

Late phase of repolarization ($T_{peakTend}$) as a prognostic marker of left ventricle remodeling in patients with anterior myocardial infarction treated with primary coronary intervention

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Abstract

Background: Left ventricle remodeling (LVR) is regarded as a marker of unfavorable outcome in patients following acute myocardial infarction (AMI). Repolarization, especially its late part ($T_{peakTend}$), is strongly related to local myocardial attributes. We assessed prospectively in this study if repolarization duration (measured from one hour of nighttime) might predict LVR occurrence in patients with anterior AMI treated with primary percutaneous coronary intervention (PCI).

Methods: The study population consisted of 111 patients with first anterior AMI (82 males, age 58 ± 11 years, LVEF $41 \pm 7\%$) treated with the primary PCI of left anterior descending coronary artery. LVR, defined as left ventricle end-diastolic volume increase by $> 20\%$ during six months follow-up, occurred in 35 patients (31 males, age 56 ± 10 years, LVEF $37 \pm 7\%$, LVR+), while the other 76 subjects were free of LVR (51 males, age 58 ± 10 years, LVEF $43 \pm 7\%$, LVR-). Holter recordings were performed in the fifth day of AMI. Repolarization parameters: QT, QT_{peak} and $T_{peakTend}$ were assessed from one hour of nighttime Holter recording (between 1–4 a.m.).

Results: LVR occurred more frequently in males ($p = 0.02$). LVEF was lower in LVR+ patients ($p = 0.001$). QT_c was similar: 441 ± 29 ms vs 434 ± 25 ms, $p = 0.37$ for LVR+ vs LVR-. Patients with LVR had shorter QT_{peakc} (333 ± 34 ms vs 345 ± 25 ms, $p = 0.03$) and remarkably longer $T_{peakTendc}$ (108 ± 15 ms vs 89 ± 17 ms, $p = 0.0001$). Receiver operating characteristics analysis revealed that the best cut-off value for LVR prediction was 103 ms — sensitivity: 65.7%, specificity: 81.6%, positive predictive value: 62%, negative predictive value: 83.8%.

Conclusions: The greater transmural heterogeneity of the repolarization processes described by $T_{peakTend}$ interval measured at discharge after AMI seems to be a prognostic marker of left ventricle remodeling occurrence during six months follow-up in patients with acute anterior infarction. (Cardiol J 2010; 17, 3: 244–248)

Key words: myocardial infarction, percutaneous coronary intervention, repolarization, transmural dispersion, remodeling

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Introduction

Identification of patients after acute myocardial infarction (MI) being at higher risk of cardiac death or sudden cardiac death (SCD) is still a primary goal of many studies. Non-invasively assessed risk markers, related to mechanical, electrical or regulatory (autonomic nervous system activity) triggers, are supposed to be predictors of the poor outcome in these patients [1]. It is also suggested that merging different risk markers may be helpful in identifying high-risk subjects. Left ventricular remodeling (LVR) refers to changes in left ventricle (LV) size and shape with rearrangement of the wall structure, leading to progressive dilatation. However, the strong correlation with left ventricle ejection fraction (LVEF) is not always present [2, 3]. A relationship between LVR occurrence and poor outcome in patients with MI was also reported. Prolongation of repolarization duration (QT) was also found to be associated with higher incidence of cardiac death or SCD in many papers, but not in all. Interestingly, QT duration was found to be prolonged in patients with LVR [4, 5].

Automatic measurement of the QT interval in Holter recordings provides more accurate information on the duration of the entire repolarization, its early (QT peak) and late (TpeakTend) phases. The most recent one, as demonstrated by Antzelevitch [6], seems to reflect the transmural dispersion of the repolarization, a difference between the action potential duration of M cells and both epicardial and endocardial layers. Therefore, it may be supposed that prolongation in TpeakTend is related to changes in myocardial attributes, which are consequences of changes in myocardial wall structure and/or persistent local ischemia despite successful percutaneous coronary intervention (PCI) of the culprit coronary artery. However, the prognostic significance of TpeakTend in post-infarction patients, and the relationship between TpeakTend and the risk of LVR development, are still open to debate.

The purpose of this study was to assess prospectively the relationship between prolongation of repolarization duration measured from one hour of nighttime and the risk of LVR occurrence in patients with anterior acute MI treated with primary PCI.

Methods

The cohort of 111 patients with first anterior MI treated with successful primary PCI (TIMI 3) of left anterior descending coronary artery was observed prospectively for six months. Coronary

angiography and primary PCI of the culprit coronary artery were performed with a percutaneous femoral approach. Antegrade flow in the culprit artery was graded according to the TIMI classification system. Echocardiographic examinations were performed twice in each patient: once on the second day of MI and once six months later with commercial system Vivid 7 (GE). Left ventricular end-diastolic (LVEDV), end-systolic (LVESV) volume and LVEF using Simpson method were assessed. LVR was defined as > 20% increase in the LVEDV at six months in comparison with the baseline study. Patients were divided into LVR (+) and LVR (–) groups according to the presence of remodeling.

The study protocol was approved by the Local Ethical Committee.

Holter recording

Holter recordings were performed at the fifth day of acute MI using three channel Lifecard Del-Mar Reynolds recorders (ECG signal recording with ‘oversampling’ rate 1,024 Hz, effective sampling rate 128 Hz) and analyzed with Pathfinder 700 system. Channel CM5, which is closest to V5 or V4 leads of standard surface 12-lead ECG recording [7] was used. All subjects were in sinus rhythm and did not have bundle-branch block or QRS complex duration > 120 ms. No frequent atrial or ventricular arrhythmias (> 10/h) were observed.

Repolarization duration measurement

Repolarization parameters were assessed from one hour (between 1–4 a.m.) in which ST-T segment pattern facilitated automatic beat-to-beat analysis of more than 95% of recording. The following parameters were used: QT-time from the beginning of the QRS complex to the end of the T wave, QT peak-time from the beginning of the QRS complex to the peak of the T wave and TpeakTend-time from the peak to the end of the T wave. All these intervals were corrected according to Bazett’s formula using preceding RR interval-QTc, QTpeakc, TpeakTendc.

Statistical analysis

All continuous variables are shown as mean \pm standard deviation and categorical variables as absolute numbers or proportions. Continuous data was compared with the Student’s t-test or Mann-Whitney U test, categorical variables with the χ^2 test or Fisher exact test, and Spearman correlation was used to assess relationships between continuous variables. Receiver Operating Curve (ROC) analysis was used to assess optimal cut-off point for TpeakTendc. P value of < 0.05 was considered

Table 1. Study groups' characteristics.

	LVR-	LVR+	p
Gender (females; males)	25; 51	4; 31	0.02
Age (years)	58 ± 10	56 ± 10	0.51
Beta-blockers	99%	100%	0.99
Angiotensin converting-enzyme inhibitors	96%	100%	0.13
Statins	98.7%	100%	0.48
Left ventricular ejection fraction (%)	43 ± 7	37 ± 7	0.001
Left ventricular end-diastolic volume [mL]	58 ± 21	72 ± 21	0.002
Left ventricular end-systolic volume [mL]	102 ± 32	113 ± 30	0.07

LVR — left ventricle remodeling

Table 2. Repolarization parameters in study groups.

	LVR-	LVR+	p
QTc [ms]	434 ± 25	441 ± 29	0.37
QTpeakc [ms]	345 ± 25	333 ± 34	0.03
TpeakTendc [ms]	89 ± 17	108 ± 15	0.0001

LVR — left ventricle remodeling

significant. Statistical analysis was performed with Statistica 7.1 PL package.

Results

The study cohort consisted of 111 patients with first anterior MI (82 males, age 58 ± 11 years, LVEF 41 ± 7%). The study group's characteristics are given in Table 1. Groups did not differ in treatment; 99% of patients were treated with beta-blockers and no true antiarrhythmics were given. LVEF was significantly lower in LVR+ (p = 0.001), as well as LVESV (p = 0.002). QTc was similar in both groups (Table 2). Patients with LVR had shorter QTpeakc (333 ± 34 ms vs 345 ± 25 ms, p = 0.03) and remarkably longer TpeakTendc (108 ± 15 ms vs 89 ± 17 ms, p = 0.0001). Weak but significant correlations were found between TpeakTendc and both LVESV and LVEF: r = 0.27, p = 0.003 and r = -0.44, p = 0.0001 respectively. There was insignificant relationship between TpeakTendc and LVEDV (r = 0.17, p = 0.08). ROC analysis revealed that the best cut-off value for TpeakTendc was 103 ms (Fig. 1) with sensitivity: 65.7%, specificity: 81.6%, positive predictive value: 62% and negative predictive value: 83.8%, with odds ratio (OR) = 8.49, 95 confidence interval: 3.42–21.03 (Fig. 2). High predictive values were found in patients with

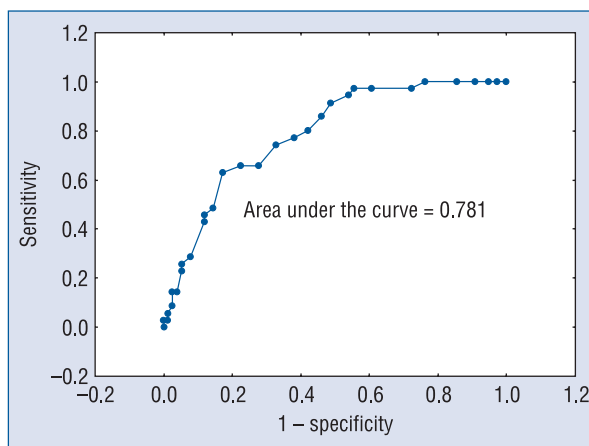


Figure 1. Receiver operating characteristics (ROC) curve for TpeakTendc.

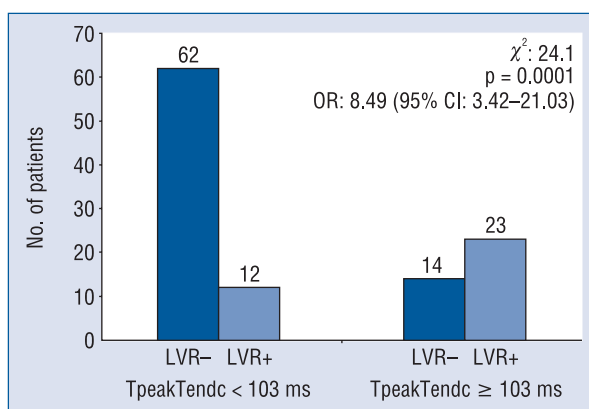


Figure 2. Distribution of TpeakTendc in study groups with respect to cut-off value of 103 ms.

both LVEF < 35% (OR = 10.5, 95% confidence interval: 1.5–73.7, p = 0.02) and LVEF ≤ 35% (OR = 5.25, 95% confidence interval: 1.68–16.4, p = 0.005).

Discussion

In this study, we demonstrated that longer late phase of repolarization is a significant predictor of left ventricular remodeling occurrence in patients with acute anterior myocardial infarction treated with primary PCI. We also found not a strong but a remarkable relationship between TpeakTendc and left ventricular ejection fraction. It should be emphasized that no medicines with possible or probable effect on repolarization duration were used at baseline of the study.

Computer analysis of QT interval in Holter recording using beat-to-beat analysis provide more accurate information on the duration and dynamicity of repolarization duration than manual assessment. However, the automatic determination of Tpeak in the entire recording in acute MI patients is often impossible due to dynamic changes of T wave shape or amplitude. Therefore, we used in our study data of QT measures taken from one hour in nighttime period, in which T waves were more stable and analysis of at least 95% of recording was possible. In our opinion, this method provides more precise measurement of both entire repolarization and its late phase, and is helpful in omitting mistakes related to biphasic or flat T waves, which are often found in ECG recordings in acute MI patients.

Gaudron et al. [4] found that non-survivor patients with LVR and LV dilatation were characterized by more remarkable QTc prolongation than survivors. This difference was the most significant at six month follow-up. They suggested that LVR may be a link between LV dysfunction, myocardial electrical instability and SCD in post-infarction patients. This observation is similar to our results presented previously [5]. We reported significant prolongation of both QTc and TpeakTendc in patients, in whom remodeling had occurred six month after MI. We also found significant relationships between repolarization parameters and changes in both LVEF and LVEDV, which were observed six months after acute MI. In the present study, we analyzed baseline data and found that these correlations at early phase of myocardial infarction are weak. This suggests, in our opinion, that transmural heterogeneity of repolarization is more related to local myocardial attributes than LV global function. We found that the baseline LVEF was lower, and both LVEDV and LVESV were higher, in patients who presented LVR during the follow-up. This observation is in concordance with results presented by Bolognese et al. [2], who described microvascular dysfunction as a marker and risk fac-

tor of LV remodeling occurrence in post-infarction patients. Therefore, we think, with respect to the observation of Bolognese, that microvascular dysfunction observed even in patients after successful PCI of the culprit coronary artery, may be a factor in increased transmural heterogeneity of repolarization. It may explain our findings of the predictive value of TpeakTendc in the prognosis of the LV remodeling occurrence, which, moreover, was found to be independent of the severity of the LV impairment.

Recently, the association between prolongation of repolarization and the presence and the degree of myocardial scarring has been found in animal studies [8]. Histological and electrophysiological studies revealed the presence of surviving subendocardial Purkinje fibers with prolonged action potentials. Acute myocardial infarction causes alterations in the function of ionic currents, known as electrical remodeling, which is responsible for abnormalities in the conduction and refractoriness in infarction and peri-infarction zones [9]. Dynamic changes in repolarization duration resulting in higher differences between infarcted, injured and ischemic zones in the myocardium of acute MI patients were also described [10]. Gupta et al. [11] found in acute MI patients that TpeakTend was significantly longer in precordial leads with ST segment elevation compared to non-ST segment elevation leads. Therefore, we think that increased transmural heterogeneity of repolarization, which was found in our study, may be related to all the above mechanisms, including alterations of ionic channels, different ischemic conditions due to microvascular dysfunction and the presence of different types of ischemic myocardial injury as a result of acute MI. Despite the controversies as to the genesis of TpeakTend measured from the surface electrocardiography [12], its clinical utility should be noticed. It is possible that myocardial stunning, observed in the subacute phase of MI, might have important influences on our results, and therefore, it may be thought as a limitation of the study. Nevertheless, in our opinion, despite this uncertainty, further studies on QT and TpeakTend in such patients should be carried out to explain and confirm the prognostic significance of such findings.

Conclusions

Greater transmural heterogeneity of the repolarization processes described by TpeakTend interval measured at discharge after acute MI seems to be a prognostic marker of left ventricle remodeling

occurrence during six month follow-up in patients with acute anterior infarction.

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