ACUTE ELECTROCARDIOGRAPHIC CHANGES ASSOCIATED WITH SUCCESSFUL CORONARY THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION

HIROSHI SATO, M.D., KAZUHISA KODAMA, M.D., TOHRU MASUYAMA, M.D.
SHINSUKE NANTO, M.D., KAZUO KOMAMURA, M.D.
AND MICHTOSHI INOUE, M.D.*

In this study ECG changes were analyzed to assess the acute effects of antegrade blood flow on the ECG in patients with AMI. The study population consisted of 22 patients with MI in whom the totally occluded left anterior descending artery (LAD) or right coronary artery (RCA) was recanalized by intracoronary urokinase infusion (recanalized group) and 14 patients in whom the occluded coronary artery was not successfully recanalized (control group). No significant difference was found in the sum of ST segment elevation (V2-V4 leads for the LAD-occluded group, II, III and aVF leads for the RCA-occluded group) before urokinase infusion. In the recanalized group $\Sigma ST$ abruptly increased at 5 min after recanalization in 13 of 16 LAD-occluded patients from $1.49 \pm 0.89 \text{ mV}$ to $2.44 \pm 1.67 \text{ mV} (p < 0.005)$, and in 4 of 6 RCA-occluded patients from $0.66 \pm 0.12 \text{ mV}$ to $1.42 \pm 0.52 \text{ mV} (p < 0.01)$. However, increased $\Sigma ST$ in the recanalized group was reduced to the control value existing before recanalization within 30 min after recanalization and continued to decline more rapidly than in the control group. These transient ST segment elevations were not correlated with long-term angiographic determinants of left ventricular function. We conclude that ST segment shows abrupt augmentation after successful thrombolysis and that continuous ST segment monitoring is useful for assessing thrombolysis in AMI.

INTRACORONARY thrombolysis is now thought to be a useful method for salvaging ischemic myocardium in patients with AMI. The importance of salvaging ischemic myocardium with successful thrombolysis has been suggested in many clinical studies using ventriculographic, echocardiographic, radionuclide and ECG parameters. It has been reported that successful intracoronary thrombolysis is accompanied by ECG changes such as regression of ST segment elevation within a few hours after thrombolysis, acceleration of Q wave development and reperfusion arrhythmias. Elevated ST segment declining to the baseline within a few hours after intracoronary thrombolysis has been reported to be a noninvasive indicator for successful thrombolysis. However, acute ST segment changes accompanying restoration of antegrade blood flow in successful thrombolysis have never been carefully studied.

The purposes of this study were to closely analyze acute ECG changes occurring before and

Key words:
ST segment
Coronary thrombolysis
Acute myocardial infarction

(Received July 30, 1986; accepted October 9, 1986)
The cardiovascular division, Osaka Police Hospital, and *The First Department of Internal Medicine, Osaka University Medical School, Osaka, Japan
Mailing address: Hiroshi Sato, M.D., The cardiovascular Division, Osaka Police Hospital, 10-31 Kitayama-cho, Tennoji-ku, Osaka 543, Japan

Japanese Circulation Journal Vol. 51, March 1987 265
TABLE I  CLINICAL AND CORONARY ANGIOGRAPHIC DATA

<table>
<thead>
<tr>
<th></th>
<th>Recanalized group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LAD</td>
<td>RCA</td>
</tr>
<tr>
<td>No. of patients</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62 ± 10</td>
<td>59 ± 12</td>
</tr>
<tr>
<td>Sex</td>
<td>13M, 3F</td>
<td>4M, 2F</td>
</tr>
<tr>
<td>Duration of symptoms before UK (hours)</td>
<td>3.6 ± 2.2</td>
<td>3.9 ± 2.6</td>
</tr>
<tr>
<td>Extent of coronary artery disease*</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>1 vessel disease</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>2 vessel disease</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Collaterals</td>
<td>8</td>
<td>2</td>
</tr>
</tbody>
</table>

Abbreviations: LAD = left anterior descending artery, RCA = right coronary artery, UK = urokinase
*coronary artery stenosis greater than 75%

after coronary thrombolysis and to examine whether any of these changes can be used to predict the occurrence and the timing of successful coronary thrombolysis.

METHODS

Patient selection
The study population consisted of 48 consecutive patients with transmural AMI in whom coronary thrombolysis was performed. Eight patients with cardiogenic shock, complete right bundle branch block, left ventricular hypertrophy, previous infarction and reinfarction or pericarditis during follow-up were excluded, as were four patients with subendocardial infarction. Therefore 36 patients, 28 men and 6 women, aged 44 to 74 years (mean 61 years) were studied. In 25 of these 36 patients, the left anterior descending artery (LAD) was found to be completely occluded in the initial angiogram, and in the remainder, the right coronary artery (RCA) was occluded. Sixteen of the 25 LAD-occluded patients and 6 of the 11 RCA-occluded patients were successfully recanalized by urokinase within six hours after the onset of chest pain (recanalized group) while the others were not successfully recanalized (control group). There was no significant difference between two groups in age distribution, sex, duration of symptom before urokinase infusion or extent of coronary artery diseases (Table I).

In all patients, the ECGs obtained before initial angiography showed ST segment elevations of at least 0.1 mV in at least two precordial leads other than V1 (LAD occlusion) and at least two of II, III and aVF (RCA occlusion). The diagnosis of MI was confirmed retrospectively by an observed increase in creatine phosphokinase (CPK) to at least three times the upper normal limits.

Coronary artery stenosis greater than 75% of the arterial diameter was recognized as significant.

Intervention and treatment
Before cardiac catheterization, 100–200 U/kg heparin sodium was infused intravenously as a bolus. Using an 8-Fr. Judkins catheter by the percutaneous femoral approach, coronary angiography of the unaffected coronary artery was first performed, followed by angiography of the coronary artery supplying the area of the evolving infarction. We then slowly injected 0.1 mg of nitroglycerin into the totally occluded artery to rule out spasm as the cause of the coronary artery occlusion and then repeated the angiography of the coronary artery. Next, we infused 240,000 U of urokinase into the occluded coronary artery for 15 min and then repeated the coronary angiography. We added another 240,000 U of urokinase into the affected coronary artery every 15 min until the artery began to open or until a total dose of 960,000 U had been given. To determine the time of recanalization, coronary angiography was repeated at about 15-minute intervals and was also performed when dysrhythmia developed or the symptom changed.
**TABLE II  TIMES OF ELECTROCARDIOGRAPHIES IN RELATION TO THE ONSET OF CHEST PAIN**

<table>
<thead>
<tr>
<th>ECG No.</th>
<th>Recanalized group (hours)</th>
<th>Control group (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>before UK</td>
<td>before UK</td>
</tr>
<tr>
<td>2</td>
<td>before rec.</td>
<td>just after UK</td>
</tr>
<tr>
<td>3</td>
<td>5 minutes after rec.</td>
<td>5 minutes after UK</td>
</tr>
<tr>
<td>4</td>
<td>10 minutes after rec.</td>
<td>10 minutes after UK</td>
</tr>
<tr>
<td>5</td>
<td>20 minutes after rec.</td>
<td>20 minutes after UK</td>
</tr>
<tr>
<td>6</td>
<td>30 minutes after rec.</td>
<td>30 minutes after UK</td>
</tr>
<tr>
<td>7</td>
<td>2 hours after rec.</td>
<td>2 hours after UK</td>
</tr>
<tr>
<td>8</td>
<td>6 hours after rec.</td>
<td>6 hours after UK</td>
</tr>
<tr>
<td>9</td>
<td>24 hours after rec.</td>
<td>24 hours after UK</td>
</tr>
</tbody>
</table>

Abbreviations: ECG = electrocardiography; UK = urokinase; rec. = recanalization

**Fig.1.** Evolution of electrocardiographic change in a recanalized group patient

During cardiac catheterization, arterial oxygen and electrolyte concentrations were measured every 30–60 min. If the PO2 was lower than 80 mmHg, oxygen was administered via a nasal cannula or face mask and if the potassium concentration was lower than 4.0 mEq/L, potassium chloride solution was infused at a rate of 10–20 mEq/hour intravenously. The anti-arrhythmia
TABLE III

<table>
<thead>
<tr>
<th>Anteroseptal Infarction</th>
<th>ECG No.</th>
<th>recanalized group</th>
<th>control group</th>
<th>Inferior Infarction</th>
<th>ECG No.</th>
<th>recanalized group</th>
<th>control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>1.59 ± 0.84</td>
<td>1.84 ± 0.88</td>
<td>2.40 ± 1.43*</td>
<td>1.86 ± 0.84*</td>
<td>1.49 ± 1.33</td>
<td>1.23 ± 0.94</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>1.83 ± 1.33</td>
<td>1.48 ± 1.07</td>
<td>1.40 ± 1.15</td>
<td>1.51 ± 1.21</td>
<td>1.48 ± 1.07</td>
<td>1.25 ± 0.45</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1.83 ± 1.60</td>
<td>1.55 ± 1.17</td>
<td>1.51 ± 1.17</td>
<td>1.51 ± 1.21</td>
<td>1.48 ± 1.07</td>
<td>1.25 ± 0.45</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>1.55 ± 1.17</td>
<td>1.51 ± 1.21</td>
<td>1.48 ± 1.07</td>
<td>1.40 ± 1.15</td>
<td>1.40 ± 1.15</td>
<td>1.25 ± 0.45</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>1.55 ± 1.17</td>
<td>1.51 ± 1.21</td>
<td>1.48 ± 1.07</td>
<td>1.40 ± 1.15</td>
<td>1.40 ± 1.15</td>
<td>1.25 ± 0.45</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>1.55 ± 1.17</td>
<td>1.51 ± 1.21</td>
<td>1.48 ± 1.07</td>
<td>1.40 ± 1.15</td>
<td>1.40 ± 1.15</td>
<td>1.25 ± 0.45</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>1.55 ± 1.17</td>
<td>1.51 ± 1.21</td>
<td>1.48 ± 1.07</td>
<td>1.40 ± 1.15</td>
<td>1.40 ± 1.15</td>
<td>1.25 ± 0.45</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>1.55 ± 1.17</td>
<td>1.51 ± 1.21</td>
<td>1.48 ± 1.07</td>
<td>1.40 ± 1.15</td>
<td>1.40 ± 1.15</td>
<td>1.25 ± 0.45</td>
</tr>
</tbody>
</table>

Table III: Comparison of $\sum ST$ between recanalized group and control group (mean ± S.D. mV)

Drug disopyramide 50–150 mg was administered intravenously to treat ventricular arrhythmias in six patients and atrial fibrillation in three patients.

**Electrocardiographic measurements**

Twelve lead ECG were recorded at one-minute intervals during cardiac catheterization and nine recordings were made (Table II). The time intervals from onset of symptoms to analysis of ECG recordings were almost identical in the recanalized group and the control group and ranged between 1 (before urokinase infusion) to 9 (24 hours after recanalization in the recanalized group or 24 hours after urokinase infusion in the control group). ST was defined in LAD-occluded patients $\sum ST$ as the sum of the ST segment elevation above the baseline determined by the preceding TP segment, 0.04 seconds after the end of the QRS, in leads V2, V3 and V4 and, in RCA-occluded patients, as the sum of the ST segment elevation in leads II, III and aVF. All ECG measurements were calculated as the mean values of 10 beats.

**Long term studies**

In 21 of 25 LAD-occluded patients, coronary angiography and left ventriculography were studied 43 ± 12 days after the initial angiography. Coronary angiograms were assessed by two independent observers.

Follow-up ejection fractions (EFs) and regional EFs (rEFs) were determined from the left ventriculogram by the area-length method. The left ventricular silhouette (30° right anterior oblique view) was divided into five areas and rEFs of anteroseptal and apical areas were measured as the difference between diastolic and systolic regional areas divided by the diastolic regional area. The percentage length of the abnormally contracting segments was determined by the method of Field et al., as follows:

%ACS = (akinetic and/or dyskinetic length of end-diastolic circumference)/(whole end-diastolic circumference)

Local wall motion was qualitatively evaluated according to the American Heart Association system for segmental left ventricular wall motion assessment.

**Statistical analysis**

Data are presented as mean ± SD. Analysis of variance and the paired t-test were used for comparing serial $\sum ST$ in both recanalized and control
ECG Changes Associated with Coronary Thrombolysis

Fig. 2. $\Sigma$ST changes of LAD-occluded patients in the recanalized group (top) and in the control group (bottom). $\Sigma$ST abruptly increased within 5 min after thrombolysis and rapidly declined to the baseline in the recanalized group. $\Sigma$ST = the sum of the ST segment elevation in leads V2, V3 and V4.

In the control group, $\Sigma$ST was $2.10 \pm 1.35$ mV before urokinase infusion, and it gradually declined for 24 hours.

In the recanalized group, $\Sigma$ST segment elevation ($1.59 \pm 0.84$ mV) before urokinase infusion did not differ significantly from that in the control group. ST segment increased abruptly in 13 of 16 LAD-occluded patients of the recanalized group within five min after intracoronary

RESULTS

Anteroseptal Infarction

thrombolysis (Fig. 1) and the mean ΣST was significantly greater five min after recanalization than before recanalization (2.40 ± 1.45 mV vs 1.48 ± 0.88 mV, p < 0.005, Table III). The augmentation of ΣST rapidly decreased within 10 min after recanalization in all but one patient. ΣST gradually declined and returned to the level existing before recanalization about 20 min after recanalization (1.49 ± 1.33 mV). The ΣST further continued to decline for 24 hours after recanalization up to 0.67 ± 0.34 mV. In the recanalized group ΣST values at two hours, six hours and 24 hours after urokinase were significantly lower than those in control group (p < 0.05 in Fig. 2).

Residual coronary stenosis after successful thrombolysis, elapsed time from the onset of chest pain and the existence of collaterals to the infarct vessel did not affect the degree of augmentation of ST segment (ΔΣST: change in ΣST from before recanalization to five min after recanalization) in successfully recanalized patients, as shown in Fig. 3.

**Inferior Infarction**

In the control group, ΣST, was 0.98 ± 0.57 mV before urokinase infusion, and it then declined gradually for 24 hours.

In the recanalized group, ΣST segment elevation (0.84 ± 0.19 mV) before urokinase infusion did not differ significantly from that in the control group. ST segment increased abruptly in four of six RCA-occluded patients of the recanalized group within five min after intracoronary thrombolysis and the mean ΣST was significantly greater five min after recanalization than before recanalization (1.41 ± 0.51 mV vs 0.70 ± 0.18 mV, p < 0.05). The augmentation of ΣST rapidly decreased within 10 min after recanalization in all four patients. ΣST gradually declined and returned to the level existing before recanalization about 20 min after recanalization (0.61 ± 0.31 mV). The ΣST further continued to decline for 24 hours after recanalization up to 0.16 ± 0.13 mV. In the recanalized group ΣST values at 30 min, two hours, six hours and 24 hours after Urokinase were significantly lower than those in the control group (p < 0.05) (Fig. 4).

**Ventricular arrhythmias**

Ventricular premature beats appeared during cardiac catheterization in 14 of 22 patients in the recanalized group and in 8 of 14 patients in the control group. Six patients of the recanalized group develop ventricular tachycardia, accelerated idioventricular rhythm or frequent ventricular premature beats precisely at the time of restoration of antegrade blood flow. However 16 of
ECG Changes Associated with Coronary Thrombolysis

Fig. 4. STE changes of RCA-occluded patients in the recanalized group (top) and in the control group (bottom). STE abruptly increased within 5 min after thrombolysis and rapidly declined to the baseline in the recanalized group. STE = the sum of the ST segment elevation in leads II, III and aVF.

TABLE IV EJECTION FRACTION, REGIONAL EJECTION FRACTION AND ABNORMALLY CONTRACTING SEGMENT IN THE CHRONIC STAGE OF INFARCTION IN LAD-OCCULDED PATIENTS

<table>
<thead>
<tr>
<th>Recanalized group (n = 14)</th>
<th>Control group (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>56 ± 13</td>
</tr>
<tr>
<td>rEF (%)</td>
<td>26 ± 10</td>
</tr>
<tr>
<td>ACS (%)</td>
<td>39 ± 10</td>
</tr>
</tbody>
</table>

Abbreviations: EF = ejection fraction, rEF = regional ejection fraction, ACS = abnormally contracting segment, NS = not significant

22 patients in the recanalized group did not have any arrhythmic episodes coincident with recanalization.

Long-term study

In LAD-occluded patients, coronary angiography and left ventriculography were performed at the chronic stage. In all 13 restudied patients in the recanalized group, no infarct vessel was occluded. On the other hand, among patients without successful thrombolysis, two of the LAD-occluded patients and two of the RCA-occluded patients showed recanalization of the infarct vessel at the site of the acute complete obstruction. In LAD-occluded patients, follow-up ventriculography showed an anterolateral and
apical aneurysm in two of six patients in the control group but in only one patient in the recanalized group. Ejection fraction, regional ejection fraction, and percentage length of abnormally contracting segments were not significantly different in the two groups but left ventricular function tended to be good in the successfully recanalized group as shown in Table IV.

DISCUSSION

In this study, ECG changes were analyzed to assess the acute effects of antegrade blood flow on the ECG in patients with AMI in whom complete obstruction of the LAD or RCA observed on the initial angiogram was recanalized by intracoronary urokinase. Abrupt augmentation of elevated ST segment within five min after coronary thrombolysis was observed in 17 of 22 patients of the recanalized group. The augmentation was transient and returned to the previous level within 30 min. ST segments in the recanalized group declined to the baseline more rapidly than those in the control group; therefore, $\Sigma$ST in the recanalized group was significantly lower than that in the control group several hours after successful coronary thrombolysis for both LAD- and RCA-occluded patients. The ECG features associated with intracoronary thrombolysis during evolving myocardial infarction has been well described in many animal experiments and patient studies. Maroko and co-workers found a significant reduction of ST segment elevation within 30 min after reperfusion of 3-hour coronary occlusion in dogs. Blanke et al. found that ST segment elevation in 14 patients treated with intracoronary streptokinase declined more rapidly than in conventionally treated control patients and concluded that these ST segment changes may be secondary to relief of ischemia rather than myocardial necrosis because of the finding of smaller infarct size in the successfully thrombolized group as determined by ECG and ventriculographic findings. Our findings were comparable to theirs. Moreover, we found new evidence that the elevated ST segment abruptly increased immediately after recanalization and was followed by the return of ST segment within 30 min to the previous level existing before recanalization. The transient ST segment elevation which was precisely coincident with the time of coronary reperfusion might indicate myocardial injury or extension of infarction; however, we could not find any residual manifestation of myocardial injury in our left ventriculographic results at the chronic stage.

The mechanism of abrupt ST segment elevation associated with thrombolysis is still unknown but several possible mechanisms can be considered. The ST segment is generally thought to be affected by numerous factors such as myocardial injury, oxygen, drugs and electrolytes. Hemorrhagic edema observed in the reperfused ischemic myocardium might abruptly alter the electrophysiological properties of myocardial cells and possibly contribute to the rapid augmentation of ST segment. However it is unlikely that these electrophysiological changes would disappear within 30 min and reduce the ST segment to that level existing before recanalization. Secondly, wash-out of ions from the interstitial space might also rapidly change the electrophysiological properties of myocardial cells. It has been reported that accumulation of extracellular potassium occurs within seconds after initiation of ischemia and that, on reperfusion, this increase of extracellular potassium rapidly returns to the control level within two min. Recently Serruys et al. reported that coronary sinus potassium did not change significantly during coronary occlusion, and that a transient rise in potassium occurred within eight seconds after removal of occlusion in two patients in whom angiography for significant stenosis of their left anterior descending arteries was performed. Thus a decrease of ST segment elevation toward the baseline may be explained by washout of potassium ions from the interstitial space. Further studies are required to assess the role of electrolytes affecting the electrophysiological properties of the myocardium.

In patients with angiographically demonstrable collaterals, infarction may proceed more slowly and the restoration of antegrade flow may be less effective than in patients without collaterals; however the degree of abrupt ST segment augmentation was not significantly different between patients with and without angiographically demonstrable collaterals.

Residual coronary stenosis after recanalization by thrombolysis may regulate antegrade blood flow pressure and volume. In this study six of the 13 LAD-occluded patients and one of the 4 RCA-occluded patients had severe stenosis greater than 99% in diameter after successful thrombolysis. The high degree of residual stenosis after recanalization did not affect the degree of ST.

*Japanese Circulation Journal Vol. 51, March 1987*
segment augmentation.

The time from the onset of symptoms to recanalization is thought to be one of the significant factors affecting relief of the ischemic myocardium during coronary thrombolysis. In this study a majority of the patients in both control and recanalized groups underwent coronary angiography within four hours after the onset of symptoms and obtained successful recanalization within six hours. Although the degree of elevated ST segment augmentation was slightly greater in patients whose coronary artery was recanalized within four hours than in patients who were recanalized four to six hours after the onset of chest pain, there was no significant difference.

Antegrade blood flow has been reported to produce various electrocardiographic changes such as decline of ST segments toward the baseline, acute reduction in R-wave amplitude, development of Q wave and reperfusion arrhythmias. In this study ventricular arrhythmias were observed in 14 patients of the recanalized group (64%) and in eight patients of the control group (72%) during cardiac catheterization and there was no significant difference between them. This may be explained by the frequent treatment of electrolyte and oxygen disorders during this study. We found reperfusion arrhythmia such as ventricular tachycardia and accelerated idioventricular rhythm in only six of the 22 recanalized patients precisely at the time of restoration of antegrade blood flow. Ventricular arrhythmias and 'reperfusion' arrhythmias developed less frequently in this study than in previous reports. In such circumstance ventricular arrhythmia might not be as good a marker for successful coronary thrombolysis as augmentation of ST segment elevation.

Thus we conclude that augmentation of ST segment elevation is a good marker for successful coronary thrombolysis in patients with acute transmural infarction. It is noted that re-elevation of ST segment might also be observed when variant-type of angina, re-infarction and left ventricular aneurysm are complicated with evolving acute myocardial infarction. However it is possible to differentiate between them by observing the symptoms accompanying such ischemic events. ST segment elevation by left ventricular aneurysm would not be transient as in the case of augmentation of ST segment elevation with coronary thrombolysis.

The mechanisms of the abrupt augmentation of ST segment elevation are still unknown, but ST segment seems to be a simple and useful marker for the occurrence and the timing of successful coronary thrombolysis when recanalization is undertaken and when coronary angiography is not available.

REFERENCES


11. FIELD BJ, RUSSEL O, DOWLING JT, RACKLEY CE: Regional ventricular performance in the year.


