Survival data management in patients with acute myocardial infarction

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ABSTRACT: The aim of this study is to analyse survival data of the patients with acute myocardial infarction. We studied a sample of 424 patients with a mean age of 67.1±12.3 years. The overall mortality rate after 5 years was 233.4‰. The presence of late potentials in patients with associated arrhythmias, low ejection fraction or low RR variability is associated with higher mortality risk.
KEYWORDS: survival analysis, myocardial infarction, late potentials, Cox regression.

Introduction

In developed countries, cardiovascular diseases represent the first cause of mortality [NHL07]. Within this group of patients, the acute myocardial infarction (AMI) is responsible for 75% of heart disease mortality.

Late potentials (LPs) represent slow or delayed conduction originating from viable cells within or surrounding myocardial infarct regions. They are cardiac signals of very low amplitude (between 1 and 20 μV) and high frequency content (between 40 and 250 Hz), which are located at the end of the QRS complex and at the beginning of the ST segment [BS00]. They are defined as abnormal signals that outlast the normal QRS period during normal sinus rhythm.

Due to their particular characteristics, the LPs are not detectable in the conventional surface electrocardiogram (ECG). The Signal Averaging High-Resolution ECG (SAECG) is the specific electrocardiographic technique

which detects LPs. SAECG utilizes computer processing to amplify signals, mediate and filter them in order to record low-amplitude signals free of noise not normally observed on standard electrocardiogram and defined as magnitude vector [Gom93, OL09].

Three parameters are identified on the vector magnitude: a) the entire duration of the filtered signal-averaged QRS complex; b) the root mean square voltage of the terminal 40 ms of the QRS complex (RMS40); and c) the duration of low-amplitude signals (LAS) of less than 40□V.

LPs are noninvasive markers for reentrant arrhythmias with negative predictive value for cardiovascular deaths. They proved their utility in risk stratification of patients with AMI [G+96].

The RR variability (RRV) or Heart rate variability (HRV) is a non-invasive index of the autonomic control of the heart. It can be quantified by the simple calculation of the standard deviation of the RR intervals. In September 1993, the Cardiovascular Technology Assessment Committee of the American College of Cardiology published a position statement on heart rate (actually RR interval) variability for risk stratification [Ame93].

The present prospective study was undertaken to determine if the presence of late potentials in patients with acute myocardial infarction identifies a subgroup of patients who are at particularly high risk of sudden death and/or ventricular arrhythmias.

1. Methods

The prognostic significance of late ventricular potentials recorded from the body surface using high-resolution amplification and signal averaging was assessed prospectively in consecutive patients with acute myocardial infarction admitted to the Timis County Emergency Hospital. A total number of 600 patients were potential eligible subjects. From this pool of patients only 424 were suitable. Within the 176 excluded patients, 44 were lost during follow-up, 40 had a mean noise >0.7 μV (the accepted noise should be less than 0.7 μV as recommended in the manual for the bedside unit) and 92 patients had intraventricular conduction disturbances. This cohort study was carried out between June 2001 and June 2010. The procedure was explained to all the patients, they were informed about the potential adverse and side effects, risks and benefits and they finally signed an agreement previously approved by the local ethic committees.

At the time of enrollment each patient was the subject of a complex evaluation (demographics, medical history, clinical examination, laboratory

tests, chest X-ray, standard and signal-averaged electrocardiography, RRV in time domain analyses, Holter monitoring in selected cases and M, 2D, CW, PW and color Doppler echocardiography. Follow-up of the patients included repeated evaluations at one month, 3 months, and then every three month during the first year and every six months in the next years for a minimum follow-up period of 5 years.

The criteria for ventricular late potentials were: QRS duration >114 ms in men or >104 ms in women and RMS40 <20 μV. The RMS40 value was found from the vector magnitude, using the 40-msec period preceding the latest individual lead QRS offset.

Means, standard deviations and proportions are presented for continuous variables. Frequencies and percentages are shown for categorical data. Chi-square test was used to compare categorical data. Survival time was calculated as the time from acute myocardial infarction to death, censoring at the date of last contact. The Kaplan-Meier method was used to compute survival rates. Survival curves were compared using the log-rank test. The Cox regression model was applied to evaluate the effect of independent variables on overall survival. Relative risk rates (RR) and their 95% confidence intervals (95% CIs) were calculated. The P values for all hypothesis tests were two-sided, and we set statistical significance at P<0.05.

Statistical analyses were performed using Open Epi and SPSS version 10 software.

2. Results and discussions

We studied a sample of 424 patients (67.69% males, 32.31% females), with a mean age of 67.1±12.3 years. Characteristics of the patients are shown in Table 1. Ninety nine patients died during the follow-up period (Table 2). The overall mortality rate after 5 years was 233.4‰ (99 deaths), with a rate of 236.9‰ in males (68 deaths) and 226.2‰ in females (31 deaths).

Deaths were significantly higher among patients who presented LPs (determined by the value of RMS40) compared to those who had no LPs (44.02% versus 3.26%), *P* <0.001.

The highest death rate occurred in patients who had low ejection fraction (EF 0-40) compared to those with ejection fraction values ranging between 41 and 55, respectively > 55 (91.01% vs. 3, 27% and 2.23%), *P*<0.001.

Heart rate variability, determined by following RR intervals in standard derivations showed that deaths were about four times more

common in patients who had changes in RR intervals compared to those who did not have this variation (29.07% versus 7.21 %), *P*<0.001.

Among patients with QRS complex prolongation deaths were recorded more frequently than in patients who had normal QRS complex (40.27% versus 14.18%), *P*<0.001.

Table 1. Patients' characteristics

Characteristics (n=424)	N	%
Males	287	67.7%
Females	137	32.3%
Mean age ± Standard deviation	67.1±12.3	
Follow-up period	5 -10 years	
Acute Anterior Myocardial Infarction	272	64.2%
Acute Inferior Myocardial Infarction	152	35.8%
Hypertension	227	53.53%
Diabetes	139	32.78%

Table 2. Deceased by gender and age group

Age group	Females	Males	Total
<34 years	0	2	2
35 - 44 years	1	0	1
45 – 54 years	3	11	14
55 - 64 years	11	14	25
>65 years	16	41	57
Total	31	68	99

In our study, ventricular arrhythmias increased the risk of cardiac death by seven times (Fig. 1).

If both the ejection fraction and the presence of late potentials are used as prognostic factors, statistical analysis by Cox regression and survival curves documents highly statistically significant differences. The presence of late potentials in patients with ejection fraction below 0.4 documents an increased risk of death by almost seven times at an extreme level of significance, *P*<0.0001.

Survival curves depending on the presence or absence of late potentials and heart performance show a severe evolution in those who develop concomitant alteration of potential parameters and cardiac function (Fig. 2, Table 3).

Applying the same analysis model in patients with low RR variation shows that association of vegetative alteration with the presence of LPs increases the risk of cardiac death 3 times (Fig. 3, Table 4).

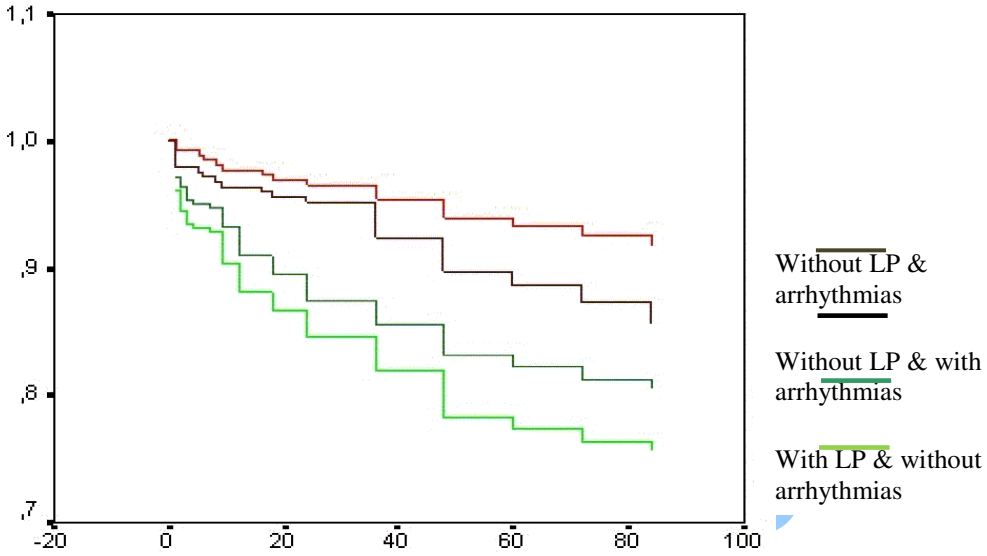

Fig. 1 Survival curves according to the presence of late potentials and arrhythmias

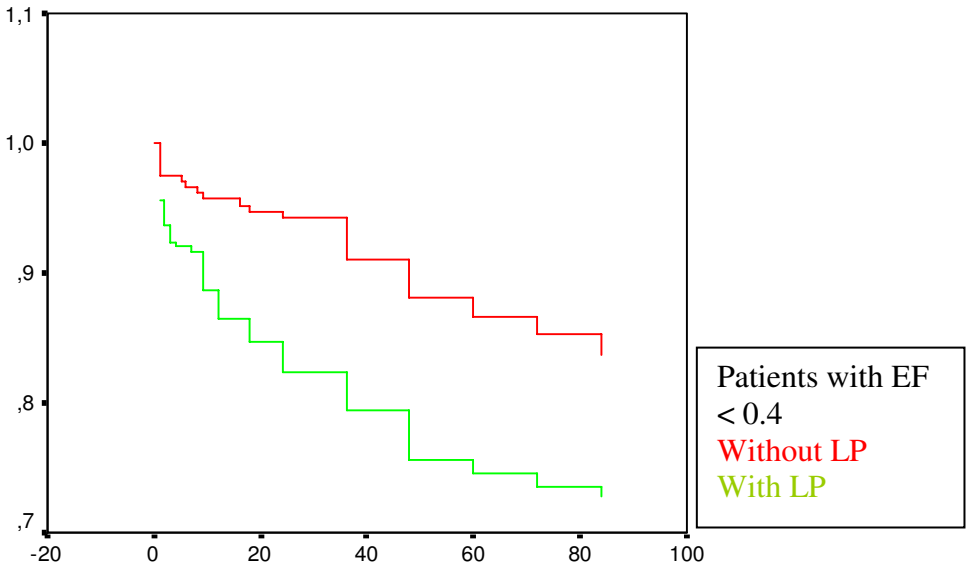

Fig. 2 Survival curves in patients with or without late potentials and impaired cardiac performance

Table 3. Relative risk in patients with EF<0.4

	P value	Relative risk RR	95.0% CI	
			Min	Max
EF	<0.0001	6.691	4.247	10.542

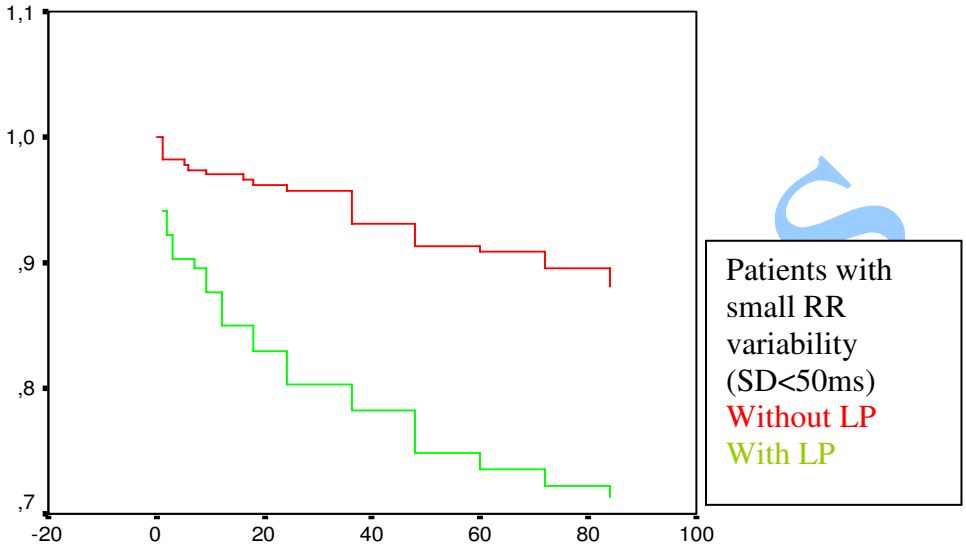

Fig. 3 Survival curves in patients with or without late potentials and impaired autonom activity

Table 4. Relative risk in patients with small RR variability

	P value	Relative risk RR	95.0% CI	
			Min	Max
Var. RR	0.016	2.790	1.208	6.445

Numerous studies have shown increased predictive power of LPs if associated with data obtained by Holter monitoring [KTS86, T+94, Z+93]. Occurrence of sustained ventricular arrhythmias in patients with LPs increases the risk of cardiac death. These observations demonstrate that LPs help identifying those patients with severe ventricular dysfunction or ventricular arrhythmias, who have conditions to develop fatal arrhythmia and, conversely, the need for severe ventricular impairment or the presence of cardiac arrhythmic triggers to initiate and maintain these fatal arrhythmias.

Association of the presence of LPs in patients with documented sustained ventricular arrhythmia increases the risk of cardiac death by 7 times. (Fig. 4, Table 5).

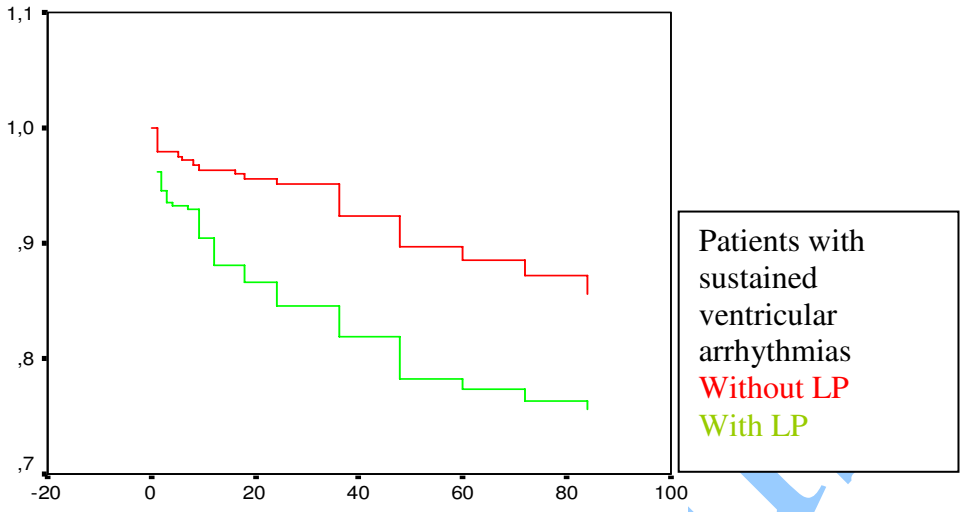

Fig. 4 Survival curves in patients with or without late potentials and ventricular arrhythmias

Table 5. Relative Risk in patients with arrhythmias

	P value	Relative risk RR	95.0% CI	
			Min	Max
Arrhythmias	<0.0001	7.096	4.669	10.783

Conclusions

- Presence of late potentials particularly identifies patients prone to develop life threatening arrhythmias.
- RRV as marker of autonomic imbalance proved to be an independent risk for sudden cardiac death.
- Ejection fraction is the most powerful prognostic factor but the association LP, RRV and EF in risk scale after myocardial infarction augment the sensitivity and sensibility of risk stratification and individualize treatment in order to improve survival.

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