J Nephrol (2016) 29:835–845
DOI 10.1007/s40620-016-0281-x

ORIGINAL ARTICLE

Diabetes mellitus does not affect the incidence of acute kidney injury after cardiac surgery; a nested case–control study

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Received: 20 November 2015 / Accepted: 3 February 2016 / Published online: 29 February 2016
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Abstract

Background Acute kidney injury (AKI) after cardiac surgery is a common complication associated with increased mortality. However, the heterogeneity of the definitions used results in high variance of incidence rates in the literature. Data on the effect of diabetes mellitus on AKI incidence in this setting are scarce. We thus aimed to compare the incidence of AKI (defined by the AKIN, RIFLE and KDIGO criteria) in diabetic vs. non-diabetic patients undergoing cardiac surgery.

Methods This is a nested case–control study from a cohort of patients undergoing cardiac surgery between 1/1/2013 and 30/6/2014 in a single center. Exclusion criteria were: type-1 diabetes, end-stage renal disease, death during surgery and AKI prior to surgery. We identified 199 type-2 diabetic patients and matched them for gender, age and estimated glomerular filtration rate (eGFR) to 199 non-diabetic individuals. The incidence of AKI between the two groups was compared in the total population and in subgroups according to preoperative eGFR. Univariate and multivariate logistic regression analysis were conducted to identify factors associated with AKI.

Results The incidence of AKI was moderately high, but similar between the two study groups (AKIN and KDIGO: 24.1 vs. 23.1 %; $p = 0.906$, RIFLE: 25.1 vs. 25,1 %; $p = 1.000$, in diabetics and non-diabetics respectively). A trend towards increased incidence of AKI from eGFR subgroup 1 to subgroup 3a was noted in diabetic patients ($p = 0.04$). No significant differences were detected between the two study groups within any eGFR subgroup studied. At multivariate analysis, age [per year increase: odds ratio (OR) 1.034, 95 % confidence interval (CI) 1.001–1.068] and duration of cardiopulmonary bypass [per minute increase: OR 1.009 (1.003–1.015)] were associated with AKI. Diabetes was not related to AKI development in regression analysis [OR 1.057 (0.666–1.679)].

Conclusions Incidence of AKI after cardiac surgery is high, but diabetes is not a risk factor for AKI. Baseline renal function in diabetics is related inversely to the incidence of AKI. Age and cardiopulmonary bypass duration are independent predictors of cardiac surgery-associated AKI.

Keywords Acute kidney injury · Cardiac surgery · Chronic kidney disease · Diabetes mellitus · Incidence

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Introduction

Cardiac surgery, with or without the use of cardiopulmonary bypass, is commonly associated with the onset of acute kidney injury (AKI) [1, 2]. In the literature, a number of different definitions have been used for AKI, a fact resulting in highly variant estimations of postoperative AKI incidence [3]. In general, about 3–30 % of patients undergoing cardiac surgery are reported to experience an acute drop in renal function postoperatively, and 1–5 %

require extracorporeal renal replacement therapy [4]. Renal function deterioration after such operations is considered a serious complication, as testified by a prospective cohort study of 2488 patients in which occurrence of AKI led to a 4 % increase in all-cause hospital mortality [5]. Notably, observational data from a prospective cohort of 4118 patients who underwent cardiac and thoracic aortic surgery suggested that even mild increases of serum creatinine ($\geq$0.5 mg/dl) within 48 h postoperatively were associated with a 6 % increase in adverse outcomes with regard to 30-day mortality [6]. In patients with more severe cardiac surgery-related AKI, requiring renal replacement therapy postoperatively, 30-day mortality rate can be as high as 58 % [7].

In order to optimize clinical decision-making and implement preventive strategies in cardiac surgery, predictive models for high-risk patient identification have been developed. The most widely used system is perhaps the European System for Cardiac Operative Risk Evaluation (EuroSCORE) I and its more recent modified version EuroSCORE II [8, 9]. These morbidity scores correlate strongly both with mortality and incidence of AKI in several studies [1, 5, 6]. Moreover, since researchers tried to cope with different definitions for AKI and the consequent problems, in previous years three definition and classification systems for AKI were developed, with small differences between them. In 2002, the Acute Dialysis Quality Initiative (ADQI) group introduced the RIFLE (Risk, Injury, Failure, Loss and End-stage renal disease) criteria for diagnosis and staging of AKI based on serum creatinine, estimated glomerular filtration rate (eGFR) and urine output changes [10]. In 2007, the Acute Kidney Injury Network (AKIN) proposed a RIFLE modification known as the AKIN criteria and 5 years later the most recent definition was proposed, in the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for AKI [11, 12].

The pathophysiologic mechanisms leading to AKI after cardiovascular operations are multiple and complex. Intraoperative hypotension, nephrotoxic agents used in anesthesia, postoperative cardiac complications that impair renal perfusion, hemolysis and atheroembolism are some of the possible causes of AKI [13]. Further, a synergistic role of other injury pathways during and after surgery, such as neurohormonal activation, inflammation, oxidative stress activated by kidney ischemia and reperfusion and several endogenous toxins, has been proposed [14, 15]. In addition to the above, preoperative non-controllable risk factors that impair the kidney autoregulatory mechanisms, such as older age, advanced atherosclerotic vascular disease, hypertension and left ventricular ejection fraction (EF) decrease, have been associated with higher incidence of AKI [13, 16]. Presence of chronic kidney disease (CKD) *per se* is independently correlated with the post-surgery occurrence of AKI and need for renal replacement therapy [17]. The extent of renal dysfunction (higher serum creatinine, lower eGFR) and renal injury (higher proteinuria) before cardiac surgery is associated with AKI incidence [17–19].

Diabetes mellitus (DM) is present in about 20–25 % of patients undergoing cardiac surgery [1, 5] and has been associated with an increase in post-surgery cardiovascular events in some, but not all, studies [20, 21]. No study so far has focused mainly on the effect of DM on AKI incidence after cardiac surgery and current data are contradictory; some studies showed a similar prevalence of DM between patients with and without occurrence of AKI [5, 22], whereas others indicated that DM is an independent predictor of AKI, among several studied factors [1, 19]. Thus, the aim of this study was to compare the incidence of AKI (defined by the AKIN, RIFLE and KDIGO criteria) in matched patients with and without DM undergoing cardiac surgery and to directly examine the effect of DM on AKI development in these individuals.

Materials and methods

Study design and population

This is a nested case–control study with both cases and controls deriving from a prospectively assembled cohort of patients undergoing elective, urgent or emergency cardiac surgery (coronary artery bypass grafting [CABG], aortic or mitral valve replacement, thoracic aortic aneurysm repair, aortic dissection repair, atrial septal defect closure or a combination of these procedures) during an 18-month period (from 1/1/2013 to 30/6/2014) in the Department of Cardiothoracic Surgery, Papanikolaou Hospital in Thessaloniki, Greece. Exclusion criteria were: (a) type-1 DM; (b) stage 5 renal disease (eGFR <15 ml/min/1.73 m^2); (c) death during surgery; (d) ongoing AKI of any cause before surgery; (e) patients with missing data for the parameters studied. A total of 199 type-2 diabetic patients were identified and represented the cases. After the case group was formed, one of the investigators, blinded to patient data apart from matching parameters, selected an equal number of non-diabetic patients as controls, matched for gender, age ($\pm$5 years) and pre-surgery kidney function (eGFR values $\pm$ 5 ml/min/1.73 m^2).

Data collection and definitions

Upon admission, demographic and anthropometric parameters were recorded for each patient, as well as existing risk factors and comorbidities, e.g. hypertension, dyslipidemia, DM, coronary heart disease, stroke, peripheral vascular disease, chronic obstructive pulmonary disease, heart failure according to the New York Heart Association (NYHA) classification, as well as pre-surgery use of diuretics or renin-angiotensin-aldosterone system (RAAS) inhibitors. Additional preoperative risk factors included in the EuroSCORE I and II models were recorded. Pre-surgery cardiac function was evaluated by echocardiography. Intraoperative parameters such as type of intervention, duration of intubation (hours), duration of cardiopulmonary bypass use (minutes) and use of intra-aortic balloon pump, as well as factors related to intensive care unit (ICU) hospitalization were recorded. Possible postoperative complications were documented in all study participants; e.g. postoperative myocardial infarction, onset of atrial fibrillation, deep sternal wound infection, ventilator-associated pneumonia, stroke, requirement for re-intubation or renal replacement therapy, persistent hemodynamic instability, septicemia and multiple organ dysfunction syndrome.

Renal function was estimated on the basis of a series of serum creatinine measurements before surgery (baseline), when the operation was finalized, as well as exactly 24 and 48 h after the baseline blood samples were acquired. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation, as described elsewhere [23]. Patient's urinary excretion rate was monitored every 6 h on the day of surgery and on a daily basis thereafter. Diagnosis of AKI was made separately with the use of RIFLE, AKIN and KDIGO criteria [24], which are depicted in Fig. 1. The period of observation was restricted to 48 h post-surgery. The incidence of AKI and requirement for renal replacement therapy were compared between the diabetic and non-diabetic patients in the total population and in subgroups of renal function, according to their eGFR levels prior to surgery (Group 1: $\geq$90 ml/min/1.73 m^2; Group 2a: $\geq$75 < 90 ml/min/1.73 m^2; Group 2b: $\geq$60 <75 ml/min/1.73 m^2; Group 3a: $\geq$45 <60 ml/min/1.73 m^2; Group 3b: $\geq$30 < 45 ml/min/1.73 m^2). Patients with stage 4 CKD were very few (n = 4) and, thus, were not analyzed separately. A further analysis to examine the effect of CKD severity on AKI incidence was performed.

Statistical analysis

The Shapiro–Wilk test was applied to examine the normality of distribution for quantitative variables. Continuous variables are described as mean ± 1 standard deviation (SD) or median and range according to the normality of distribution, while categorical variables are described as frequency and percentage (n, %). Incidence of AKI, existing comorbidities, medication use, surgery and procedure related data, occurrence of post-operative complications, as well as laboratory parameters were compared between the two study groups with the Chi-square test or Fisher's exact test for qualitative variables, and with Student's *t* test or the Mann–Whitney test and analysis of variance (ANOVA) or Kruskal–Wallis test by ranks for quantitative variables. Moreover, uni- and multivariate logistic regression analysis was performed to evaluate the correlation of various demographic, clinical and laboratory characteristics with occurrence of AKI defined by the KDIGO criteria. Variables were tested for interactions and included in the multivariate model if p was <0.20 at the univariate analysis. The adjusted odd ratios (OR) are reported with 95 % confidence intervals (CI) and values of $p < 0.05$ (two-tailed) were considered statistically significant. Statistical analysis was performed with the 21st version of the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA).

Results

Baseline demographic and clinical characteristics

A total of 398 patients were included in this study, allocated into two equal groups (n = 199) based on the diagnosis of DM prior to study entry. Mean age of patients was 67 years (diabetics: 66.4 ± 9.1, non-diabetics: 67.4 ± 8.3, p = 0.289) and each group consisted of 164 males and 35 females. Pre-operative renal function, in means of serum creatinine and eGFR, was similar in the two groups (creatinine: diabetics: 1.10 ± 0.2, non-diabetics: 1.09 ± 0.2, p = 0.817; eGFR: diabetics: 68.3 ± 28.5, non-diabetics: 67.5 ± 16.1, p = 0.724). The only parameters that were significantly more prevalent in diabetic patients were hypertension (54 vs. 46 %, p = 0.013) and dyslipidemia (58.7 vs. 41.3 %, p = 0.010). EuroSCORE I was higher in non-diabetics (4.9 ± 4.6 vs. 5.8 ± 5.9, p = 0.084), but the difference was of borderline significance and its newer modification EuroSCORE II was similar (1.9 ± 1.7 vs. 2.1 ± 2.1, p = 0.353) in the two groups. The pre-surgery use of diuretics and RAAS inhibitors was higher in the diabetic patient group, but did not reach significant levels (Table 1).

Surgery-related factors

As shown in Table 2, there were differences in the types of operation performed between the two groups. CABG was performed more often in diabetics, while combined surgery was more frequent in non-diabetics. Intra-aortic balloon pump was used more often in non-diabetic patients (3.5 vs. 10.6 %, p = 0.010). However, duration both of cardiopulmonary bypass and of intubation did not differ

RIFLE criteria		
Risk	1-7 Days	50-99% Creatinine rise (1.5-1.99 x Baseline) eGFR decrease ≥25%
Injury	1-7 Days	100-199% Creatinine rise (2.00-2.99 x Baseline) eGFR decrease ≥50%
Failure	1-7 Days	>200% Creatinine rise (≥3 x Baseline) Creatinine ≥4mg/dl Acute Creatinine rise ≥0.5 mg/dl eGFR decrease ≥75%
Loss	4 weeks	Persistent acute renal failure: complete loss of kidney function
End Stage	3 months	End-Stage Renal Disease

AKIN criteria		
Stage 1	1-7 Days	50-99% Creatinine rise (1.5-1.99 x Baseline)
	1-48 hours	Acute Creatinine rise ≥0.3 mg/dl
Stage 2	1-7 Days	100-199% Creatinine rise (2.00-2.99 x Baseline)
Stage 3	1-7 Days	>200% Creatinine rise (≥3 x Baseline) Creatinine ≥4mg/dl with acute rise ≥0.5 mg/dl
	Any time	Requirement for Renal Replacement Therapy

KDIGO criteria		
Stage 1	1-7 Days	50-99% Creatinine rise (1.5-1.99 x Baseline)
	1-48 hours	Acute Creatinine rise ≥0.3 mg/dl
Stage 2	1-7 Days	100-199% Creatinine rise (2.00-2.99 x Baseline)
Stage 3	1-7 Days	>200% Creatinine rise (≥3 x Baseline)
	1-48 hours	Creatinine ≥4mg/dl with acute rise ≥0.3 mg/dl
	1-7 Days	Creatinine ≥4mg/dl with 50% rise (1.5 x Baseline)
	Any time	Requirement for Renal Replacement Therapy

Urine Output	
Risk / Stage 1	<0.5 mL/kg/h for 6 hours
Injury / Stage 2	< 0.5 mL/kg/h for 12 hours
Failure / Stage 3	< 0.3 mL/kg/h for 12 hours Anuria for 12 hours

Fig. 1 RIFLE, AKIN and KDIGO Staging for acute kidney injury severity [9–11] (Urine output definition is common for the 3 classification systems)

significantly between groups (cardiopulmonary bypass: 100.3 ± 36.8 min in diabetics vs. 107.1 ± 45.2 min in non-diabetics, $p = 0.319$; duration of intubation: 10.8 ± 13.8 h in diabetics vs. 13.4 ± 29.7 h in non-diabetics, $p = 0.263$). The most common complications were the onset of atrial fibrillation (140 cases in total) and hemodynamic instability (25 cases in total). No differences in incidence rates of any post-surgery complications were noted between the two groups (Table 2).

Renal outcomes

Baseline creatinine and eGFR levels were, respectively, 1.1 ± 0.2 mg/dl and 68.3 ± 28.5 ml/min/1.73 m^2 in diabetic vs. 1.09 ± 0.2 mg/dl and 67.5 ± 16.1 ml/min/1.73 m^2 in non-diabetic patients ($p = 0.817$, and $p = 0.724$, accordingly). Similarly, creatinine and eGFR levels at the end of surgery, as well as 24 h and 48 h after the first blood sample acquisition did not differ between the two groups (Table 3). Urine excretion during the first day post-surgery (diabetics: 3553 ± 887 ml vs. non-diabetics: 3766 ± 822, $p = 0.053$) and post-surgery day 2 (diabetics: 2998 ± 1083 ml vs. non-diabetics: 3296 ± 1111, $p = 0.013$) were significantly lower in the diabetic patient group. A similar analysis conducted within each renal function category, as defined above, showed no significant changes between groups (data not shown).

The incidence of AKI was moderately high, but also similar between the two study groups regardless of the set of criteria used. Defined by the AKIN criteria, incidence of AKI was 24.1 % (48 cases) in diabetic and 23.1 % (46 cases) in non-diabetic patients ($p = 0.906$) (Table 3). Using the RIFLE criteria, AKI was found in 25.1 % (50 cases) from each group ($p = 1.000$). With the KDIGO definition of AKI, the results were identical to those of the AKIN criteria (Table 3). Renal replacement therapy in the ICU was needed for 7 (3.5 %) diabetics and 3 (1.5 %) non-diabetics ($p = 0.169$). Notably, requirement for renal replacement therapy was significantly higher for diabetics in the renal function subgroup 2b (6.8 vs. 0 %, $p = 0.022$), but incidence rates and sample sizes in this comparison are relatively small. Moreover, there were no significant differences between diabetic and non-diabetic patients in AKI incidence with any definition used within each baseline renal function subgroup (Table 4).

We also analyzed the incidence of AKI and the need for renal replacement therapy in the ICU between baseline renal function categories in the study population as a whole and in the two study groups separately

Table 1 Basic demographic, anthropometric and clinical parameters of diabetic and non-diabetic patients

Parameters	Diabetics	Non-diabetics	p
N	199	199	–
Age (years)	66.42 ± 9.1	67.36 ± 8.3	0.289
Gender			
Female	35 (8.8 %)	35(8.8 %)	1.000
Male	164 (41.2 %)	164 (41.2 %)	1.000
Creatinine (mg/dl)	1.10 ± 0.2	1.09 ± 0.2	0.817
eGFR (ml/min/1.73 m^2)	68.3 ± 28.5	67.5 ± 16.1	0.724
Weight (kg)	80.9 ± 14.4	79.4 ± 12.8	0.261
Height (cm)	167.1 ± 9.7	167.7 ± 8.3	0.548
BMI (kg/m^2)	29.120 ± 6.5	28.209 ± 4.1	0.097
Hypertension (n, %)	157 (54 %)	134 (46 %)	**0.013**
Dyslipidemia (n, %)	149 (58.7 %)	105 (41.3 %)	**0.010**
Coronary heart disease (n, %)	197 (99 %)	193 (97 %)	0.284
Stroke (n, %)	25 (12.6 %)	17 (8.5 %)	0.253
Peripheral vascular disease (n, %)	28 (14.1 %)	23 (11.6 %)	0.549
Chronic obstructive pulmonary disease (n, %)	42 (21.1 %)	48 (24.1 %)	0.472
NYHA classification			
No heart failure	6 (3 %)	2 (1 %)	0.483
Class 1	81 (40.7 %)	87 (43.7 %)	
Class 2	103 (51.8 %)	102 (51.3 %)	
Class 3	9 (4.5 %)	7 (3.5 %)	
Class 4	0 (0 %)	1 (0.5 %)	
Ejection fraction (%)	53.2 ± 11.5	55.1 ± 11.7	0.107
EuroSCORE I	4.9 ± 4.6	5.8 ± 5.9	0.084
EuroSCORE II	1.9 ± 1.7	2.1 ± 2.1	0.353
Renal function groups			
Group 1	21 (10.6 %)	19 (9.5 %)	1.000
Group 2a	36 (18.1 %)	39 (19.6 %)	
Group 2b	74 (37.2 %)	83 (41.7 %)	
Group 3a	48 (24.1 %)	40 (20.1 %)	
Group 3b	18 (9 %)	16 (8 %)	
Pre-surgery use			
Diuretics	92 (46.2 %)	76 (38.2 %)	0.104
ACEIs/ARBs	48 (24.1 %)	38 (19.1 %)	0.223

eGFR estimated glomerular filtration rate, *BMI* body mass index, *ACEI* angiotensin-converting-enzyme inhibitor, *ARB* angiotensin II receptor blocker

(Table 5). When AKIN or KDIGO criteria were used (identical results), a trend towards increased incidence of AKI from eGFR subgroup 1 to subgroup 3a was noted in the total study population; this trend was significant in diabetic patients, starting from 14.3 % in subgroup 1 and progressively increasing to 35.4 % in subgroup 3a ($p = 0.04$), but not in non-diabetic patients. With regard to renal replacement therapy, no particular trend was noted, apart from the fact that all non-diabetic patients in need of support were classified in subgroup 3a at baseline ($p = 0.018$).

Factors associated with AKI occurrence

The univariate and multivariate regression analysis in the total study population is shown in Table 5. Diabetes was clearly not correlated with the development of AKI in our study [OR 1.057 (95 % CI: 0.666–1.679)]. CKD severity defined by the aforementioned subgroups of renal function was associated with progressively increasing risk for AKI from group 1 to group 3a at univariate, but not multivariate analysis. Older age was independently associated with AKI occurrence both at univariate and multivariate [per year

Table 2 Surgery-related parameters and postoperative complications in diabetic and non-diabetic patients

Parameters	Diabetics	Non-diabetics	p
N	199	199	–
Surgery type			
Coronary artery bypass grafting (n, %)	156 (78.4 %)	132 (66.3 %)	**0.004**
Aortic or mitral valve replacement (n, %)	25 (12.6 %)	20 (10.1 %)	
Thoracic aortic aneurysm repair (n, %)	3 (1.5 %)	10 (5 %)	
CABG and valve replacement (n, %)	12 (6 %)	17 (8.5 %)	
CABG and aneurysm repair (n, %)	0 (0 %)	6 (3 %)	
Valve replacement and aneurysm repair (n, %)	2 (1 %)	7 (3.5 %)	
CABG and valve replacement and aneurysm repair (n, %)	0 (0 %)	4 (2 %)	
Other (n, %)	1 (0.5 %)	3 (1.5 %)	
Surgery procedures			
Cardiopulmonary bypass (min)	100.3 ± 36.8	107.1 ± 45.2	0.319
Intubation (h)	10.8 ± 13.8	13.4 ± 29.7	0.263
Intra-aortic balloon pump	7 (3.5 %)	21 (10.6 %)	**0.010**
Post-Surgery complications			
Postoperative myocardial infarction	2 (1 %)	3 (1.5 %)	1.000
Atrial fibrillation	69 (34.7 %)	71 (35.7 %)	0.916
Deep sternal wound infection	5 (2.5 %)	10(5 %)	0.292
Ventilator-associated pneumonia	1 (0.5 %)	2 (1 %)	0.624
Stroke	5 (2.5 %)	3 (1.5 %)	0.253
Re-intubation	4 (2 %)	1 (0.5 %)	0.372
Days in ICU	1.7 ± 1.1	1.8 ± 1.4	0.237
Hemodynamic instability	11 (5.5 %)	14 (7.1 %)	0.544
Septicemia	2 (1 %)	2 (1 %)	1.000
Multiple organ dysfunction syndrome	5 (2.5 %)	2 (1 %)	0.449

CABG coronary artery bypass graft, *ICU* intensive care unit

increase; OR 1.034 (1.001–1.068)] analysis. Another factor independently associated with elevated odds for AKI development was the duration of cardiopulmonary bypass use [per minute increase; OR 1.009 (1.003–1.015)]. EUROSCORE II score, total intubation time and occurrence of complications postoperatively displayed also significant ORs in the univariate analysis, but failed to reach statistical significance when adjusted for other factors.

Discussion

This study aimed to examine in comparison the incidence of AKI after cardiac surgery in matched diabetic and non-diabetic patients and to evaluate possible associations with factors that may contribute to its occurrence. The study included two groups of patients (diabetic and non-diabetic), carefully matched for age, gender and baseline renal function, that underwent cardiac surgery. As the sample size was relatively high, the two groups had almost no significant differences for a large set of demographic and clinical parameters studied, with the exception of hypertension and dyslipidemia, which cluster with type 2 diabetes within the setting of the metabolic syndrome [25]. Our main finding was that the prevalence of AKI as a whole was moderately high, but there were no differences between diabetic and non-diabetic patients with all three of the definitions used. This suggests that presence of DM is not a pre-disposing factor for AKI in individuals undergoing cardiac surgery.

Incidence of AKI after a cardiac operation in the population studied was 23.6 % based on the AKIN and the KDIGO criteria and 25.4 % based on the RIFLE criteria. In the literature, earlier studies, using definitions such as: (1) ≥25 % increase in serum creatinine by the third postoperative day or initiation of hemodialysis, or (2) postoperative decrease ≥10 % in creatinine clearance calculated with the Cockroft-Gault formula suggested incidence rates between 11 and 45 % [26–28]. With the development of new definitions, more reproducible data have become available. In a cohort study of about 25,000 patients undergoing cardiac surgery, over a period of 7 years, incidence rates of AKI were 30 % using the AKIN criteria and 31 % using the RIFLE criteria [29]. A study of 4836 individuals found a

Table 3 Serum creatinine, eGFR, 24-hour urine excretion at different time points of the study and incidence of AKI during the first 48 h post-surgery in diabetic and non-diabetic patients

Parameters	Diabetics	Non-diabetics	p
N	199	199	
Pre-surgery			
Creatinine (mg/dl)	1.1 ± 0.2	1.09 ± 0.2	0.817
eGFR (ml/min/1.73 m^2)	68.3 ± 28.5	67.5 ± 16.1	0.724
Post-surgery			
Creatinine (mg/dl)	1.08 ± 0.3	1.06 ± 0.2	0.438
eGFR (ml/min/1.73 m^2)	69.1 ± 17.4	69.6 ± 16.7	0.800
After 24 h			
Creatinine (mg/dl)	1.2 ± 0.3	1.2 ± 0.3	0.925
eGFR (ml/min/1.73 m^2)	62.4 ± 18.2	62.5 ± 19.7	0.960
Urine output (ml)	3,553 ± 887.1	3,766 ± 822.6	**0.053**
After 48 h			
Creatinine (mg/dl)	1.1 ± 0.4	1.1 ± 0.3	0.207
eGFR (ml/min/1.73 m^2)	64.3 ± 20.2	67.5 ± 22.1	0.138
Urine output (ml)	2,998 ± 1083	3,296 ± 1111	**0.013**
AKI with AKIN (n, %)	48 (24.1 %)	46 (23.1 %)	0.906
AKI with RIFLE (n, %)	50 (25.1 %)	50 (25.1 %)	1.000
AKI with KDIGO (n, %)	48 (24.1 %)	46 (23.1 %)	0.906
Renal replacement therapy in ICU	7 (3.5 %)	3 (1.5 %)	0.169

AKI acute kidney injury, *AKIN* acute kidney injury network, *RIFLE* risk, injury, failure, loss and end-stage renal disease criteria, *KDIGO* kidney disease: improving global outcomes, for other abbreviations, see previous tables

Table 4 Incidence of AKI during the first 48 h post-surgery in the total study population and in diabetic and non-diabetic patients based on the baseline renal function

Parameters	Subgroups	Group 1	Group 2a	Group 2b	Group 3a	Group 3b	p
N		40	75	157	88	34	N/A
AKI with AKIN (n, %)	Total	6 (15 %)	13 (17.3 %)	37 (23.6 %)	28 (31.8 %)	9 (26.5 %)	0.151
	Diabetics	3 (14.3 %)	7 (19.4 %)	15 (20.3 %)	17 (35.4 %)	5 (27.8 %)	**0.040**
	Non-Diabetics	3 (15.8 %)	6 (15.4 %)	22 (26.5 %)	11 (27.5 %)	4 (25 %)	0.610
	P	1.000	0.643	0.358	0.427	0.855	
AKI with RIFLE (n, %)	Total	12 (30 %)	14 (12.7 %)	40 (25.5 %)	26 (29.5 %)	8 (23.5 %)	0.541
	Diabetics	6 (28.6 %)	8 (22.2 %)	17 (23 %)	15 (31.3 %)	4 (22.2 %)	0.629
	Non-Diabetics	6 (31.6 %)	6 (31.6 %)	23 (27.7 %)	11 (27.5 %)	4 (25 %)	0.737
	P	1.000	0.448	0.496	0.701	0.849	
AKI with KDIGO (n, %)	Total	6 (15 %)	13 (17.3 %)	37 (23.6 %)	28 (31.8 %)	9 (26.5 %)	0.151
	Diabetics	3 (14.3 %)	7 (19.4 %)	15 (20.3 %)	17 (35.4 %)	5 (27.8 %)	**0.040**
	Non-Diabetics	3 (15.8 %)	6 (15.4 %)	22 (26.5 %)	11 (27.5 %)	4 (25 %)	0.610
	P	1.000	0.643	0.358	0.427	0.855	
Renal replacement therapy in ICU	Total	0 (0 %)	1 (1.3 %)	5 (3.2 %)	3 (3.4 %)	1 (2.9 %)	0.729
	Diabetics	0 (0 %)	1 (2.8 %)	5 (6.8 %)	0 (0 %)	1 (5.6 %)	0.284
	Non-Diabetics	0 (0 %)	0 (0 %)	0 (0 %)	3 (7.5 %)	0 (0 %)	**0.018**
	P	N/A	0.480	**0.022**	0.090	1.000	

For abbreviations, see previous tables

significantly higher incidence of AKI as defined by the AKIN criteria (26.3 %) than the RIFLE criteria (18.9 %) [30] while another study found an AKI incidence of 25.9 % with the AKIN and KDIGO criteria and of 24.9 % with RIFLE criteria [31]. Our findings are in general agreement with the above studies [3, 5, 29–31] and further support the

Table 5 Univariate and multivariate regression analysis for occurrence of AKI defined by KDIGO criteria in the total studied population

Parameter	Univariate analysis		Multivariate analysis	
	Unadjusted odds ratio (95 % CI)	p	Adjusted odds ratio (95 % CI)	p
Gender				
Male	Reference group			
Female	1.148 (0.634–2.079)	0.649		
Age (per year increase)	1.047 (1.017–1.078)	0.002	1.034 (1.001–1.068)	0.043
BMI (per kg/m^2 increase)	1.035 (0.993–1.078)	0.108	1.027 (0.986–1.070)	0.211
eGFR groups				
Group 1	Reference group		Reference Group	
Group 2a	1.188 (0.414–3.409)	0.748	1.107 (0.370–3.314)	0.856
Group 2b	1.747 (0.681–4.486)	0.246	1.296 (0.480–3.499)	0.608
Group 3a	2.644 (1.001–7.025)	0.050	1.676 (0.579–4.855)	0.341
Group 3b	2.040 (0.643–6.474)	0.226	1.211 (0.341–4.304)	0.767
Diabetes	1.057 (0.666–1.679)	0.813		
Chronic obstructive pulmonary disease	1.242 (0.895–1.942)	0.107	1.550 (0.881–2.728)	0.125
Hypertension	1.095 (0.646–1.857)	0.735		
Dyslipidemia	1.202 (0.737–1.960)	0.460		
Coronary heart disease	0.932 (0.279–3.985)	0.897		
NYHA classification				
No heart failure	Reference group			
Class 1	0.877 (0.170–4.523)	0.875		
Class 2	0.917 (0.179–4.694)	0.917		
Class 3	1.800 (0.271–11.957)	0.543		
Class 4	n/a	n/a		
Ejection fraction (per % increase)	0.996 (0.977–1.016)	0.710		
Pre-surgery use				
Diuretics	1.019 (0.638–1.626)	0.939		
ACEIs/ARBs	1.058 (0.606–1.847)	0.844		
EuroSCORE II (per unit increase)	1.173 (1.048–1.314)	0.006	1.001 (0.863–1.161)	0.990
Cardiac surgery				
Elective	Reference group			
Urgent	0.853 (0.430–1.692)	0.650		
Emergency	2.133 (0.350–12.993)	0.411		
Cardiopulmonary bypass (per min)	1.010 (1.005–1.016)	<0.001	1.009 (1.003–1.015)	0.004
Intra-aortic balloon pump use	1.321 (0.562–3.105)	0.523		
Intubation time (per hour)	1.019 (1.003–1.034	0.017	1.008 (0.996–1.020)	0.192
Post-surgery complications	2.093 (1.310–3.343)	0.002	1.503 (0.897-2.520)	0.122

For all abbreviations, see previous tables

significance of AKI as one of the most frequent postoperative complications in cardiac surgery, despite the development of predictive indices to identify high risk patients and the evolvement of a few protecting procedures, among various tried and showed to be ineffective [32].

The role of DM as a risk factor for AKI has not been conclusively determined. In non cardiac surgery settings, such as in 936 patients undergoing elective percutaneous coronary angioplasty, diabetes was a significant factor for AKI [33]. However, in a systematic review evaluating occurrence of AKI in patients undergoing transcatheter aortic valve implantation, DM was found as an independent predictor in 2 of the total 13 studies included [34]. Further, a meta-analysis including more than 1.2 million participants with general population characteristics and 80,000 CKD patients suggested that not the presence of DM *per se* but rather the presence of diabetic kidney injury (i.e. increased urine albumin excretion and particularly proteinuric diabetic nephropathy) were associated with increased occurrence of AKI [35]. The role of DM as a risk factor for renal function deterioration after cardiac surgery is much less studied. In a cohort study of 3219 patients who underwent cardiac surgery with cardiopulmonary bypass in a single center, DM was an independent predictor for AKI [OR 2.035 (1.172–3.534)], defined by the AKIN criteria [1]. Similarly, in a cohort of 995 patients DM was independently correlated with increased AKI incidence [OR 2.080 (1.080–4.040)] [3] defined as 50 % in eGFR. However, the use of suboptimal definitions for AKI may have affected these results. In contrast, in a retrospectively assembled cohort of 2488 patients, prevalence of diabetes was similar in patients with or without cardiac surgery-associated AKI defined by the RIFLE criteria and, thus, diabetes was not an independent predictor of AKI [5]. Similar were the findings in a multivariate analysis of a study in 267 patients undergoing aortic arch surgery [22]. Our study further clarifies this issue, as we found no significant differences between diabetic and non-diabetic patients, in the overall study population and when compared in subgroups based on preoperative renal function, in the incidence of AKI and need for renal replacement therapy in the ICU. Moreover, the uni- and multivariate logistic regression analysis performed did not indicate significant associations between DM and occurrence of AKI in the whole population studied.

Occurrence of post-surgery AKI and requirement of renal replacement therapy are considered established complications of CKD in the literature, possibly due to the impaired autoregulatory response of the kidneys [14]. Results from a cohort study including 964 patients with mean baseline eGFR 54 ml/min/1.73 m^2 indicated an increasing risk for AKI and hemodialysis initiation with the progression of CKD from stage 1 towards stage 5; 7 % of the total population required renal replacement therapy and this rate was 75 % for patients at stage 5 [17]. Another observational study concluded that lower pre-operative eGFR values can independently predict the development of AKI defined by the AKIN and the RIFLE criteria [19]. In our study, progressive decline of renal function from CKD stage 1 to stage 3a was associated with higher post-surgery incidence of AKI with the AKIN and KDIGO definitions in both diabetic and non-diabetic patients. Regarding the results from the regression analysis, an interesting trend was noted with OR values gradually increasing from renal subgroup 1 towards 3a and slightly falling in subgroup 3b. With regard to other factors affecting incidence of AKI, an independent correlation with age was found, as noted in other observational studies [1, 5, 13]. Duration of cardiopulmonary bypass was also independently related to AKI development. Cardiopulmonary bypass during cardiac operations is believed to cause AKI through renal ischemia and reperfusion and it has been suggested that off-pump surgery, when indicated, may decrease this risk [15]. In most observational studies in the field, the mean time for cardiopulmonary bypass was significantly longer in those with AKI postoperatively [5, 30]. Results from a multicenter cohort study of 3500 patients indicated that for every 15-min increase of bypass time patients had an 11 % increased risk for AKI [14].

This study has strengths and limitations. Firstly, a direct comparison of carefully matched individuals was used to evaluate post cardiac surgery incidence of AKI in diabetic and non-diabetic patients with CKD. Secondly, as data from different studies are ambiguous, we examined AKI incidence using all three contemporary definitions of AKI. Lastly, our study included information on most of the possible factors affecting AKI incidence in the setting of cardiac surgery, following rigorous prospective recordings. However, this is still an observational study, and definite cause and effect associations cannot be established. The patients were not matched for type of surgery and this may have slightly affected the results, although almost all of many relevant factors (including target organ damage, EuroSCORE, cardiopulmonary bypass and intubation times) did not differ between groups. Lastly, the follow-up period was up to 48 h post-surgery, when all relevant data were routinely recorded for all patients.

In conclusion, this study shows that incidence of AKI after cardiac surgery remains relatively high, but diabetes mellitus does not constitute a separate risk factor for AKI development. This is in contrast to other settings, such as in patients undergoing percutaneous coronary angioplasty where DM increases the incidence of AKI significantly, possibly due to contrast-induced nephropathy. Among patients with DM, baseline renal function is the main parameter related inversely to the incidence of AKI. Age and cardiopulmonary bypass time are factors associated with AKI development in all patients. Thus, these are the factors that should be mainly considered when it comes to planning adequate measures for AKI prevention.

Sources of support This paper was not supported by any source and represents an original effort of the authors.

Compliance with ethical standards

Conflict of interest All authors disclose that they do not have any conflict of interest.

Ethical approval This is a retrospective study of patients' routinely recorded data, approved by the Institutional Ethical Committee.

Informed consent All study participants provided an informed consent for the use of their personal medical records.

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