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Original research article

Prognostic value of cystatin C in relation to other markers of renal function in early prediction of hospital mortality and major cardiac adverse events in patients with ST elevation myocardial infarction treated by primary percutaneous coronary intervention

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ABSTRACT

Introduction: Cystatin C has been implicated as a prognostic marker in cardiovascular diseases. The aim of prospective study was to evaluate the benefits of measuring cystatin C for prognostic stratification to predict hospital mortality and the rates of major cardiac adverse events (MACE) in ST elevation myocardial infarction (STEMI) patients and to compare cystatin C to other markers of renal function and Global Registry of Acute Coronary Events (GRACE) score.

Methods: A total of 659 consecutive patients (479 men, mean age 65 years) from a prospective study on acute STEMI treated by primary percutaneous coronary intervention (PCI) were evaluated. Standard laboratory tests including cystatin C, troponin T, NT-terminal fragment of brain natriuretic peptide (NT-proBNP), markers of renal function were assessed on admission in all patients. Using *c*-statistic, the ability of cystatin C, other biomarkers and GRACE score to predict hospital mortality and MACE (acute coronary syndrome recurrence, stroke event, definite in-stent thrombosis and mortality) rate was evaluated.

Results: All-cause hospital mortality and MACE occurrence were 4% ($n = 26$) resp. 6.8% ($n = 45$). Cystatin C, creatinine, urea, glomerular filtration rate, troponin T, NT-proBNP and GRACE on admission were identified as significant prognostic risk markers.

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Serum cystatin C level and GRACE score were significantly higher in non-survivors (1.65 ± 0.91 vs. 0.97 ± 0.41 mg/mL; $P < 0.001$ resp. 138 ± 43 vs. 99 ± 31; $P < 0.001$). The area under the curve (AUC) values for mortality and MACE rate prediction for cystatin C and GRACE score were 0.83 and 0.88, respectively 0.66 and 0.72 (all $P < 0.001$) with optimal cut-off values of 1.3 mg/mL for cystatin C and 136 for GRACE score.

Cystatin C above cut-off >1.30 mg/L was associated with the highest adjusted odds ratio (OR) 3.85 (95% confidence interval 2.36–6.38; $P < 0.001$), and predicted in-hospital mortality with 77% sensitivity and 86% specificity. The addition of cystatin C to the GRACE score (OR 1.05, 95% confidence interval 1.04–1.07; $P < 0.001$) was not significantly associated with improved risk stratification.

Conclusions: Cystatin C is a predictor of early outcome comparable with the GRACE score in patients with STEMI.

Introduction

The prognosis for patients with acute ST elevation myocardial infarction (STEMI) is variable and is determined by many factors. The early distinguishing of patients with high risk of complications and also on the other hand spectrum of low risk patients with very good prognosis is crucial for selection of the appropriate therapy, and it also has not insignificant socio-economic consequences. In the risk stratification of patients with STEMI it is possible to use many predictors, including evaluation of biomarkers.

One of the prognostic factors for a whole range of cardiovascular illnesses is the initial level of renal functions. Patients with reduced level of glomerular filtration are at a greater risk of acute myocardial infarction, and the presence of chronic kidney disease is also associated with higher mortality rate and the development of complications in the context of STEMI [1]. Cystatin C is an intensely studied renal function biomarker. It is appreciated mainly for the greater accuracy in the evaluation of glomerular filtration compared to creatinine and also for its ability to independently predict the overall and cardiovascular mortality rate for many cardiovascular diseases, even in the absence of significant chronic kidney disease [2].

The aim of prospective study was to evaluate the benefits of measuring cystatin C for prognostic stratification to predict hospital mortality and the rates of major cardiac adverse events (MACE) in ST elevation myocardial infarction (STEMI) patients and to compare cystatin C to other markers of renal function and Global Registry of Acute Coronary Events (GRACE) score.

Subjects and methods

A prospective observational single center study covering all cases of STEMI, hospitalized in a medical intensive care unit in a tertiary care hospital, in order to assess in-hospital mortality and MACE during hospitalization was conducted.

Six hundred fifty-nine consecutive acute STEMI patients treated by direct percutaneous coronary intervention (PCI) were enrolled between January of 2012 and December of 2013. The diagnosis of STEMI was based on symptoms consistent with MI in conjunction with appropriate changes on electrocardiography (ECG), that is ST-segment elevation or new left bundle branch block and detection of rise and/or fall of high sensitivity troponin T with at least one value above cut-off 14 ng/L.

In all enrolled patients, the type of initial PCI treatment was recorded (STEMI culprit lesion intervention). Standard pharmacotherapy (ACE inhibitors, β-blockers, high-dose statins and dual antiplatelet therapy) was initiated as soon as possible. Patients were treated in accordance with current guidelines for the management of acute STEMI [3]. The diagnosis of acute heart failure was assessed according to clinical signs on hospital admission and/or during hospitalization (Killip class I–IV).

At baseline, all patients underwent: (1) transthoracic echocardiography focused on left ventricular morphology and function; (2) laboratory assessment of specific cardiac and renal function markers and (3) GRACE score estimation [4].

Echocardiography

Transthoracic echocardiography (TTE) was performed on the first day of hospitalization with a Vivid 7 machine (GE Healthcare Technologies, Waukesha, WI, USA) with a M3S probe (2–5 MHz) and focused on the quantification of left ventricular morphology and regional/global systolic function on admission.

A detailed evaluation was done off-line in the Echopac 7 Option program (BT 10.0.0 version) by two independent examiners who were blinded to the results of other examinations.

Laboratory tests

All laboratory analyses were performed in the certified laboratories of our hospital on Cobas 8000 modular analyzer system (Roche Diagnostics, Mannheim, Germany). Samples of venous blood for cystatin C analyses, standard biochemical and hematological blood tests were drawn immediately on hospital admission.

Samples for cystatin C analysis were centrifuged within 10 min in a refrigerated centrifuge, and the plasma and serum

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