Prediction of Life-Threatening Arrhythmia in Patients after Myocardial Infarction by Late Potentials, Ejection Fraction and Holter Monitoring

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SUMMARY

In order to compare the prognostic significance of late potentials (LPs) on signal-averaged electrocardiogram (SA-ECG), left ventricular ejection fraction (EF) and 24-hour Holter monitoring (HM) following myocardial infarction, a prospective study on 60 patients (age 61.7±8.02 years old) just after acute myocardial infarction (AMI) was done. LPs, EF and HM were performed in all patients. Coronary arteriography had been done in 25 patients. The results showed that LPs were associated with a slightly higher incidence of life-threatening arrhythmia (34.8%) than HM (28.6%) and EF (25%). During the follow-up period (10±6 months), 9 patients had serious ventricular arrhythmic events, among whom 3 had sudden death due to ventricular fibrillation. The event rate in patients with abnormal LPs was higher than in patients with normal LPs ($p=0.01$, odds ratio=19.2). The study showed that there was no correlation between abnormal LPs and sex, age, number of narrowed coronary arteries, ventricular aneurysm, location of myocardial infarction, or EF alone. But there was a correlation between abnormal LPs and high grade ventricular ectopic activity detected by HM ($r=0.62899$, $p=0.024$). In addition, the combination of abnormal values of LPs, EF and HM could predict sustained ventricular tachycardia or sudden death in the first year after myocardial infarction with very high sensitivity (100%) as well as high specificity ($p=0.0009$, odds ratio=19).

Key Words:
Late potentials Life-threatening arrhythmia Ejection fraction
Holter monitoring

LIFE-THREATENING arrhythmias remain the main cause of cardiac death in the first year after acute myocardial infarction (AMI).[1] In

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order to identify those patients at high risk for such arrhythmic events, a number of clinical noninvasive tests such as exercise stress test, cardiac function index and Holter monitoring (HM) have been utilized. The results have shown that most of them are of limited value. Recently, a number of studies have shown that the late potentials (LPs) on signal-averaged ECG (SA-ECG) might prove to be a more valuable predictor in the prognosis of patients with AMI. The purpose of this study is to determine if there is any prognostic significance of abnormal LPs on SA-ECG in the first year after AMI, and to determine whether factors such as sex, age, ejection fraction (EF), ventricular aneurysm, location of AMI, the mean peak creatine kinase level (during the acute phase of AMI), the number of narrowed coronary arteries ($\geq$75%) and HM are related to abnormal LPs.

Methods

Patients: From November 1989 to August 1990, 60 patients with AMI were enrolled in the present study. The mean age was 61.7$\pm$8.0 (range 40 to 78) years. Patients with previous myocardial infarction, bundle branch block and age >78 years were excluded. The diagnosis of AMI was based upon clinical findings, electrocardiogram (ECG), serum creatine kinase (CK) and CK-MB enzymatic changes. Among the 60 patients, 28 had anterior wall AMI, 15 had inferior wall AMI, 14 patients had infarctions over two sites, and 3 had non-Q-wave AMI.

Data: The following tests were performed: (1) LPs (ART-12000 system, US) was accomplished within 10$\pm$3 days (range 7–14 days) after AMI; (2) EF by radionuclide (^{99m}Technetium, ^{99m}Tc) ventriculography; (3) 24-hour HM; (4) the peak serum creatine kinase values were determined during the first 14 days after AMI. Coronary arteriography was done in 25 of the 60 patients, and this was always done within 2 weeks after the onset of AMI. Examinations (2) and (3) above and coronary arteriography were done within 2 weeks after the onset of AMI. Antiarrhythmic agents were not withdrawn during the LPs procedure. To obtain a signal-averaged surface QRS complex more than 150 beats were averaged in all patients. A vector magnitude was calculated for each point of the averaged X, Y and Z waves as $\sqrt{x^2+y^2+z^2}$. All data were analyzed at filter frequencies of 40–50 Hz. The criteria of abnormal LPs on SA-ECG were: (1) the total duration of QRS vector complex $\geq$120 ms; (2) the duration of the low amplitude signals of <25 μv in the terminal 40 ms of the QRS complex, and (3) the duration of the terminal 40 ms of the QRS complex $\geq$40 ms. LPs were considered to be positive when the first or both the second and third items were present.

Radionuclide ventriculography: The left ventricular EF and presence of a ventricular aneurysm were determined by ^{99m}Tc.

Twenty-four hour Holter monitoring data: The average VPB per hour was calculated by dividing the total number of VPBs seen on 24-hour HM recording, and classified as follows: (1) no ventricular premature beats (VPB); (2) averaged number of VPBs <10/hour; (3) averaged number of VPBs ≥ 10/hour; (4) couplets;[2] (5) nonsustained ventricular tachycardias; and (6) ventricular tachycardia (defined by Josephson et al[3]). Patients who fulfilled any of the criteria for grades 3 to 6 were considered as having high grade ventricular ectopic activity. The life-threatening arrhythmic event was defined as ventricular tachycardia of >120 beats/min of ventricular origin lasting ≥ 30 sec, or ventricular tachycardia associated with hemodynamic compromise. Sudden death was defined as instantaneous, unexpected death or death occurring within 1 hour of the onset of symptoms.

Follow-up: Patients were followed through clinic visits, direct contact with their relatives or by phone for 10 ± 6 months.

Statistical analysis: Data were analyzed by using the chi-square analysis. The odds ratio was calculated with the Yates correction. The correlation between LPs and other various factors was explored by the logistic regression covariates.

Results

LPs: Twenty-three patients (38.3%) had abnormal LPs on SA-ECG. Among the 23 patients with abnormal LPs, 9 patients had an abnormal prolongation of duration (≥ 120 ms) of the signal-averaged QRS vector. The other 14 had the terminal 40 ms <25 μv and the duration of the low amplitude signals was prolonged ≥ 40 ms. The other 37 patients (61.7%) had normal LPs. The ejection fraction (EF) was $\leq 45\%$[4] in 20 patients (33.3%), while the other 40 patients (66.7%) had normal ventricular ejection fractions. Twenty-four-hour Holter monitoring (HM); Twenty-one (35%) of the 60 patients had high-grade ventricular ectopic activity, and the remaining 39 patients (58.3%) had low-grade or no ventricular ectopic activity.

Correlation between the LPs on SA-ECG and clinical features: The data are presented in Tables I and II. Table II shows that there was no correlation in patients with abnormal LPs with age (age was divided according to each decade from 40 to 78 years), sex, location of AMI, EF and ventricular aneurysm. The mean peak creatine kinase level was higher in patients with abnormal LPs than in patients with normal LPs, but the difference was not statistically significant ($p>0.05$). Abnormal LPs in the pa-

Table I. Clinical Features in 60 Patients with AMI

	Abnormal LPs	Normal LPs
Number of cases	23	37
Age (years)	60.9±8.1	62.2±8.1
Sex		
Male	19 (83%)	31 (84%)
Female	4 (17.4%)	6 (16.2%)
Location of MI		
Anterior	12 (52%)	16 (43.2%)
Inferior	4 (17.4%)	11 (29.7%)
Location of MI ≥2	6 (26.1%)	8 (21.6%)
Non-Q-wave MI	1 (4.3%)	2 (5.4%)
Mean peak creatine kinase	1517±763.59	1016.21±999.79
Number of involved coronary vessels		
One branch	2 (8.7%)	7 (18.9%)
Two branches	5 (21.7%)	7 (18.9%)
Three branches	1 (4.3%)	3 (8.1%)
Ventricular aneurysm	5 (21.7%)	3 (8.1%)
Ejection fraction	47±8.03%	53±7.61%

Table II. The Correlation between Abnormal LPs on SA-ECG and Other Factors in Patients with AMI

	r	Sx	t value	p value
Sex	−0.4124	0.8213	−0.502	0.618
Age	−0.0189	0.0434	−0.436	0.665
Location of AMI	−0.2128	0.46507	−0.458	0.649
EF	−0.0198	0.0556	−0.356	0.724
Ventricular aneurysm	−0.49115	0.9851	0.449	0.620
Holter monitoring	0.62899	0.2693	2.335	0.024*

* Indicates a good correlation statistically.

tients with ventricular aneurysm were higher than in patients without ventricular aneurysm, although not statistically significant ($p>0.05$). Table II shows that there was a good correlation between abnormal LPs and high-grade ventricular ectopic activity detected by HM ($r=0.62899$, $p=0.024$). Table I shows that in patients with abnormal LPs, the mean EF was 47± 8.03%, and the EF was 53±7.61% in patients with normal LPs. Judging by EF alone, there was no statistically significant difference between EF and abnormal LPs ($r=-0.0198$, $p=0.724$).

Clinical ventricular arrhythmic events: All 60 patients were followed for a mean of 10±6 months; 9 (15%) of the 60 patients had life-threatening arrhythmic events during the follow-up period. Six of the 9 pa-

Table III. The Incidence of Life-Threatening Arrhythmic Events in Patients with Normal and Abnormal LPs, EF and Holter Monitoring Findings

	Normal (%)	Abnormal (%)	p value	odds ratio
LPs	1/37 (2.7)	8/23 (34.8)	0.01	19.2
HM	3/39 (7.7)	6/21 (28.6)	0.02	4.8
EF	4/40 (10)	5/20 (25.0)	0.20	3
LPs+HM	0/31 (0)	4/12 (33.3)	0.001	8.3
LPs+EF	1/27 (3.7)	4/14 (28.6)	0.01	10.4
EF+HM	3/33 (0)	4/15 (26.7)	0.001	6.9
LPs+EF+HM	0/26 (0)	3/5 (60)	0.0009	19

LPs=late potentials; EF=ejection fraction; HM=Holter monitoring.

tients had documented sustained ventricular tachycardia, and the remaining 3 had sudden death with sustained ventricular tachycardia degenerating into ventricular fibrillation. These 3 cases with sudden death all had abnormal LPs and high-grade ventricular ectopic activity. The total cardiac mortality rate in this study was 5% during the follow-up period. None of them had ventricular aneurysm. Among the 9 patients, only one had an EF of less than 45%; the EF of the other two were 50% and 52%, respectively.

Correlation between life-threatening arrhythmic events and LPs, HM and EF variables: Table III shows that the incidence of life-threatening arrhythmic events in patients with abnormal LPs on SA-ECG was 34.8% (8/23). Among 37 patients with normal LPs only one patient (1/37 or 2.7%) had arrhythmic events. This difference was statistically significant ($p=0.01$). Similarly, among the 21 patients with high-grade ventricular ectopic activity, 6 patients had life-threatening arrhythmic events (28.6%). Among the remaining 39 patients with lower grade ventricular premature beats, only 3 patients had life-threatening arrhythmic events (7.7%). Judging from this alone, there was no statistically significant difference between the 2 groups of the patients with and without high-grade ventricular ectopic activity ($p=0.02$). The incidence of life-threatening arrhythmias in patients with abnormal ventricular EF ($\leq 45\%$) was 25% (5/20). Of the other 40 patients with normal EF, 4 patients had arrhythmic events (10%). Thus EF alone was not statistically significantly different between the patients with normal and abnormal EF ($p=0.20$).

Our study showed that the sensitivity of LPs was 89%, and the odds ratio=19.2. Whereas, the sensitivity of EF and Holter monitoring was 56% and 67%, respectively. Likewise, the specificity of these three tests was the same (71%). It seemed that the sensitivity of LPs was definitely higher than EF and Holter monitoring. Combination of abnormal LPs and Holter moni-

toring was associated with a higher rate of life-threatening arrhythmic events (33.3%) than any single abnormal test. In contrast, the rate of arrhythmia was lower (0 to 3.7%) if both of these tests were normal. Therefore, a combination of the two tests for the prediction of life-threatening arrhythmic events provided a higher sensitivity (80 to 100%), while the specificity did not change.

Analysis showed that if all three tests (the EF, HM and LPs) were abnormal, it was associated with the highest arrhythmic event rate of 60% (odds ratio=19). In contrast, there were no life-threatening events in patients when the three tests were normal. The combination of these three tests had a very high sensitivity (100%) as well as a very high specificity (93%).

Discussion

Josephson et al believed that the finding of late potentials (LPs) on SA-ECG may indicate an area of delayed activation which is the basis of reentrant ventricular tachycardia.[3] Many studies have shown that this noninvasive test may be a moderately sensitive predictor of sustained ventricular tachycardia in patients with chronic ischemic heart disease.[1] Some studies have also shown that LPs on SA-ECG may be an independent predictor of sustained ventricular tachycardia, which was not related to the presence of ventricular aneurysm, cardiac function or other factors.[5],[6] The results of our study suggest that the abnormal LPs in patients with AMI did not have any correlation with factors such as sex, age, location of AMI, mean peak creatine kinase, number of narrowed coronary vessels, EF or ventricular aneurysm (Table II). Some authors reported that the correlation between LPs and location of AMI was significant. But recently, many investigators[2] and our study found that there was no correlation between these two parameters. Our data also show that if the presence of LPs on SA-ECG test was used alone to predict life-threatening ventricular arrhythmic events, the prediction would be more sensitive than that by EF or HM alone in the first year after AMI. This result was similar to that of Gomes et al.[7],[8]

A question remained unanswered as to the predictive value of high grade ventricular arrhythmias detected by HM in postinfarct patients. Some authors[9] believed that Holter monitoring can give information about the role of the autonomic nervous system and the frequency of occurrence of ectopic activity. Unfortunately, however, 35 to 50% of patients with documented sustained ventricular tachycardia or ventricular fibrillation could not be detected by HM. The results of our study showed that HM has a good correlation with LPs ($r=0.62899$, $p=0.024$). This result was similar to that

of Califf's et al,[10] but differed from that of Simson et al.[5] This might be due to the fact that the high grade ventricular arrhythmias in our study were the result of a reentrant mechanism.[3] As noted by Gomes,[9] the detection of high grade ventricular arrhythmia not only has prognostic significance, but also can clarify the mechanism by which the sustained ventricular tachycardia was induced. If reentrant pathways were present, the high grade ventricular premature beats could easily induce a life-threatening ventricular arrhythmia.[11] In the present study, only 28.6% of patients with life-threatening arrhythmias had abnormal HM was limited. Our study also indicated that the incidence of life-threatening ventricular arrhythmias in patients with both abnormal LPs and HM reached 33.3%. In contrast, no such ventricular arrhythmias occurred in our patients when both LPs and HM were normal. Thus, the results of the present study suggest that LPs can detect the presence of a reentrant pathway, and the high-grade ventricular ectopic activity may be the factor inducing life-threatening arrhythmic events. Therefore, the combination of these two tests might provide more valuable predictive information than HM alone.

In our study, there was a poor correlation between EF and LPs. Judging by EF alone the incidence of life-threatening ventricular arrhythmias was about 20%[5] in patients with abnormal ventricular function after AMI. This suggested that abnormal ventricular wall motion may cause the conduction delay, and form the basis of sustained reentrant ventricular tachycardia accompanied with the decreased EF. But, life-threatening ventricular arrhythmias also occurred in 15.6% of patients with normal cardiac function in the clinic. Gomes believed that such arrhythmias occurring in patients with normal ventricular wall motion and cardiac function might correlate with changes in the histology and electrophysiologic properties in myocardial infarction and/or peripheral tissues.

With the analysis by logistic regression covariates, the prediction of life-threatening arrhythmic events can be greatly increased when LPs are combined with EF and Holter monitoring compared with these tests alone. The results showed that these three tests in combination can be a very valuable predictor of the rate of life-threatening arrhythmic events. The sensitivity and specificity are significantly higher (100% and 93%, respectively) than those of any single or a combination of any two of these tests. Our study demonstrated that if all three tests were abnormal in patients with AMI, the incidence of life-threatening arrhythmias was significantly higher than that in those patients with three normal tests (Table III). It is apparent that those patients with three abnormal tests should be considered as a high risk group for life-threatening arrhythmia after AMI, and that these tests can be used

as a valuable noninvasive index to predict life-threatening arrhythmia in patients with AMI.

Since our study did not exclude the effect of antiarrhythmic drugs on LPs, EF and left ventricular function, some of our results in this study have to be confirmed by further investigations.

In conclusion, LPs on SA-ECG can be used as an independent predictive index for life-threatening arrhythmias occurring in the first year after AMI. If the LPs are combined with EF and HM, the predictive value can be greatly increased. These noninvasive tests may prove beneficial in defining a subset of patients at very high risk for sustained ventricular tachycardia.[12] Patients with abnormal results in all three tests (LPs, EF and HM) must be followed up carefully even if they appear to be stable.

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