The Role of Cystatin C in the Prognosis of Adverse Outcomes after the Coronary Artery Bypass Graft Surgery During Hospitalisation



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Background	This study has been aimed to assess clinical significance of cystatin C in the prognosis of a risk of hospital complications among the patients with coronary artery disease CAD who have undergone coronary artery bypass surgery (CABG).
Methods	We have recruited 719 consecutive Caucasian (Russian) patients who underwent CABG in 2011-2012.
Results	No statistically significant differences in the serum creatinine concentration (sCr) and glomerular filtration rate before and seven days after the surgery have been found among the patients belonging to different EuroSCORE risk groups. A statistically significant elevation of serum cystatin C concentration (sCC) before and seven days after the surgery has been demonstrated in EuroSCORE medium- and high-risk groups in comparison with the low-risk group. In addition, we have revealed increased pre-surgical levels of sCC in patients who had died earlier than seven days after CABG. Regarding the cardiovascular complications, a statistically significant elevation of sCC has been observed in patients with and without myocardial infarction (MI), stroke, or acute kidney injury (AKI) in the postoperative period.
Conclusions	We suggest that the determination of sCC before and after CABG surgery may help in the prognosis of adverse cardiovascular and renal outcomes after the CABG surgery.
Keywords	Coronary artery disease • Coronary artery bypass graft surgery • Complications • Adverse outcomes • EuroSCORE • Cystatin C.

Introduction

Coronary artery bypass graft (CABG) surgery is one of the effective methods of coronary artery disease (CAD)

treatment [1]. Myocardial infarction (MI), stroke, and acute kidney injury (AKI) with a further development of chronic renal failure are the leading causes of hospital death after CABG. European System for Cardiac Operative Risk

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Evaluation (EuroSCORE) is conventionally used for the prognosis of hospital death risk in patients after the CABG surgery. However, according to EuroSCORE, "kidney dysfunction" is diagnosed only when the serum creatinine concentration (sCr) exceeds 200 µmol/L. An adequate kidney dysfunction risk assessment by other biological markers may have greater prognostic value in comparison with conventional methods based on the quantitative measurements which can reveal the disease only in the late stage. It is also known that cardiovascular and renal complications of the CABG surgery evolve as a result of a decrease of the left ventricular ejection fraction and systemic inflammatory response development [2]. Therefore, it is possible to use a number of early markers of kidney dysfunction, including cystatin C, for the prognosis of the cardiovascular complications [3,4]. This study was aimed to assess clinical significance of cystatin C in the prognosis of the risk of complications in patients with CAD who underwent CABG surgery.

Materials and Methods

We have recruited 719 consecutive Caucasian (Russian) patients (576 males and 143 females) who underwent CABG surgery in the Research Institute for Complex Issues of Cardiovascular Diseases (Kemerovo, Russia) from March, 2011 till April, 2012. The study has been approved by the local ethics committee and written informed consent was provided by all the participants after a full explanation of the study was given to them.

The age of patients ranged from 33 to 78 (average 59) years. Serum creatinine and cystatin C concentration along with the glomerular filtration rate (GFR, calculated by MDRD formula) were determined twice (24 hours before the operation and seven days after the operation). Patients were classified into one of the EuroSCORE risk groups before the operation by a surgeon. According to recent studies, cystatin C reference values range from 0.52-0.90 mg/L for females and from 0.56-0.98 mg/L for males [5]. Clinicopathological features of the patients are presented in Table 1. Chronic kidney disease was defined by the presence of certain kidney injury markers persisting at least for three months or more according to the Russian Guidelines on chronic kidney disease. These markers included: 1) renal structural lesions revealed by ultrasound investigation (abnormalities of renal development, hydronephrosis, kidney cysts, kidney stones); 2) albuminuria/proteinuria; 3) erythrocyturia, cylindruria, leukocyturia; 4) decrease of GFR less than 60 ml/min/1,73 m² [6]. Arterial hypertension was defined as values >140 mmHg systolic blood pressure and/or >90 mmHg diastolic blood pressure, according to the ESH/ESC Guidelines for the management of arterial hypertension [7]. Dyslipidaemia was defined as highdensity lipoprotein cholesterol less than 1 mmol/L, or/and triglycerides more than 2 mmol/L, or/and atherogenic index more than 3, or/and low-density lipoprotein cholesterol more than 4 mmol/L, or/and total cholesterol more than 5 mmol/L,

Table 1 Clinicopathological features of the patients who have undergone CABG surgery.

Feature	Value, N(%)
Male gender	576 (80.1%)
Median of the age, years	59,0 (54.0-64.0%)
Arterial hypertension	635 (88.3%)
Dyslipidaemia	346 (48.0%)
Smoking status	257 (35.7%)
Previous history of MI	61 (8.5%)
Previous history of stroke	57 (7.9%)
Angina pectoris, grade III-IV	294 (40.8%)
Chronic heart failure, grade III	183 (25.4%)
Ventricular arrhythmia	100 (13.9%)
Supraventricular arrhythmia	66 (9.2%)
Type 2 diabetes mellitus	126 (17.5%)
Chronic kidney disease	308 (42.8%)

according to ESC/EAS Guidelines for the Management of Dyslipidaemias [8].

Most of the patients underwent elective surgery. Operative features of the patients who underwent CABG surgery are presented in Table 2. We used standardised anaesthesiological and perfusion supply such as cold blood cardioplegia or Custodiol solution (Kohler Chemie, Germany) in all patients. The volume repletion was performed by the infusion of 1.2 L of modified gelatine, mannitol, sodium bicarbonate, and balanced polyionic solution without fresh frozen plasma. The induction of anaesthesia was carried out using propofol (2 mg/kg body weight), the maintenance of anesthaesia was conducted by the infusion of propofol under the bispectral index monitoring and fentanyl infusion. On-pump surgery was started when activated clotting time was more than >400 seconds; heparin reversal was performed by protamine sulfate (1 mg/1 mg); the target haemoglobin level was 90 g/L with ≥65% of venous oxygen saturation. Normothermia was maintained during the whole time of the operation. A water balance at the end of surgery was 12 (6; 15) ml/kg. About 72% of patients were admitted to the intensive care unit with the prescription of dopamine up to 8 mcg/kg/min; in case of vasoplegia (about 12% of patients) dopamine was combined with norepinephrine up to 0.04 mcg/kg/min; the duration of usage was up to 16 hours of postoperative period. There were no statistically significant differences between the duration of inotropic support and mean therapeutic dosage in all groups of patients.

Regarding the drugs, 690 (96.0%) patients were treated by beta-blockers, 702 subjects (97.7%) used angiotensin-converting enzyme (ACE) inhibitors, 654 (91.0%) individuals were administered with calcium channel blockers, 258 (36%) patients were treated by prolonged nitrate therapy, and 194 (27%) subjects used statins. All patients 719 (100%) used antiplatelet drugs which, however, were cancelled seven days before the surgery. In addition, patients with angina

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