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Incidence, risk factors, and outcomes of perioperative acute kidney injury in noncardiac and nonvascular surgery

Murat Biteker, M.D.[a,*], Akın Dayan, M.D.[b], Ahmet İlker Tekkeşin, M.D.[c], Mehmet M. Can, M.D.[d], İbrahim Taycı, M.D.[e], Erkan İlhan, M.D.[f], Gülizar Şahin, M.D.[g]

[a]Medipol University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey; [b]Department of Family Medicine, Haydarpaşa Numune Education and Research Hospital, Istanbul, Turkey; [c]Department of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Research and Training Hospital, Istanbul, Turkey; [d]Department of Cardiology, Bagcılar Education and Research Hospital, Istanbul, Turkey; [e]Department of Internal Medicine, Haydarpaşa Numune Education and Research Hospital, Istanbul, Turkey; [f]Department of Cardiology, Van Erciş State Hospital, Van, Turkey; [g]Department of Nephrology, Haydarpaşa Numune Education and Research Hospital, Istanbul, Turkey

KEYWORDS:
Perioperative acute kidney injury;
Noncardiac surgery;
Outcome

Abstract

BACKGROUND: The aim of this study was to determine the incidence rate, identify the risk factors, and describe the clinical outcome of perioperative acute kidney injury (AKI) in patients undergoing noncardiac, nonvascular surgery (NCS).

METHODS: A total of 1,200 adult consecutive patients undergoing NCS were prospectively evaluated. Patients with pre-existing renal dysfunction were excluded. The primary outcome of this study was perioperative AKI defined by the RIFLE (risk, injury, failure, loss of function, and end-stage kidney disease) criteria.

RESULTS: Eighty-one patients (6.7%) met the AKI criteria. Multivariate analysis identified age, diabetes, revised cardiac risk index, and American Society of Anesthesiologists physical status as independent predictors of AKI. Patients with AKI had more cardiovascular (33.3% vs 11.3%, $P < .001$) complications and a higher in-hospital mortality rate (6.1% vs 0.9%, $P = .003$) compared with patients without AKI.

CONCLUSIONS: Several preoperative predictors are found to be associated with AKI after NCS. Perioperative AKI is an independent risk factor for outcome after NCS.

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Perioperative acute renal failure remains a leading cause of morbidity and mortality in patients undergoing surgery.[1–4] The incidence varies between 1% and 36% depending on the type of surgery and the definition of renal failure.[5–9] Most of the previous studies used the term acute renal failure, which is a nonspecific description of an acute decrease in renal function, and they considered patients to have acute kidney injury (AKI) only when a deterioration in renal function requiring postoperative dialysis was documented. However, AKI has now replaced the term acute renal failure. To address the lack of a universal definition for AKI, a collaborative network of international experts established the Acute Dialysis Quality Initiative and devised the

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* Corresponding author. Tel.: +90-216-414-4502; fax: +90-216-336-0565.

E-mail address: murbit2@yahoo.com

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RIFLE (risk, injury, failure, loss of function, and end-stage kidney disease) definition and staging system for AKI.[10] Although it has been shown that there is an AKI risk associated with noncardiac and nonvascular surgeries, relatively few data are available regarding the incidence, risk factors, and effect on the outcome of perioperative AKI for these surgeries.[11–13] Therefore, we aimed to determine the incidence, risk factors, and outcome of perioperative AKI using the RIFLE criteria in patients with previously normal renal function undergoing noncardiac, nonvascular surgery.

Methods

Study population

The study population consisted of 1,200 consecutive patients older than 18 years who underwent noncardiothoracic, nonvascular surgery between January 2010 and February 2012 at Haydarpaşa Numune Education and Research Hospital, which is a tertiary medical center in Istanbul, Turkey. Written informed consent was obtained from each patient before entry into the study. We received study approval from our local institutional review board. The following variables were recorded on admission: age, sex, body mass index, preoperative medications, American Society of Anesthesiologists (ASA) physical status,[14] and comorbidities. The Revised Cardiac Risk Index (RCRI) was used for the prediction of cardiac risk based on 6 prognostic factors: high-risk type of surgery (defined as intraperitoneal, intrathoracic, or suprainguinal vascular procedures), ischemic heart disease, congestive heart failure, history of cerebrovascular disease, insulin therapy for diabetes, and preoperative serum creatinine >2.0 mg/dL.[15] One point was assigned for each of the prognostic factors. Anesthetic management, monitoring, and other aspects of perioperative management were at the discretion of the attending physician. Electrocardiography (12-lead) and cardiac biomarkers (creatine kinase-MB and troponin I) were evaluated 1 day before surgery; immediately after surgery; and on postoperative days 1, 3, and 7. All serum creatinine measurements were performed preoperatively, daily for 7 days after surgery, and on request thereafter. Standard transthoracic echocardiography was performed in all patients using the Vivid Three System (Vivid 3 pro; GE Vingmed, Milwaukee, WI) before surgery. Left ventricle ejection fraction was measured using the modified Simpson rule.

Standard, 2-dimensional M-mode and Doppler echocardiographic measurements were obtained in all patients. Patients presenting for surgery requiring only local anesthesia or monitored anesthesia care and day case surgical procedures were excluded. Emergent surgical cases, patients with an ASA classification of 5 (moribund, not expected to live 24 hours irrespective of operation), and patients with pre-existing renal dysfunction (serum creatinine level greater than 1.6 mg/dL for men and greater than 1.4 mg/dL for women or preoperative dialysis-dependent renal failure) were also excluded. Vascular and intrathoracic surgery is not performed in our institution. In our study patients, major gastrointestinal surgery (laparotomy, advanced bowel surgery, and gastric surgery), major gynecologic cancer surgery (abdominal hysterectomy and oophorectomy for cancer), major open or transurethral urologic surgery (cystectomy, radical nephrectomy, and total prostatectomy), head and neck surgery, and hip or knee arthroplasty were included. Cardiac risk assessment, preoperative preparation, drug therapy, and postoperative follow-up were completed according to current American College of Cardiology/American Heart Association guidelines.[16] Patients were followed up by the study team until discharge after surgery. Preoperative risk factors and laboratory test results were measured and evaluated for their association with the occurrence of in-hospital perioperative adverse events and AKI. All pre- and postoperative complications were systematically registered and classified during the study period.

Definition of outcomes

The primary outcome of this study was perioperative AKI defined by the RIFLE criteria using the maximal change in serum creatinine and estimated glomerular filtration rate during the first 7 postoperative days compared with baseline values before surgery.[10] The glomerular filtration rate was estimated by using the Chronic Kidney Disease Epidemiology Collaboration formula.[17]

Secondary outcome measures included the postoperative length of stay in the hospital, perioperative cardiovascular and noncardiovascular events, acute ischemic stroke, and mortality. To assess the effect of perioperative AKI on the length of stay, the mean length of stay was calculated for patients without complications and for those experiencing AKI. The perioperative cardiovascular events were defined as the occurrence of severe arrhythmias requiring treatment, acute heart failure, acute coronary syndrome (nonfatal acute myocardial infarction or unstable angina), pulmonary thromboembolism, nonfatal cardiac arrest, and arterial thromboembolism. Perioperative myocardial infarction was defined according to the universal definition of myocardial infarction.[18] Arterial thromboembolic events were defined as any symptomatic systemic embolism except cardioembolic stroke confirmed by arteriography, magnetic resonance angiography, spiral computed tomography imaging, or Doppler studies.

Noncardiovascular complications were lobar pneumonia confirmed by a chest radiograph and requiring antibiotic therapy, respiratory failure requiring intubation for more than 2 days or reintubation, wound infection, bacteremia, and major and minor bleeding. Major bleeding was defined as fatal or life threatening, bleeding at a critical location (retroperitoneal, intracranial, intraocular, or intraspinal), the necessity of acute medical diagnostic procedures or

medical intervention or repeat surgery, or the administration of at least of 2 U packed red blood cells. Minor bleeding was defined as all other reported bleeding events not meeting criteria for a major bleed that did not require hospital admission or transfusion. Acute ischemic stroke was defined as rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of a vascular origin.[19] A focal disturbance lasting less than 24 hours was classified as a transient ischemic attack and was excluded from the study. Cases of in-hospital mortality because of cardiac or noncardiac causes were also recorded.

Statistical analysis

Data were analyzed using SPSS for Windows (version 15; SPSS Inc, Chicago, IL). The continuous variables were expressed as mean ± standard deviation and were compared between groups by using the 2-tailed Student *t* test. Nonparametric tests were also used when necessary (Mann-Whitney *U* test). The Fisher exact (chi-square) test was used to compare categoric variables. Statistical differences among groups were tested by using 1-way analysis of variance and Kruskal-Wallis tests for parametric and nonparametric variables, respectively. Kaplan-Meier methods were used to estimate the rates of death and cardiovascular and noncardiovascular complications after surgery. Univariate and multivariate logistic regression analyses were applied to determine crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between AKI and adverse events. For all analyses, $P < .05$ was considered statistically significant.

Results

Of the 1,200 patients (mean age 65.7±13.9 years) who underwent noncardiac surgery, 81 patients (6.7%) experienced the primary outcome of AKI. The baseline clinical and demographic characteristics are summarized in Table 1, and the perioperative characteristics are presented in Table 2 in patients with and without AKI. The 2 groups were comparable in terms of sex, tobacco use, body mass index, chronic obstructive pulmonary disease, history of cerebrovascular disease, and type of surgical procedure.

Predictors of acute kidney injury

Patients with AKI were older (72.8 ± 11.3 vs 65.2 ± 13.9 years, $P < .001$); had diabetes (58% vs 23.1, $P < .001$), heart failure (38.2% vs 9%, $P < .001$), hypertension (71.6% vs 54.4%, $P < .001$), atrial fibrillation (30.9% vs 12.2%, $P < .001$), and coronary artery disease (45.6% vs 25.2%, $P < .001$) more frequently; and had higher ASA and RCRI scores. Patients who had perioperative AKI had higher values of C-reactive protein but lower levels of albumin and hemoglobin at presentation. Univariate analysis showed a significant association between age, diabetes, coronary artery disease, atrial fibrillation, hypertension, heart failure, ASA status, RCRI, hemoglobin, albumin, left ventricle ejection fraction, and perioperative AKI (Table 3). On multivariate logistic regression analysis, age (OR = 1.14; 95% CI, 1.11 to 1.37; $P = .004$), diabetes mellitus (OR = 1.53; 95% CI, 1.19 to 3.46; $P < .001$), RCRI (OR = 1.58; 95% CI, 0.75 to 4.22; $P = .032$), and ASA physical status (OR = 1.69; 95% CI, 0.99 to 2.86; $P = .047$) remained as independent predictors of AKI.

Effect of acute kidney injury on secondary outcomes

The distribution of in-hospital perioperative adverse events and postoperative length of stay data is summarized in Table 4 in patients with and without AKI. The postoperative length of stay was significantly prolonged in patients who experienced postoperative AKI (10.3 ± 9.2 vs 8.1 ± 7.6 days, $P < .001$). The most common cardiovascular complications were acute coronary syndrome, acute heart failure, and arrhythmia, and the most common noncardiac complications were minor bleeding, wound infection, and lobar pneumonia. Cardiovascular complications occurred in 27 patients (33.3%) with AKI and in 127 patients (11.3%) without this complication ($P < .001$) (Fig. 1A). Noncardiovascular complications occurred in 29 patients (35.8%) with AKI and 270 patients (24.1%) without AKI ($P = .435$). Although the overall noncardiovascular complication rates were similar in the 2 groups, Kaplan-Meier analysis showed that the rate of noncardiovascular complications was similar in the 2 groups during the first 2 weeks after surgery (22.2% vs 20.3%, $P = .456$), but thereafter the rate of noncardiovascular complications was higher in patients with AKI (13.6% vs 3.8%, $P < .001$) (Fig. 1B). Patients with perioperative AKI had a greater incidence of in-hospital mortality (6.1% vs 0.9%, $P = .003$) (Fig. 1C) but a similar incidence of stroke (2.5% vs 1.7%, $P = .351$) compared with those who never developed AKI. After the adjustment for age, sex, comorbidities, and clinical risk indicators, perioperative AKI remained as a significant predictor for cardiovascular adverse events (OR = 3.56; 95% CI, 1.13 to 8.52, $P < .001$) and mortality (OR = 3.83; 95% CI, 1.09 to 13.40; $P = .036$). Perioperative AKI was not a predictor of noncardiovascular complications within the first 2-week period of surgery, but it was an independent predictor of noncardiovascular complications after the first 2 weeks of surgery (OR = 1.83; 95% CI, 1.09 to 3.46; $P = .036$).

Comments

In this single-center, prospective study of consecutive patients with preoperative normal renal function who underwent noncardiac and nonvascular surgery, we found that

Table 1 Baseline clinical and demographic characteristics

	All patients (N = 1,200)	AKI (+) (n = 81)	AKI (−) (n = 1,119)	*P* value
Demographics				
Age	65.75 ± 13.90	72.78 ± 11.31	65.24 ± 13.93	<.001
Male	634 (52.8)	45 (55.5)	589 (52.6)	.611
Body mass index	28.22 ± 11.39	27.28 ± 3.60	28.29 ± 11.75	.874
Medical history				
Current smoking	145 (12.1)	10 (12.3)	135 (12)	.544
Diabetes mellitus	306 (25.5)	47 (58)	259 (23.1)	<.001
Hypertension	667 (55.6)	58 (71.6)	609 (54.4)	<.001
Atrial fibrillation	162 (13.5)	25 (30.9)	137 (12.2)	<.001
Hyperlipidemia	440 (36.7)	33 (40.7)	407 (36.4)	.423
Heart failure	130 (10.8)	31 (38.2)	99 (9)	<.001
Coronary artery disease	320 (26.7)	37 (45.6)	283 (25.2)	<.001
History of cerebrovascular disease	89 (7.4)	7 (9)	82 (7.3)	.663
Chronic obstructive pulmonary disease	139 (11.6)	10 (12)	129 (11.5)	.824
Malignancy	199 (16.6)	12 (14.8)	187 (16.7)	.758
NYHA functional class				
1	741 (61.8)	48 (59.2)	705 (63)	.326
2	423 (35.3)	29 (35.8)	384 (34.3)	
3	36 (3)	4 (4.9)	30 (2.6)	
4				
Revised cardiac risk index				
0	160 (13.3)	3 (3.7)	157 (14)	<.001
1	542 (45.2)	17 (20)	525 (46.9)	
2	339 (28.3)	22 (27)	317 (28.3)	
3	145 (12.1)	36 (44.4)	109 (9.7)	
4	14 (1.2)	3 (3.7)	11 (1)	
ASA status				
ASA I	188 (17.5)	2 (2.4)	186 (16.6)	<.001
ASA II	600 (50)	35 (43.2)	575 (51.3)	
ASA III	296 (24.7)	30 (37)	266 (23.7)	
ASA IV	97 (8.1)	14 (17.3)	83 (7.4)	
Laboratory				
C-reactive protein (mg/dL)	1.96 ± 3.38	2.08 ± 2.86	1.95 ± 3.41	.003
Mean platelet volume (fL)	8.80 ± 5.56	8.52 ± 1.08	8.81 ± 5.75	.734
Hemoglobin (g/dL)	12.38 ± 1.86	11.87 ± 2.03	12.41 ± 1.85	.007
White blood count ($\times 10^3$cells/mL)	8.55 ± 4.84	8.67 ± 3.09	8.54 ± 4.94	.304
Fasting glucose (mg/dL)	108.87 ± 38.3	108.32 ± 38.88	108.49 ± 37.90	.228
Creatinine (mg/dL)	1.22 ± 1.36	1.21 ± 1.33	1.22 ± 1.39	.329
Albumin (g/dL)	3.82 ± 0.59	3.69 ± 0.59	3.83 ± 0.59	.018
Left ventricle ejection fraction	58.52 ± 8.75	49.77 ± 13	59.15 ± 8.05	<.001

Values are given as mean ± standard deviation or number (percentage) unless otherwise indicated.
AKI = Acute kidney injury; ASA = American Society of Anesthesiologists; NYHA = New York Heart Association.

the incidence of perioperative AKI was 6.7%. Age, diabetes mellitus, RCRI, and ASA physical status independently predicted AKI. Perioperative AKI was strongly and independently associated with perioperative outcomes, postoperative length of stay, and in-hospital mortality. Previous clinical studies have largely investigated risk factors and outcomes of acute renal failure occurring during the perioperative period in cardiac and vascular surgery, with rates up to 40% depending on how it is defined.[20–23] Most of these studies defined acute renal failure as the deterioration of renal function sufficient to require dialysis and focused on patients without pre-existing renal insufficiency. However, data regarding AKI in a noncardiovascular surgery population are very limited. Kheterpal et al[24] investigated the incidence and risk factors for postoperative acute renal failure after major noncardiac surgery among patients with previously normal renal function. They evaluated adult patients in a prospective, observational, and single-center study

Table 2 Perioperative characteristics

	All patients (N = 1,200)	AKI (+) (n = 81)	AKI (−) (n = 1,119)	*P* value
Type of surgery, n (%)				
General	510 (42.5)	36 (44.4)	474 (42.3)	.436
Urologic	237 (19.8)	10 (12.3)	227 (20.2)	
Plastics	66 (5.5)	3 (3.7)	63 (5.6)	
Gynecologic	59 (4.9)	6 (7.4)	54 (4.8)	
Orthopedic	281 (23.4)	22 (27)	259 (23.1)	
Neurologic	32 (2.7)	2 (2.4)	30 (2.7)	
Ear/nose/throat	14 (1.2)	2 (2.4)	12 (1)	
Preoperative medications, n (%)				
Angiotensin-converting enzyme inhibitor	384 (32)	31 (38.2)	353 (31.5)	.219
Beta-blocker	276 (23)	26 (32)	352 (31.4)	.386
Statin	116 (9.7)	9 (11.1)	109 (9.6)	.447
Aspirin	308 (25.7)	25 (30.8)	283 (25.2)	.292
Calcium inhibitor	176 (14.7)	16 (19.7)	160 (14.2)	.192
Diuretics	77 (6.4)	5 (6.2)	72 (6.4)	.196

AKI = acute kidney injury.

undergoing major noncardiac surgery with a preoperative creatinine clearance of 80 mL/min or greater calculated using the Cockcroft-Gault formula.[25] They found a 0.8% incidence and 7 independent preoperative predictors (age, emergent surgery, liver disease, body mass index, high-risk surgery, peripheral vascular occlusive disease, and chronic obstructive pulmonary disease necessitating chronic bronchodilator therapy) of postoperative acute renal failure, which was defined as a calculated creatinine clearance of 50 mL/min or less within the first 7 postoperative days.

Although the incidence and predictors of postoperative acute renal failure were identified in this preliminary study, the effect of renal failure on cardiac and noncardiac outcomes were not investigated. A second study performed by the same investigators revealed a 1% incidence of AKI defined as an increase in serum creatinine of at least 2 mg/dL or acute renal failure necessitating dialysis and showed that the development of AKI was associated with an 8-fold increase in all-cause 30-day mortality.[26] Abelha et al[27,28] studied postoperative AKI, which was defined by Acute Kidney Injury Network criteria[29] in 2 different retrospective studies. In the first study, 1,166 patients with no previous renal insufficiency who were admitted to the intensive care unit after noncardiac surgery were evaluated.[28] Multivariate analysis identified ASA physical status, RCRI score, high-risk surgery, and congestive heart failure as preoperative determinants for postoperative AKI, which was detected in 7.5% of the patients. Patients who developed AKI had a longer length of stay in the hospital and a higher 6-month mortality rate. In the second study, 1,200 patients

Table 3 Univariate and multivariate analyses of risk factors for AKI

	Univariate analysis				Multivariate analysis			
		95% CI				95% CI		
Variable	OR	Lower	Upper	*P* value	OR	Lower	Upper	*P* value
Age	1.050	1.028	1.071	.000	1.141	1.113	1.370	.004
Diabetes mellitus	1.869	4.014	10.459	.000	1.534	1.193	3.459	<.001
Hypertension	0.748	1.285	3.472	.003	0.827	0.406	1.685	.601
Atrial fibrillation	1.163	1.933	5.298	.000	0.217	0.574	2.691	.581
Heart failure	1.854	3.901	10.461	.000	0.410	0.166	1.010	.052
Coronary artery disease	0.910	1.572	3.925	.000	1.690	0.818	3.489	.156
Revised cardiac risk index	1.010	2.128	3.542	.000	1.585	0.755	4.227	.032
ASA physical status	1.046	2.160	3.750	.000	1.686	0.993	2.862	.047
Hemoglobin	−0.157	0.757	0.965	.012	0.910	0.758	1.091	.309
Albumin	−0.365	0.488	0.987	.042	1.696	0.935	3.077	.082
LVEF	−0.077	0.909	0.943	.000	0.965	0.927	1.004	.081

AKI = acute kidney injury; ASA = American Society of Anesthesiologists; CI = confidence interval; LVEF = left ventricle ejection fraction; OR = odds ratio.

Table 4 Association of AKI with adverse perioperative outcomes

	All patients (N = 1,200)	AKI (+) (n = 81)	AKI (−) (n = 1,119)	*P* value
Cardiovascular complications	154 (12.8)	27 (33.3)	127 (11.3)	<.001
Acute coronary syndrome	40 (3.3)	9 (11.1)	31 (2.8)	<.001
Acute heart failure	35 (2.9)	7 (8.6)	28 (2.5)	.002
Severe arrhythmia	26 (2.2)	4 (4.9)	22 (2)	.076
Pulmonary embolism	19 (1.6)	4 (4.9)	15 (1.3)	.012
Nonfatal cardiac arrest	10 (0.8)	2 (2.5)	8 (0.7)	.094
Arterial thromboembolism	24 (2)	5 (6.1)	19 (1.7)	.019
Noncardiovascular complications	299 (24.9)	29 (35.8)	270 (24.1)	.435
Wound infection	81 (6.7)	6 (7.4)	75 (6.7)	.807
Respiratory failure	14 (1.2)	2 (2.5)	12 (1.1)	.258
Lobar pneumonia	21 (1.8)	3 (3.7)	18 (1.6)	.165
Bacteremia	13 (1.1)	1 (1.2)	12 (1.1)	.892
Minor bleeding	128 (10.7)	12 (14.8)	116 (10.3)	.196
Major bleeding	42 (3.5)	5 (6.1)	37 (3.3)	.198
Stroke	21 (1.8)	2 (2.5)	19 (1.7)	.351
Length of stay (d)	8.2 ± 8.1	10.3 ± 9.2	8.1 ± 7.6	<.001
Mortality	16 (1.3)	5 (6.1)	11 (0.9)	.003

AKI = acute kidney injury.

admitted to the postoperative anesthesia care unit after major noncardiac surgery were retrospectively analyzed.[29] Patients with AKI (9.6%) stayed longer in the postoperative anesthesia care unit, had a 9-fold increased risk of mortality during hospitalization, and had a 4-fold risk of mortality at 6 months after discharge. Unfortunately, none of these 4 studies examined the effect of perioperative AKI on cardiac or noncardiac outcomes. In a recent, observational single-center study, Licker et al[30] showed that AKI occurred in approximately 7% of patients undergoing lung cancer resection and was associated with a 3- to 4-fold higher risk of cardiopulmonary complications.

The previously mentioned studies and our study showed that the incidence of AKI after adult noncardiac surgery varies from 0.8% to 10% largely because of nonuniform definitions of AKI and is highly dependent on pre-existing renal function and the type of surgery. Our study also showed that the presence of perioperative AKI is associated with a 3- to 4-fold increased risk of cardiovascular adverse events and in-hospital mortality. Another finding of our study is that noncardiac complications were not more common in patients with AKI during the first 2 weeks after surgery, but thereafter the rate of noncardiovascular complications was higher in patients with AKI. This could be partly because of the older age and higher prevalence of preoperative comorbidities in patients with perioperative AKI, and it is also partly presumed to be because of the prolonged length of stay in these patients.

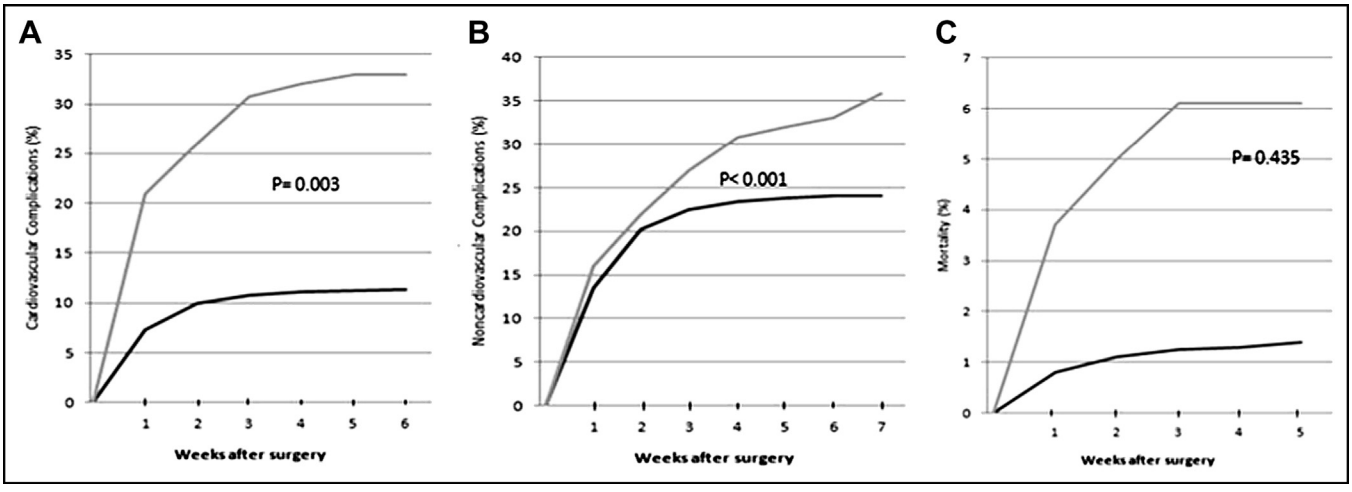

Figure 1 Kaplan-Meier curves for the cardiovascular complications (A), noncardiovacular complications (B), and in-hospital mortality (C) after noncardiac, nonvascular surgery in patients with (thin line) and without perioperative AKI (bold line).

Although our study cohort included a heterogeneous group of patients and procedures, it reflects practice and outcomes at a single institution and may not be replicable in other settings. Patients undergoing emergent surgery, high-risk surgery (vascular surgery), and thoracic surgery were not included. Because long-term follow-up after discharge was not performed, complications that may have developed after discharge in some patients may lead to an underestimation of their incidence. Our study cannot establish a causal relation between AKI and cardiac or noncardiac complications. In conclusion, perioperative AKI is associated with a prolonged length of stay in the hospital, increased cardiovascular/noncardiovascular adverse events, and increased in-hospital mortality in this cohort of patients undergoing noncardiothoracic, nonvascular surgery.

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