Electrocardiographic changes after streptokinase-induced recanalization in patients with acute left anterior descending artery obstruction

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ABSTRACT ECG changes were assessed in 15 patients in whom intracoronary streptokinase recanalized a totally occluded left anterior descending artery during acute myocardial infarction. These results were compared retrospectively with those in 22 comparable conventionally treated patients who underwent catheterization during the acute stage of infarction. Before angiography no significant differences were found in the sum of ST elevation (ΣST (V1-V6)), the sum of R waves (ΣR (V1-V6)), or the number of Q waves (nQ (V1-V6)) in leads V1 through V6. ΣST (V1-V6) was significantly lower in the streptokinase group than in control patients at all times after angiography. ΣR (V1-V6) declined and nQ (V1-V6) increased in both groups during the first 12 hr, but there was no further change in the control group, whereas in the streptokinase group a significant increase in ΣR (V1-V6) and decrease in nQ (V1-V6) followed. There was a significant correlation between long-term electrocardiographic (ΣR (V1-V6); nQ (V1-V6)) and angiographic findings (ejection fraction, akinetic segment length). Thus, the Q wave regression and increase in ΣR (V1-V6) after streptokinase suggest, in accordance with angiographic findings, that jeopardized myocardium was salvaged by reperfusion. Circulation 68, No. 2, 406–412, 1983.

THE PURPOSE of intracoronary streptokinase (SK) therapy is to relieve ischemia and thereby limit infarct size; preliminary studies of changes in left ventricular function after reperfusion suggest that this can be achieved. In this study electrocardiographic (ECG) changes in reperfused and conventionally treated patients were compared to determine whether there are ECG signs that indicate relief of ischemia and limitation of infarct size by reperfusion. ECG and ventriculographic parameters of infarct size were correlated.

Patients and methods

Patient selection. ECG changes were assessed in 15 patients in whom complete left anterior descending artery (LAD) obstruction was recanalized by intracoronary SK infusion during acute myocardial infarction. The following exclusion criteria were applied in selecting the SK group from the first 18 consecutive patients who underwent recanalization for an acute LAD obstruction: cardiogenic shock, complete bundle branch block, left ventricular hypertrophy by ECG criteria, axis changes during follow-up, previous anterior wall infarction, and reinfection or pericarditis during follow-up.

These results were compared with ECG changes in a control group of 22 patients who were selected from a total group of 32 patients with complete LAD obstruction who underwent angiography during the acute stage of infarction, before the advent of interventional techniques. The same exclusion criteria were applied to this group.

In all patients the ECGs obtained immediately before angiography showed ST elevations of at least 0.15 mV in at least two precordial leads other than V1. The diagnosis of infarction was confirmed retrospectively by an increase in creatine kinase (CK) to at least twice the upper limit of normal. During the first 6 hr patients were entered into the study regardless of whether or not symptoms persisted; beyond 6 hr, only those with persistent symptoms were included.

All patients were studied at the same institution between January 1977 and December 1980. There were no differences between the two groups in age distribution, duration of symptoms before angiography, or history of previous myocardial infarction (table 1). One patient in each group had had a known prior inferior wall myocardial infarction. No other patients had Q waves outside of the anterior precordial leads, and no others had angiographic wall motion abnormalities outside the region supplied by the LAD. Although there were more patients with two-vessel coronary artery disease in the control group, the number of coronary arteries with greater than 50% stenoses per patient was comparable in both groups.

A constant left anterior hemiblock was present throughout the observation period in three SK group patients and four control group patients. Four of the patients with left anterior hemiblock (two in each group) had no Q waves in leads V1 through V3 on
TABLE 1
Clinical and coronary angiographic data

<table>
<thead>
<tr>
<th></th>
<th>SK group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56±7</td>
<td>57±8</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>14/1</td>
<td>18/4</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>prior to angiography (hr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.9±4.5</td>
<td>5.6±4.2</td>
<td></td>
</tr>
<tr>
<td>Extent of coronary artery disease (50% stenoses)</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>One-vessel disease</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>1.60</td>
<td>1.64</td>
</tr>
<tr>
<td>No. of &gt; 50% stenoses/patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>1 (infect)</td>
<td>1 (infect)</td>
</tr>
</tbody>
</table>

The initial ECG. The other patients with left anterior hemiblock—one in the SK group and two in the control group—had Q waves wider than 30 msec in leads V1 through V3 on presentation.

Intra-aortic counterpulsation was applied during acute infarction in eight control patients who were enrolled in a concurrent study of counterpulsation in routine myocardial infarction. These patients were neither hypotensive nor in shock. No SK group patients underwent counterpulsation. There were no significant differences in blood pressure at the time of initial angiography between patients in the SK and control groups.

Interventions and treatment. The techniques used for initial angiography and selective intracoronary SK administration have been previously described. Recanalization was demonstrated angiographically after 23 ± 22 min of SK infusion. The total duration of the infusion was 69 ± 17 min, with a total dose of 90,000 to 180,000 U. In two patients recanalization was achieved by a combination of guidewire perforation of the clot and intra coronary SK. Before angiography all patients in the SK group received a single dose of prednisolone (747 mg).

In all patients of both groups, an intravenous nitroglycerin infusion (1.5 to 9 mg/hr) was begun on hospital admission. All patients in the SK group were maintained on more than 15,000 units/day heparin by continuous intravenous infusion for 3 to 4 days after interventional angiography. Overlapping warfarin (Coumadin) therapy was instituted and maintained throughout the follow-up period. In the control group 17 patients were treated with more than 15,000 units of heparin by intravenous infusion during the initial stage, followed by warfarin in all patients. The remaining five control patients received 15,000 units/day heparin subcutaneously during the initial stage. During the follow-up period aortocoronary bypass surgery was performed in only two SK patients (days 2 and 3), whom we continued to follow.

Long-term studies. Angiography was repeated in 14 SK group patients 26 ± 12 days and in 15 control patients 88 ± 77 days after the initial angiogram. In all 14 restudied patients in the SK group the infarct vessel was patent at repeat angiography and at the site of previous occlusion there was a greater than 60% lesion. In the control group seven patients showed spontaneous recanalization of the infarct vessel with a greater than 70% lesion at the site of acute obstruction.

Angiographic assessments. Initial and follow-up ejection fractions (EFs) were determined from biplane contrast cineventriculograms by the area-length method. The length of the akinetic segments (AKS) was determined by the method of Feild. Local wall motion was qualitatively assessed with the criteria of Herman and Gorlin7 and the severity of coronary artery lesions was determined by the criteria of Gensini.8 Stenoses occluding greater than 50% of the arterial diameter were regarded as significant.

ECG measurements. In each patient six 12-lead ECGs were obtained at intervals shown in table 2. Time intervals I through V were almost identical in the SK and control groups, while the follow-up ECG was obtained significantly later in the control group. In both groups, the locations of leads V1 through V6 were marked on each patient's chest on admission to ensure consistent electrode placement in the recording of ECGs I through V.

The following parameters were calculated: (1) ΣST ↑ Vr-V6 (the sum of ST elevations above the baseline defined by the preceding TP segment, 20 msec after the end of the QRS complex, in leads V1 through V6 [figure 1]), (2) nQVr-V6 (the number of pathologic Q waves in the precordial leads, with any Q waves in leads V1 through V3 and Q waves wider than 20 msec in V4, and than 30 msec in V5 and V6, considered pathologic), and (3) ΣR Vr-V6 (the sum of R wave height in V1 through V6).

Statistical analysis. Data are presented as mean ± SD. The paired t test or Student's t test for unpaired data was used. Linear regression equations were calculated that related the ECG variables (ΣR Vr-V6 and nQVr-V6) and the angiographic measurements (EF and length of AKS). A p greater than .05 was considered nonsignificant.

Results

ΣST ↑ Vr-V6. Two examples of the evolution of ECG changes in ruptured patients are illustrated in figure 2.

Before angiography (ECG I) ΣST ↑ Vr-V6 was not significantly different in the two groups. From before angiography to immediately afterwards, the sum decreased 60% (p < .0025) in the SK group, while decreasing only 13% (NS) in the control group at compa-
rable times after the onset of infarct symptoms (figure 3). Thus, $\Sigma ST \uparrow_{V_1-V_6}$ after angiography in the SK group was less than half that in the control group. A significant difference persisted on all subsequent ECGs.

$\Sigma R_{V_1-V_4}, \Sigma R_{V_1-V_6}$ was not significantly different in the two groups before angiography (ECG I). There was a significant decrease in $\Sigma R_{V_1-V_6}$ from ECG I to ECG III in both groups (figure 4). In the control group, $\Sigma R_{V_1-V_6}$ did not change from ECG III to ECG VI. In the SK group, however, $\Sigma R_{V_1-V_6}$ increased significantly from ECG III to ECGs V and VI. In ECGs IV through VI,
FIGURE 3. Changes in \( \Sigma S T_{V1-V6} \) during the study period.

\( \Sigma R_{V1-V6} \) was significantly higher in the SK group than in the control group. In the SK group \( \Sigma R_{V1-V6} \) in ECG VI was not significantly different from that in ECG I; in the control group, however, \( \Sigma R_{V1-V6} \) was significantly lower in ECG VI than in ECG I.

\( nQ_{V1-V6} \) was not significantly different in the two groups before angiography (figure 5). There was a significant increase in \( nQ_{V1-V6} \) from ECG I to ECG III in both groups. In the control group there was no significant change in \( nQ_{V1-V6} \) from ECG III to ECG VI, whereas in the SK group \( nQ_{V1-V6} \) significantly decreased from ECG III to ECGs V and VI. In ECGs IV to VI, \( nQ_{V1-V6} \) was significantly smaller in the SK group than in the control group. In the control group \( nQ_{V1-V6} \) was significantly larger in ECG VI than in ECG I; in the SK group, however, \( nQ_{V1-V6} \) was not significantly different in ECG VI than in ECG I.

In the control group, no significant differences between patients with spontaneous recanalization and those with persistent occlusion were noted with respect to \( \Sigma S T_{V1-V6} \) or other ECG variables. There were also no differences between those who underwent intra-aortic balloon counterpulsation and the remaining control patients. ECGs were examined before and after surgery in the two SK group patients who received bypass grafting. In one patient there were no immediate perioperative changes; in the other small precordial \( Q \) waves developed after surgery.

Changes in left ventricular function in relation to ECG changes. In the SK group there was a significant increase in EF from the initial to the follow-up stage, as well as a significant decrease in the length of the AKS. Neither EF nor the length of the AKS changed in the control group (table 3). The follow-up angiogram showed an anterolateral and apical aneurysm in five patients of the control group but in no patient of the SK group. For those patients in the total population (SK

FIGURE 4. Changes in \( \Sigma R_{V1-V6} \).

FIGURE 5. Changes in \( nQ_{V1-V6} \).
TABLE 3
Changes in EF, length of AKS, and $\Sigma R_{v_1-v_6}$ from the acute to the chronic stage of infarction

<table>
<thead>
<tr>
<th></th>
<th>SK group (n = 14)</th>
<th>Control group (n = 15)</th>
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<tbody>
<tr>
<td>EF (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>50 ± 10</td>
<td>50 ± 11</td>
</tr>
<tr>
<td>Chronic</td>
<td>57 ± 14</td>
<td>51 ± 13 NS</td>
</tr>
<tr>
<td>AKS (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>14.0 ± 2.7</td>
<td>12.2 ± 3.8</td>
</tr>
<tr>
<td>Chronic</td>
<td>5.7 ± 5.4</td>
<td>12.9 ± 11.7</td>
</tr>
<tr>
<td>$\Sigma R_{v_1-v_6}$ (mV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>3.3 ± 1.8</td>
<td>3.1 ± 2.0</td>
</tr>
<tr>
<td>Chronic</td>
<td>2.7 ± 1.7</td>
<td>1.8 ± 1.0 p &lt; .01</td>
</tr>
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</table>

and control groups) who had a repeat ventriculogram, there was a significant correlation at follow-up between each of the ECG measurements ($\Sigma R_{v_1-v_6}$ and $nQ_{v_1-v_6}$) and each of the angiographic variables (EF and length of the AKS, table 4).

Discussion

In this study ECG changes were analyzed only in patients who demonstrated a complete obstruction of the LAD on the initial angiogram, since the effect of fibrinolysis on subtotal lesions is difficult to assess. The LAD was selected for this study on the basis of previous data that indicated that only patients with infarction in the distribution of this artery consistently manifested at least one of the three classical ECG signs of acute myocardial infarction (ST elevation, new pathologic Q waves, and diminution or loss of R waves). In addition, anterior wall myocardial infarctions are particularly suitable for the measurement of evolving ECG changes in the six anterolateral leads. Zmyslinski et al. found that the six standard precordial leads can be used as an alternative to a 35-lead precordial map in following changes of anterior wall myocardial infarction because, as they observed, there is a good correlation between these two different sets of leads with respect to the sums of ST elevation, Q wave area, and R wave area.

Rapid decline in ST elevation in the setting of acute occlusion followed by reperfusion, as we found in our SK group, has been well described in many animal experiments. Gillmann et al. found that ST elevation in patients treated with intravenous SK declined more rapidly than in conventionally treated control patients. Angiographic data were not obtained in this study; however, it is conceivable that recanalization occurred in a significant percentage of patients treated with intravenous SK. The disparate rate of ST decline between patients in our SK group and those in the control group might be explained by relief of ischemia in the SK group or by more rapid death of the cells that produce ST elevation.

It is generally accepted that the loss of R waves and new Q waves after acute myocardial infarction represent loss of myocardium. In our SK group, $nQ_{v_1-v_6}$ increased and $\Sigma R_{v_1-v_6}$ decreased throughout the first 12 hr in parallel with the control group; this was followed by a reversal of this trend in the SK group only. In the follow-up period there were significantly fewer ECG signs of infarction in the SK group than in the control group.

Transient Q waves have been reported by several authors in patients with Prinzmetal’s angina and during a variety of transient ischemic events such as coronary angiography, bypass surgery, and exercise stress testing. Reports of the disappearance of Q waves in established myocardial infarction are controversial; its incidence varies tremendously from study to study and its mechanism is unknown. In almost all cases, Q waves disappeared only in the follow-up stage, weeks to years after myocardial infarction. Kalbfleisch et al. observed this phenomenon in 6.7% of 775 patients, generally by the end of the second year after infarction. Only six of their 775 patients showed regression of pathologic Q waves within 1 month. In our control group two out of 22 patients demonstrated regression of Q waves: the first, 3 days after infarction, the other at some point between discharge on day 21 and a repeat ECG recorded 3 months after infarction. Reports of Q wave regression in the subacute phase of myocardial infarction, however, are extremely rare. Six days was the shortest time interval for regression observed by Kalbfleisch. Hiat reported one patient with anterior myocardial infarction and only moderate enzyme elevation who showed a loss of Q waves within 48 hr and normalization of the ECG within 6 days.

Transient Q waves have also been described in animal models of reperfusion. Gross et al. ligated the coronary arteries of dogs until Q waves appeared and observed their disappearance several minutes after the reestablishment of blood flow. Subsequent studies of the disease process revealed slight necrosis of the subendocardial zone. Because of the short duration of

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TABLE 4
Correlations between angiographic and ECG findings in the chronic stage of infarction in 29 patients

<table>
<thead>
<tr>
<th></th>
<th>AKS = 15.7 - 2.9 $\Sigma R_{v_1-v_6}$</th>
<th>$r = -0.4454; p &lt; .025$</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF</td>
<td>$= 46.1 + 3.6 \Sigma R_{v_1-v_6}$</td>
<td>$r = 0.4130; p &lt; .05$</td>
</tr>
<tr>
<td>AKS = 2.2 + 2.8 $nQ_{v_1-v_6}$</td>
<td>$r = 0.4922; p &lt; .01$</td>
<td></td>
</tr>
<tr>
<td>EF = 61.2 - 2.9 $nQ_{v_1-v_6}$</td>
<td>$r = -0.3770; p &lt; .05$</td>
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</tr>
</tbody>
</table>
ischemia this phenomenon may be comparable to the findings of transient Q waves in Prinzmetal's angina. In a dog model of reperfusion, Kordenat and Kezdi found that Q wave regression occurred after clot lysis, but only if the occlusion lasted 1 hr or less. ECGs were not recorded beyond the acute stage. Working with primates, Smith et al. observed that the short-term decline in the sum of R and S wave heights after coronary occlusion was reversed only when reperfusion was induced within 1 hr. Reperfusion after 2, 4, or 6 hr interrupted the progressive decline in the sum of R and S wave heights but did not actually reverse it. The ECG studies were only continued for several hours and no long-term evaluation was made.

Regarding the significance of time to reperfusion in our study, it must be realized that the pathophysiology of myocardial infarction in human beings is different from that in animals. The onset of symptoms and time of occlusion are not necessarily coincident. It should be noted that a majority of the patients in both groups underwent angiography within the first 4 hr after the onset of symptoms and that only those patients with persistent chest pain were entered into the study after 6 hr. In this latter group of patients collaterals to the distribution of the infarct vessel were found more often than in patients entered into the study within the first 6 hr. In patients with angiographically demonstrable collaterals, the infarct may proceed more slowly so that patients may remain symptomatic longer and reperfusion may be successful in achieving myocardial salvage after a longer time interval.

In animal reperfusion experiments Theroux et al. observed a deterioration in left ventricular function during the first 24 hr, followed by an improvement. He hypothesized that local edema, an inflammatory reaction, or hemorrhage could explain this observation. Similar mechanisms might explain the delay we observed in regression of Q waves and the increase in height of R waves.

In agreement with previous authors we found a correlation in the chronic phase of myocardial infarction between the ECG infarct parameters and angiographic measurements. The finding of smaller infarct size in the SK group, as determined by ECG and ventriculographic parameters, suggests that the more rapid decrease in ST elevation seen in that group was probably secondary to relief of ischemia rather than to more rapid necrosis after reperfusion. In the chronic stage, the significantly higher sum of ST elevation in the control group might be attributable to the findings of ventricular aneurysm in five of the 15 patients in this group who underwent repeat angiography. In each of these five patients $\sum ST_{V_1-V_6}$ was greater than 0.6 mV.

In comparing the data from the two groups the fact that patients were compared with historical controls and that patient selection was not randomized must be kept in mind, along with those variables that differed in the two otherwise comparable groups. These variables, however, did not favor the SK group. Intra-aortic balloon counterpulsation in eight patients in the control group might have minimized the differences observed. The longer time interval between initial and follow-up measurements in the control group probably did not exaggerate the observed differences, since left ventricular function and ECG findings tend to improve with time in the follow-up stage. Recently reported data suggest that the administration of steroids to patients in the SK group is not likely to cause substantial changes in values of the parameters measured. Furthermore, in another study from our group, five patients who received both steroids and SK but did not undergo recanalization showed no improvement in left ventricular function from the initial to the follow-up stage, unlike those who did undergo the procedure.

We view coronary artery bypass grafting as a technique to be used subsequent to reperfusion in selected patients. Early coronary artery bypass surgery in two SK group patients did not appear to increase the differences observed. In one of the patients there were no immediate perioperative changes and in the other there was a worsening of the ECG infarct parameters, with the development of small anterior precordial Q waves.

The ECG data in this study, in correlation with angiographic findings, suggest that reperfusion may reduce acute ischemia and thereby limit infarct size. However, it is known from the analysis of many studies that retrospectively studied control patients tend to fare worse than those in prospectively randomized control groups. It will therefore be necessary to confirm these results in a prospectively randomized study.

References


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