

Preoperative blood morphology and incidence of acute kidney injury after on-pump coronary artery bypass grafting – a single-center preliminary report



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Abstract

Introduction: Acute kidney injury (AKI) after coronary artery bypass grafting (CABG) performed in cardiopulmonary bypass (CPB) may complicate the postoperative course and has a negative impact on outcome. In some cases, postoperative AKI develops in spite of normal baseline creatinine concentration and estimated glomerular filtration rate (eGFR).

Aim: To examine whether there is any association between the preoperative blood morphology and incidence of postoperative AKI.

Material and methods: The study involved 62 consecutive patients with the mean age of 64.0 ± 7.4 years who underwent CABG in CPB. Before surgery, blood morphology and biochemistry were analyzed. Patients with eGFR below 60 ml/min/1.73 m² were excluded. After the operation, parameters of renal function were checked systematically. Acute kidney injury was defined according to the Acute Kidney Injury Network (AKIN) classification.

Results: Twenty-one (33.9%) patients presented AKI (group AKI), although in the majority of them ($n = 16$) it was temporary and medical management was enough to cure AKI. Only in 1 (1.6%) case was renal replacement therapy necessary. In group AKI, patients' preoperative hemoglobin concentration (8.46 ± 0.72 mM/l), red blood cell count (4.51 ± 0.39 × 10¹²/l) and hematocrit (0.40 ± 0.04) were significantly lower ($p < 0.05$) than in group C (9.07 ± 0.57 mM/l; 4.78 ± 0.36 × 10¹²/l; 0.43 ± 0.03, respectively). Interestingly, the baseline parameters of renal function were comparable between groups.

Conclusions: Hemoglobin concentration and red blood cell counts close to the lower limit of the normal range may enable identification of patients at risk of AKI early after CABG in CPB among individuals with normal preoperative biochemical parameters of renal function.

Key words: coronary surgery, blood morphology, kidney injury.

Streszczenie

Wstęp: Ostre uszkodzenie nerek (AKI) po operacjach pomostowania aortalno-wieńcowego (CABG) w krążeniu pozaustrojowym (CPB) może być istotnym powikłaniem i mieć negatywny wpływ na wynik kliniczny. W niektórych przypadkach pooperacyjne AKI rozwija się pomimo prawidłowego wyjściowego stężenia kreatyniny i współczynnika przesączania kłębuszkowego (eGFR).

Cel: Ocena, czy istnieje związek między przedoperacyjną morfologią krwi a częstością występowania pooperacyjnego AKI.

Materiał i metody: Badaniem objęto kolejnych 62 chorych w wieku średnio 64,0 ± 7,4 roku, którym poddano CABG w CPB. Przed operacją analizowano morfologię krwi i wykonywano badania biochemiczne. Do badania nie kwalifikowano chorych z eGFR poniżej 60 ml/min/1,73 m². Po operacji systematycznie analizowano wartości parametrów oceniających czynność nerek. Ostre uszkodzenie nerek definiowano wg klasyfikacji Acute Kidney Injury Network (AKIN).

Wyniki: U 21 (33,9%) chorych stwierdzono AKI (grupa AKI), choć u większości z nich ($n = 16$) było ono czasowe i leczenie zachowawcze było skuteczne. Jedynie w 1 (1,6%) przypadku niezbędne było leczenie nerkozastępcze. U chorych z grupy AKI przedoperacyjne stężenie hemoglobiny (8,46 ± 0,72 mmol/l), liczba krwinek czerwonych (4,51 ± 0,39 × 10¹²/l) i hematokryt (0,40 ± 0,04) były istotnie niższe ($p < 0,05$) niż w grupie kontrolnej (C) (odpowiednio 9,07 ± 0,57 mmol/l; 4,78 ± 0,36 × 10¹²/l i 0,43 ± 0,03). Co ciekawe, wyjściowe wartości parametrów nerkowych były porównywalne między grupami.

Wnioski: Stężenie hemoglobiny i liczba krwinek czerwonych bliskie dolnej granicy normy mogą być przydatne w identyfikacji chorych wyższego ryzyka wystąpienia AKI we wczesnym okresie po operacji CABG w CPB z prawidłowymi biochemicznymi parametrami czynności nerek.

Słowa kluczowe: pomostowanie aortalno-wieńcowe, morfologia krwi, ostre uszkodzenie nerek.

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Introduction

Acute kidney injury (AKI), either temporary or persistent, is a well-recognized adverse event after cardiac surgical procedures, including coronary artery bypass grafting (CABG) particularly performed in cardiopulmonary bypass (CPB) [1]. It may involve even more than 30% of all cardiac surgical patients [2, 3]. Acute kidney injury was proved to have an unfavorable impact not only on late survival but also development of chronic kidney disease (CKD) stages 3 to 5 [3]. Even if patients recover after AKI, their survival rate is still reduced in comparison to patients without kidney dysfunction in the early postoperative period [4]. Up to now, many factors predisposing to develop AKI after CABG have been reported. Among them, one of the most potent is application of CPB [5, 6]. Prolonged CPB time (< 90 minutes) was shown to correspond with a markedly higher rate of AKI [7]. Currently, many CABG procedures, particularly in high-risk patients with pre-existing renal disease, are done on the beating heart (off-pump coronary artery bypass – OPCAB), which was proved to significantly reduce the rate of postoperative complications [8]. However, some cardiac surgeons still prefer CABG in CPB instead of OPCAB. They stress that CABG in CPB enables them to perform meticulous distal anastomoses of aorto-coronary grafts with the recipient coronary arteries.

In some cases, AKI can develop in spite of normal preoperative renal performance assessed on the basis of creatinine concentration and estimated glomerular filtration rate (eGFR). Normally functioning kidneys produce and release erythropoietin, which is crucial in hemoglobin synthesis, and thus CKD may be reflected in hemoglobin level [9].

Aim

In view of the above, we examined whether patients with eGFR above 60 ml/min/1.73 m² who developed AKI in the early postoperative period after CABG procedures carried out in CPB manifested any differences in the findings of the routine baseline examination of blood morphology.

Material and methods

Patients

The study involved 62 consecutive patients (48 male and 14 female) with the mean age of 64.0 ± 7.4 years (range: 42–81 years) who underwent CABG in CPB between January and December 2012. All patients satisfied the following criteria of enrollment: isolated severe CAD requiring elective surgical treatment, relatively well-preserved kidney function (creatinine concentration below 1.0 mg/dl in women or 1.2 mg/dl in men and eGFR above 60 ml/min/1.73 m²). Patients with any pre-existing form of anemia or with at least moderate CKD defined as eGFR less than 60 ml/min/1.73 m² were excluded from the study.

Patients were retrospectively divided into two groups. In the first group, postoperative AKI was diagnosed according to the Acute Kidney Injury Network classification ($n = 21$; 33.9%), which is based on an absolute increase

in serum creatinine concentration of > 26 mmol/l within 48 hours or an a relative increase to at least 150% within 7 days of surgery accompanied by urine output less than 0.5 ml/kg/h for more than 6 hours [10]. The second group (control one; group C; $n = 42$) comprised subjects without any laboratory signs or clinical symptoms of postoperative renal dysfunction.

Baseline data

All patients before surgery had blood samples taken to examine morphology (hemoglobin concentration (HBG), white blood cells (WBC), red blood cells (RBC) and platelet count (PLT)), red blood cell indices (mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), hematocrit (HCT)) and biochemistry. In the latter, special attention was paid to biochemical parameters of kidney function such as creatinine and eGFR.

Surgery

All subjects underwent CABG from median sternotomy using CPB and cold cardioplegic cardiac arrest with St Thomas Hospital II solution. Additionally, local and systemic moderate hypothermia (approx. 28°C) was applied. At the beginning of surgery, all necessary grafts were harvested. After the heart was arrested, distal anastomoses were performed. Following declamping of the ascending aorta, proximal anastomoses of the “free” grafts were performed applying the technique of partial side-clamp of the ascending aorta.

The intraoperative parameters such as CPB time, aortic cross-clamping time (ischemic time for myocardium) and mean arterial pressure (MAP) during the procedure were analyzed.

Postoperative management

All patients after surgery were transferred to a postoperative care unit (ICU), usually for 24 hours, then to a surgical one. Routinely, 7 to 10 days following surgery patients were discharged and transferred to cardiac rehabilitation centers.

Blood samples were taken three times a day up to 2 days following surgery then at least once a day. Peak concentrations of creatinine throughout the early postoperative period were recorded and eventually analyzed. Post-procedural urine output was the clinical parameter of the most interest. Moreover, the volume of transfused red blood cells was also evaluated.

Data management and statistical analysis

To check normality of continuous variables the Shapiro-Wilk W test was performed. Normally distributed data are presented as the means ± standard deviations and compared with the unpaired Student's *t*-test. The categorical or ordinal variables are expressed as the numbers (*n*) and percentages (%) and they were analyzed using the Mann-

Whitney *U* test. A *p*-value < 0.05 was considered statistically significant. All statistical analyses were performed using Statistica 10.0 for Windows software (StatSoft, Inc., Tulsa, OK, USA).

Results

Patients

Among 77 patients undergoing elective or urgent CABG in CBP, only 62 were considered eligible for the study. The remainder either had preoperative eGFR lower than 60 ml/min/1.73 m² (*n* = 12) or anemia related to iron (*n* = 2) or folic acid deficiency (*n* = 1).

Table I. Preoperative demographic and clinical variables

Variables ¹	Group AKI (<i>n</i> = 21)	Group C (<i>n</i> = 41)	<i>P</i> -value
Age [years]	67.4 ±7.2	62.2 ±7.0	0.008*
Gender (M/F)	15/6	33/7	0.428
Height [m]	1.65 ±0.10	1.71 ±0.09	0.017*
Weight [kg]	74.5 ±11.8	84.2 ±17.7	0.030*
BMI [kg/m ²]	27.6 ±4.2	28.7 ±4.3	0.321
BMI > 30 kg/m ²	6 (28.6)	13 (31.7)	0.804
DM ²	5 (23.8)	11 (26.9)	0.754
Arterial hypertension	16 (76.2)	30 (73.2)	0.645
PVD	6 (28.6)	12 (29.3)	0.875
PCI in history	13 (61.9)	24 (58.5)	0.665
Urgent CABG ³	4 (19.0)	5 (12.2)	0.310

¹Continuous variables are expressed as mean ± standard deviation, categorical variables as numbers (%); ²treated with either insulin and/or oral medications; ³defined if surgery had to be performed during the same in-hospital stay. **P*-value of statistical significance, group AKI vs. group C. BMI – body mass index, CABG – coronary artery bypass grafting, DM – diabetes mellitus, PCI – percutaneous coronary intervention, PVD – peripheral vascular disease.

Table II. Preoperative hematological parameters

Parameter ¹	Group AKI (<i>n</i> = 21)	Group C (<i>n</i> = 41)	<i>P</i> -value
Blood morphology:			
WBC [$\times 10^9/l$]	6.9 ±1.8	7.5 ±1.7	0.216
PLT [$\times 10^9/l$]	220 ±65	246 ±49	0.080
RBC [$\times 10^{12}/l$]	4.51 ±0.39	4.78 ±0.36	0.012*
HBG [mM/l]	8.46 ±0.72	9.07 ±0.57	< 0.001*
HCT [l/l]	0.40 ±0.04	0.43 ±0.03	0.004*
MCV [fl]	89.0 ±5.1	90.1 ±4.4	0.390
MCH [fM]	1.88 ±0.10	1.91 ±0.11	0.157
MCHC [mM/l]	21.0 ±0.5	21.2 ±0.6	0.209
Biochemistry:			
Creatinine [mg/dl]	0.89 ±0.21	0.90 ±0.16	0.928
eGFR [ml/min/1.73 m ²]	85.1 ±23.5	85.7 ±15.6	0.913

¹Continuous variables are expressed as mean ± standard deviation. *Statistically significant *p*-value, group AKI vs. group C. eGFR – estimated glomerular filtration rate, HBG – hemoglobin concentration, HCT – hematocrit, MCH – mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration, MCV – mean corpuscular volume, PLT – platelet count, RBC – red blood cell count, WBC – white blood cell count.

Incidence of AKI

In 21 (33.9%) patients AKI was noted, although in the majority (*n* = 16; 76.2% of AKI) as stage 1 according to the AKIN classification. Stage 2 was seen in 4 (19.0%) patients, whereas another 1 (4.8%) subject required renal replacement therapy by means of continuous veno-venous hemofiltration (CVVHF). Fortunately, in all but two cases (one of them treated with CVVHF soon after surgery) this injury was temporary and at discharge eGFR was above 60 ml/min/1.73 m² and creatinine concentration was comparable to baseline. Patients with persistent renal dysfunction (*n* = 2) were referred to nephrologists.

Demographic data and postoperative AKI

Patients with postoperative AKI were significantly older than the remainder in group C (*p* = 0.008). Although they were slightly shorter, BMI and obesity prevalence were similar. Other demographic and preoperative clinical variables did not differ markedly between groups (Table I).

Intraoperative data

None of the analyzed intraoperative parameters differed between groups. Mean CPB and ACC times were 78.8 ±17.8 and 47.5 ±12.6 minutes, and 80.4 ±19.7 and 46.9 ±13.6 minutes, respectively, in group C and AKI (NS). Moreover, MAP values during CBP in group C (72.5 ±17.4 mm Hg) and AKI (71.7 ±15.8 mm Hg) were also comparable (NS).

Blood products utilization

The majority of patients received red blood cells in the perioperative period, 35 (85.3%) in group C and 18 (85.1%) in group AKI (NS). Total volume of red blood cells transfused did not differ significantly between group C (388 ±134 ml) and group AKI (380 ±123 ml).

Laboratory data and postoperative AKI

Interestingly, eGFR and creatinine concentration were comparable between groups (Table II). Otherwise, marked differences were seen in blood morphology. Preoperative RBC, HBG and HCT were significantly lower in group AKI than group C (Table II).

Detailed analysis of preoperative HBG showed that the majority of patients (11/16; 68.8%) in the first quartile of HBG concentration (below 8.5 mM/l; *n* = 16) presented postoperative AKI, compared to one third (10/30; 33.3%) of individuals in the second quartile (HBG 8.6 to 9.2 mM/l; *n* = 30), and only 1 subject (1/16; 6.3%) in the third quartile (i.e., HBG above 9.2 mM/l; *n* = 16).

Discussion

The real incidence of AKI following on-pump CABG differs between several reports with a relatively wide range from less than 10% to even 30% and more [11–15]. The AKI rate in our preliminary report is within this range but rather close to the upper limited reported by other authors. It must be noted that the incidence seems to be higher in prospective

single-center analyses [11–13] than in retrospective cohort studies of large national databases [14, 15]. In the latter it may be underestimated and underreported as it based predominantly on analyses of the medical records where AKI was identified using International Classification of Diseases, 9th Revision diagnosis codes. It is not common clinical practice to code mild and transient post-procedural AKI. Otherwise, AKI incidence requiring renal replacement therapy found in our study (below 2%) is comparable even with aforementioned database analyses [15]. This method indicating severe AKI is usually associated with a significant increase in costs and prolonged in-hospital stay and thus is probably reported in 100% of cases.

The most important message of this preliminary report, from a practical point of view, is the finding that even some of the most routine and basic parameters assessed before surgery in all patients as blood morphology may be helpful in identification of subjects at high risk of AKI following CABG. It must be stressed that our study involved only patients with hematological parameters within the normal physiological range and relatively well-preserved renal function assessed on the basis of creatinine concentration and eGFR (see *Patients* section). The majority of patients who developed AKI had HBG below the 25th percentile and the red blood cell indices revealed normocytemia. Normocytic normochromic anemia was shown previously to be a frequent comorbidity of patients with diagnosed CKD [16]. The pathogenesis of this phenomenon is well known. The main humoral regulator of erythropoiesis, the hormone erythropoietin, which stimulates proliferation and differentiation of erythroid precursor cells, is mainly produced in the kidneys [17]. Thus in estimating the real risk of postoperative AKI we should take into consideration not only biochemical parameters of renal performance but also blood morphology. In some patients even slightly lower HBG as compared to the previous examinations but still within the physiological range might precede clinically evident renal disease diagnosed by means of classic renal parameters such as elevated serum creatinine concentration accompanied by markedly reduced eGFR.

Our results may be applicable in daily clinical practice with cardiac surgery patients. We are aware that probably in many patients with post-procedural AKI it would not be possible to avoid it, but having in mind this potentially severe adverse event optimal management of the surgical team could have minimized its rate. Up to now, several risk factors with a potential negative impact on renal function have been identified, but only some of them are modifiable [11, 18, 19]. Patients who develop AKI are usually older, which was also supported by our findings. It is expected, as aging is associated with morphological and structural changes in glomeruli [20, 21]. Not only does the overall number of functioning nephrons steadily decline, but also the remaining ones lose their mass [21]. It was previously reported that intraoperative anemia and very HCT low during CPB were risk factors for the development of the post-procedural AKI [18]. However, blood morphology before

surgery and its impact on AKI incidence soon after CABG in CPB have not been studied extensively. Additionally, low MAP (area under curve MAP < 50 mm Hg) during CPB added additional risk (OR more than 3.0) but only among patients with severe anemia (< 25th percentile of lowest HBG) [18].

In high-risk patients, preventative measures must be applied. In consequence we should avoid hypotonia and maintain adequate hemodynamics, particularly in patients with borderline HBG before surgery and in the elderly. Because patients who developed AKI were older than the remainder and had comparable MAP during CPB, it is possible that elderly persons require higher perfusion pressure to preserve normal kidney function after surgery. Moreover, maximal reduction in time of CPB is of paramount importance [18]. Avoiding nephrotoxic agents and optimizing preoperative hemoglobin levels to avoid excessive transfusions would also be beneficial [1]. Moreover, it is possible to reduce the priming volume of CPB leading to excessive hemodilution in this group of CABG subjects by applying a miniaturized cardiopulmonary circuit. The latter was shown to lower the incidence of AKI when compared with conventional CPB [11].

We are aware of some study limitations. Our group is relatively small and confined to the experience of a single cardiac surgical center. It resulted from management with CABG patients in our department. The majority of them have been treated off-pump for at least 10 years. Almost all patients involved in this study were treated by one, very experienced surgeon who still prefers CABG in CPB over off-pump operations. As the patients enrolled in this study were consecutive, in our opinion these data should be reliable and conclusions may be useful for planning optimal management to prevent post-operative AKI.

Conclusions

Hematological parameters such as hemoglobin concentration, red blood cell counts and hematocrit close to the lower limit of the normal range may be helpful in identification of patients at risk of early AKI among subjects undergoing CABG in CPB with normal baseline biochemical parameters of renal function. However, this preliminary observation requires further research on a much larger group of patients.

Disclosure

Authors report no conflict of interest.

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