Effects of Acebutolol on Myocardial Infarct Extension: A Randomized Electrocardiographic, Enzymatic and Angiographic Study

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SUMMARY The effect of acebutolol (1 mg/kg i. v. during the first 2 days followed by a daily oral dose of 600 mg for 3 weeks) was studied in a randomized trial involving 26 patients seen within 24 hours after the onset of uncomplicated anterior transmural myocardial infarction (TMI). Myocardial ischemia and necrosis were evaluated by precordial maps recorded daily for 9 days. Left ventricular pump function and dysynchrony were quantitatively measured on 30° right anterior oblique cineangiograms. Angiography was performed, using the postextrasystolic potentiation technique, within the first 24 hours after TMI and was repeated 1 month later. The basal and postextrasystolic beats from the initial angiography were computerized and compared with those from the final angiogram. MB-CK serum level was measured from blood samples drawn every 3 hours for the first 72 hours.

Fourteen patients selected at random received acebutolol within the first 24 hours; 12 subjects were untreated and served as controls. During the 1-month study, no other drugs were administered. Treated patients showed a significant reduction in capillary wedge pressure, extent of hypokinesia and ST-segment elevation; no significant differences were observed in the control group. However, the predictability based on the angiographic data was the same in both groups, and β blockade did not alter this predictability significantly. Furthermore, no significant difference was found during the final evaluation for treated compared with control patients for any single variable or set of variables. The incidence of infarct extension was not decreased, but only significantly delayed in treated patients. The high variability of the measurements, probably related to the high variability of the pathophysiologic factors, may account for the failure to demonstrate the efficacy of acebutolol.

BENEFICIAL EFFECTS from β-blockade therapy have been demonstrated in experimental coronary artery occlusions and clinical acute myocardial infarction (MI). Several studies have suggested that the delay in instituting adrenergic blockade is critical for limiting infarct size; reduction of myocardial infarct size can be expected only when therapy is begun within 4–6 hours after the onset of experimental or clinical acute coronary occlusion. However, not all patients can reach a coronary care unit that soon after MI. Further, extension of necrosis occurs in more than half of them within the first few days after the onset of symptoms. Thus, the question arises whether β-blocking therapy can prevent or reduce the incidence of infarct extension when it is initiated at 6–24 hours after MI.

Previous studies have suggested that ST and QRS changes are valuable indicators of myocardial ischemia and necrosis. Hence, serial observations of precordial ST and QRS mapping for several days after onset should detect extension in the early stages of MI. But the efficacy of interventions designed to prevent infarct extension and then limit final infarct size should be ultimately assessed only from quantitative measurements of objective indexes of myocardial function. In this regard, regional wall motion abnormalities estimated from left ventricular cineangiograms have been identified as a sensitive and specific index of myocardial ischemia or necrosis. An investigation in our laboratory showed the ability of postextrasystolic potentiation (PESP) to predict reversible wall motion abnormalities from contrast ventriculograms in untreated patients with acute transmural myocardial infarction (TMI).

A few studies of infarct size limitation have used a randomization procedure. In these studies, precordial mapping has not been done, angiography has failed to show significant improvement from β-blocking therapy, and the efficacy of propranolol has been assessed only from enzyme measurements in patients treated within 4 hours after the onset of symptoms.

The present randomized clinical trial was designed to determine the effects of an established β-blocking drug (acebutolol) given within the 24 hours after acute anterior TMI in patients without signs of cardiac failure. Infarct extension was detected by mapping and by enzyme measurements. Myocardial function was assessed by angiography during PESP on the first day and by comparing the initial angiographic data with those obtained 1 month later.

Methods

Selection of Patients

All patients selected for study had an acute anterior TMI less than 24 hours after the onset of pain, as documented by serial 12-lead ECGs and characteristic elevations in serum enzymes (CK and MB-CK). Patients 70 years and older and those with previous in-
fractures, associated cardiovascular or systemic disease, mechanical complication, persistent or recurrent ischemic pain not relieved by opiates and nitroglycerin after 12 hours, clinical signs of coronary insufficiency present more than 3 months before the current TMI, atrioventricular or intraventricular conduction disturbances, or refractory arrhythmias were excluded from the study. Patients taking chronic drug therapy (such as β-blocking agents, digitalis, lidocaine or other antiarrhythmic drugs) were also excluded. All patients who met the selection criteria were in Killip class I and in sinus rhythm.

These selection criteria were carefully controlled for each patient so we could study a homogeneous sample of untreated subjects without previous cardiovascular problems within 24 hours after a first anterior TMI not complicated by clinical pump failure or persistent chest pain.

All the patients selected underwent cardiac catheterization for further hemodynamic selection. Right-heart pressure, capillary wedge pressure (CWP), femoral arterial pressure, and thermodilution cardiac output (Edwards 9520) were measured. When CWP was 15 mm Hg or more, or when cardiac index was 2.5 l/min/m² or less, the patient was rejected from the study. As a result, four patients who were in Killip class I were excluded. Twenty-six patients fulfilled all selection criteria.

Randomization Procedures

The 26 patients were assigned at random to one of two groups. Group A included 12 patients, ages 29–61 years (mean 52 years), who received only heparin during their 1-month hospitalization and served as controls. Group B included 14 patients, ages 31–63 years (mean 51 years), who, in addition to heparin, received acebutolol immediately after the initial measurements and in all the cases within 24 hours. Acebutolol was infused intravenously at a rate of 1 mg/kg body weight for 48 hours, and heart rate, arterial pressure and CWP were monitored continuously. Thereafter, a daily oral dose of 600 mg was given for 3 weeks. Cardiac dynamics studied by PESP in the 12 control patients have been reported in detail.

Protocol

All patients underwent electrocardiographic, enzymatic, and angiographic evaluation 6–24 hours after the onset of chest pain. Pulmonary angiography was first performed in the 30° right anterior oblique (RAO) position immediately after the hemodynamic measurements while a right ventricular stimulus was delivered at 50% of the RR interval through a bipolar pacing catheter to obtain PESP, as described previously.

The initial mapping was done immediately after catheterization (mean 15 hours, range 11–21 hours). With the patient supine, precordial maps were recorded from a grid of 42 recording sites arranged in seven horizontal rows and six vertical columns. The seven rows were designated A to G, starting from above. The top right electrode (A1) was placed in the first intercostal space at the right parasternal line. The A2 mark was made at the second intercostal space to the left of the sternum. Mark A3 was made at the anterior axillary line and A4 was placed equidistant between A2 and A3. A5 and A6 were put on the midline and posterior axillary line. The first row served as a guideline for placing the remaining six rows. The second row was at the second intercostal space. Rows C to G were placed at distances identical to that between the first to second intercostal space. The marks were made with a skin pencil to assure exact repositioning of the "V" electrode. The 42 electrodes lead to a switch box connect- ed to a direct-writing, three-channel, ink-jet Mingo grap recorder (Elema-Schonander).

During the first 72 hours, an i.v. catheter was inserted percutaneously into an antecubital vein in all patients so blood could be withdrawn every 3 hours for measurement of CK and MB-CK.

All patients were hospitalized for 1 month. During this period, only heparin (group A) or heparin and acebutolol (group B) were administered. No other drugs, particularly antiarrhythmic drugs, were required. ECGs and precordial maps were recorded each morning for 9 consecutive days.

Because concern that ST-segment changes alone may be unreliable indicators for myocardial necrosis extension, a further extension was defined using the following criteria: (1) an increase of more than 20% in the number of sites showing ST elevations totaling 1 mm or more (NST) and of more than 10% in the sum of Q waves (EQ) between two consecutive days; (2) a secondary rise in MB-CK > 10 IU/l compared with the preceding value. When a further extension was suspected from electrocardiographic data, including patients with ECG evidence of extension past the first 3 days (when routine MB-CK values were obtained), blood samples were drawn every 3 hours for 48 hours for CK-MB measurements.

A final set of measurements was recorded at 30 days in all patients. In group B, acebutolol was discontinued 5 days before. This final study included the same hemodynamic evaluation as the initial one, LV angiography in the 30° RAO projection and coronary arteriography in several projections with Bourassa catheters. During LV angiography, right atrial pacing was performed to drive the heart at the same rate (± 3 beats/min) as during initial angiography. This was done to compare the initial and final angiograms at the same atrial heart rate.

Technical Data Evaluation

Angiographic data were processed with a specially programmed calculator (Hewlett-Packard 9845-T) as previously described. For each patient, three angiographic cycles were systematically analyzed and compared: the basal cycle of the initial angiographic study (within 24 hours), the postextrasystolic cycle of the initial angiogram, and the basal cycle of the final angiogram (1 month). Three variables were obtained for each frame: the ejection fraction, determined by dividing the angiographically calculated stroke volume...
by the end-diastolic volume; the percentage of the end-diastolic perimeter showing a shortening value ≤ 20% (hypokinesis); and the percentage of the end-diastolic perimeter showing a shortening value ≤ 5% (akinesia). Coronary angiograms were read separately by two observers without accompanying clinical data. The number of major coronary vessels that showed critical narrowing, the degree and the location (proximal or distal) of luminal occlusion, the quality of distal runoff and collateral circulation were studied. The distal runoff beyond the main obstructions was empirically coded as follows: 0 = excellent; 1 = good; 2 = relatively poor with thin or stenotic vessels; 3 = nearly absent; 4 = absent. Likewise, collateralization beyond the obstruction was judged to be adequate (1), slight (2), or absent (3). The sum of the significant lesions in the major coronary branches was calculated to give a score for each coronary item. The interobserver variability was very low, and the final assigned codes were those resulting from the best agreement between observers.

ST-segment elevation was measured to the nearest 0.5 mm, 0.06 second after the nadir of the S wave or the peak of the R wave using the TP segment as the isoelectric line. When the TP segment was difficult to delineate because of tachycardia, the PQ segment was used as a baseline. All the ST elevations were summed for each study and expressed as ΣST. The number of sites that had ST-segment elevation of 1 mm or more (NST) was taken as an index of the extent of ischemic injury. The number of points showing pathologic Q waves (Q-wave amplitude ≥ 0.2 mV; duration ≥ 40 msec) was also evaluated (NQ). All these Q waves were measured to the nearest 1.0 mm and summed (ΣQ). The number of R waves with an amplitude greater than 1.0 mm (NR) and the sum of all the R waves (ΣR) were also determined.

CK-MB values were determined from the blood samples withdrawn every 3 hours for 72 hours; the serum level was measured by electrophoresis. In case of recurrent chest pain or ECG reextension (as defined previously), samples were continued for 48 hours more. Enzymatic infarct weight and enzymatic infarct size were calculated as previously reported.

### Statistical Analysis

No distribution hypothesis of single variables was assumed. Accordingly, intragroup and intergroup comparisons were performed with nonparametric tests, the Mann-Whitney test and the Wilcoxon signed-rank test. However, multivariate normal distribution was assumed to compare groups with the Hotelling T² statistic. Linear regression analyses were carried out in both groups to study the relationship between the angiographic data obtained from a postextrasystolic cycle of the initial angiography and those obtained from a spontaneous cycle during the final angiography. Slopes and intercepts from the two groups were then compared. The null hypothesis stated that β-blocking therapy does not induce beneficial changes in the evolution in group B compared with the control group.

### Results

#### Comparison of Initial Data Values

Initial data recorded in the control group and in the treated patients are listed in tables 1 and 2. There were no significant differences between groups for any variable or set of variables on the first day of the study. However, the coronary angiograms showed that group B patients had significantly worse peripheral runoff and collateral flow than the control group. The number, the degree, and the localization of luminal occlusions were similar in the two groups. Therefore, the groups were considered comparable and suitable for evaluation of β-blocking drug efficacy.

#### Comparison of Initial and Final Data Values

The most meaningful evolutionary changes observed are summarized in tables 1 and 2. There was no

### Table 1. Hemodynamic and Enzymatic Variables

<table>
<thead>
<tr>
<th></th>
<th>AI</th>
<th>AF</th>
<th>BI</th>
<th>BF</th>
<th>Homogeneity</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>82 ± 21</td>
<td>82 ± 21</td>
<td>87 ± 19</td>
<td>80 ± 12</td>
<td>6% NS</td>
<td>-1% NS</td>
</tr>
<tr>
<td>CWP (mm Hg)</td>
<td>9.0 ± 3.8</td>
<td>7.1 ± 3.3</td>
<td>10.0 ± 3.0</td>
<td>5.2 ± 2.3</td>
<td>11% NS</td>
<td>-28% NS</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>127 ± 9</td>
<td>110 ± 17</td>
<td>129 ± 21</td>
<td>108 ± 13</td>
<td>2% NS</td>
<td>-2% NS</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>92 ± 6</td>
<td>83 ± 13</td>
<td>92 ± 15</td>
<td>82 ± 7</td>
<td>0% NS</td>
<td>-1% NS</td>
</tr>
<tr>
<td>CI (l/min/m²)</td>
<td>3.27 ± 0.84</td>
<td>3.84 ± 0.62</td>
<td>3.19 ± 0.43</td>
<td>3.01 ± 0.69</td>
<td>-2% NS</td>
<td>-7% NS</td>
</tr>
<tr>
<td>SI (ml/m²)</td>
<td>40 ± 11</td>
<td>41 ± 11</td>
<td>37 ± 8</td>
<td>37 ± 7</td>
<td>-10% NS</td>
<td>-11% NS</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>195 ± 46</td>
<td>201 ± 39</td>
<td>198 ± 39</td>
<td>197 ± 56</td>
<td>2% NS</td>
<td>-4% NS</td>
</tr>
<tr>
<td>EF (%)</td>
<td>42 ± 8</td>
<td>44 ± 13</td>
<td>40 ± 8</td>
<td>44 ± 11</td>
<td>-5% NS</td>
<td>-1% NS</td>
</tr>
<tr>
<td>HK (%)</td>
<td>43 ± 18</td>
<td>37 ± 19</td>
<td>44 ± 8</td>
<td>37 ± 12</td>
<td>3% NS</td>
<td>2% NS</td>
</tr>
<tr>
<td>AK (%)</td>
<td>24 ± 14</td>
<td>18 ± 14</td>
<td>29 ± 7</td>
<td>20 ± 15</td>
<td>22% NS</td>
<td>11% NS</td>
</tr>
<tr>
<td>EIV (g-Eq)</td>
<td>30 ± 18</td>
<td>29 ± 25</td>
<td>-3% NS</td>
<td>-7% NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EIS (%)</td>
<td>16 ± 10</td>
<td>15 ± 9</td>
<td>-7% NS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: HR = heart rate; CWP = capillary wedge pressure; SAP = systolic arterial pressure; MAP = mean arterial pressure; CI = cardiac index; SI = stroke index; EDV = end-diastolic volume; EF = ejection fraction; HK = hypokinesia; AK = akinesia; EIW = enzymatic infarct weight; EIS = enzymatic infarct size; AI = initial measurements in group A; AF = final measurements in group A; BI = initial measurements in group B; BF = final measurements in group B; BI/AF = comparison of BI and AF; BI/AL = comparison of BI and AI; BF/BI = comparison of BF and BI.
difference between the heart rates recorded during the initial and the final angiograms, for atrial pacing was instituted during the final angiographic examination to avoid any heart rate difference. Before atrial pacing, however, heart rate was significantly \( p < 0.05 \) reduced in both groups (group A 82 ± 21 to 68 ± 8 beats/min; group B 87 ± 19 to 66 ± 11 beats/min). CWP decreased in both groups, but the decrease was significant only in group B. Mean and systolic arterial pressures decreased in both groups. Cardiac index and stroke index did not change. Ejection fraction increased by 5% in group A and 8% in group B (NS). The percent hypokinesis and akinesis decreased, but the decrease was significant only in group B.

The comparison of the initial and final mapping data showed that group B (acebutolol) had a significantly lower \( \Sigma ST \); the decrease in \( \Sigma ST \) in the control group was not significant (fig. 1). Despite the significant reduction of \( \Sigma ST \) in group B patients, there was no significant change of \( \Sigma Q \) and \( \Sigma R \) in either group (table 2).

Figure 2 shows how the final functional myocardial status can be predicted from the PESP data recorded in both groups. The linear relationships between the initial angiographic data recorded during a postextrasystolic cardiac cycle and those at 1 month are significant, as shown by analysis of variance. However, no significant differences between groups are found for slopes and intercepts, except for the intercepts concerning the ejection fraction \( p < 0.05 \) and akinesis \( p < 0.01 \) (unilateral test). This suggests that the predictability based upon the PESP angiographic data is nearly the same in both groups and that \( \beta \) blockade does not significantly alter this predictability.

### Daily Evolutionary Changes Based on Electrocardiographic Evaluations

Figures 1 and 3 show the mean evolutionary changes of NST, \( \Sigma ST \), \( NQ \), and \( \Sigma Q \) in both groups. During the 9-day observation period, the groups remained comparable. All the variations between paired measurements of each variable 1–8 days apart were examined. These comparisons showed no significant difference between groups. Indeed, there was a larger increase of NST and \( \Sigma ST \) mean differences in group B than in group A from the beginning to the end of the observation period (table 3). But the variances were so high that no significance level was attained at any time. The highest degree of variability for NST paired measurements occurred at day 4 for both groups.

Fourteen of the 26 patients had an infarct extension: six in group A and nine in group B (fig. 4). The number of NST augmentations and the maximal peak increase were not significantly different between the two groups. However, the NST augmentations in group B were significantly delayed (mean 6.4 ± 1.6 days; range 3–8 days) compared with those in group A (mean 3.2 ± 1.2 days; range 2–5 days) \( p < 0.01 \).

### Table 2. Electrocardiographic Variables in Control and Treated Patients During the First and Ninth Days

<table>
<thead>
<tr>
<th>Group</th>
<th>Day 1</th>
<th>Day 9</th>
<th>Group B</th>
<th>Day 1</th>
<th>Day 9</th>
<th>Homogeneity</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR</td>
<td>27 ± 9</td>
<td>28 ± 9</td>
<td>25 ± 6</td>
<td>22 ± 9</td>
<td></td>
<td>( B_1/A_1 ), ( p )</td>
<td>( A_0/A_1 ), ( p )</td>
</tr>
<tr>
<td>( \Sigma R )</td>
<td>164 ± 88</td>
<td>161 ± 47</td>
<td>112 ± 58</td>
<td>109 ± 72</td>
<td></td>
<td>( B_2/A_0 ), ( p )</td>
<td>( B_0/B_1 ), ( p )</td>
</tr>
<tr>
<td>( NQ )</td>
<td>23 ± 8</td>
<td>19 ± 11</td>
<td>18 ± 9</td>
<td>20 ± 12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \Sigma Q )</td>
<td>109 ± 54</td>
<td>114 ± 112</td>
<td>94 ± 67</td>
<td>137 ± 109</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NST</td>
<td>20 ± 8</td>
<td>19 ± 7</td>
<td>25 ± 8</td>
<td>21 ± 8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Abbreviations:

- NR = number of sites showing R waves;
- \( \Sigma R \) = sum of R waves;
- \( NQ \) = number of sites showing Q waves;
- \( \Sigma Q \) = sum of Q waves;
- NST = number of sites showing ST elevations;
- \( \Sigma ST \) = sum of ST elevations;
- \( B_1/A_1 \) = comparison of groups A and B on day 1;
- \( B_0/A_0 \) = comparison of groups A and B on day 9;
- \( A_0/A_1 \) = comparison of group A on days 1 and 9;
- \( B_0/B_1 \) = comparison of group B on days 1 and 9.

\[ \Sigma ST = 36 ± 25 \quad 31 ± 12 \quad 51 ± 31 \quad 33 ± 14 \quad 41% \quad \text{NS} \quad 6\% \quad \text{NS} \quad -18% \quad \text{NS} \quad -72% \quad (0.10) \quad 0.05 \]
Discussion

Since the first experimental results reported by Maroko et al.,1 mapping techniques have been thoroughly investigated so as to design a noninvasive method of evaluating the magnitude and the extent of ischemia and necrosis during acute myocardial infarction and the effects of therapeutic interventions from which a reduction of final infarct size can be expected. Based on experimental,45 theoretical46-48 and clinical39,50 investigation, doubts have been expressed about the reliability of this technique for assessing acute directional changes in ischemic injury. However, most investigators have accepted its validity as an indirect estimate of the severity of infarction.26,28,51,52 In fact, controversies have mostly related to the value of the isolated ST-segment mapping, inasmuch as ST-segment changes are not directly related to necrosis.49,50 Hence, several authors have proposed other techniques, such as the study of changes in the QRS complex,17,23,26,28,30,34,51,52 the accumulated CK-MB release as a direct quantitative estimate of infarct size,7,9,15,26,36,39,53 and the analysis of contraction abnormalities by LV cineangiography.9,36,39,40

Though LV angiography assesses wall motion abnormalities of the left ventricle only, various studies have suggested that angiographic data correlate well with indexes of necrosis obtained from precordial mapping34-38 and also with enzymatic estimates of infarct size.36-39 We used both precordial mapping and LV angiography in the present trial.

We considered several points in attempting to assess myocardial ischemic injury from precordial mapping. First, the delay of the initial record from the onset of the infarct may be critical. The initial map was performed 11-24 hours after the onset of pain, while the ST segment was relatively stable, as documented by previous reports.16,22,28,34,53,57,58 Thus, comparisons with subsequent records could be made with baseline measurements taken during a relatively stable period. Second, because of the 24-hour interval between daily maps, transient ST-segment elevations may have been undetected. However, Thompson and Katavatis50 showed that when ST-segment elevation accompanies significant myocardial necrosis, it persists long enough to be detected within 24 hours. Third, nonspecific changes in precordial ST-segment elevation, such as fluctuations in serum potassium levels or the development of pericarditis, may occur and alter the relationship of the ST segment to ischemic injury. As ST-segment changes alone are unreliable detectors of ischemia, infarct extension was diagnosed only when NST increased by more than 20% and ΣQ increased by more than 10% between two consecutive days and there was significant further release of MB-CK.

The aim of the present study was to detect infarct extensions and to determine whether the incidence and magnitude of extensions were reduced by acebutolol and whether indexes of necrosis at 9 days and cardiac
The major finding in the recent study was that the incidence of extensions is not decreased but only significantly delayed in patients receiving acebutolol. No explanation of this phenomenon can be found in our results or in previously reported work. Although the release of CK activity may be delayed by β-blocking drugs, our results do not show that the delayed occurrence of extension and the delayed release of CK are related. If this assumption were true, the time course of the infarct might be protracted by β-blocking therapy.

The efficacy of acebutolol on chronic stable angina pectoris suggests that this drug should also be effective at the early stages of myocardial infarction. The precordial mapping data did not show that acebutolol had a favorable effect. Though NST and Σ ST decreased consistently in group B patients, no significant difference was present between the two groups. NQ and Σ Q followed a similar evolutionary pattern (fig. 3); the same time course for the loss of electrically active myocardium was observed by Fox et al. in patients receiving β-blocking drugs and in control patients. Thus, in contrast to some experimental findings, modifications induced by β-blocking agents in ST-segment elevations are not always representative of myocardial necrosis development.

Two factors may have contributed to smooth out the beneficial effect of the β-blocking drug therapy: the higher degree of coronary artery obstruction in treated than in control patients and the high variability of data.

First, coronary angiograms performed after 1 month showed worse peripheral runoff and collateral flow in the treated patients than in the control group. Gold et al. suggested that the response of ST-segment elevation to the β-blocking agent could be related to the presence or absence of angiographically demonstrable flow to the infarcted area. Thus, despite randomization, treated patients did not have as good a coronary bed as control patients and perhaps could not draw sufficient benefit from therapy.

Second, the evolution of MI in man is highly variable, which makes it difficult to achieve statistical significance on samples of this size. Indeed, ST-

![Figure 3](http://circ.ahajournals.org/)

**FIGURE 3.** Mean evolutionary changes of NQ and Σ Q in control patients (dotted lines) and in patients receiving acebutolol (solid lines). Vertical bars represent standard deviations. Σ Q is expressed in mV × 10. NQ = number of sites showing pathologic Q waves; Σ Q = sum of Q waves.

dynamics at 1 month were significantly improved by acebutolol. The incidence and the delay of infarct extensions in untreated patients was in good agreement with those previously reported, though von Essen et al. and reported earlier extensions in nontreated patients (12–36 hours after the onset of chest pain). The

### Table 3. Paired Measurements of the Number of Sites Showing ST Elevation and the Sum of ST Elevations

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 11)</th>
<th></th>
<th>Group B (n = 14)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NST</td>
<td>Σ ST</td>
<td>NST</td>
<td>Σ ST</td>
</tr>
<tr>
<td></td>
<td>Mean difference</td>
<td>sd</td>
<td>Mean difference</td>
<td>sd</td>
</tr>
<tr>
<td>1–2 days</td>
<td>1.82</td>
<td>2.86</td>
<td>-0.91</td>
<td>10.77</td>
</tr>
<tr>
<td>1–3 days</td>
<td>0.91</td>
<td>5.77</td>
<td>-3.64</td>
<td>17.18</td>
</tr>
<tr>
<td>1–4 days</td>
<td>0.82</td>
<td>6.19</td>
<td>-0.09</td>
<td>19.69</td>
</tr>
<tr>
<td>1–5 days</td>
<td>0.73</td>
<td>5.97</td>
<td>-2.64</td>
<td>18.96</td>
</tr>
<tr>
<td>1–6 days</td>
<td>-0.27</td>
<td>5.10</td>
<td>-3.64</td>
<td>17.94</td>
</tr>
<tr>
<td>1–7 days</td>
<td>-0.46</td>
<td>4.97</td>
<td>-2.64</td>
<td>19.41</td>
</tr>
<tr>
<td>1–8 days</td>
<td>0.55</td>
<td>5.59</td>
<td>-6.36</td>
<td>17.94</td>
</tr>
<tr>
<td>1–9 days</td>
<td>-0.27</td>
<td>4.88</td>
<td>-5.18</td>
<td>18.49</td>
</tr>
</tbody>
</table>

Abbreviations: NST = number of sites showing ST elevation; Σ ST = sum of ST elevation.
segment elevation varies considerably between patients, and ST variability increases along with the time course of the early phase of acute MI (table 3). For this reason, Hardarson et al.\(^\text{58}\) suggested that therapeutic interventions should be performed 12–36 hours after the onset of symptoms and over periods of 1–4 hours because during short-term recordings, the ST segment is relatively stable. The time course of NQ, \(\Sigma Q\), NR and \(\Sigma R\) — is also highly variable, as shown in previous work\(^\text{17, 61}\) and the present study (table 2).

The cineangiographic data also showed a high variability and an increase of variances on day 30 compared with day 1 (table 1). In a previous work,\(^\text{40}\) ejection fraction, hypokinesis and akinesis recorded on day 1 correlated poorly with those on day 30. In contrast, correlations increased markedly as the final angiograms were compared with the electrically induced postextrastolytic initial beat. In the present study, the same pattern of predictability based on the initial postextrastolytic cardiac cycle was found in both groups, though there was more scatter of values in the group B than in the control group (fig. 2). If a beneficial effect of the \(\beta\)-blocking therapy is to be expected, the final values in group B patients should be greater for ejection fraction and lower for hypokinesis and akinesis than those predicted from the postextrastolytic cycle of the initial angiography when no drug had been given. Although more favorable trends can be observed in group B (fig. 2, table 1), our results fail to confirm the beneficial effects of the \(\beta\)-blocking drug statistically. The large variances of the measured variables might have helped circumvent any significant improvement in LV function. Norris et al.\(^\text{9}\) showed that propranolol failed to improve cardiac dynamics in similar-sized samples, but they did not study predictability of final regional wall motion abnormalities using PESP in the initial course of MI.

Finally, by taking into account the number of patients and the variances, we computed the theoretical differences required to attain the 5% probability level for unilateral tests (table 4). Differences needed to significantly prove the efficacy of \(\beta\)-blocking therapy using the same samples should have reached 12–17% for ejection fraction, hypokinesis and akinesis, compared with the 3–6% observed differences. Thus, one must ask whether sufficient benefit from \(\beta\)-blocker therapy during the first 24 hours of TIMI is to be expected, taking into account the possibility of worsening pump function by depression of contractility. We found four patients who were in Killip class I but had hemodynamic signs of cardiac failure and therefore were excluded from our study. Hence, i.v. \(\beta\)-blocking agents should not be systematically given in the first 24 hours without hemodynamic monitoring in the coronary care unit. We are not certain that a significant improvement of the overall or regional LV function can be expected.

**Acknowledgment**

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**References**


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**Table 4. Evolutionary Mean Differences for Angiographic Variables**

<table>
<thead>
<tr>
<th></th>
<th>(\Delta) group A</th>
<th>(\Delta) group B</th>
<th>(\Delta (\Delta B - \Delta A))</th>
<th>Theoretical (\Delta)</th>
<th>Theoretical (\Delta/) observed (\Delta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>2.91</td>
<td>6.14</td>
<td>3.23</td>
<td>11.89</td>
<td>3.68</td>
</tr>
<tr>
<td>HK (%)</td>
<td>-7.55</td>
<td>-10.86</td>
<td>-3.31</td>
<td>-16.79</td>
<td>5.07</td>
</tr>
<tr>
<td>AK (%)</td>
<td>-7.09</td>
<td>-12.79</td>
<td>-5.70</td>
<td>-13.71</td>
<td>2.41</td>
</tr>
</tbody>
</table>

Abbreviations: \(\Delta\) group A = mean difference observed in group A between the first day and the thirtieth day; \(\Delta\) group B = mean difference observed in group B between the first day and the thirtieth day; \(\Delta (\Delta B - \Delta A)\) = \(\Delta\) group B − \(\Delta\) group A (observed); Theoretical \(\Delta\) = change required to attain the 5% probability level.
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Estimation of Infarct Size by Myocardial Emission Computed Tomography with Thallium-201 and Its Relation to Creatine Kinase-MB Release After Myocardial Infarction in Man

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SUMMARY We evaluated emission computed tomography (ECT) for thallium-201 (201TI) myocardial imaging in estimating infarct size (IS). In 18 patients in whom IS was estimated enzymatically at the time of the acute episode, planar 201TI perfusion scintigraphy and ECT with a rotating gamma camera were performed 4 weeks after the first myocardial infarction. From the size of 201TI perfusion defects, the infarct area in planar images and the infarct volume in reconstructed ECT images were measured by computerized planimetry. When scintigraphic IS was compared with the accumulated creatine kinase-MB isoenzyme release (CK-MBr), infarct volume determined from ECT correlated closely with CK-MBr (r = 0.89), whereas infarct area measured from planar images correlated less satisfactorily with the enzymatic IS (for an average infarct area from three views, r = 0.69; for the largest infarct area, r = 0.73). Although conventional scintigraphic evaluation is useful for detecting and localizing infarction, quantification of ischemic injury with this two-dimensional technique has a significant inherent limitation. The ECT approach can provide a more accurate three-dimensional quantitative estimate of infarction, and can corroborate the enzymatic estimate of IS.

THE IMPORTANCE of quantifying infarct size (IS) stems from findings that in both acute and old myocardial infarction, morbidity and mortality are related to the extent of myocardial damage. In addition, various therapeutic interventions have been proposed that may limit IS and possibly improve the patient's chances for survival. Several methods have been developed to measure IS in man, Radionuclide methods are particularly attractive because they can be used in patients in the intensive care setting and are potentially capable of measuring IS noninvasively.

Experimental studies have shown that myocardial uptake of thallium-201 (201TI) correlates inversely with myocardial creatine kinase (CK) depletion and relative decrease of myocardial blood flow. Clinical studies have proved the efficacy of 201TI imaging in detecting myocardial ischemia or scar. Good qualitative relationships between location of 201TI myocardial perfusion defects and electrophysiological, ventriculographic, cardiac enzymes, coronary angiography, or postmortem studies have been reported; but several clinical studies have suggested that the accuracy of planar imaging for sizing myocardial infarction is only fair. With conventional imaging techniques, a three-dimensional structure is compressed onto a two-dimensional image plane, so the extent of the damaged myocardium cannot be determined accurately.
Effects of acebutolol on myocardial infarct extension: a randomized electrocardiographic, enzymatic and angiographic study.
I Azancot, P Lorente, G Georgiopoulos, P Beaufils, C Masquet, Y Baudouy and R Slama

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