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Microvolt T-wave alternans predicts cardiac events after acute myocardial infarction in patients treated with primary percutaneous coronary intervention

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ABSTRACT

Background: Current risk stratification after acute myocardial infarction (MI) depends on left ventricular ejection fraction. Microvolt T-wave alternans (MTWA) is one of promising markers to predict cardiac events in patients after acute MI treated according to current guidelines.

Methods: In this single center study, 112 consecutive patients with the first anterior ST-elevation MI undergoing PCI <12 hours from symptom onset, were enrolled prospectively. Demographics, established risk factors, myocardial contrast echocardiography (MCE) perfusion, index event data and MTWA were assessed. Composite cardiac events (CCE) defined as: death, recurrent MI, sustained ventricular tachycardia (sVT) or readmission for acute heart failure (HF) were recorded during follow-up.

Results: MTWA test was negative in 76, positive in 18 and undetermined in 7 patients. MTWA negative patients had significantly higher LVEF at 30 days. At 4 years, 26 patients experienced CCE (10 died, 2 reinfarcted and 14 HF events). In multivariate Cox proportional hazard model maximum CKMB, non-negative MTWA and reduced LVEF made the best model to predict CCE. Four year CCE free survival was 77% and was significantly lower for non-negative MTWA (94% vs 50%, $p<0.003$).

Conclusions: Non-negative MTWA with infarct size index and reduced LVEF could predict cardiac events in patients with anterior STEMI treated with primary PCI. MTWA non-negative patients have significantly worse outcome.

Key words: T-wave alternans, myocardial infarction, cardiac events, prognosis

INTRODUCTION

Patients after acute myocardial infarction (MI) have relatively high mortality during the first 12 months, in half of cases the death is sudden, predominantly arrhythmic [1]. One of the most widely used stratifier with established value is depressed left ventricular ejection fraction (LVEF) [2]. Many other noninvasive stratifiers have been used to assess prognosis after MI, but their positive predictive values are low and therefore search for new markers for survival is still being conducted. Pharmacotherapy with beta-blocking agents, angiotensin converting enzyme inhibitors and statins have been proved to improve survival. In addition, use of primary percutaneous coronary interventions (PCI) with stent implantation also could influence the value of some stratifiers.

Microvolt T-wave alternans (MTWA) has been proposed as a potential indicator of susceptibility to ventricular tachycardia/fibrillation in several groups of patients, equivalent to electrophysiological study [3,4]. Occurrence of

sustained microvolt-level T-wave alternans at a specified heart rate has been suggested to predict life-threatening arrhythmic events in patients after recent MI [5]. High negative predictive value of MTWA in post MI patients with left ventricular ejection fraction ≤ 40% was also confirmed [6]. It was very attractive as it linked arrhythmia susceptibility to cellular arrhythmia mechanism [7]. Other studies in MADIT II or SCD-HeFT type patients showed that MTWA could predict total mortality [8-11]. In one of these trials, MTWA SCD-HeFT substudy, risk of ventricular arrhythmic events was not different according to MTWA test results [11]. In addition, the effects of left ventricular function on the prognostic value of MTWA in different populations are under investigation [12].

We undertook the single center prospective study to assess the value of new and already acknowledged risk stratifiers in consecutive patients with the first ST elevation myocardial infarction (STEMI) undergoing PCI during 12 hours of symptoms onset. We limited the inclusion criteria only to patients with anterior infarction for the sake of the population homogeneity. The aim of our paper was to assess presence of positive MTWA in this homogeneous population, as well as the predictive value of the test for major adverse cardiac events during long-term follow-up.

MATERIALS AND METHODS

In the single center study, 113 consecutive patients with their first MI of anterior wall undergoing primary PCI < 12 hours from symptoms onset were enrolled. In all patients, TIMI 3 flow in the left anterior descending artery after the procedure was achieved. Demographics, medical history, maximal troponin I and CK-MB levels, arrhythmias (ventricular and supraventricular) and treatment data were collected. All patients underwent echocardiographic study on the second day of MI to assess LVEF. LV volumes were calculated by the modified Simpson biplane method. Left ventricular ejection fraction (LVEF) was assessed as the percent change in LV volume from end-diastole to end-systole. Patients were treated pharmacologically according to current guidelines. All agents were titrated through the hospital stay and then at day 30. At day 30 the echocardiographic study was repeated for LVEF and the presence of LVEF improvement (LVEF+, at least 5% increase between day 2 and day 30). MTWA test was performed at day 30 during exercise treadmill test with commercially available MTWA analyzer (CH 2000; Cambridge Heart, Inc., Bedford, MA, USA) by power spectral method. MTWA was considered positive when the sustained alternans voltage was > 1.9μV, with an alternans ratio >3.0 in any orthogonal leads or 2 consecutive precordial leads during exercise with an onset rate <100 bpm for at least 1 minute and negative when above criteria were not met and artifact free data were available (at least 1 minute >105 bpm). The remaining results were considered undetermined. Coronary artery lesion extent (1-vessel or multi-vessel disease) was taken from the coronary angiograms (lesion >50% was regarded as significant). No antiarrhythmic agents were used.

At 6 months, all surviving patients underwent coronary angiography for restenosis detection and, if needed, further revascularisation in multivessel coronary artery disease. During the first six months follow-up, 19 patients presented symptoms of angina. After performing coronary angiography all patients were selected for urgent PCI. During 4 years follow-up restenosis of culprit artery was the reason to perform 12 successive PCI.

During the 48-months follow-up, composite cardiac events (CCE) defined as death, recurrent MI and urgent hospitalization due to significant worsening of heart failure were collected (primary endpoint). The secondary endpoints analyzed, included total mortality and hospitalization for significant heart failure worsening.

The study protocol was approved by the local ethics committee, (approval number NN-013-224/1/03) and all patients have given the informed consent for the participation in the study.

Statistical analysis (Statistica 7.1 PL package) was performed using the following tests: chi-square, U Mann-Whitney and t-Students. Univariate and multivariate Cox proportional hazard analysis was used. For multivariate analysis factors with $p<0.1$ were selected and step-down elimination of the poorest p was performed to achieve the final model. The primary and secondary endpoints free survival was analyzed with Kaplan-Meier method. For comparison of survival log-rank test was used. Level $p<0.05$ was considered significant.

RESULTS

Study population

From the initially enrolled 115 patients two died before day 30. The clinical characteristics of the 113 patients are presented in *Tab. 1.*

MTWA results

MTWA test was not performed in 12 patients due to continous atrial fibrillation in 6 and severe orthopedic disability in 6 patients. From 101 MTWA tests the results were positive in 18 patients (MTWA+), negative in 76 (MTWA-) and in 7 patients–undetermined. Undetermined results were primarily due to frequent ectopic beats or the inability to achieve the target heart rate. According to the published data, the positive and undetermined patients, as well as patients in whom MTWA test could not be performed were combined as the MTWA non-negative patients [MTWA non(-)] [13]. The characteristics of the separate subgroups according to MTWA test results are presented in *Tab. 2.* There were no differences in gender, age, history, treatment and extent