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ACUTE KIDNEY INJURY IN PATIENTS WITH CORONARY HEART DISEASE AND METABOLIC SYNDROME DURING BYPASS GRAFTING: CURRENT STATE OF THE PROBLEM

Abstract

The article presents a review of literature on the current efforts in research of acute kidney injury (AKI) in patients with coronary heart disease (CHD) after myocardial revascularization with coronary artery bypass grafting (CABG). Different sources provided the data on the frequency of AKI during surgical methods of myocardial revascularization with the use of the cardio-pulmonary bypass (CPB) and off pump. The article describes the epidemiology of metabolic syndrome (MS) both in the world and in the Russian Federation. It also considers several options for making a MS diagnosis basing on various criteria, including the presence of CKD, as a likely predictor of developing MS and vice versa. An analysis of the current data showed the contribution of concomitant MS in the development of CKD and proved it an important risk factor for AKI. The study was based on the concept of endothelial dysfunction (ED), as a key element in the pathogenesis of cardiovascular diseases, MS and renal pathology. Concomitant proteinuria, microalbuminuria and decreased glomerular filtration rate (GFR), as well as the phenomenon of insulin resistance (IR) were proven to contribute to the development of perioperative AKI in patients with MS. The study covers the entire pathogenetic chain of development of cardiorenal syndrome (CRS), as an integral part of the cardiorenal continuum. It also considers the social and medical problem due to the high morbidity and mortality, as well as increased economic costs of treating this group of patients. The authors endeavored to determine the most rational approach when choosing the tactics of treatment and management of these patients. The methods for the prevention and treatment of AKI in patients with MS were considered. Based on the global positive experience of using statins, angiotensin converting enzyme (ACE) inhibitors, calcium antagonists and beta-blockers, these groups of drugs were considered as promising ones for pharmacological prevention of AKI in patients during myocardial revascularization with the use of bypass grafting.

Keywords: coronary heart disease, metabolic syndrome, off-pump coronary artery bypass grafting, acute kidney injury, statins.

Coronary heart disease (CHD) is a pathological condition characterized by an absolute or relative disorder of myocardial blood supply due to coronary artery diseases [22]. Amounting to 13.2%, or 7.4 million cases per year, CHD ranks first among causes of death in the world. According to official data, in 2015, the Russian Federation had the overall CHD incidence at 6,425.2 per 100 thousand of the population (Rosstat, 2015). From 2011 to 2015, the number of cases with CHD diagnosis established for the first time increased 1.5 times from 633.2 to 911.0 per 100 thousand of the population. The CHD structure is dominated by stable angina – 3,059.9 thousand people. In Russia annually registers an average of 520,000 new cases of acute coronary syndrome (ACS), breaking down into 63.6% cases of unstable angina and 36.4% cases of myocardial infarction [11].

Bypass surgeries are considered the most effective methods of CHD treatment. However, these surgeries are associated with a high risk of developing various undesirable dysfunctions of the organs and body systems, as well as with a number of serious complications, including acute kidney injury (AKI). In the recent years, off-pump bypass grafting surgeries have become widespread. Although less invasive, this method of surgical myocardial revascularization does not significantly reduce the risk of severe postoperative complications, including AKI. Thus, according to a number of international multifocal studies, off-pump bypass grafting results in renal dysfunction in 28% of patients, and 1.2-2.9% of them need hemodialysis due to the AKI development [3].

The postoperative AKI leads to changed patient's management, longer duration of treatment and significantly worse prognosis, increasing hospital mortality from 7.6% to 26.3% among AKI patients [4]. The studies indicate a higher risk of developing perioperative renal complications in patients with concomitant chronic kidney diseases (CKD), diabetes mellitus, and overweight.

It has been established that one of the factors contributing to impaired renal function in patients with cardiovascular pathology is concomitant MS [23]. Patients with MS are 2.5 times more likely to have a high risk of developing CKD [6]. Therefore, for the patients with coronary artery disease and concomitant MS, who have undergone surgeries, in particular off-pump coronary artery bypass grafting, the management tactics requires a special approach, mandatory assessment of the initial state of the kidney function and the measures aimed at preventing their dysfunction in the pre-and postoperative periods.

1. Surgeries for CHD and acute kidney injury.

CHD surgeries involve shunting myocardial revascularization and percutaneous coronary intervention (PCI) with or without drug-eluting stents. Should PCI be impossible to perform due to technical difficulties or anatomical features, an open-heart surgery using CPB or an off-pump operation is an option. As any cardiac surgery using CPB, coronary artery surgeries are always associated with a high risk of developing undesired dysfunctions of organs and systems, as well as a number of serious complications, with AKI being quite common [7].

In the recent decades, off-pump bypass surgeries have become an alternative to traditional operations on coronary vessels using CPB. These surgeries are less invasive, and up to 25% of all myocardial revascularizations in the world practice are performed off-pump [1]. However, despite the exclusion of major factors triggering AKI (platelet activation and damage, disruption of the blood coagulation system, production of free radicals, activated systemic inflammatory response), CABG still has the risk of postoperative kidney dysfunction [24].

The analysis of the information provided by various researchers on AKI following bypass grafting shows a large scatter of the data on frequency of this complication. Therefore, first, it is important to take into account the criteria of kidney injury that is used. For example, the AKI frequency following CABG with the use of the AKIN (Acute Kidney Injury Network) criteria is 26.3%, while with the use of RIFLE criteria (Risk, Injury, Failure, Lost of kidney function, End-stage renal failure) – 18.9% [16].

According to several authors, in terms of developing pronounced renal dysfunction, patients with concomitant MS make

another particular risk group [7]. The AKI following off-pump bypass grafting was observed in 17.5% of patients [12]. The combination of MS and cardiovascular diseases, and CHD in particular, is now a proven fact.

2. Relationship between metabolic syndrome and kidney failure.

MS is a topical issue in the modern medicine and is of interest for various specialists. According to epidemiological studies, nowadays, MS is characterized as a "XXI century non-infectious pandemic" and is regarded in many countries as a major socio-economic problem. The prevalence of MS in different countries varies from 10% to 84% among the total adult population and depends on ethnicity, age, gender, and race [25]. In Russia, according to the Ministry of Health, the MS prevalence varies from 20% to 35% among adults, its frequency increasing with age and being 2.5 times more common in women [5].

The World Health Organization (WHO) defines MS as a combination of type 2 diabetes mellitus (DM) with at least two of the following factors: arterial hypertension (AH), high blood lipids, obesity, and microalbuminuria [15]. The nature of MC is reflected most accurately and fully in the guidelines of the Russian Society of Cardiology (RSC). According to the RSC guidelines, MS is characterized by increased mass of visceral fat, decreased sensitivity of peripheral tissues to insulin and hyperinsulinemia, which causes the development of disorders of carbohydrate, lipid, and purine metabolism, and hypertension [10].

Along with the above clinical manifestations, MS also includes various renal dysfunctions, which often eventually leads to the development of CKD. MS has been linked with markers of chronic renal pathologies, including reduced GFR, proteinuria and/or microalbuminuria, as well as with histopathological markers, such as tubular atrophy and interstitial fibrosis [17].

Kidney injury can be considered both as one of the MS criteria and as an independent risk factor for CKD [18]. The presence of MS increases the likelihood of developing CKD in patients over 20 years of age by 2.6 times, and the risk goes higher with increasing MS criteria. With the MS lasting over nine years, the risk of developing CKD may increase by about 50% [19].

The early stages of CKD are most often asymptomatic and are not diagnosed during the initial examination of the patient. At the same time, it is not completely clear what develops earlier – CKD or MS. Indeed, there are common factors in the development mechanisms of the both pathologies: insulin resistance, inflammation, lipid metabolism, and hypertension [14]. In addition, obesity is accompanied by increased adipose tissue secretion of such pro-inflammatory cytokines as leptin, IL-6, and TNF, which also contributes to the production of type IV collagen, as well as the formation of reactive oxygen species, which in turn can lead to kidney endothelial cell (EC) dysfunction, secondary growth of mesangial cells and the formation of glomerulosclerosis [28].

Currently, it is recognized that endothelial dysfunction (ED) is one of the leading links in the pathogenesis of nephrosclerosis, as well as the majority of chronic forms of kidney pathology of both immune and non-immune genesis [2]. The unique position of endothelial cells at the interface between circulating blood and tissues makes them most vulnerable to various pathogenic factors in the systemic and tissue circulation. EC are the first to come in contact with free radicals, and are exposed to high hydrostatic pressure of blood with a high content of cholesterol and glucose. All these factors cause damage to the vascular endothelium, its dysfunction as an endocrine organ, and the accelerated development of angiopathy and atherosclerosis [29]. Thus, it can be stated that ED and MS syndrome are closely associated conditions and form a vicious circle leading to metabolic, cardiorenal and cardiovascular conditions.

In general, the existence of a close relationship between the development and progression of cardiac and renal pathology is a proven fact and must be taken into account in clinical practice. With the increased group of such patients, practitioners began to separate their condition into a single syndrome complex, which has been lately referred to in the Russian and international literature as cardiorenal syndrome (CRS), or cardiorenal continuum. Moreover, in 2008, the concept of cardiorenal interactions was adopted and developed, and various types of the CRS were identified [30].

This term is a collective one that emphasizes the interaction between the kidneys and the heart, when an acute or chronic dysfunction of one of these organs leads to an acute or chronic dysfunction of the other. MS patients have CKD without its manifestation and belong to the group with a high risk of perioperative renal complications [6].

In patients after myocardial revascularization, the presence of latent renal dysfunction as a manifestation of chronic CRS can significantly worsen the immediate and late postoperative cardiorenal prognosis, and presents a medical and social problem due to high mortality and significant pharmaceutical and economic costs.

Thus, comorbidity in the form of a combination of CHD, MS and nephropathy in patients undergoing myocardial revascularization bypass grafting is a serious clinical problem.

Undoubtedly, improved surgical methods for the treatment of coronary heart disease, early detection of patients with a high risk of renal dysfunction and prediction of their development, elimination of nephrotoxic drugs, a more balanced approach to the use of radiopaque research methods have contributed to the reduction of postoperative AKI in MS patients [20]. Along with this, targeted prophylactic pharmacotherapy is an equally important direction in reducing perioperative renal complications, taking into account the mechanisms of its development, especially in patients with concomitant MS.

3. The use of statins as a preventive method for kidney injury following bypass grafting in CHD patients with concomitant MS.

The main measures for the prevention of perioperative kidney injury following surgical interventions are set out in the National Guidelines for the diagnosis, prevention and treatment of AKI, clinical guidelines for the management of patients with the risk of AKI [8], and the management of patients with MS [9].

The main objectives of treating MS patients are weight loss, better metabolic control, the maintenance of an optimal level of blood pressure, as well as the prevention of acute and remote cardiovascular complications. At the same time, taking into account the key pathogenesis of the syndrome, as well as the modern concept of ED, for patients with coronary pathology and concomitant MS, an important component of preventive measures is pharmacotherapy with drugs that can directly affect the state of the endothelium and its dysfunction, as well as correct lipid exchange.

There are several pharmacological groups used to correct ED. These are antioxidants, angiotensin II receptor blockers, angiotensin converting enzyme (ACE) inhibitors, calcium antagonists, beta-blockers, nonsteroidal anti-inflammatory drugs, and statins. The data on the effect of many medications in the presented groups on the endothelium

function are insufficiently studied and controversial. To date, there is evidence of various "pleiotropic" effects of statins. It has been revealed that statins regulate ED, proliferation of mesangial cells, have anti-inflammatory and immunomodulatory effect, as well as a positive effect on renal hemodynamics. The positive effect of statins in the event of perioperative AKI has been also revealed [17].

HMG-CoA reductase inhibitors are suitable for most patients with albuminuria and proteinuria, especially with the amount of protein in the urine exceeding 1 g/day [18].

The mediated nephroprotection and increased GFR with various signs of renal dysfunction observed in clinical practice [21] require further study of this effect of statins. Therefore, it continues to be relevant to study the effect of HMG-CoA reductase inhibitors on the course of AKI with its various etiologies. In addition, there is insufficient information about the optimal timing of statin administration from the standpoint of their nephroprotective effect.

Thus, currently the problem of kidney injury following bypass grafting in patients with coronary heart disease, especially with concomitant MS, remains relevant; there is no consensus on the choice of methods for its prevention, and the use of statins as nephroprotective agents remains the subject for discussion.

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POINT OF VIEW

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THE EFFECT OF PREGNANT AGE ON THE PROBABILITY OF THE OCCURRENCE OF COMPLICATIONS DURING PREGNANCY AND CHILDBIRTH

ABSTRACT

Until now, there has not been a consensus in the literature as to what plays a leading role in the occurrence of complications of pregnancy and childbirth in minors: biological immaturity or social risk factors. **The aim of this work** was to determine the influence of the age of the pregnant woman on the probability of complications of pregnancy and childbirth.

Materials and methods. Minors pregnant women surveyed (n=483) observed and gave birth in SPbGPU "Maternity hospital № 10" in 2004-2014 [1 group 13-15 years (n=49); 2 group - 16-17 years (n=434)]. The comparison group consisted of 110 women of middle reproductive age. Medical and social aspects of the life and behavior of patients were assessed by analyzing unified specially designed questionnaires. Statistical analysis of obtained data was performed using the programs STATISTICA V. 7.0 (Statsoft Inc., Tulsa, USA) and SPSS 19 (SPSS: An IBM Company, USA). Multivariate statistical analysis was performed using logistic regression for dichotomously dependent variables. In addition to age group indicators, the following control (independent) variables were used to separate the effect of age from other factors in the construction of regressions: age of menarche; the age of sexual activity; the period of registration in the women's consultation.

Results. In minors 13-15 years, compared with women of average reproductive age, significantly higher was the chance of occurrence of early rupture of membranes (OR=13,2; 95% CI: 2,1-81,9; p<0.01) and the implementation of perineotomy (OR=8,3; 95% CI: 2,6-27,0; p<0.01), and significantly lower the chances of occurrence polyhydramnios (OR=0,2; 95% CI: 0.1 to 0.6; p<0.01). In minors 16-17 years, compared with women of middle reproductive age, significantly higher were the chances of occurrence of chronic placenta insufficiency with hemodynamic disorders during pregnancy (OR=2,5; 95% CI: 1,3-5,0; p<0,05), premature (OR=3,3; 95% CI: 1,2-9,0; p<0,05) and early (OR=12,5; 95% CI: 2,7-57,1; p<0,01) rupture of membranes and production of perineotomy (or=2,6;% CI: 1,3-5,1; p<0.01) during childbirth, and significantly lower chances of occurrence of polyhydramnios (OR=0,1; 95% CI: 0,1-0,3; p<0,01).

Conclusion. The results confirm the literature data on the complicated course of pregnancy and childbirth in minors. Moreover, it is likely that the morpho-functional immaturity of the reproductive system, as well as other body systems, homeostasis systems of minors pregnant women is most important, and adverse social factors are the background to which the work of the systems and organs is imposed on the limit of their functional capabilities with a rapid ability to decompensate.

Keywords: age of childbirth, childbirth in minors, pregnancy in minors.

Introduction. In 2016, In Russ. Federation women gave birth to 51 thousand children less than in 2015, which may be the beginning of the second "Russian cross". Another very important fact is of particular concern: in 2016, 175 thousand fewer marriages were registered than in 2015 [2, 5]. Therefore, every pregnancy is a value for the family and society. Though small, but important segment in a cohort of women in labor occupy minors.

In Russia, 30-40 thousand minors give birth every year [2, 5].

Until now, there is no consensus in the literature on what plays a leading role in the occurrence of complications of pregnancy and childbirth in minors: biological immaturity or social risk factors [1, 4, 6].

There are also conflicting opinions as to whether the frequency and severity of complications of pregnancy, childbirth and the postpartum period increases with the decrease in the age of the minor [1, 3, 7].

The aim of this work was to determine the influence of the age of the preg-