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Preoperative renal dysfunction is associated with an adverse in-hospital and long-term outcome after cabg surgery

Предоперационная почечная дисфункция связана с неблагоприятным госпитальным и отдаленным исходом после аортокоронарного шунтирования

Abstract

We carried out this study with the aim to compare the prevalence of an adverse in-hospital and long-term outcome after coronary artery bypass graft (CABG) surgery in patients with and without preoperative renal dysfunction [RD, defined as glomerular filtration rate (GFR) <60 ml/min/1.73 m²]. We recruited 720 consecutive Caucasian (Russian) patients who underwent CABG surgery in 2011–2012. Before the surgery, we measured serum creatinine concentration along with the calculation of GFR (MDRD formula) and risk of hospital death (EuroSCORE). Preoperative GFR<60 ml/min/1.73 m² was significantly associated with a higher prevalence of hemodynamically significant (≥50%) stenosis of extracranial arteries and lower extremity arteries, adverse in-hospital cardiovascular and renal outcomes compared to GFR ≥60 ml/min/1.73 m². After one year of follow-up, preoperative GFR<60 ml/min/1.73 m² was significantly associated with a recurrent angina and progression of chronic heart failure. In addition, combined adverse outcome after one year of follow-up was significantly more frequent in a medium risk group (EuroSCORE 3–5) with a preoperative GFR<60 ml/min/1.73 m². Therefore, RD is significantly associated with an adverse in-hospital and long-term outcome after CABG surgery.

Keywords: CABG surgery, renal dysfunction, glomerular filtration rate, prognosis, adverse outcome.

Резюме

Данное исследование было проведено с целью сравнения распространенности неблагоприятного госпитального и отдаленного исхода после аортокоронарного шунтирования (АКШ) у пациентов с и без почечной дисфункции [ПД, определяемая как скорость клубочковой фильтрации (СКФ) <60 мл/мин/1,73 м²]. В исследование вошли 720 пациентов, подвергшихся АКШ в 2011–2012 гг.; до проведения АКШ измерялся уровень креатинина в сыворотке и рассчитывалась СКФ (формула MDRD) вместе с риском госпитальной летальности (EuroSCORE). Предоперационная СКФ <60 мл/мин/1,73 м² была статистически значимо ассоциирована с повышенной распространенностью гемодинамически значимых (≥50%) стенозов экстракраниальных артерий и артерий нижних конечностей, а также неблагоприятным сердечно-сосудистым и

почечным исходом на госпитальном этапе в сравнении с СКФ ≥60 мл/мин/1,73 м². После одного года наблюдения предоперационная СКФ <60 мл/мин/1,73 м² была статистически значимо ассоциирована с возобновлением приступов стенокардии и прогрессированием хронической сердечной недостаточности. Кроме того, комбинированный неблагоприятный исход после одного года наблюдения статистически значимо чаще встречался в группе среднего риска (EuroSCORE 3–5) с предоперационной СКФ <60 мл/мин/1,73 м². Таким образом, ПД статистически значимо ассоциирована с неблагоприятным госпитальным и отдаленным исходом после АКШ.

Ключевые слова: аортокоронарное шунтирование, почечная дисфункция, скорость клубочковой фильтрации, прогноз, неблагоприятный исход.

■ INTRODUCTION

According to the World Health Organization estimates, cardiovascular disease (CVD) is responsible for an almost one-third (17.5 million) of all deaths worldwide [1, 2]. Coronary artery disease (CAD) and stroke, in turn, are responsible for 7.4 million and 6.7 million of deaths, respectively, out of these 17.5 million [1, 2]. Coronary artery bypass graft (CABG) surgery efficiently improves a quality of life and even prognosis in patients with CAD [3]. Age, past medical history of myocardial infarction and stroke, reduced left ventricular ejection fraction, arterial hypertension, peripheral artery disease, and diabetes mellitus are predictors of adverse outcome after CABG surgery but patients with renal dysfunction (RD) are often excluded from the large clinical studies on CVD [3]. However, RD may possess particular predictive significance due to its association with increasing age and a growing number of elderly patients [4, 5]. It is known that RD is associated with an adverse outcome in patients with CAD [6]; however, its prognostic significance in patients undergoing CABG surgery is still under discussion. We performed this study to clarify this issue.

■ MATERIALS AND METHODS

We recruited 720 consecutive Caucasian (Russian) patients who underwent CABG surgery in Research Institute for Complex Issues of Cardiovascular Diseases (Kemerovo, Russia) from March 2011 till April 2012. The study was performed in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki, was approved by the local ethical committee, and written informed consent was provided by all the participants after a full explanation of the study was given to them.

Before the surgery, colour duplex screening of the extracranial arteries (ECA) and lower extremity arteries (LEA) was performed in all patients using the cardiovascular ultrasound system Vivid 7 Dimension (General Electric Healthcare, USA) with a 5.7 MHz linear array transducer (for ECA), a 2.5-3 MHz curved array transducer and a 5 MHz linear array transducer (for LEA). Arterial stenosis was assessed by B-mode ultrasonography and Doppler ultrasonography. Common and internal carotid arteries, vertebral, and

subclavial arteries were visualized from both sides during the ECA screening; common and deep femoral arteries, popliteal, anterior and posterior tibial arteries were visualized from both sides during the LEA screening. An intima-media thickness (IMT) of the common carotid artery was measured in automatic mode (the value <1 mm was considered as normal). Selective coronary angiography was also performed before the surgery using GE Healthcare Innova 3100 Cardiac Angiography System (General Electric Healthcare, USA). Luminal stenosis ≥50% was defined as a hemodynamically significant stenosis.

Serum creatinine level (sCr) and glomerular filtration rate [GFR, calculated by Modification of Diet in Renal Disease (MDRD) formula] were determined 24 hours before and 7 days after the surgery. RD was defined as GFR<60 ml/min/1.73 m^2. Risk of death was calculated using the additive EuroSCORE [7]. Patients were classified into the one of the EuroSCORE risk groups before the operation by a surgeon. Clinicopathological features of all patients are represented in the Table 1.

Regarding the drugs, 691 (96.0%) patients were treated by beta-blockers, 703 subjects (97.7%) used angiotensin-converting enzyme inhibitors,

Table 1
Clinicopathological features of the patients

Feature	Value, n (%)
Male gender	577 (80.1)
Median age, yrs	59.0 (54.0–64.0)
Arterial hypertension	636 (88.3)
Dyslipidemia	347 (48.2)
Smoking status	249 (34.5)
Past medical history of myocardial infarction	61 (8.5)
Past medical history of stroke	57 (7.9)
STable angina, CCS class	
I	22 (3.0)
II	344 (47.7)
III	279 (40.8)
IV	15 (2.0)
UnsTable angina	58 (8.0)
Chronic heart failure, NYHA class	
I	27 (3.75)
II	462 (64.1)
III	184 (25.5)
IV	10 (1.4)
Ventricular arrhythmia	100 (13.8)
Supraventricular arrhythmia	66 (9.1)
Type 2 diabetes mellitus	126 (17.5)
Stenosis of lower extremity arteries	217 (30.1)
<50%	170 (23.6)
≥50%	47 (6.5)
Stenosis of extracranial arteries	232 (32.2)
<50%	172 (23.8)
≥50%	60 (8.3)
Past medical history of kidney diseases	309 (42.9)
Preoperative glomerular filtration rate <60 ml/min/1.73 m^2	116 (16.1)

655 (91.0%) individuals were treated by calcium channel blockers, 259 (36%) patients were treated by long-acting nitrates, and 195 (27%) subjects used statins. All 720 patients used antiplatelet drugs which, however, were cancelled 7 days before the surgery. In this period, patients with angina pectoris of grade III or IV were treated by low-molecular-weight heparin.

In most of the patients (692, 96.1%) elective CABG surgery was performed. Urgent CABG surgery (without any discharge after coronary angiography) was performed only in 24 (3.3%) patients, in most of the cases, they had subtotal left main coronary artery (LMCA) stenosis together with subtotal stenosis and/or occlusion of right coronary artery (RCA), anterior descending artery (ADA), or circumflex artery (CA). Emergent CABG surgery was performed in 4 (0.6%) patients due to non-ST-segment elevation acute coronary syndrome (NSTE-ACS). We used standardized anesthesiological 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 anesthesia was carried out using propofol (2 mg/kg body weight), the maintenance of anesthesia 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 hemoglobin 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 μg/kg/min; in case of vasoplegia (about 12% of patients) dopamine was combined with norepinephrine up to 0.04 μg/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.

On the day 10th–12th after the surgery, we assessed the status (presence or absence) of cardiovascular (death, myocardial infarction, stroke, transient ischemic attack, acute kidney injury, chronic renal failure progression, critical lower limb ischemia, or re-mediastinotomy due to a bleeding) and non-cardiovascular complications (pancreonecrosis, ileus, acute cholecystitis, urgent operations on another organs, septic mediastinitis, urethritis, or sepsis). The presence of any of these complications was considered as an adverse hospital outcome. After one year of follow-up, the following endpoints were considered: coronary and non-coronary deaths, myocardial infarction, stroke, sTable angina CCS (Canadian Cardiovascular Society) class III–IV, and chronic heart failure NYHA (New York Heart Association) class III. The presence of any of these endpoints was considered as an adverse long-term outcome.

The diagnosis of post-operative myocardial infarction was defined by the 5-fold elevation of troponin I level 6 hours following surgery. Transient ischemic attack was defined as transient neurologic deficit of cerebrovascular origin (contralateral paralysis, sudden weakness or numbness, sudden dimming or loss of vision, aphasia, dysarthria, and mental confusion) resolving in 24 hours. In the case if this neurological deficit lasted more than 24

hours and became permanent, it was defined as a stroke. The diagnosis of transient ischemic attack or stroke was performed by a neurologist and was further proved by magnetic resonance imaging. Acute kidney injury was defined according to the RIFLE criteria [8]. 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 [9]. Dyslipidemia was defined as high-density 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, according to ESC/EAS Guidelines for the management of dyslipidaemias [10].

Statistical analysis was performed using MedCalc (MedCalc Software, Belgium). A sampling distribution was assessed by D'Agostino-Pearson test. Regarding descriptive statistics, data were represented by the median, the interquartile range (25th and 75th percentiles), the mean and confidence intervals (CIs) for the both median and mean. Depending on the sampling distribution, two independent groups were compared by either Mann-Whitney U-test or Student's t-test, three and more independent groups were compared using either Kruskal-Wallis test or analysis of variance (ANOVA) with the further pairwise multiple comparisons by Mann-Whitney U-test or Student's t-test in the case if statistically significant differences were revealed by Kruskal-Wallis test or ANOVA, respectively. Two paired samples were compared by either Wilcoxon test or paired Student's t-test according to the sample distribution. An adjustment for multiple comparisons was performed using false discovery rate (FDR). P-values, or q-values if FDR was applied (q-values are the name given to the adjusted p-values found using an optimized FDR approach), ≤0.05 were regarded as statistically significant.

■ RESULTS

All the patients were divided into two groups, with and without preoperative RD. Most of the clinicopathological features did not significantly differ between the groups; however, past medical history of kidney diseases and ≥50% stenosis of ECA and LEA were significantly more prevalent amongst patients with RD (Table 2). Mean EuroSCORE and median number of grafts were also significantly higher in patients with RD (Table 3).

Mean sCr was significantly higher in patients with RD compared to those without RD both 24 hours before [131.6 (124.8–138.8) and 80.5 (79.1–81.8) μmol/L, respectively, P=0.0001] and 7 days after the surgery [119.5 (107.7–131.2) and 105.7 (103.7–107.8) μmol/L, respectively, P=0.0001]. Noteworthy, there were no patients with sCr>200 μmol/L, which is a risk factor in EuroSCORE, in both groups. An adverse in-hospital outcome was observed significantly more frequently in patients with RD in comparison with those without RD (37.0 and 22.6%, respectively, P=0.0006). The in-hospital case fatality rate was 1.8% and was significantly higher in patients with RD than in those without RD (5.1% and 1.2%, respectively, P=0.006).

Nine (1.25%) patients were excluded from the study sample after one year of follow-up due to incomplete follow-up data. Combined adverse outcome was observed in 298 (41.9%) patients. Recurrent angina and progression of chronic heart failure were significantly more prevalent in

Table 2
Clinicopathological features of the patients depending on the glomerular filtration rate GFR)

Feature	GFR≥60 ml/min/1.73 m² N=604 (84.0%)	GFR<60 ml/min/1.73 m² N=116 (16.0%)	P-value
Male gender	467 (77.3%)	110 (94.8%)	0.09
Median age, yrs	59.3 (33.0–81)	58.5 (33.0–76.0)	0.07
Arterial hypertension	525 (86.9%)	111 (95.6%)	0.3
Dyslipidemia	293 (48.5%)	54 (46.5%)	0.1
Median body mass index, kg/m²	27.9 (25.1–31.2)	28.4 (25.2–31.14)	0.5
Smoking status	206 (34.1%)	43 (37.0%)	0.1
Past medical history of myocardial infarction	46 (7.6%)	15 (13.7%)	0.1
STable angina CCS class III-IV	246 (40.7%)	48 (41.3%)	0.4
Chronic heart failure, NYHA class III	155 (25.6%)	29 (25.0%)	0.3
Past medical history of stroke	48 (7.9%)	9 (7.7%)	0.8
Ventricular arrhythmia	83 (13.7%)	17 (14.6%)	0.8
Supraventricular arrhythmia	52 (8.6%)	14 (12.0%)	0.4
Past medical history of kidney diseases	243 (40.2%)	66 (56.8%)	0.03
Type 2 diabetes mellitus	106 (17.5%)	20 (17.3%)	0.5
Past medical history of CABG surgery	5 (0.8%)	1 (0.8%)	0.9
Stenosis of extracranial arteries			
<50%	136 (22.5%)	36 (31.0%)	0.04
≥50%	33 (5.4%)	27 (23.2%)	0.001
Stenosis of lower extremity arteries			
<50%	140 (23.1%)	30 (25.8%)	0.3
≥50%	34 (5.6%)	16 (13.7%)	0.02
Median left ventricular ejection fraction	60.0 (50.0–64.0)	60.0 (49.0–64.0)	0.5

Table 3
Surgical features of the patients depending on the glomerular filtration rate (GFR)

Feature	GFR≥60 ml/min/1.73 m² n=604 (84.0%)	GFR<60 ml/min/1.73 m² n=116 (16.0%)	P-value
Elective surgery	581 (96.1%)	111 (95.6%)	0.7
Urgent surgery	20 (3.3%)	4 (3.4%)	0.6
Emergency surgery	2 (0.3%)	2 (1.7%)	0.6
On-pump surgery	515 (85.2%)	100 (86.2%)	0.6
Mean duration of on-pump surgery, min	99.5 (96.6–102.4)	103.8 (96.1–111.5)	0.6
Median number of grafts	2 (2–3)	3 (2–3)	0.003
Aneurysmectomy With left ventricular reconstruction	28 (4.6%)	5 (4.3%)	0.4
Without left ventricular reconstruction	8 (1.3%)	1 (0.8%)	0.9
CABG surgery along with carotid endarterectomy	9 (1.5%)	4 (3.4%)	0.2
Complete myocardial revascularization	543 (89.9%)	98 (84.4%)	0.13
Mean EuroSCORE	3.1 (2.9–3.3)	3.9 (3.4–4.3)	0.0006

Table 4
Treatment of patients after the CABG surgery depending on the glomerular filtration rate (GFR)

Drug	GFR≥60 ml/min/1.73 m² n=603 (84.8%)	GFR<60 ml/min/1.73 m² n=108 (15.2%)	P-value
Asetylsalicylic acid	404 (66.9%)	73 (67.5%)	0.5
Clopidogrel	37 (6.1%)	5 (4.6%)	0.5
Angiotensin-converting enzyme inhibitors	321 (53.2%)	60 (55.5%)	0.7
Nitrates	170 (28.1%)	98 (90.7%)	0.002
Angiotensin receptor blockers	54 (8.9%)	4 (3.7%)	0.06
Aldosterone antagonists	40 (6.6%)	18 (16.6%)	0.0005
Calcium channel blockers	119 (19.7%)	10 (9.2%)	0.009
Loop diuretics	42 (6.9%)	14 (12.9%)	0.03
Statins	407 (67.5%)	79 (73.1%)	0.2

patients with preoperative RD (16.3% and 12.9%, respectively) compared to those without it (7.4% and 7.3%, respectively), P=0.003 and 0.04, respectively. However, there were no statistically significant differences regarding any other endpoints between the groups. During one year of follow-up, patients with preoperative RD were treated by aldosterone antagonists, loop diuretics, and nitrates significantly more frequently than patients without it; however, they significantly less frequently used calcium channel blockers (Table 4).

There were no significant differences in prevalence of RD amongst the EuroSCORE risk groups (Table 5). After one year of follow-up, combined adverse outcome was significantly more prevalent in medium risk patients with RD compared to those without it (Table 6).

Table 5
Prevalence of the renal dysfunction depending on EuroSCORE

Glomerular filtration rate (GFR)	Low risk (EuroSCORE 0–2) n=436 (61.3%)	P-value	Medium risk (EuroSCORE 3–5) n=211 (29.6%)	P-value	High risk (EuroSCORE ≥6) n=64 (9.0%)	P-value
GFR≥60 ml/min/1.73 m²	370 (61.3%)	0.09	179 (29.6%)	0.06	54 (8.9%)	0.7
GFR<60 ml/min/1.73 m²	66 (61.1%)		32 (29.6%)		10 (9.2%)	

Table 6
Prevalence of an adverse outcome after one year of follow-up depending on EuroSCORE and glomerular filtration rate (GFR)

EuroSCORE	GFR≥60 ml/min/1.73 m² n=603 (84.8%)	GFR<60 ml/min/1.73 m² n=108 (15.1%)	P-value
Low risk	145 (39.1%)	29 (43.9%)	0.06
Medium risk	81 (42.2%)	17 (53.1%)	0.04
High risk	22 (40.7%)	4 (40.0%)	0.6
Total	248 (41.1%)	50 (46.3%)	0.3

■ DISCUSSION

It was demonstrated that even moderate elevation of sCr after CABG surgery is a risk factor for an adverse outcome [11]. In addition, preoperative RD is associated with increased hospital stay after CABG surgery [11]. Moreover, GFR 30–59.9 ml/min/1.73 m^2 and <30 ml/min/1.73 m^2 was associated with 1.8- and 5.2-fold higher risk of death, respectively, in comparison with GFR>90 ml/min/1.73 m^2 after five years of follow-up after CABG surgery [12]. In another investigation, GFR 15–45 ml/min/1.73 m^2 was associated with 1.8-fold higher risk of death compared to GFR>60 ml/min/1.73 m^2 [13]. However, it was also found that RD is not significantly associated with early and long-term adverse cardiovascular outcomes in patients who underwent CABG surgery [14]. In our study, an adverse in-hospital outcome and in-hospital case fatality rate were observed significantly more frequently in patients with preoperative RD in comparison with those without RD. After one year of follow-up, recurrent angina and progression of chronic heart failure were significantly more prevalent in patients with preoperative RD compared to those without it; however, there were no statistically significant differences regarding any other endpoints between the groups.

Additive and logistic EuroSCORE are successfully used for the prediction of the risk of hospital death after CABG surgery [15]. EuroSCORE takes into consideration a number of preoperative risk factors such as sCr>200 μmol/L. and it is rather simple for clinicians [16]. However, sCr may depend not only on renal function but on a number of other non-renal factors and therefore cannot be considered as the best marker of RD [17]. In our study, combined adverse outcome was significantly more prevalent in medium risk (EuroSCORE 3-5) patients with RD compared to those without it after one year of follow-up. Therefore, preoperative measurement of GFR may be particularly useful in these patients. Although there are many novel biomarkers of RD such as microalbuminuria, serum cystatin C, interleukin-18, neutrophil gelatinase-associated lipocalin, or kidney injury molecule-1, they were not assessed in this study since we evaluated them in previous articles [18-22]. However,, technical possibilities and financial issues restrict their wide application in medical units, whereas this is not the case for GFR.

■ CONCLUSIONS

RD is significantly associated with an adverse in-hospital and long-term outcome after CABG surgery.

Conflict of Interest Statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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