Quantitative ECG changes and patency of infarct-related arteries after intravenous streptokinase

J. GOURASSAS, J. M. BENNETT, S. KONSTANTINIDES, LAURA MATZNER, C. C. VAN DER MERWE

Summary

Thirty-three patients with acute inferior myocardial infarction (MI), who were treated with intravenous streptokinase, were studied by serial 12-lead ECGs for 48 hours to determine the relationship between early changes in the sum of elevations above the baseline 40 ms after the end of the QRS complex in leads II, III and AVF (SumST), the sum of amplitude of R waves in leads II, III and AVF, the sum of the Q waves in leads II, III and AVF, the sum of ST-segment depression in leads V1 - V4 as measured from the baseline to 80 ms after the J point (SumST (V1 - V4)) and the patency of the infarct-related artery at angiography after MI. Patients with patent arteries had a faster rate of decline in the SumST during the first 2.5 hours; reached the steady state earlier; had a more pronounced decrease in the SumST at 1.25 hours; a larger percentage drop in SumR at 4.5 hours and a more pronounced SumST (V1 - V4) early on but resolution times similar to that of patients with closed arteries. Several ECG indices may indicate reperfusion of the infarct-related artery in patients with inferior MI.

Patients and methods

The study population consisted of 35 consecutive patients who were admitted to hospital within 6 hours after the onset of pain and qualified for inclusion in our intravenous SK protocol.

Inclusion criteria were: typical chest pain, duration < 6 hours but > 30 minutes, and diagnostic ECG ST-segment elevation (> 2 mm in two or more contiguous leads - II, III, AVF). Myocardial necrosis was confirmed by elevated serum levels of the cardiac enzymes in every patient.

Exclusion criteria were: the presence of bundle-branch block; QRS complex width exceeding 110 ms; and where coronary arteriography was not done.

Standard 12-lead ECGs were recorded at 25 mm/s (10 mm = 1 mv) on a 3-channel Hewlett-Packard cardiograph (model HP4700A) before the administration of SK and up to 48 hours thereafter. During the first 2 hours after the end of SK administration an ECG was recorded every 15 minutes, then every 30 minutes for the next 2 hours then at 8, 12, 16, 24 and 48 hours after the end of SK administration.

The serial ECGs were digitised by a single observer by means of a digitiser interfaced with a computer system. A QRS complex with no or minimal baseline drift was identified and a horizontal line connecting consecutive TP segments was drawn, all measurements were referred to this baseline. The following were calculated: (i) SumST (the sum of elevations above the baseline 40 ms after the end of the QRS complex in leads II, III and AVF); (ii) SumR (the sum of amplitude of R waves in leads II, III and AVF); (iii) SumQ (the sum of the Q waves in leads II, III and AVF); and (iv) SumST (V1 - V4) (the sum of ST-segment depression in leads V1 - V4 as measured from the baseline to 80 ms after the J point).

The steady state SumST was defined as the mean of the SumST at 24 hours and 48 hours. The achievement of steady state was considered to be the time when the first of the serial ECGs was found in which the SumST was equal to less than 80% of the initial SumST. The coronary angiograms were analysed by two experienced observers. The coronary angiograms were analysed by two experienced angiographers who were unaware of the ECG findings. The infarct-related artery was identified easily in 24 patients because they had single-vessel disease. In the remaining 10 patients (7 with double-vessel disease and 3 with triple-vessel disease) the vessel was identified by angiographic evidence of an intracoronary thrombus or angiographic features of an ulcerated atheromatous plaque. Patients were defined as having a patent infarct-related artery if a mild delay in antegrade filling with complete filling of the distal part occurred, or if no antegrade delay was found. The artery was considered to be occluded if no antegrade filling was present or if a marked delay of flow without complete filling of the distal vessel was observed.

Statistical methods

Nonparametric methods were employed in analysing the data since the underlying distribution does not lend itself to

Division of Cardiology, Department of Internal Medicine, University of Pretoria and H. F. Verwoerd Hospital, Pretoria

J. GOURASSAS, DIP. IN MED. (ATHENS)
J. M. BENNETT, M.B. CH.B., M.MED. (INT.)
S. KONSTANTINIDES, DIP. IN MED. (THESSALONIKA)
LAURA MATZNER, B.ESC.
C. C. VAN DER MERWE, D.COMM.

Reprint requests to: Professor J. M. Bennett, Dept of Cardiology, H. F. Verwoerd Hospital, PB X 169, Pretoria, 0001 RSA.
Accepted 8 Aug 1988.
statistical methods based on a normal distribution. Throughout the study, statistical analyses were performed at a 5% level of significance.

The Mann-Whitney U-test, Wilcoxon matched-pairs signed-ranks and Fisher's exact test were performed where applicable. The rate of decline was expressed in mm/h. The percentage decrease was calculated for each time interval with reference to the initial values before SK administration.

The Breslow test for survival analysis tested the median times for the patent and occluded groups to reach a steady state in the ST segment. The same test was applied to test the normalisation time between the patent and occluded groups in the ST (V1 - V4) segment. Numerical values are expressed as mean ±1 SD. The values in the graphs are presented as the mean ±SEM.

Results

From the 35 patients initially enrolled in the study, 2 were excluded, because 1 refused coronary angiography and the other developed left bundle branch block. The mean age of the patients was 51 ± 9.11 years. The time elapsed from onset of pain until administration of SK was 3.3 ± 1.4 hours. Coronary angiography was performed in 3.3 ± 2.2 days. A patent infarct-related artery was found in 19 patients (57.6%) (group A) and in 14 patients (42.9%) the artery was occluded (group B).

**SumST.** The changes in the decline of the SumST are graphically represented in Fig. 1. Before administration of SK the SumST was similarly elevated in both groups. During the next 2.5 hours the decline in the SumST as expressed in mm/h was steeper in group A than in group B (3.3 ± 2.4 mm/h v. 2.0 ± 2.0 mm/h) (P = 0.036) with a significant difference in the SumST between the two groups at 2.25 - 3.5 hours (P < 0.05). After this, the SumST decline did not differ significantly in the two groups (P > 0.05); except at 24.5 hours (P = 0.040) (Fig. 1). The median time to reach the steady state was 136 minutes for patients in group A and 210 minutes for patients in group B (P = 0.039). The percentage decrease of SumST from the initial values before administration of SK to the various time intervals (Table I) reached a significant statistical difference from 1.25 hours to 3.5 hours and at 4.5 hours and 24.5 hours after the start of SK administration (P < 0.05).

**SumR.** The fall in the SumR was nearly parallel in the two groups and no statistical difference was found at the various time intervals (Fig. 2). Within both groups the SumR decreased significantly at 48 hours from their initial values (P < 0.05). The percentage drop of SumR tended to be greater in group A than in group B and reached a significant difference at 2, 2.25, 4.5 and 24.5 hours (P < 0.05) (Table I).

**SumQ.** The pattern of evolution of the SumQ was nearly parallel for both groups during the first 8.5 hours. This pattern was punctuated with differences at 1.25 hours (P = 0.041), 1.75 hours (P = 0.042) and 2.5 hours (P = 0.049). Thereafter the SumQ in patients with an occluded artery was consistently greater than in patients with a patent artery and remained so up to 48 hours (P < 0.05) (Fig. 3). The percentage increase of SumQ did not differ between the two groups at any of the time intervals.

**SumST (V1 - V4).** Of all 33 patients examined, 26 (78.8%) presented with significant ST- segment depression in V1 - V4. This occurred in 16 of the patients in group A (84.2%) and in 10 of those in group B (71.4%) (P > 0.05). The reduction in the mean SumST (V1 - V4) values did not differ significantly between patients with patent and occluded arteries and a significant difference was only observed at 0.75 h (P = 0.0293) (Fig. 4). The median time of the SumST (V1 - V4) to normalise was 180 minutes for both groups. The
### TABLE I. % ECG CHANGES IN SumST AND SumR FROM START OF STREPTOKINASE ADMINISTRATION TO 48 H

<table>
<thead>
<tr>
<th>Time from start of STK administration (h)</th>
<th>% decrease of SumST</th>
<th>% decrease of SumR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patent</td>
<td>Occluded</td>
<td>P value</td>
</tr>
<tr>
<td>0.75</td>
<td>33.74 ± 35.19</td>
<td>18.60 ± 26.10</td>
</tr>
<tr>
<td>1.00</td>
<td>39.02 ± 32.64</td>
<td>22.49 ± 29.27</td>
</tr>
<tr>
<td>1.25</td>
<td>32.32 ± 23.29</td>
<td>29.27 ± 28.01</td>
</tr>
<tr>
<td>1.50</td>
<td>35.22 ± 33.56</td>
<td>35.22 ± 30.70</td>
</tr>
<tr>
<td>1.75</td>
<td>37.03 ± 32.27</td>
<td>37.03 ± 27.39</td>
</tr>
<tr>
<td>2.00</td>
<td>39.16 ± 27.86</td>
<td>39.16 ± 27.86</td>
</tr>
<tr>
<td>2.25</td>
<td>45.37 ± 27.06</td>
<td>45.37 ± 27.06</td>
</tr>
<tr>
<td>2.50</td>
<td>46.74 ± 30.56</td>
<td>46.74 ± 30.56</td>
</tr>
<tr>
<td>3.00</td>
<td>52.61 ± 29.01</td>
<td>52.61 ± 29.01</td>
</tr>
<tr>
<td>3.50</td>
<td>61.53 ± 27.35</td>
<td>61.53 ± 27.35</td>
</tr>
<tr>
<td>4.00</td>
<td>65.27 ± 29.59</td>
<td>65.27 ± 29.59</td>
</tr>
<tr>
<td>4.50</td>
<td>64.75 ± 24.65</td>
<td>64.75 ± 24.65</td>
</tr>
<tr>
<td>5.00</td>
<td>59.63 ± 44.09</td>
<td>59.63 ± 44.09</td>
</tr>
<tr>
<td>12.50</td>
<td>68.35 ± 27.14</td>
<td>68.35 ± 27.14</td>
</tr>
<tr>
<td>16.50</td>
<td>59.70 ± 33.05</td>
<td>59.70 ± 33.05</td>
</tr>
<tr>
<td>24.50</td>
<td>61.08 ± 33.11</td>
<td>61.08 ± 33.11</td>
</tr>
<tr>
<td>48.00</td>
<td>70.54 ± 25.56</td>
<td>70.54 ± 25.56</td>
</tr>
</tbody>
</table>

Fig. 2. The decrease in the SumR of the two groups (△ = patent; • = occluded).

The percentage decrease of SumST (V1 - V4) from the initial values to the various time intervals did not reach significance. From these 26 patients, 11 (42.3%) had an increase of more than 5% in the SumST (V1 - V4) depression in one or more of the serial ECGs compared with the initial value before the administration of SK. Seven of these patients (63.6%) had a patent infarct-related artery and 4 (36.4%) had an occluded artery. The occurrence of this phenomenon was not found to be statistically different between the two groups. This depression occurred earlier in patients with a patent artery (49.3 ± 7.3 min) than in patients with an occluded artery (60.0 ± 21.2 min).

### Discussion

A need exists for a reliable non-invasive marker of myocardial reperfusion in patients with acute MI who receive thrombo-
Fig. 3. The SumQ for the two groups. Note the significant difference from 8.5 hours to 48 hours (Δ = patent; ● = occluded; * = P < 0.05).

Fig. 4. The reduction in the mean SumST (V1 - V4) (Δ = patent; ● = occluded; * = P < 0.05).
lytic drugs. If this marker provides this information accurately and early, patients can be treated in a coronary care unit with adjunctive therapy in order to sustain coronary artery patency or, where possible, taken to a catheterisation laboratory for angiography and possible angioplasty.

Several ECGs in patients treated with intracoronary thrombolysis showed a resolution of ST segments after successful reperfusion,\(^2,3\) and descriptive analysis was used for intra-
venously treated patients.\(^10\) Blanke et al.\(^3\) have found that in patients with anterior MI the ST segment in the recanalised group was less than half of that in the control group at 3 hours after treatment with intracoronary SK. In our study, we found that patients with patent arteries had a more rapid decline of SumR than patients with occluded arteries during the first 2,5 hours. At 2,25 - 3,5 hours after the start of SK admini-
stration the SumR in patients with patent arteries was half of that in patients with occluded arteries. These results are in
accord with the studies mentioned above.

Madias\(^11\) has observed an unpredictable late ST-segment elevation during the course of acute MI, which could not be attributed to clinical changes. Krucoff et al.\(^4\) applying Holter monitoring, were not able to separate patients with recanalisa-
tion from those without when examining their data, anticipating a return of the ST segment to the iso-electric line. We have found a significant difference in the time when the steady state was achieved between patients with patent or occluded arteries. Although our results are in agreement with those of Krucoff et al.,\(^6\) the time intervals in which the steady state was achieved were more prolonged in the present study. This can be explained by the fact that our time intervals between examinations were longer than those of Holter monitoring. The significant statistical difference between patients with
patent and occluded infarct-related arteries may reflect the changes in coronary artery patency.

A more than 55% drop of the ST segment was found within 1 hour after recanalisation in intracoronary SK-treated patients.\(^7\) We have found that in 1,25 hours the SumST dropped to 62% of its initial amplitude in patients with a patent artery, whereas in patients with an occluded vessel the SumST dropped only 29%. This simple ECG criterion seems useful for judging coronary artery patency.

**SumR.** In human studies in acute anterior MI,\(^12\) a good correlation was found between the loss of R waves and the MI size. We found no significant difference in the SumR of patients with an occluded artery compared with those with a patent artery, the fall in the SumR in the two groups was parallel up to 48 hours. In anterior MI the R waves fall in parallel during the first 24 hours and after that a regrowth of R waves was observed in patients whose vessels recanalised after thrombolysis with SK.\(^7\) These findings may be explained by a very late regrowth of R waves in our patient group, which is beyond the studied time interval; or as Yusuf et al.\(^13\) have observed, the SumR for inferior MI does not correlate well with the infarct size as estimated by the cumulative creatine phosphokinase (myocardial band). This may reflect the inability to discriminate between patients with small or big infarcts and by extrapolation, patients whose vessels recanalise or remain occluded.

The percentage shift of SumR from its initial value before the administration of SK showed that the trend of percentage shift was always greater in patients with a patent artery than in patients with an occluded artery. At 2, 2,25, 4,5 and 24,5 hours a significant difference was found in the percentage drop of SumR between the two groups. This may constitute a useful tool in everyday clinical practice, since nearly 45% of SumR was lost at 4,5 hours in patients with patent arteries compared with only 28% in patients with occluded arteries. These results in patients with an occluded infarct-related artery are similar to those of Madias,\(^11\) who examined patients with inferior MI treated conventionally. The trend of a greater percentage drop of SumR in patients with patent arteries in this study is in accord with the observation of Ganz et al.\(^14\) that reperfusion results in disappearance of R waves. Early augmentation of the R wave in acute MI has been described;\(^15\) animal studies have shown that after an initial augmentation of R waves an immediate reduction occurs with reperfusion of the coronary artery.\(^16\)

**SumQ.** Traditionally the development of Q waves correlates with the presence of myocardial necrosis. In recent years, transient Q waves have been observed during ischaemia and have disappeared after cessation of ischaemia.\(^17\) It has been suggested that hypoperfusion may result in transient metabolic standstill to the point where even electrical activity is not generated.\(^18\) Transient Q waves in patients with small MIs have been described; the mechanism is still unclear but it is believed that shrinking of scar and hypertrophy of the myocytes in the border zone is the most likely explanation.\(^19\)

Interventional studies have shown that patients with recanalisation of vessels after an acute MI developed smaller Q waves than those whose vessels did not recanalise.\(^20\) In this study the SumQ increased nearly in parallel in patients with patent and occluded arteries during the first 8,5 hours. From 8,5 hours up to 48 hours the SumQ for patients with patent arteries was nearly half that of patients with occluded arteries. These results are in accord with those previously described and may be useful in distinguishing patients with open vessels from those without.\(^10\)

**SumST (V1 - V4).** During acute inferior MI the reported incidence of anterior ST-segment depression varies widely from 54%\(^21\) to 100%.\(^22\) In our study it was 78,8% and seems to be a frequent finding in the early hours after MI. The mechanism and the clinical significance is still conven-
tional.\(^23,24\)

Liddle et al.\(^24\) have observed a prompt resolution of anterior ST-segment depression when the right coronary artery was reperfused with SK, even in those patients with left anterior descending coronary artery disease.

We have documented only one difference in the changes of SumST V1 - V4 between the two groups. At 0,75 hours after the start of SK the SumST (VI - V4) depression in patients with a patent artery was twice that of patients with an occluded artery. The resolution of SumST (V1 - V4) was achieved at the same time in patients with patent and occluded arteries and our results differ from Little et al.\(^24\) Eleven of the patients had a further increase of SumST (V1 - V4) depression in the subsequent one or more ECGs compared with that before administration of SK; this happened earlier in patients with an patent artery than in patients with an occluded artery. Larger studies are needed to clarify the mechanism and the precise significance of these observations, and a definite conclusion cannot be reached.

A limitation of this study is the fact that coronary angiography was not done during thrombolytic therapy. It could therefore be possible that some patients' vessels recanalised later and that in some of those whose vessels initially recanalised, re-occlusion occurred. Another problem is that although statistically significant differences were found between the two groups, the SDs were relatively large, making the evaluation of an individual patient difficult. Ascertain- ing recanalisation at the time of thrombolytic therapy may be useful in defining the two groups accurately and may also reduce the SD.

In patients with inferior MI treated with intravenous SK, the following ECG changes may indicate reperfusion of the infarct-related artery: (i) a rapid decline of the ST-segment elevation during the first 2,5 hours; (ii) a ST-segment reduction of 62,6 - 75% from 1,25 hours to 3,5 hours respectively; and (iii) achievement of the steady state at/or before 136 minutes.
The value of these criteria are limited by the large SDs but remain useful when studying the effects of coronary thrombolysis in patient groups.

We thank Rina Reynierse for secretarial assistance and the nursing staff of the Coronary Care Unit, H. F. Verwoerd Hospital, who recorded the ECGs.

REFERENCES