Late Potentials and Ventricular Enlargement After Myocardial Infarction
A New Role for High-Resolution Electrocardiography?

A.G. Zaman, MRCP; J.L. Morris, MRCP; J.H. Smyllie, MRCP; J.C. Cowan, MRCP, DPhil

Background. Arrhythmias are common in patients who have developed ventricular enlargement after myocardial infarction.

Methods and Results. A prospective study was undertaken to assess the relation between ventricular dilatation and the development of late potentials after myocardial infarction. Echocardiograms and signal-averaged ECGs were recorded on days 1, 3, 7, and 42 in 52 patients with a first anterior myocardial infarction. Twenty-nine percent of patients were late potential-positive on their initial signal-averaged ECG recorded on the day of admission. The incidence of late potentials rose during the next week to a peak of 42% at day 7, declining to 13% by day 42. The presence of late potentials on the day of admission was associated with an increase in end-diastolic volume index of 16.1 ± 6.0 mL/m² (mean ± SEM), compared with a decrease of 4.7 ± 2.7 mL/m² among late potential-negative patients (P < .006). Qualitatively similar results were evident for late potentials on day 3 and day 7. By contrast, there was no association between late potentials on day 42 and ventricular dilatation. Marked dynamic changes in late potentials were evident during the first week. Patients with persistent late potentials (n = 9) on all three recordings in the first week showed a marked increase in end-diastolic volume index of 21.3 ± 8.1 mL/m² (P < .005 in comparison with patients who were persistently negative [n = 20]). Patients demonstrating dynamic positivity (n = 15) not present on all three recordings in the first week showed no significant increase in end-diastolic volume index.

Conclusions. It is concluded that late potentials during the first week after infarction are associated with subsequent ventricular dilatation. These early-phase late potentials may be a manifestation of cell slippage. They arise before gross topographical enlargement and may serve as a predictor of ventricular dilatation. (Circulation. 1993:88:905-914.)

KEY WORDS • infarcts • left ventricle

Infarct expansion and ventricular remodeling are important determinants of ventricular function after myocardial infarction.1 Ventricular function is in turn a major determinant of arrhythmogenesis and sudden death, yet little is known of the consequences of ventricular remodeling for arrhythmogenesis. That a relation may exist is evident in the well-known association between left ventricular aneurysm formation, an extreme form of infarct expansion, and susceptibility to arrhythmias.2 It is unclear, however, whether a similar association exists for lesser degrees of infarct expansion.

Indirect evidence supporting a relation between ventricular remodeling and arrhythmogenesis can be inferred from recent studies concerning the benefits of thrombolysis. Successful thrombolysis is known to prevent infarct expansion.3-5 Persistent occlusion of the infarct-related artery results in thinning and expansion of the infarct zone and an increase in ventricular dimensions. Several authors have shown that successful thrombolysis is also associated with a decreased incidence of late potential development.6-9 Furthermore, patients who have received thrombolytic therapy manifest a decreased susceptibility to sustained ventricular arrhythmias during programmed stimulation.10,11 However, the mechanism whereby reperfusion influences the arrhythmogenic substrate is unclear.

There are, moreover, similarities between the histological changes underlying infarct expansion and the pathophysiological processes underlying slow conduction and arrhythmogenesis. Infarct expansion initially involves myocyte stretch and slippage with loss of gap junctions in the peri-infarct zone.12 Subsequently, fibrosis develops between surviving myocytes.13-15 Either early slippage or late fibrosis or both might result in slow conduction and arrhythmogenesis.

The purpose of the present investigation was to assess the possible relation between ventricular remodeling and the development of an arrhythmogenic substrate after myocardial infarction. Patients with anterior myocardial infarction were studied because of their susceptibility to infarct expansion and the higher specificity of late potentials in this group.16 Serial changes in ventricular volumes over the first 6 weeks after infarction were determined echocardiographically. These changes were correlated with the evolution of late potentials as an index of arrhythmia susceptibility.
Patients
Seventy-nine consecutive patients with a first acute anterior myocardial infarction were eligible for investigation. Myocardial infarction was diagnosed from the presence of two of three standard criteria: a history consistent with myocardial infarction, a creatine kinase rise greater than three times normal, and the development of new Q waves in the ECG. Patients were excluded if it was not possible to record a high-quality echocardiogram (19 patients). Other reasons for exclusion included the presence of bundle branch block or atrial fibrillation (2 patients) in the presenting ECG. Patients receiving treatment with steroids (1 patient) or nonsteroidal anti-inflammatory drugs (2 patients) were also excluded, since these agents may adversely influence ventricular remodeling.17,18 Three patients were unable or unwilling to give consent. Over a 10-month period, 52 patients entered the investigation.

The study was approved by the hospital’s ethics committee.

Timing of Investigations
Initial echocardiograms were recorded within 12 hours and initial signal-averaged ECGs within 24 hours of admission to the coronary care unit (day 1). Echocardiograms and signal-averaged ECGs were repeated on day 3 after admission, on day 7 (before hospital discharge), and on day 42. With the exception of the initial echocardiogram, all echocardiograms and signal-averaged ECGs were recorded between 8 AM and 12 noon, at least 12 hours after the administration of any cardioactive drug. The echocardiographic and signal-averaging data sets were 95% and 96% complete, respectively. Creatine kinase was estimated daily for the first 3 days after admission.

Echocardiography
Two-dimensional echocardiographic images of the left ventricle were recorded on S-VHS tape with a Hewlett-Packard Sonos 500 machine. Standard apical four-chamber and apical two-chamber long-axis views were obtained on each visit, with the patient lying on his left side at an angle of 45°, with breath held in end expiration. A simultaneous ECG tracing was recorded. Patients were entered into the study only if there was clear visualization of at least 90% of the endocardium in systole and diastole. The optimal transducer position was noted and marked with indelible ink for subsequent echocardiographic recordings.

Recordings were coded for subsequent analysis by a single operator blinded to the signal-averaging results. Videos were replayed through a computer-assisted video-overlay system. Signals from the computer, digitizer, and video were processed through a custom-built video mixer and displayed on a high-resolution monitor. End-diastolic and end-systolic frames were selected, and the endocardial outline of each was traced with a digitizer pad and displayed on the monitor. The system differed from a frame-grabbing facility in that it allowed echocardiographic images to be displayed in real time while one could still view the computer contour. This enabled the computer contour to be adjusted to provide the closest fit to the endocardial contour of the real-time images. End diastole was defined as the first frame after the start of the QRS complex and end systole as the frame immediately preceding mitral valve opening.19 Long-axis length was defined as the longest distance from midbase to apex. Volumes were calculated by the disk-summation method.20 Measurements were averaged over two consecutive cardiac cycles.

Signal Averaging
Signal-averaged ECGs were recorded with subjects lying quietly supine. After careful skin preparation, silver/silver chloride electrodes were applied in a standard bipolar orthogonal X, Y, Z lead system. The resultant signals were digitized with a sampling frequency of 2000 Hz (Predictor II, Corazonix Corp, Oklahoma City, Okla). Noisy or abnormal complexes were rejected by a template recognition algorithm. The signal-averaged QRS vector magnitude was calculated as the square root of (X²+Y²+Z²). The QRS vector magnitude was then bidirectionally filtered at a high-pass filter frequency of 40 Hz and low-pass filter frequency of 250 Hz.

For each recording, 300 beats were averaged. Recordings were accepted only if the noise level was <0.7 μV, the latter being measured over an interval of 40 milliseconds in the ST segment. The end of the QRS complex was determined by computer algorithm and was defined as the midpoint of the 5-millisecond segment in which the mean voltage exceeded the mean noise level plus three times the SD of the noise sample.

The QRS vector indices were measured by an automated algorithm, and the presence of late potentials was determined from the presence of two of the following three criteria21: (1) filtered QRS duration ≥114 milliseconds; (2) RMS voltage of the terminal 40 milliseconds <20 μV; and (3) low-amplitude (<40 μV), high-frequency signal (LAS) duration >38 milliseconds.

Reproducibility
The reproducibility of signal-averaged ECGs was assessed by selecting 15 of the study patients at random and repeating the signal-averaged ECG recording 1 to 3 hours after the initial recording. Concordance for the determination of the presence or absence of late potentials was 87%.

The reproducibility of echocardiographic volume measurements was assessed by repeating an echocardiogram on 15 patients at random 1 to 3 hours after the initial recording. Each study was coded and blindly analyzed. The SD of repeated measurements of end-diastolic volume index was 4.6 mL/m². The beat-to-beat reproducibility for end-diastolic volume index was 3.9 mL/m².

Statistical Analysis
Patients were classified into groups based on the presence or absence of late potentials at stated time points. Ventricular volume measurements were normalized for body surface area, and end-diastolic and end-systolic volume indices were calculated. The change in each index was measured relative to the day 1 value. Results are presented as mean±SEM.

To avoid assumptions about the distribution of the data, nonparametric analyses were performed. The statistical significance of change in ventricular volumes
within the groups from day 1 to day 42 was calculated by the Wilcoxon matched-pairs signed-rank test. The changes in each group from day 1 to day 42 were compared by the Mann-Whitney U test. Two-sided P values are reported.

Results

Patient demographic criteria are presented in Table 1. Forty-eight patients received thrombolytic therapy (46 streptokinase, 2 tissue-type plasminogen activator). The median time to thrombolysis from onset of symptoms was 3 hours 20 minutes (range, 45 minutes to 18 hours). One patient died of cardiogenic shock within 48 hours of admission. Five more patients died after hospital discharge during the 6-week follow-up period. All of these deaths were sudden. No patients received antiarrhythmic drugs during the study period. At hospital discharge, 48% of patients were on a β-blocker, 8% on an angiotensin converting enzyme inhibitor, 16% on a nitrate, 14% on a calcium antagonist, and 20% on a diuretic. There were no subsequent changes in drug therapy from day 7 to day 42 and no significant differences in drug therapy between late potential–positive and late potential–negative patients. One patient had a second infarction during the study period.

Change in Late Potential Status With Time

Twenty-nine percent of patients were late potential–positive on their initial signal-averaged ECG on day 1. During the next week, there was a slight rise in the number of patients who were late potential–positive, reaching a peak of 42% on day 7 (Table 2). Subsequently, the incidence of late potentials fell to 13% on day 42.

To exclude any possible bias arising because of deaths, the incidence of late potentials was reassessed, excluding the six patients who died during the course of the study (Table 2). The pattern of late potential positivity remained qualitatively similar.

<table>
<thead>
<tr>
<th>TABLE 1. Demographic Data (%)</th>
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<tbody>
<tr>
<td>Male (no.)</td>
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<tr>
<td>Mean age (years)</td>
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<tr>
<td>Thrombolysis (no.)</td>
</tr>
<tr>
<td>Median time to thrombolysis</td>
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<tr>
<td>Hypertension (no.)</td>
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<tr>
<td>Diabetes (no.)</td>
</tr>
<tr>
<td>Smokers (no.)</td>
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</table>

Changes in End-Diastolic Volume

The mean end-diastolic volume index showed no significant change over the 6-week study period (Table 3). This apparent lack of change in the mean end-diastolic volume index conceals substantial variation between individual patients. The distribution of end-diastolic volume index changes over the 6-week study period is illustrated in Fig 1. In this figure, a volume change of 10 mL/m² is equivalent to the reproducibility of the echocardiographic technique, corresponding to approximately twice the SD of repeated estimates of end-diastolic volume index.

It is not possible to assess the extent of ventricular dilatation between the onset of infarction and the initial echocardiogram, but the absolute ventricular volumes for late potential–positive and –negative groups on day 1 were similar in the initial echocardiogram (60.5±5.8 and 67.1±3.4 mL/m², P<.3, NS).

In view of the dynamic nature of late potentials in the early infarct period and the changing pattern of late potentials with time, their relation (Table 4) to ventricular dilatation was considered separately for each recording period. The patient who died before day 3 was excluded from further consideration, since change in ventricular volume could not be determined.

Patients who were late potential–negative on day 1 showed no significant change in ventricular end-diastolic volume index with time (Fig 2, A). By contrast, late potential–positive patients showed a progressive and statistically significant increase in ventricular end-diastolic volume (P<.006 on day 42 compared with the late potential–negative group).

Similar results were evident for patients who were categorized according to late potential status on day 3 (Fig 2, B). The late potential–positive group showed a progressive increase in ventricular end-diastolic volume index compared with the late potential–negative group (P<.002 on day 42).

For patients who were late potential–positive on day 7 (Fig 2, C), increase in end-diastolic volume index was again significantly greater among late potential–positive patients (P<.04), although the difference was less marked than on days 1 and 3.

Consideration of patients who were late potential–positive on day 42 (Fig 2, D) is more difficult because of the relatively small numbers (n=6 in this group). An initial trend of volume increase was evident to day 7. By day 42, this trend had disappeared, and the extent of volume enlargement was similar in the two groups (P=.54) but with a wide standard error in the late potential–positive group, reflecting the small number of patients.

Separating late potentials at each time point in this way, it is apparent that the presence of late potentials on days 1, 3, and 7 was predictive of subsequent ventricular dilatation. By contrast, late potentials on day 42 did not identify patients who had undergone ventricular dilatation.

Change in End-Systolic Volume

The relation between late potentials and change in end-systolic volume index was qualitatively similar to the diastolic volume results (Fig 3). Late potentials on day 1 (Fig 3, A) were associated with a significant

<table>
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<tr>
<th>TABLE 2. Incidence of Late Potential Positivity</th>
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<tr>
<td></td>
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<tr>
<td>All patients</td>
</tr>
<tr>
<td>Day 1 (%)</td>
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<tr>
<td>Day 3 (%)</td>
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<tr>
<td>Day 7 (%)</td>
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<tr>
<td>Day 42 (%)</td>
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</table>

Excluding deaths

<table>
<thead>
<tr>
<th>All patients</th>
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<tbody>
<tr>
<td>30</td>
</tr>
<tr>
<td>Excluding deaths</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>Excluding deaths</td>
</tr>
<tr>
<td>43</td>
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<tr>
<td>13</td>
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</tbody>
</table>

Five patients died suddenly after discharge and before day 42. The late potential status of these patients on days 1, 3, and 7 was: patient 1, positive day 7; patient 2, positive days 3 and 7; patient 3, positive days 1, 3, 7; patient 4, positive day 3; patient 5, negative days 1 and 3, no recording day 7.
increase in end-systolic volume index to day 42, compared with the late potential-negative group \( (P<.004) \). Late potentials on day 3 (Fig 3, B) or day 7 (Fig 3, C) were similarly associated with a significant increase in end-systolic volume index to day 42 \( (P=.001 \) and \( P<.006 \), respectively). By contrast, late potentials on day 42 showed no association with change in end-systolic volume index (Fig 3, D).

**Change in Ejection Fraction**

In contrast to diastolic and systolic volumes, ejection fraction did not show a clear relation to the presence of late potentials (Fig 4). There was no statistically significant association between late potentials on day 1 (Fig 4, A) or day 3 (Fig 4, B) and change in ejection fraction to day 42. There was a weak association between late potentials on day 7 and change in ejection fraction (Fig 4, C, \( P=.04 \)). There was no association between late potentials on day 42 and change in ejection fraction.

**Individual Signal-Averaging Parameters**

The correlations between the three individual signal-averaging parameters (QRS duration, RMS voltage, and LAS duration) and change in end-diastolic volume index over the 6-week study period are presented in Table 5. On day 1, the three parameters were only weakly correlated with change in end-diastolic volume index, with results bordering on statistical significance. On days 3 and 7, highly significant correlations were observed; correlations were significant for all three parameters, but QRS duration and LAS duration were more closely related to ventricular dilatation than was RMS voltage.

**Variation in Late Potential Positivity**

Considerable variability was observed in late potential activity among the three recordings in the first week after infarction (Table 6). The patients were divided into three groups: those positive for late potentials on all 3 recording days \( (n=9) \), those negative for late potentials on all 3 days \( (n=20) \), and those demonstrating dynamic late potentials present on one or two of the recording days but not all three \( (n=15) \).

Change in end-diastolic volume index among these three groups was considered (Fig 5). Persistent late potentials throughout the first week were associated with a particularly marked increase in end-diastolic volume index of 21.3±8.2 mL/m\(^2\), amounting to an increase in end-diastolic volume of 41±16% \( (P<.005 \) vs persistent negative group). Interestingly, the group of patients demonstrating dynamic late potentials, present in one or two recording periods but not in all three, showed no significant increase in end-diastolic volume index compared with persistently negative patients. Dynamic positivity, therefore, was not associated with significant ventricular dilatation.

Further analysis of the late potential-negative recordings in the dynamic group was undertaken to assess whether the individual signal-averaging parameters differed significantly from the persistent negative group. The mean QRS duration, RMS\(_{100}\), and LAS duration for the former group were 100.3±2.3 milliseconds, 33±3 \( \mu V \), and 30.7±1 milliseconds compared with 97.1±1.4 milliseconds, 47.8±2.8 \( \mu V \), and 28±1 milliseconds for the latter \( (P=.24, P<.001, \) and \( P=.12, \) respectively), indicating that individual parameters differed in the two

**TABLE 3. Ventricular Volumes**

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 7</th>
<th>Day 42</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-diastolic volume index (mL/m(^2))</td>
<td>66.0±2.8</td>
<td>62.6±2.7</td>
<td>68.2±2.8</td>
<td>68.8±3.4</td>
</tr>
<tr>
<td>End-systolic volume index (mL/m(^2))</td>
<td>42.2±2.3</td>
<td>40.4±2.4</td>
<td>41.3±2.2</td>
<td>42.3±3.1</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>37.3±1.4</td>
<td>37.0±1.6</td>
<td>40.6±1.5</td>
<td>40.8±2.6</td>
</tr>
</tbody>
</table>

No significant change was observed in any parameters from day 1 to day 42 (Wilcoxon signed-rank test). Values are mean±SEM.

**FIG 1. Bar graph showing distribution of change in end-diastolic volume.** The distribution of change in left ventricular end-diastolic volume index (EDVi) from day 1 to day 42 is shown. A change of 10 mL/m\(^2\) approximates to 2×SD of repeat estimates of EDVi. Hence, a change of EDVi <10 mL/m\(^2\) is within the reproducibility of the technique. There were 19 patients (43%) in this category. Twelve patients (27%) showed a significant decrease in EDVi; i.e., a decrease of >10 mL/m\(^2\). Thirteen patients showed a significant increase of EDVi, >10 mL/m\(^2\).
groups, even when conventional criteria of late potential activity were negative.

Of the nine patients who were persistently late potential-positive throughout the first week, only two remained positive on day 42; six were late potential-negative; one patient died. Persistent late potentials throughout the first week, therefore, do not result in long-term late potential positivity.

Comparison With Enzymatic and 12-Lead ECG Parameters

Peak creatine kinase activity was compared in the late potential-positive and -negative groups on each of the recording days (Table 7). Positive late potentials were associated with a trend toward larger creatine kinase values, although this achieved statistical significance only on day 3 (P<.05).

No patients developed bundle branch block during the study. For both late potential-positive and late potential-negative groups, the mean QRS duration of the standard 12-lead ECG showed no significant change throughout the 6 weeks of the investigation. When patients were categorized into two groups according to the presence or absence of ventricular dilatation (defined as an increase in end-diastolic volume index of ≥10 mL/m²), there was no significant difference in mean QRS duration at baseline on day 1 in the two groups (expanders, QRS duration 98.7±5.2 milliseconds; non-expanders, 93.6±2.3 milliseconds; P=.4). No significant changes with time were observed in either group over the 6-week study period.

The presence or absence of Q waves on a standard 12-lead ECG 48 hours after admission was assessed as an alternative means of distinguishing patients susceptible to ventricular enlargement. The presence of Q waves was not predictive of changes in end-diastolic volume index (Fig 6).

Discussion

The purpose of this investigation was to consider the possibility of a relation between ventricular remodeling and the development of late potentials after myocardial infarction. There are similarities between the histological changes underlying infarct expansion and those

### Table 4. Change in Ventricular Volumes

<table>
<thead>
<tr>
<th>Signal-averaging time point</th>
<th>End-diastolic volume index (mL/m²)</th>
<th>End-systolic volume index (mL/m²)</th>
<th>Ejection fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LP-negative</td>
<td>−4.7±2.7</td>
<td>−5.0±2.7</td>
<td>+3.8±2.3</td>
</tr>
<tr>
<td>LP-positive</td>
<td>+16.1±5.9</td>
<td>+11.4±4.8</td>
<td>−1.0±2.2</td>
</tr>
<tr>
<td>Day 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LP-negative</td>
<td>−5.6±2.6</td>
<td>−4.8±2.6</td>
<td>+3.0±2.1</td>
</tr>
<tr>
<td>LP-positive</td>
<td>+15.8±5.4</td>
<td>+9.8±5.0</td>
<td>+1.3±3.2</td>
</tr>
<tr>
<td>Day 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LP-negative</td>
<td>−4.4±2.6</td>
<td>−6.3±2.6</td>
<td>+5.7±2.1</td>
</tr>
<tr>
<td>LP-positive</td>
<td>+11.4±5.4</td>
<td>+9.2±4.4</td>
<td>−1.5±2.6</td>
</tr>
<tr>
<td>Day 42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LP-negative</td>
<td>+0.8±2.7</td>
<td>−0.1±2.4</td>
<td>+2.3±1.7</td>
</tr>
<tr>
<td>LP-positive</td>
<td>+7.9±10.6</td>
<td>+0.7±9.8</td>
<td>+5.1±5.5</td>
</tr>
</tbody>
</table>

LP, late potential. At each signal-averaging time point, patients were divided into two groups according to late potential status. For each group, changes in ventricular volumes and ejection fraction between day 1 and day 42 are presented.

**FIG 2.** Graphs showing relation of end-diastolic volume to late potential positivity. Change in end-diastolic volume index (EDVI) from the day 1 value is plotted for late potential-positive (●) and late potential-negative (●) patients, divided according to the signal-averaging results in each of the four recording periods: A, signal averaging on day 1; B, signal averaging on day 3; C, signal averaging on day 7; and D, signal averaging on day 42. Results are presented as the mean±SEM. Statistical comparisons in this and subsequent figures have been made only for the change in EDVI on day 42. *P<.05; **P<.01.
believed to underlie slow conduction and arrhythmogenesis. Infarct expansion arises because of myocyte slippage, a process that is limited by the laying down of collagen.\textsuperscript{1,14,15} This results in the separation of myocytes by areas of fibrosis. Slow conduction arising in such zones is believed to underlie the chronic phase of late potential development and arrhythmogenesis.\textsuperscript{22,23}

It was surprising, therefore, to find no relation between late-phase late potential activity (assessed at 6 weeks) and ventricular dilatation. Ventricular dilatation did not lead to late-phase late potentials. On the contrary, the development of late potentials preceded ventricular enlargement. Early-phase late potentials in the first week after infarction were predictive of ventricular enlargement. Early-phase late potentials in the early postinfarct period and subsequent ventricular enlargement has not been reported previously.

**Pathogenesis of Early-Phase Late Potentials**

It is recognized that late potentials develop early after myocardial infarction.\textsuperscript{24,25} The fibrosis believed to underlie late-phase late potentials cannot represent the explanation for this early phase of late potential development. The pathogenesis of early-phase late potentials is unclear, but it seems probable that a number of diverse factors are contributory. Ischemia and necrosis in the peri-infarct zone may be important. Although studies in patients with angina have failed to show any link between ischemia and late potentials,\textsuperscript{26-28} it is still possible that the more profound ischemia associated with infarction might give rise to slow conduction and late potentials. Alternatively, necrosis in the peri-infarct zone may result in islets of preserved myocyte activity separated by necrotic tissue and give rise to slow conduction.

Our results suggest another, hitherto unrecognized, possibility. Patients who showed early-phase late potentials during the first week underwent subsequent ventricular dilatation. It is possible that early-phase late potentials are a forerunner of ventricular dilatation and represent an early manifestation of cell slippage. Such cell slippage would result in breakage of gap junctions with resultant conduction delay between adjacent myocytes.

**Fig 3** Graphs showing relation of end-systolic volume index (ESVi) to late potential positivity. Change in ESVi from the day 1 value is plotted for late potential–positive (■) and late potential–negative (○) patients. A, signal averaging on day 1; B, signal averaging on day 3; C, signal averaging on day 7; and D, signal averaging on day 42. **P<.01.

**Fig 4** Graphs showing relation of ejection fraction (EF) to late potential positivity. Change in EF from the day 1 value is plotted for late potential–positive (■) and late potential–negative (○) patients. A, signal averaging on day 1; B, signal averaging on day 3; C, signal averaging on day 7; and D, signal averaging on day 42. *P<.05.
TABLE 5. Correlation Between Signal-Averaging Parameters and Change in End-Diastolic Volume Index Between Day 1 and Day 42

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 7</th>
<th>Day 42</th>
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<tbody>
<tr>
<td>QRS duration</td>
<td>r = .28</td>
<td>r = .44†</td>
<td>r = .49‡</td>
<td>r = .09</td>
</tr>
<tr>
<td>RMS voltage</td>
<td>r = -.30</td>
<td>r = .36*</td>
<td>r = -.32*</td>
<td>r = -.12</td>
</tr>
<tr>
<td>LAS duration</td>
<td>r = .31*</td>
<td>r = .40†</td>
<td>r = .46‡</td>
<td>r = .00</td>
</tr>
</tbody>
</table>

LAS, low-amplitude, high-frequency signal.

*P < .05; †P < .01; ‡P < .001.

After myocardial infarction, a marked derangement of gap junctions around the area of necrosis has been demonstrated. Smith and coworkers29 have reported a decrease in the density of gap junctions per myocyte in the peri-infarct zone together with a redistribution of surviving gap junctions. This derangement results in increased intercellular resistance and a reduction in conduction velocity. Transversely oriented gap junctions in the infarct border zone have been shown to be particularly vulnerable, enhancing the anisotropy of normal cellular connections.12 Conduction velocity of a wave front conducting perpendicularly to the long-fiber axis is therefore likely to be significantly reduced. Weissman and coworkers14 have demonstrated that cell slippage occurs very early in the course of infarction, before the gross topographical changes that are subsequently detected as ventricular enlargement. Some cases of early-phase late potential positivity, therefore, may be a result of cell slippage and may be a forerunner of ventricular dilatation.

There are, however, other explanations for our results. It is possible that early-phase late potentials and subsequent ventricular enlargement are merely manifestations of extent of infarction. It is certainly the case that large infarcts are more prone to ventricular enlargement. Information on the relation between early-phase late potentials and infarct size is limited. Gomes and coworkers30 found no relation between infarct size and late potentials recorded at a mean of 3 days after infarction. McGuire and coworkers31 reported a similar lack of relation for late potentials recorded throughout the hospital stay. In the present study, there was a trend toward a larger creatine kinase rise among patients with positive late potentials in the first week, and this trend achieved statistical significance on day 3. Clarification of the relation between early-phase late potentials and infarct size will require further investigation.

Both angiotensin converting enzyme inhibitors and nitrates are known to influence ventricular dilatation after myocardial infarction.1 The use of these drugs among late potential–positive and late potential–negative groups was similar. It is unlikely, therefore, that differences in pharmacological intervention underlay the greater ventricular dilatation among late potential–positive patients.

Evolution of Late Potentials After Myocardial Infarction

We have shown a relatively high incidence of late potentials (29%) in the first 24 hours after admission. Over the course of the next week, there was a gradual increase in the overall incidence of late potentials. This progressive increase in frequency over the first week is well recognized.31,32 More striking, however, was the dynamic nature of the late potentials recorded during this period. With the exception of a small group of patients who remained positive throughout the first week, there was marked crossover between the groups at the different time points. This early dynamic phase of

**TABLE 6. Variation in Late Potential Positivity During the First Week After Infarction**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 7</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistently positive</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Persistently negative</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dynamic changes in positivity</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>+</td>
<td>+</td>
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<tr>
<td></td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Recordings incomplete</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

The patient who died in the first 48 hours was excluded. In seven patients, only two of the three recordings could be made, and these patients are listed as recordings incomplete. Fifteen patients showed dynamic changes in late potential positivity during the first week after infarction.

**TABLE 7. Peak Creatine Kinase Values**

<table>
<thead>
<tr>
<th>Day of signal averaging</th>
<th>Peak creatine kinase (IU/L)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LP positive</td>
<td>LP negative</td>
</tr>
<tr>
<td>1</td>
<td>2587±547</td>
<td>1852±307</td>
</tr>
<tr>
<td>3</td>
<td>2894±488</td>
<td>1583±278</td>
</tr>
<tr>
<td>7</td>
<td>2758±416</td>
<td>1719±313</td>
</tr>
<tr>
<td>42</td>
<td>2253±735</td>
<td>2105±280</td>
</tr>
</tbody>
</table>

LP, late potential. Values are mean±SEM.
late potentials is readily apparent in other investigations.\textsuperscript{25,31,32} Just as the pathogenesis of early-phase late potentials is unclear, the reason for these dynamic changes is uncertain.

A relation between late potential status and ventricular dilatation was most clearly seen among patients with persistent late potentials throughout the first week. There are a number of possible explanations for this observation. The pathogenesis of persistent and dynamic late potentials may differ, and the former may be more closely associated with ventricular dilatation. Alternatively, there may be a continuous relation between delayed activation and ventricular dilatation, the persistence of late potentials merely indicating more extensive delayed activation. Two aspects of the current investigation favor the latter possibility. First, a continuous relation was shown between the individual signal-averaging parameters and ventricular dilatation. Second, negative recordings in the dynamic positive group differed significantly from recordings in patients who were persistently negative.

We observed a marked decrease in late potentials from day 7 to day 42. A decrease in late potentials from the time of hospital discharge is well recognized,\textsuperscript{32-34} although the factors underlying this normalization of conduction are unclear. The lack of an association between late potential status at 6 weeks and ventricular dilatation may imply a differing pathogenesis of late potentials at differing times after infarction. It is also possible, however, that the apparent disappearance of a relation merely reflects the relatively small number of patients with positive late potentials at 6 weeks.

**Predischarge Signal Averaging and Prognosis**

The value of predischarge signal averaging as an indicator of prognosis for arrhythmic events after myocardial infarction is well established.\textsuperscript{32,35,36} El-Sherif and coworkers\textsuperscript{32} have demonstrated that the prognostic significance of late potentials varies in relation to the time of recording in the postinfarction period. They found that transient abnormalities during the first 5 days after infarction were not associated with late arrhythmic events. Late potentials recorded in the phase from 6 to 30 days after infarction (of which 93% of abnormal recordings were made between 6 and 14 days) were the strongest predictor of arrhythmic events. The fibrosis believed to underlie the chronic phase of late potential activity is unlikely to be extensive at this time. It seems improbable, therefore, that the prognostic significance of predischarge signal averaging could be related solely to a long-term arrhythmicogenic fibrotic substrate.

Our findings suggest a further perspective concerning the prognostic significance of predischarge signal averaging. In some patients, late potentials may indicate that the patient is undergoing early ventricular dilatation. The adverse prognosis associated with the presence of late potentials may be a reflection of ventricular dilatation and the ensuing electrical abnormalities resulting from myocyte slippage.

Of critical interest is whether patients with predischarge late potentials that subsequently resolve have a different prognosis from patients with persistent late potentials. If the prognostic significance of predischarge late potentials is related solely to conduction abnormalities arising from a fibrotic substrate, then resolution of late potential activity might be expected to reflect resolution of the conduction abnormality and result in a normalization of prognosis. By contrast, if the prognostic significance of late potentials at discharge is related to ventricular dilatation, their subsequent disappearance would not necessarily be accompanied by a reduction in arrhythmic risk. This is an important issue that requires further study. A preliminary report has suggested that disappearance of late potentials is not accompanied by an improvement in prognosis.\textsuperscript{37}

**Late Potentials as an Index of Ventricular Enlargement**

Our study differs in a number of ways from previous investigations that have related late potential activity to ventricular function. First, we have considered change in ventricular volume during the course of infarction rather than isolated measurements at a single time point. Second, we have considered diastolic and systolic volumes individually rather than the composite measure, ejection fraction. Finally, we have concentrated on early-phase late potentials during the first week after infarction. In the late postinfarction phase, late potentials have been found to be independent of ejection fraction.\textsuperscript{30,32,38} The findings of the present investigation are consistent with this observation.

Our findings suggest the possibility of a new application for signal averaging. The importance of ventricular enlargement as a determinant of subsequent prognosis is well recognized. The prevention of ventricular enlargement with angiotensin converting enzyme inhibitors in both the SAVE\textsuperscript{39} and SOLVD\textsuperscript{40} studies, corresponding to subacute and chronic phases after infarction, has been shown to improve mortality. However, the only large study of angiotensin converting enzyme inhibitors in the immediate postinfarction period (CONSENSUS II) failed to show any benefit in prognosis.\textsuperscript{41} CONSENSUS II treated all patients after infarction. It is apparent from our work and that of other investigators that only a relatively small proportion of patients who undergo thrombolysis will subsequently develop ventricular enlargement and are hence likely to benefit from therapeutic intervention to limit infarct expansion. Therefore, there is a need for an index in the immediate postinfarction period that will identify patients at risk of subsequent infarct expansion. It is tempting to suggest that early-phase late potentials
might fulfill this role through providing an indication of early myocyte slippage. This suggestion will, of course, require detailed prospective evaluation and comparison with other predictors of ventricular enlargement. In the present study, late potentials were much superior to Q waves in predicting ventricular enlargement.

It is possible, moreover, that different criteria of late potential activity would be superior in predicting ventricular enlargement. In the present investigation, conventional criteria derived from late-phase arrhythmia susceptibility studies have been used. It is conceivable that these criteria will benefit from modification when applied in the early postinfarct period to predict ventricular dilatation.

**Relation to Thrombolysis**

Recent studies have shown that persistent occlusion of the infarct-related artery predisposes to the development of late potentials. Similarly, persistent occlusion is known to predispose to infarct expansion and ventricular enlargement. It is possible, therefore, that persistent late potentials and delayed activation are merely an index of failed reperfusion.

Our study highlights the difference in incidence between late potentials in the first week after infarction and at 6 weeks in a population of patients, 92% of whom received thrombolytic therapy. Of 21 patients who were late potential–positive on day 7, only 7 (33%) remained positive at 6 weeks. Studies demonstrating a decreased incidence of late potentials in patients who received thrombolytic therapy have relied predominantly on late potentials assessed 1 week after infarction. Turitto and coworkers have shown that thrombolyis does not influence the incidence of late potentials recorded at a mean of 13 days after admission. There is growing evidence that the predictive value of late potentials after thrombolysis may differ from their value in the prethrombolytic era. Our results indicate a need for caution in extrapolating from late potential activity in the first week to make inferences concerning the long-term effects of thrombolysis on late potential development.

**Limitations of the Present Investigation**

The study was intentionally limited to anterior infarcts. Anterior infarcts show a greater tendency to infarct expansion and ventricular dilatation than inferior infarcts and a higher specificity in the predictive value of late potentials. It was for these reasons that we chose to study this group. In the late postinfarct period, inferior infarcts are known to show a higher incidence of late potential positivity than anterior. It is possible, therefore, that the relations we have observed will not hold true for inferior infarction. This issue will require further investigation.

**Acknowledgments**

We thank Janice Catchpole and Margaret Mundy for technical assistance and Shirley Rutter for typing the manuscript. This study was supported by a British Heart Foundation junior research fellowship (A.G.Z.).

**References**


Late potentials and ventricular enlargement after myocardial infarction. A new role for high-resolution electrocardiography?
A G Zaman, J L Morris, J H Smyllie and J Č Cowan

_Circulation._ 1993;88:905-914
doi: 10.1161/01.CIR.88.3.905
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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