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Acute kidney injury after cardiac surgical operations specially including coronary artery bypass graft operations

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ABSTRACT

Introduction. Acute kidney injury as abrupt loss of kidney function leads to accumulation nitric and non-nitric metabolites, toxins. It coexists with deep disorder of fluid balance. Most of cardiac surgical operations are performed using extracorporeal circulation (ECC). To the main risk factors of the postoperative dysfunction of kidneys belong: age above 70, congestive heart failure, previous CABG, preoperative creatinine concentration 124–177 $\mu\text{mol/L}$, diabetes type I, glucose concentration $> 16,6 \text{ mmol/L}$, ECC longer than 3 hours and decreased cardiac output (CO).

Material and methods. The serum creatinine is not enough sensitive marker to diagnose early period of acute kidney injury because the serum creatinine increase occur later than true GFR changes and it needs time to accumulate. It depends on factors like: age, sex, weight, hydration status and what patient eat. NGAL (neutrophil-gelatinase associated lipocalin), cystatin C, KIM-1, IL-18, L-FABP are new markers of acute kidney injury which better than the serum creatinine concentration correspond with kidney injury. The risk factors of the acute kidney injury (AKI) are kidney hypoperfusion, microembolisation by bubbles or material particles and significant activation of humoral factors.

Results. One of the methods reducing mortality CSA-AKI (cardiac surgery associated kidney injury) is renal replacement therapy (RRT), which should be used in early period of acute kidney disease before severe symptoms and complications develop.

Conclusions. There is necessity to find early, easy and cheap markers of acute kidney injury which help decide if use renal replacement therapy. It increases the effectiveness of treatment and improves prognosis in this group of patients.

Keywords: Acute kidney injury (AKI), Cardiac surgery associated kidney injury (CSA-AKI), Renal replacement therapy (RRT).

Definition of acute kidney injury

Acute kidney injury as abrupt loss of kidney function leads to accumulation nitric and non-nitric metabolites, toxins. It coexists with deep disorder of fluid balance. Acute kidney injury (AKI) is defined (according to KIDGO 2012)^[1] as increasing of creatinine concentration in serum 0,3 mg/dl (26,5 $\mu\text{mol/l}$) within 48 hours, or

1,5 times more of creatinine within 7 days, or diuresis $< 0,5 \text{ ml/kg/h}$ within 6 h. According to international RIFLE criteria (Risk, Injury, Failure, Loss and End-stage renal disease) (Table 1) we can evaluate risk, injury and development of kidney disease (loss of function and end-stage renal disease).

Table 1. Criteria RIFLE

Class	GFR Criteria	Urine Output Criteria
Risk	Increased Serum Creatinine x 1.5 or GFR decrease >25%	< 0.5 ml/kgmc/h within 6 h
Injury	Increased Serum Creatinine x 2 or GFR decrease > 50%	< 0.5 ml/kgmc/h within 12 h
Failure	Increased Serum Creatinine x 3 or GFR decrease > 75% or Serum Creatinine \geq 4mg/dl with acute rise \geq 0.5 mg/dl	< 0.3 ml/kgmc/h within 24 h or anuria within 12 h
Loss of function	Persistent acute renal failure = complete loss of kidney function >4 weeks	
End-stage renal disease (ESRD)	End stage kidney disease (> 3 months)	

Risk factors of acute kidney insufficiency

Among the most often performed cardiac surgical operations we can mention Coronary Artery Bypass Graft (CABG) with or without off-pump coronary artery bypass (OPCAB), surgery of the mitral, aortic and tricuspid valve, surgery of aneurysm of the ascending aorta, aneurysm of the arch, surgery of aorta dissection. Apart from OPCAB most of these procedures are performed using extracorporeal circulation (ECC). To the main risk factors of the postoperative dysfunction of kidneys belong:

age above 70, congestive heart failure, previous CABG, preoperative creatinine concentration 124–177 μ mol/L, diabetes type I, glucose concentration > 16,6 mmol/L, EEC longer than 3 hours and decreased cardiac output (CO) (**Table 2**).

Etiology of acute kidney injury after cardiac surgical operations

Prevalence of acute kidney injury after cardiac surgical operations are between 7,7% [2] and 42% [3]. One of the main acute kidney injury (AKI) risk factors is kidney hypoperfusion connected with low blood volume and

Table 2. Risk factors of postoperative AKI for patients who were underwent CABG

Risk factors	Relative risk (95% CI-Cardiac index)
preoperative	
age	
70–79	1.6 (1.1–2.3)
80–95	3.5 (1.9–6.3)
congestive heart failure	1.8 (1.3–2.6)
Previous CABG	1.8 (1.2–2.7)
Preoperative creatine concentration 124–177 μ mol/L	2.3 (1.6–3.4)
Diabetes	
Diabetes type I	1.8 (1.1–3.0)
Glucose concentration > 16.6 mmol/L	3.7 (1.7–7.8)
Midoperative and postoperative	
ECC longer than 3 hours	2.8 (1.9–7.2)
Decreased cardiac output*	
significantly	4.5 (2.9–7.2)
moderately	3.1 (1.9–4.9)
mildly	4.3 (2.2–8.5)

*Significantly: Intra-aortic balloon pump (IABP); moderately: 1) cardiac index < 1.5 L/min/m² surface of the body during at least 30 minutes or at least three inotropes, 2) congestive heart failure confirmed by CI < 1.5 L/min/m², 3) PCWP – pulmonary capillary wedge pressure > 18 mmHg, or 4) central venous pressure > 12 mmHg; mildly: congestive heart failure confirmed by rales, murmurs, chest radiograph, or widening of the jugular veins.

disorder of blood pressure. If there were not appropriate procedure the condition of GFR functional decreasing lead to actin cytoskeleton disintegration, loss intercellular tight junctions, disorder of integrins functions and in result epithelium of convoluted tubule desquamation [4–6]. Another reason of acute kidney injury after cardiac surgical operations is microembolisation which is caused bubbles or material particles [7]. During cardiac surgical operation blood is undergone shear strain when it has contact with artificial material in extracorporeal circulation. It leads to red blood cells damage and hemoglobin and iron release that have redox activity. Redox reactions induce lipid peroxidation and tissue damage [8]. After cardio surgical operation with using cardiopulmonary bypass there is significant activation of humoral factors. Artificial surface activates XII coagulation factor and stimulates coagulation cascade and in result also fibrinolysis. Complement system is activated in classical pathway and alternative pathway. In the same time there are platelet activation, degranulation, adhesion to endothelium, neutrophil and endothelium activation. They result in increasing concentration of adhesion molecule, cytokines, chemokines, lytic enzymes and reactive oxygen species [9–16].

Markers of acute kidney injury

The serum creatinine is not enough sensitive marker to diagnose early period of acute kidney injury because the serum creatinine increase occur later than true GFR changes and it needs time to accumulate. The serum creatinine concentration depends on factors which is not directly connected with kidney like: age, sex, weight, hydration status and what patient eat.

NGAL (neutrophil-gelatinase associated lipocalin) is protein secreted into urine by thick ascending limb of loop of Henle and collecting duct cells. NGAL takes part in iron complex chelation and recirculation of iron complex by endocytosis that protects renal tubule from ischemic [17]. Excretion NGAL with urine significantly increases in AKI caused ischemia [18], especially after cardiac surgical operations [19] or kidney transplant [20, 21], after application big dose contrast agents [22] or other nephrotoxic substance [23, 24]. There was not observed significant increase of NGAL excretion after coronary catheterization [25].

Cystatin C in serum is earlier than creatinin marker of kidneys' function used as well to identify progressive changes as to detect dysfunction. Cystatin C is non-glycosylated protein, endogenous inhibitor of

cysteine proteases, produced and released into blood in constant rate by all nucleated cells. The concentration of cystatin C in serum is independent of age, sex, race, body weight and hydration status and can be measured using easy nephelometric method. Relatively high concentration in body fluid, low mass (13,3 kDa) and positive electric charge of this protein ensure easy glomerular filtration to primary urine. In proximal coils it's completely reabsorbed and catabolized. Because of constant rate of production the value of concentration cystatin C can be a marker of glomerular filtration what is more it does not depend on any factors as: infection, liver diseases, inflammatory diseases [26, 27]. Using cystatin C dysfunction of kidney's can be detected in critical state patients with AKI (24–48 hours earlier than using creatinin). However it is not a specific marker for AKI, because it is rather an early marker of glomerular filtration than a marker of dysfunction of coils [28–30].

KIM-1 (kidney injury molecule 1) – it is a transmembrane orphan receptor produced produced in a large amount in proximal coil because of toxic or ischemic injury. The extracellular domain is removed in urine. vi the increase its excretion is combined with surgery of abdominal aorta aneurysm, heart (precedes the increase of creatinine), but it was not detected in contrast nephropathy [31, 32].

IL-18 is proinflammatory cytokin released into urine by epithelium of proximal ducts after some kind nephrotoxic factor occurred. Concentration above 100 pg/mg creatinin corresponds well with risk of AKI and death in patients with acute respiratory disorders syndrome [33] and it predicts that the kidney will work with delay after trasplantation [34]. Increase in concentration of IL-18 can be detected in first hours after cardiovascular surgery in children [35]. Examination of IL-18 in urine allows to discern very early stage of kidney injury caused by ischemia or coil nephrotoxin and let us excluded prerenal azotemia, chronic kidney disease and urinary tract infection [36]. Furthermore IL-18 is a predictor of AKI severity and probability of death.

L-FABP is cytoplasmic protein responsible for intracellular transport of long-chain fatty acid. There are known 9 types of proteins transporting fatty acid and L-FABP is one of them. They are relatively specific to the tissue. L-FABP can be found in hepatocytes, enterocytes, and the proximal coil cells. In different kidneys injuries concentration L-FABP in urine increases. It was proved that L-FABP is a adequate marker of AKI after cardiac surgery. Its concentration increased in urine 94 times and 45 times more than in people who were not

underwent such procedures properly in 4. and 12. hour after surgery. The concentration of L-FABP increases faster than of creatinin [37]. It was revealed that the concentration of L-FABP is useful in in the monitoring of contrast-induced nephropathy [38], cis-platin induced nephropathy [39], and also in the staging of chronic kidney disease [40].

Methods of reduction mortality connected with acute kidney injury (AKI)

Prevalence of acute kidney injury connected with cardiac surgical operations (cardiac surgery associated kidney injury – CSA-AKI) in early after-operation period may be even 30% and it increases because more people are operated in old age and with co-exited disease e.g. diabetes or chronic kidney disease [41] One of the methods reducing mortality CSA-AKI is renal replacement therapy (RRT), which should be used in early period of acute kidney disease before severe symptoms and complications develop. Increase serum creatinine concentration and GFR decrease occur in 2nd–3rd day after damaging agent. It provides big loss of nephrons which often is irreversible. In many department of cardiac surgery the serum creatinine serum concentration is still main way to evaluate kidney function. There is necessity to find early, easy and cheap markers of acute kidney injury which help decide if use renal replacement therapy. It increases the effectiveness of treatment and improves prognosis in this group of patients.

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Conflict of interest statement

The authors declare that there is no conflict of interest in the authorship or publication of contribution.

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