CLINICAL STUDY OF LATE POTENTIALS
- SERIAL CHANGES OF LATE POTENTIALS IN RELATION TO VENTRICULAR ARRHYTHMIAS AND HEMODYNAMIC FINDINGS IN ACUTE MYOCARDIAL INFARCTION -

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Late potentials (LPs) recorded using the signal averaging technique were studied sequentially in 12 cases with acute myocardial infarction (AMI) in order to clarify how LPs develop in relation to ventricular arrhythmias (VA) in this disorder. Within 7 days after the onset of AMI there were no significant differences between LP durations with and without VA, and the overall mean value was relatively short (15.9 ± 5.0 msec). On the 14th day, these cases were clearly divided into two groups according to LP duration. The group with LP duration over 20 msec (n = 5, average: 24.3 ± 1.5 msec) exhibited a higher VA score and the other group with a shorter LP duration (n = 7, average: 15.0 ± 2.1 msec) had a lower VA score (4.3 ± 0.9 vs 0.6 ± 0.5, p < 0.001). This tendency was observed even in the late phase, and data such as peak CPK, cardiac index and mean pulmonary capillary pressure obtained in the acute phase could not predict this separation. In conclusion, LPs appear slightly later following the onset of AMI and correspond with the appearance of VA in the late phase; thus, LPs are useful for the prediction of VA in the course of AMI.

THE development of the monitoring system for life-threatening ventricular arrhythmias (VA) in the coronary care unit has contributed to a decrease in the incidence of rhythm death in acute myocardial infarction (AMI) by allowing the immediate therapeutic application of electric defibrillation and antiarrhythmic agents. But the treatment of VA is occasionally troublesome and prediction of ventricular tachycardia (VT) and sudden death during the course of myocardial infarction (MI) is currently under debate. The mechanism of VT in MI has been considered as reentry1-4 or enhanced automaticity5,6 based on the observations obtained from various investigations, particularly those on experimental animal models. The mechanism and clinical features of VA in MI appear to be different in relation to the time course after episode. Therefore, a question is raised about which major factors provoke VA during the sequential time course following the onset of AMI. From ample animal experiment models, conduction delay is certainly considered as one of the major factors in the first few days after the onset of AMI7,8 but clinically there are few data9,10 to support this concept because of the difficulty of performing electrophysiologic studies in patients with AMI. On the other hand, many investigators have actively studied VT in old myocardial infarction (OMI) using the electrophysiologic

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TABLE I NAMING AND CLASSIFICATION OF VENTRICULAR ARRHYTHMIA SCORE IN THIS STUDY

<table>
<thead>
<tr>
<th>Ventricular arrhythmia</th>
<th>VA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PVCs</td>
<td>0</td>
</tr>
<tr>
<td>PVCs &lt; 120 / hr</td>
<td>1</td>
</tr>
<tr>
<td>PVCs &gt; 120 / hr</td>
<td>2</td>
</tr>
<tr>
<td>2 successive PVCs</td>
<td>3</td>
</tr>
<tr>
<td>Short run of PVCs (three to 10 successive PVCs)</td>
<td>4</td>
</tr>
<tr>
<td>Ventricular tachycardia (more than 10 successive PVCs)</td>
<td>5</td>
</tr>
</tbody>
</table>

Abbreviations: VA = Ventricular arrhythmia; PVC = premature ventricular contraction.

and studied whether or not they corresponded with the appearance of VA.

SUBJECTS AND METHODS

Study patients: Twelve cases with AMI (9 men and 3 women) were studied serially in this study. Three of them revealed findings of previous MI, and the remaining 9 cases had experienced their first episode. Five cases with anterior infarction, 3 cases with anterolateral infarction and 4 cases with inferior infarction were included. None of the cases had any other organic heart disease. AMI was diagnosed by typical chest pain, significant elevation of cardiac enzymes and ECG findings. The average age of these patients was 59 ± 7 years.

Signal averaged ECGs: For detection of LPs, we used modified X, Y, Z bipolar leads. Electrodes were placed at the fifth intercostal space on the right and left maxillar lines for the X lead, at the third intercostal space along the right sternal border and at about 3 cm lateral from the apical impulse for the Y lead, and at the midsternal area and the identical position on the back for the Z lead. After careful recording from each lead, the LP with the longest duration was selected. In the majority of cases the Y lead was the best for detection of LPs. We recorded LPs only during sinus rhythm, excluding the ectopic beats and noisy beats. The ECG signals were amplified by biophysical amplifier (NEC-SANEI polygraph recorder 142-8), and passed through the bandpass filter (NF FV-604T) at a frequency range of 100 to 300 Hz. After pretrigger averaging, filtered signals were recorded on an X-Y recorder (WX-4402) with the unfiltered
original ECG, which was also averaged. The time constant of the biophysical amplifier was set at 0.3 sec, the stabilizing trigger level of signal averaging. LPs were designated as those vibrations exceeding the end of the non-filtered QRS and lasting to the noise. The endpoint of QRS was determined to be the turning point at which the slope of the tangential line became smaller than ±2.5 mv/sec. The end of LP was decided to be the point where the voltage level was less than twice the baseline noise level. Using these criteria, the duration of LPs could easily be measured in almost all cases (Fig. 1). Oral antiarrhythmic agents and digitalis were discontinued at least 24 hours prior to the study in each case, but intravenous lidocaine was continued until 30 mins before the recording in several cases.

Scoring of VA: The severity of VA was graded from 0 to 5 by modifying the Lown's classification (Table I). All of the studied cases were under continuous monitoring from the admission day to the 7th day, and the cases with serious arrhythmias were on continuous monitoring for a longer period. After the 7th day the patients underwent ambulatory Holter ECG monitoring 2 to 3 times on different days. Several cases were treated continuously by drip infusion of lidocaine and oral medication with either disopyramide or procainamide at the time when the arrhythmia score was determined.

Cardiac catheterization and infarct size determination: Eleven of the patients underwent hemodynamic measurement with Swan-Ganz catheter at the acute phase of MI. Pulmonary capillary pressure or pulmonary arterial diastolic pressure was monitored and cardiac index was obtained by the thermodilution method. After 4 to 5 weeks of the episode, 9 patients underwent cardiac catheterization, including left ventriculography and coronary angiography. Ventricular volume was calculated by the area-length method. Infarct size was assessed by peak CPK at the acute phase and also by thallium-201 myocardial scintigram in the late phase. Scintigraphic defect score was calculated by a point scoring system of 0 to 3 points by visual inspection of the uptake ratio in each segment (Table II).

Statistics: Values were expressed as mean ± one standard deviation (SD). Statistical com-
Fig. 3. Change of LPs in the case with a previous episode of AMI (A to C). Each panel shows filtered and averaged ECG (upper) and original non-filtered ECG (lower). Duration of LPs is 24 msec in the second day (A). This patient expired suddenly due to intractable ventricular fibrillation on the 23rd day.

Fig. 4. Time course of duration of LPs in AMI. Closed circles indicate long LPs group (equal to or longer than 20 msec, shaded area) and open circles show the short LPs group (less than 20 msec). The long LPs group includes 2 cases exhibiting LPs duration over 20 msec within one week and 3 cases revealing gradually increased LPs duration exceeding 20 msec after the 14th day following the onset of AMI. The other 7 cases with LPs duration within 20 msec in the time course are designated as the short LPs group.

Comparisons of mean values were undertaken using the nonpaired t-test.

RESULTS

Figure 2 represents the serial change of LPs in a case with AMI. The duration of LPs was 10 msec on the third day after the episode and 9 msec on the 7th day. It was then prolonged to 20 msec and 24 msec on the 14th day and the 28th day, respectively. The voltage of LPs also changed in this time course. Figure 3 represents a case with a second episode of AMI. Duration of LPs was already 24 msec on the second day and it was then prolonged to 27 msec on the 7th day. It was measured until the 21st day when the value was 24 msec; this patient died suddenly of intractable VT and ventricular fibrillation on the 23rd day despite every possible treatment. Change in duration of LPs in relation to the time course of AMI in 12 cases are exhibited in Fig. 4. As an LP duration of 20 msec was regarded as the criterion for positive LPs to predict the development of sustained VT in OMI in our previous study, all of the cases studied were subdivided into two groups according to this span. That is, the group with long LP duration included the cases with an LP duration equal to or longer than 20 msec during the course of AMI. In this group there were two cases in which the duration of LPs was longer than 20 msec even in the acute phase, and both were cases with recurrent episodes of MI. In the group with short LP duration, representing a duration of less than 20 msec during the course of AMI, LP duration in the majority of the studied cases was prolonged until the 7th or 14th day and then it tended to decrease slightly at the later phase. Mean duration of LPs for each group was compared, as shown in Fig. 5, and it was noted that the mean value of LP duration was not significantly different between the two groups within the first week after the episode, but in the group of long LP duration it was markedly prolonged on the 14th day and the 28th day with statistically significant differences.
compared to the short duration group. In Fig. 5, the lower column shows the VA scores in both groups. On the first and the third day after the episode, there was no significant difference in the VA score between the two groups. However, after the 7th day, this VA score decreased only in the group with short LP duration. On the contrary, the score gradually exhibited a larger value corresponding to the prolonged duration of LPs in the long duration group. A statistically significant difference was observed in the VA scores of the two groups at the later phase of
AMI, as is shown in Fig. 5.

Peak CPK, cardiac index and mean pulmonary capillary pressure were compared in the two groups within 3 days after the onset of MI for the purpose of clarifying whether or not the factors of infarct size and cardiac function could affect the duration of LPs at the late phase of MI. The mean values of these parameters were not different between two groups, as indicated in Fig. 6. Approximately one month later following the onset of AMI, we compared the several parameters indicating left ventricular function obtained by cardiac catheterization (Fig. 7). Left ventricular end-diastolic pressure was significantly higher in the long duration group than in the short duration group. The mean ejection fraction value was smaller in the long LP duration group, and all indices of left ventricular end-diastolic volume index, left ventricular end-systolic volume index and scintigraphic defect score indicating infarct size tended to be larger in the long duration group than in the short duration group, though these differences were statistically insignificant. Aneurysm of the left ventricle was noted in 40% of the cases in the long duration group and in 14% of the cases in the short duration group. The number of involved coronary vessels exhibiting luminal stenosis equal to or more than 75% was not different in the two groups.

DISCUSSION

LPs analysed using the signal averaging technique have gradually been utilized to screen high risk patients who later develop VT, especially associated with MI. It is also known that LPs recorded from the body surface reflect the fractionated activity which is known to be recorded at the localized endocardium\textsuperscript{21,32–34} or epicardium\textsuperscript{18,35} in cases of MI. These directly and/or indirectly recorded electrical activities are thought to correspond to the conduction delay which is essential for creating reentry\textsuperscript{36,37} Simson et al\textsuperscript{21} reported in their previous papers on the recording of LPs that the delayed ventricular activation could be detected from the body surface in canine models up to 60 to 90 mins after acute coronary occlusion. Berbari et al\textsuperscript{38} studied canine experimental models 3–6 days after inducing MI by coronary ligation, and they found small potentials in the ST-T segment which correlated with delayed ventricular activation directly recorded from the infarcted myocardium. In general, after complete occlusion of the left anterior descending artery, fractionated electrograms were not found in the isolated preparations during the first week but they were frequently noted at the later period.\textsuperscript{38} Gardner et al\textsuperscript{39} reported in their experimental study on infarcted canine hearts that fractionated electrograms were recorded in the regions where healing from necrosis caused wide separation of the individual myocardial fibers, distorting their orientation. They found that fractionated electrograms were frequently recorded in preparations from infarcts 2 weeks or older but were only rarely recorded in preparations from the early phase of 5-day-old infarcts. These results support our current clinical findings. Gardner proposed in his paper that fractionated electrograms in the healed infarct were not caused by abnormal or depressed activation potentials but by slow and non-homogeneous conduction and the summation of the extracellular currents occurring at disparate times. On the other hand, they might be caused by depressed transmembrane potentials at the site where fractionation has been recorded during acute ischemia.\textsuperscript{4} Thus, if the mechanism with which fractionated electrograms develop is different in the early and the late phase of MI, this may be the reason why LPs can not be detected in the acute phase and why they become evident at 2 weeks or later. It is thought that the electrical activity of the infarcted area, where the action potentials are depressed and conduction is delayed, is involved in wide QRS complex and LPs are not clearly identified. In addition, these activities will consist of lower frequency vibrations and our filtering range of 100 to 300 Hz may not necessarily be suitable for detection of such electrical activity. Since all of the cases in our study had not been examined previously, it is not known whether or not LPs were present previously before the episode of AMI in each individual case. Three cases had documented previous episodes of AMI, and the study was done after the second episode. Two of them exhibited long duration LPs within 7 days after the onset of the second episode. Thus, it is assumed that these two cases revealed positive LPs prior to this study. Furthermore, the additional development of myocardial ischemia in the case of OMI may produce more prominently delayed conduction and may prolong the duration of LPs which is not so evident before the second episode of MI.

A close relationship between LPs and VA in OMI has been reported by many investigators\textsuperscript{19,20,22,26} and our study also demonstrated similar results on the 14th and the 28th day following AMI. One of the most important findings in this study is that the VA score gradually increases with the prolongation of LP duration in the long LP group in the late phase of AMI. It is suggested from this finding that serial study of LPs in AMI has substantial importance for predicting VA in the time course of AMI. Prolonged duration of LPs could not be predicted by peak CPK, cardiac index and mean pulmonary capillary pressure in the acute phase of MI. It is suggested from the findings above that LPs are not closely related to infarct size or the severity of hemodynamic deterioration but are related to the quality of damaged myocardium. Therefore, it is possible that the appearance of VA in the late phase of AMI is not dependent mainly upon the severity of infarction at the onset but upon the electrical alteration of the damaged myocardium in the healing stage. Serial changes of LPs might well document this dispersion of refractoriness and conduction of the impulse at the healing infarct zone, and might correspond to the appearance of VA.

When the patients underwent cardiac catheterization about one month after the episode of AMI, there was a direct correlation between the duration of LPs and left ventricular end-diastolic pressure. Other hemodynamic data and the
findings of left ventricular function tended to be worse in the group with long duration LPs than in the group with short duration LPs. It was reported that the group of patients who developed recurrent ventricular fibrillation and/or sudden death during the follow up period exhibited a higher incidence of severe coronary artery disease such as triple vessel involvement, lower ejection fraction, and further abnormalities in left ventricular contraction. LPS were highly prevalent in the cases with ventricular aneurysms, and it was reported that the LPs disappeared following successful endocardial resection or left ventricular aneurysmectomy. Thus, LPs may, to some extent, demonstrate the relationship between left ventricular function and the severity of coronary artery morphology. Kanovsky et al. undertook a correlative study on signal-averaged electrocardiogram, Holter monitoring and findings of cardiac catheterization in patients with VT, and reported that multivariate logistic regression analysis revealed that only three parameters were independently significant, listing them in order of power as presence of LPs, maximal frequency of premature ventricular contractions greater than 100/hr, and presence of left ventricular aneurysm. LPs relate indirectly to left ventricular function and probably are essential for the development of VT.

There may be some limitations in this study. For example, the recording method and criteria for LPs have not yet been unified, so it is difficult to compare these results with other studies. We measured LP duration as the vibration which lasted after the end of the original QRS complex. Because electrical ringing delay was observed up to 10 msec as was mentioned in our other paper, we designate LPs longer than 10 msec as generally positive. Actually, LP duration was within 10 msec and mean value was 3.1 ± 2.8 msec in 30 healthy normal volunteers. But it must be emphasized that LP duration is different depending on the underlying heart disease and in AMI LPs longer than 20 msec will be meaningful as positive for developing severe VA. It is still unclear whether or not antiarrhythmic agents or digitalis affect LP duration. In this study the long LP group included 4 cases (80%) treated with antiarrhythmic drugs and 2 cases (40%) treated with digitalis. On the other hand, in the short LP group 3 cases (43%) were medicated with antiarrhythmic agents and one (13%) with digitalis. Although these agents were discontinued, when recording LPs it is uncertain if these drugs affect LP duration.

In conclusion, LPs are very useful for predicting VA in patients with AMI in the second week or later following onset, and important information regarding indications for treatment of VA in MI will be obtained by this method of investigation in the late phase of AMI.

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