FULL LENGTH ARTICLE

Cystatin C: A prognostic marker after myocardial infarction in patients without chronic kidney disease

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Aims: **Cystatin C is an endogenous marker of renal function. It is a well established better marker of glomerular filtration rate than serum creatinine. There is also evidence that cystatin C is associated with atherosclerotic disease. The present prospective study evaluated the prognostic value of cystatin C after myocardial infarction in patients without chronic kidney disease.**

Methods and results: **A total of 127 patients who underwent coronary angiography after an acute coronary syndrome (ACS) were included. Cystatin C was associated with the severity of coronary artery disease (CAD). Cystatin C levels were significantly higher in patients with 3-vessels disease and severe CAD according to GENSINI score ($p = 0.01$ and $p < 0.001$ respectively). Among the patients admitted for ST elevation myocardial infarction, Cystatin C concentration was correlated with the initial TIMI flow in the culprit artery ($p < 0.001$). Mean duration of the follow-up period was 10.76 þ 2.1 months. High Cystatin C concentrations were associated to the occurrence of unfavourable outcomes and cardiovascular mortality during follow-up (1.19 þ 0.4 vs. 1.01 þ 0.35 mg/L, $p = 0.01$ and 1.21 þ 0.36 vs. 0.96 þ 0.27 mg/L, $p = 0.03$). Among different laboratory parameters, cystatin C was the best marker to predict the occurrence of major adverse cardiovascular events during the follow-up (Area under the receiveroperating characteristic curve = 0.743).**

Conclusion: **High cystatin C levels are associated with the severity of coronary artery disease in patients presenting an acute coronary syndrome and a normal renal function. Cystatin C is also associated to unfavourable cardiovascular outcomes during follow-up and appears as a strong predictor for risk of cardiovascular events and death.**

Keywords: Cystatin C, Myocardial infarction, Cardiovascular mortality, Coronary artery disease, Major adverse cardiovascular events

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Introduction

The risk stratification of patients with coronary artery disease (CAD), especially death and acute heart failure, has been the subject of research in recent years [1–3]. Renal impairment is frequent in patients with cardiovascular disease and increases morbidity and mortality. The search for new biomarkers with better and accurate profiles has been very intense. Cystatin C (Cys C) is a novel marker for renal dysfunction and is better than serum creatinine, especially for mild renal impairment [4–6]. Cys C is a cysteine protease inhibitor produced in all nucleated cells at a constant rate and is freely filtrated by the glomeruli to be reabsorbed and degraded in the proximal tubules. Cys C is not affected by sex, age, and muscle mass. Recently, a close relationship has been established between Cys C and various subsets of atherosclerotic disease including CAD, stable CAD, as well as acute coronary syndromes (ACS). Therefore, Cys C might be a useful biomarker for prognostic stratification in patients with ACS [7–9].

The aim of the present study was to evaluate whether the concentration of Cys C could predict the severity of CAD after myocardial infarction in patients with normal or mildly impaired renal function estimated from the concentration of serum creatinine, and to determine the prognostic value of Cys C in predicting cardiovascular death during follow up.

Abbreviations

CKD	Chronic kidney disease
HD	hemodialysis
LVFS	left ventricular fractional shortening
TDI	Tissue Doppler imaging
BSA	Body surface area
BNP	brain natriuretic peptide
BP	blood pressure
TTE	transthoracic echocardiography
LA	left atrial
IVST	interventricularseptal thickness
LVPWT	left ventricular posterior wall thickness
LVEDd	left ventricular end-diastolic dimension
LVESd	left ventricular end-systolic dimension
LVMi	left ventricular mass index
2D-LVEDVi	two-dimensional left ventricular end diastolic volume index
2D-LVESVi	two-dimensional left ventricular end systolic volume index
LVFS	left ventricular fractional shortening
LVEFs	left ventricular ejection fraction calculated by biplane Simpson method
3D-LVEDVi	three-dimensional left ventricular end diastolic volume index
3D-LVESVi	three-dimensional left ventricular end systolic volume index
3D-LAEDVi	three-dimensional left atrial end diastolic volume index
3D-LAESVi	three-dimensional left atrial end systolic volume index
3D-LVEF	three-dimensional left ventricular ejection fraction
3D-LAEF	three-dimensional left atrial ejection fraction
GLS	two-dimensional global longitudinal strain
GRS	two-dimensional global regional strain
GCS	two-dimensional global circumferential strain
LAS	left atrial strain
RVS	right ventricular strain
3D-GLS	three-dimensional global longitudinal strain

Methods

Our study was prospective observational including Tunisian patients admitted to the department of cardiology of Hédi Chaker Hospital with the diagnosis of myocardial infarction who underwent urgent coronary angiography from May 2012 to December 2012. All patients have the following criteria: (1) chest pain at rest within the past 24 hours; (2) ST-segment elevation; (3) new presumed left bundle brunch block; or (4) ST segment or T wave abnormalities with troponin Ic rise. All patients were admitted in the hospital within the past 24 hours. Patients were divided into two groups: Group 1 was defined by patients admitted with non-ST segment elevation myocardial infarction (NSTEMI) with troponin Ic rise and Group 2 included patients with ST-segment elevation myocardial infarction (STEMI). We excluded patients with chronic renal failure and those who had an estimated glomerular filtration rate (eGFR) <60 mL/min, calculated using the Modification of Diet in Renal Disease equation based on the level of serum creatinine from this study. Patients with significant valvular or structural heart disease were excluded. All the study participants provided their consent before entering the study. Patients with hypertension were defined by a blood pressure $\geqslant$140/90 mmHg or having history of antihypertensive drug use. Diabetes mellitus was defined as fasting glucose level >1.26 g/L (7 mmol/L) or having history of hypoglycemic drug or insulin use. Dyslipidemia was defined as a low density lipoprotein-cholesterol level >1.4 g/L (3.6 mmol/L) or if patients were taking a hypolipidemic drug. Smokers were defined as patients actively inhaling tobacco smoke. The hemodynamic status was evaluated at admission, including blood pressure measurement and the KILLIP class. For patients admitted with NSTEMI,