<tr>
<td>6–19</td>
<td>6/41 (15)</td>
</tr>
<tr>
<td>31–68</td>
<td>0/4 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>25/77 (32)</td>
</tr>
</tbody>
</table>

There is a significant difference between the totals for each group (p < 0.005).

Arrhythmias During ST-segment Elevation

Arrhythmias were observed in 12% of 364 episodes of ST-segment elevation. Arrhythmias were more common in painful episodes than in painless ones. However, more severe forms of ventricular arrhythmias, such as bigeminy, couplets and VT, were also observed during the painless episodes. This finding indicates that painless episodes of ST-segment elevation, like those with chest pain, are also a potential cause of sudden death. Therefore, in patients with variant angina, silent ST-segment elevation should be sought by 24-hour ambulatory ECG monitoring.

Some of the arrhythmias occurred while the ST segment was still rising, but most occurred when the ST segment started to decline. All episodes of VT occurred during the latter period. Arrhythmias at this period may be explained by the so-called reperfusion arrhythmias shown in experimental myocardial ischemia. If this is the case, these arrhythmias will be difficult to control by antiarrhythmic agents and the prevention of ST-segment elevation by calcium antagonists or long-acting nitrates will be very important.
References

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