Our viewpoint on the impact and outcome that risk factors have on acute kidney injury of the postoperative cardiac surgical patient

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Abstract

Aim: Cardiac surgery interventions can often be associated with complications. One of the most important of them is postoperative acute kidney injury (AKI) that can significantly contribute in a higher postoperative morbidity and mortality. The risk and prevention of acute kidney injury (AKI) following cardiac surgical interventions is less well understood and still remains a challenge. By conducting the study, we evaluated the factors that may predispose the appearance of AKI in terms of cardiac surgery.
Methods: The study was based on the recorded clinical and demographic data of 72 adult patients (age ≥ 18 years) who underwent coronary artery bypass graft (CABG) surgery and valve surgery (with or without concomitant CABG) at the Hygeia Hospital Tirana, Albania, in cardiac surgery department during September 2011 – May 2012. According to RIFLE/AKIN classifications, risk factors such as patient's condition, lowest mean arterial pressure during intervention, aortic clamp time, bypass time, intubation total time and hemorrhage and creatinine levels were studied during the first five postoperative days.
Results: 72 patients were included in the study. Mean age was 61.3±9.7 years; 76.4% were men and 23.6% were women. About 78% were intervened of cardiopulmonary bypass, 11% underwent valvular replacement surgeries and 7% combined surgeries. Around 14% of patients developed signs of AKI within the fifth postoperative day. Pre, intra- and postoperative risk factors for acute renal failure were evaluated. By studying the variables' correlation with AKI, we found a highly significant association (P<0.001) for values like total intubation time and ICU (intensive care unit) stay time as well as mean value of urea and creatinine within five days. A less significant association was found with lactate values taken 24 hours after cardiac interventions (P=0.05).
Conclusion: In patients that undergo surgical procedures in cardiac surgery, the postoperative renal function tests, as well as intubated and ICU time, play a very important role in development of the postoperative AKI. Reducing these factors to their lowest limits, can directly help in minimizing the postoperative development of AKI and will surely reduce the treatment costs of the postoperative patient. Quality improvement strategies should be incorporated at all institutions in order to identify and track quality indicators relevant to the prevention of postoperative renal dysfunction during the index admission for cardiac surgery. Once identified, clinicians can implement preventative measures for high-risk patients.

Keywords: cardiopulmonary bypass, kidney, postoperative acute renal injury, risk factors.

Introduction

Cardiac surgery interventions can often be associated with complications. One of the most important of them is postoperative acute kidney injury (AKI) that can significantly contribute in a higher postoperative morbidity and mortality. Physicians strive to provide optimal care for their patients by first performing a thorough evaluation of all organ systems. In the perioperative period, a preventive therapy can be instituted according to patient's risk. Many studies have focused on the risk and prevention of perioperative and postoperative cardiac events (1-5). The risk and prevention of acute kidney injury (AKI) following cardiac surgical interventions is less well understood and still remains a challenge. By conducting the study, we evaluated the factors that may predispose the appearance of AKI in terms of cardiac surgery.

Definition of Perioperative AKI

Until recently, the definition of AKI was not standardized. Authors have used terms such as renal insufficiency, renal dysfunction, acute renal failure (ARF), and renal failure requiring dialysis somewhat interchangeably. The system RIFLE criteria of the Acute Dialysis Quality Initiative consist of a worsening function progressing from Risk to Injury to Failure to Loss to End-Stage Renal Failure (6). More recently, the Acute Kidney Injury Network (AKIN), a consensus panel involving national and international societies in nephrology and critical care, proposed standard defnitions of AKI, and graded the severity of kidney injury into three stages (7). These criteria define AKI as an increase in serum creatinine level by 0.3 mg/dL (or 1.5 times) relative to baseline. Subsequently, the severity is divided into three stages based on the degree of

Table 1. Definitions of Acute Kidney Injury *(Adapted from Crit Care 2007;11:R317)*

Acute Kidney Injury Network Criteria			RIFLE Criteria		
	Creatinine/ GFR	**Urine Output**		**Creatinine/ GFR**	**Urine Output**
Stage 1	Increased Cr 0.3mg/dL Or Cr 150%	UOP<0.5 mL/kg/h for>6h	Risk (R)	Increased Cr 1.5 or GFR Decreased <25%	UOP <0.5mL/kg/h for >6h
Stage 2	Baseline Cr 200%-300%	UOP<0.5 mL/kg/h for >12h	Injury (I)	Increased Cr 2 or GFR Decreased <50%	UOP <0.5mL/kg/h for >12h
Stage 3	Baseline Cr >300% of baseline or >4mg/dL with 0.5mg/dL acute Increase	UOP<0.3 mL/kg/h for 24 h or Anuria for 12h	Failure (F)	Increased Cr 3 or GFR Decreased <75% or Cr >4mg/dL with 0.5mg/dL	UOP <0.3mL/kg/h for 24h or Anuria for 12 h

creatinine elevation (stage I: 1.5 to 2 times increase; II: >2 to 3 times increase; and III: >3 times increase, new requirement of dialysis, or an acute increase ARF indicates acute renal failure; Cr, chromium; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; UOP, urine output:

absolute creatinine value of >4 mg/dL with at least a 0.5 mg/ dL increment). There are caveats to these criteria, in that they await broader validation across all patient care settings. However, it allows a streamlined approach in recognition of the disease, clinical research, as well as future delivery of care. Given the wide range of definitions previously used in the literature, for the purposes of this article we will not be able to specifically group kidney injury by current definitions. The rate of perioperative AKI is difûcult to know precisely as it is dependent on definitions used and type of surgery studied. In cardiac surgery, rates of kidney injury range between 7.7% and 11.4% (8-10).

Materials and methods

The study was based on the recorded clinical and demographic data of 72 adult patients (age≥18 years) who underwent coronary artery bypass graft (CABG) surgery and valve surgery (with or without concomitant CABG) at the Hygeia Hospital Tirana, Albania, in cardiac surgery department during September 2011 – May 2012. According to RIFLE/ AKIN classifications, risk factors as patient's condition, lowest mean arterial pressure during intervention, aortic clamp time, bypass time, intubation total time and hemorrhage and creatinine levels were studied during the five first postoperative days. The Cockroft-Gault formula was used to estimate preoperative creatinine clearance (11).

Patients on dialysis in the moment of intervention, those with intra aortic balloon pump and off pump surgeries (OPCABG) were excluded from the study. All queries were resolved by reference to the patients' original records.

This study was approved by the Committee of Medical Ethics.

Operation and CABG

All surgeries were performed through a midline sternotomy with the use of cardiopoulmonary bypass (CPB). CPB was instituted using standard techniques with cannulation of the right atrium with the proper number of cavoatrial venous cannula and the ascending aorta with recpective aortic cannula. A membrane oxygenator (Medtronic Trillium Affinity™) and roller pump (Stöckert S-4, Stöckert Instrument GmbH, Munich, Germany) was used in all patients. The circuit was primed with Lactated Ringer solution (RL) 500 ml, Voluven by Fresenius Kabi 500 ml, Mannitol 25g and 10,000 units of heparin. Permissive hypothermia was allowed, temperature was measured with a rectal probe and maintained at >33°C. Heparin (400 units/kg) was given prior to cannulation. Activated clotting time was maintained at ≥480 seconds during the procedure. Nonpulsatile pump flow rates were kept at 2.4 L/min/m^2 and the mean arterial pressure (MAP) was adjusted to keep the surgical field bloodless and to avoid severe hypotension <50 mmHg. In general the targeted MAP was 60 mmHg. To maintain the filling volume of the extracorporeal circuit, colloids (Voluven) and Ringer's Lactate solution were added. When the hemoglobin was less than 7mg/ dL, packed red blood cells were transfused. Blood cardioplegia with modified Buckberg solution at a ratio of 4:1 with high potassium (20mmol/L) at induction, and at a ratio of 16:1 with low potassium (8mmol/L) for maintenance was used for myocardial protection. Cardioplegic solution was delivered in an antegrade fashion via the aortic root or by direct cannulation of the coronary ostia. Heparin was reversed with protamine following decannulation.

Standard anesthesia monitoring included, ECG x 5 leads, SpO2, invasive blood pressure (IBP) and central venous pressure (CVP) measuring and in some cases thermodilution pulmonary artery catheters (Baxter Healthcare Corp, Santa Ana, USA) to measure cardiac index (CI), and in in some cases pulmonary artery. Anesthesia consisted of intravenous drugs as Benzodiazepines, Fentanyl, Propofol and short acting miorelaxants. All surgical procedures were performed using the median sternotomy. After the surgery, all patients were transferred to the cardiovascular surgical intensive care unit ICU and extubated from mechanical ventilation according to standard weaning protocols. All fluid, inotropes, hemodynamics and lab values including creatinine were recorded for five days post-operatively.

Statistical analysis

Pre-operative clinical variables, procedural details, and laboratory test results, including creatinine, were obtained from electronic medical records and cardiovascular surgery charts. Those variables are presented as means ± one standard deviation, or as percentages. Continuous variables were compared with *t*-test when normally distributed and non-parametric Mann–Whitney *U* test when skewed. Multivariable logistic regression modeling was also performed to assess the adjusted associations of measured perioperative variables with the three thresholds of AKI. Initially, bivariate analyses (using the statistic for categorical variables and the *t*- test or Wilcoxon rank sum test for continuous variables) were performed to identify which variables were associated with the dependent variables. The mathematical relationships between the continuous predictor variables and AKI were assessed with cubic spline functions (12,13). Variables that were not linearly related were either mathematically transformed, categorized along clinically sensible cut points, or converted into multiple dichotomous variables (14). The variables with $P<0.1$ in univariate analysis and variables that are known to be associated with AKI were included in the multivariable model. Data analyses were performed using SPSS statistical software, version 16.0. All analyses were two-sided. $P<0.05$ was considered statistically significant.

Table 2. Coefficients*

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
Model	**B**	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**
(Constant)	-0.103	0.849		-0.122	0.904	-1.823	1.616
TypeSurgery	-0.007	0.124	-0.008	-0.059	0.954	-0.259	0.244
TotalTimeop	0.118	0.041	0.436	2.89	0.006	0.035	0.2
Age	0.001	0.006	0.027	0.185	0.855	-0.012	0.014
Gender	-0.073	0.154	-0.078	-0.474	0.638	-0.386	0.24
BSA	0.353	0.323	0.189	1.095	0.281	-0.301	1.008
Grafts	0.019	0.048	0.065	0.405	0.688	-0.078	0.117
DM	-0.122	0.077	-0.244	-1.585	0.122	-0.278	0.034

* Dependent Variable: AKI calculated by Linear regression / Confidence Interval / Durbin – Watson & Model Fit.

Results

72 patients were included in the study. The mean age was 61.3±9.7 years; 76.4% were men and 23.6% were women. 77.8% were intervened of cardio-pulmonary bypass, 11.1% underwent valvular replacement surgeries and 6.9% combined surgeries (Table 3). 13.9% of patients developed signs of AKI within the fifth postoperative day. Pre, intra-and postoperative risk factors for acute renal failure were evaluated (Table 4). By studying the variables' correlation with AKI, we found a very significant association (P<0.001) for values like total intubation time and ICU (intensive care unit) stay time as well as mean value of urea and creatinine within five days. A less significant association was found with lactate values taken 24 hours after cardiac interventions (P=0.05).

Table 3. Surgery types

		Frequency	Percent
Valid	CABG	56	77.8
	Valve	8	11.1
	Combined system	5	6.9
Missing		3	4.2
Total		72	100.0

Table 4. Incidence of AKI in the overall group of patients

		Frequency	Percent
Valid	non AKI	37	51.4
	AKI	10	13.9
	Total	47	65.3
Total		72	100.0

Table 5. Bivariate correlations of risk factors and AKI

		AKI
AKI	Pearson Correlation	1
	Sig. (2-tailed)	
	N	47
ICU hr	Pearson Correlation	.404**
	Sig. (2-tailed)	0.005*
	N	47
Intubated (hr)	Pearson Correlation	.384**
	Sig. (2-tailed)	0.008*
	N	47
Mean CK of 5 days	Pearson Correlation	.477**
	Sig. (2-tailed)	0.003
	N	37
Mean BUN of 5 days	Pearson Correlation	.663**
	Sig. (2-tailed)	0
	N	42
Mean Scr of 5 days	Pearson Correlation	.839**
	Sig. (2-tailed)	0
	N	42

** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed)

Discussion

Patient-specific risk for severe renal insufficiency can be predicted before undergoing CABG surgery for patients with normal or near-normal renal function. We identified preoperative patient and disease characteristics most predictive of a patient before CABG surgery at risk of developing severe renal insufficiency after the procedure. In our study, the AKI resulted strongly associated to the above factors as presented in Table 5. For values of $P<0.05$, the longer the time length of CPB, the more are the patient's possibilities to develop AKI. We found comparable results to our findings with other similar studies (15). Studies indicate that longer CPB and cross-clamp times are with an increased incidence of AKI. A safe time cutoff has not been determined (16). Nevertheless, prolonged cardiopulmonary bypass and aortic cross-clamp times are relatively well-accepted as being linked to increased postoperative AKI, although this finding has not been present in all studies (17). That can be due to the heterogeneous patient populations, no specific time frame been established after which the risk of AKI increases. Additionally, although prolonged bypass times may play a role in postoperative AKI, it is likely a combination of all of the previously mentioned factors that will decide each individual patient's propensity for postoperative renal dysfunction (18). Our model extends this analysis by using estimated Scr of the first post operation week of stay, too. Other models have been found in other geographic areas and validated across other institutions (19). Janssen et al used a combined outcome for predicting renal dysfunction after CABG surgery (20). They identified similar preoperative risk factors to our model: age≥75, diabetes, and hypertension (21). Nally and colleagues have identified several prevention strategies to help reduce the occurrence of renal insufficiency after CABG surgery (22).

However, this model should be validated by another national or regional registry to confirm these preoperative risk factors among patients with normal or near-normal renal function are predictive of developing severe renal insufficiency after CABG surgery.

Conclusion

In patients that undergo surgical procedures in cardiac surgery, the postoperative renal function tests, as well as intubated and ICU time, play a very important role in developing of the postoperative AKI. Reducing these factors to their lowest limits, can directly help in minimizing the postoperative development of AKI and will surely reduce the treatment costs of the postoperative patient. Quality improvement strategies should be incorporated at all institutions in order to identify and track quality indicators relevant to the prevention of postoperative renal dysfunction during the index admission for cardiac surgery. Severe renal insufficiency is a serious consequence to cardiac surgery, even among patients with normal preoperative renal function. A prediction card can be developed and used to risk stratify patients for developing severe renal insufficiency. Once identified, clinicians can implement preventative measures for high-risk patients.

Conflicts of interest: None declared.

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