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Awareness, incidence and clinical significance of acute kidney injury after non-general anesthesia

A retrospective cohort study

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Abstract

Postoperative acute kidney injury is associated with high mortality and poor prognosis. Additional investigations into the risk factors for this condition and the outcomes of patients who undergo surgeries under non-general anesthesia (GA) are necessary.

This retrospective cohort study included data on all surgeries performed in adult patients from January 2006 to December 2015 at a tertiary hospital in Korea. Patients were divided into those undergoing surgeries with non-GA and those undergoing surgeries with GA. We analyzed the nephrological evaluation patterns, the risk factors for acute kidney injury, and prognoses after acute kidney injury by reviewing mortality, progression to end-stage renal disease, and serum creatinine doubling/estimated glomerular filtration rate halving from baseline.

Of 74,524 patients, 20,332 underwent surgery with non-GA. These patients had baseline (adjusted odds ratio [OR], .68, 95% confidence interval [CI], .63–.72; $P < .01$] and follow-up serum creatinine levels (adjusted OR, .34; 95% CI, .33–.36; $P < .01$) less frequently measured than those undergoing GA. However, the incidence of acute kidney injury did not differ significantly between the 2 groups. Moreover, postoperative acute kidney injury after non-GA surgery showed a worse clinical prognosis which was similar with that of GA operations.

Patients undergoing surgeries under non-GA did not receive sufficient evaluation for their risks of acute kidney injury. As an acute kidney injury in non-GA was associated a worse prognosis as in GA surgeries, more clinical attention should be considered.

Abbreviations: AKI = acute kidney injury, ASA class = American Society of Anesthesiologists (ASA) class, BMI = body mass index, CI = confidence interval, CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate, GA = general anesthesia, NSAIDs = non-steroidal-anti-inflammatory drugs, OR = odds ratio, RAAS = renin-angiotensin-aldosterone-system, sCr = serum creatinine.

Keywords: acute kidney injury, anesthesia

1. Introduction

Acute kidney injury (AKI) is associated with an increased risk of patient mortality and deterioration of kidney function.[1,2] Although there have been numerous studies on the risk factors and clinical outcomes of AKI, there remains a need to raise awareness of AKI.[3]

Postoperative AKI is one of the main categories of AKI.[1,4] It is strongly associated with poor prognosis,[5–9] and even a small elevation in serum creatinine (sCr) level was shown to be associated with an increased risk of patient mortality or progression to end-stage renal disease.[10–13] However, most studies on postoperative AKI were performed in patients undergoing major surgeries that are mainly performed under general anesthesia (GA).[11,12,14] Also, clinicians commonly consider that surgeries under non-GA are relatively safer than GA surgeries regarding AKI risks, but evidence concerning this issue is scarce. Therefore, the risk factors, prognoses, clinical awareness regarding postoperative AKI undergoing surgeries under non-GA need further investigation.

In this study, we evaluated whether postoperative AKI after surgeries under non-GA bears similar characteristics and clinical significance as that after GA surgeries. We also assessed the clinical awareness of postoperative AKI in non-GA operations. Above investigations were performed to report the necessity of an additional attention to the postoperative AKI after non-GA surgery considering the comparable clinical significance of AKI after non-GA surgeries to the AKI of GA operations.

2. Materials and methods

2.1. Ethical considerations

The institutional review board of the Seoul National University Bundang Hospital approved the study (approval number: B-1706/403–101). Informed consent was waived as this was a retrospective cohort study. The study was conducted in accordance with the principles of the Declaration of Helsinki and performed following the STROBE guideline.

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SP and SL contributed equally to this study.

The authors report no conflicts of interest.

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2.2. Study population

We retrospectively reviewed all surgeries that were performed in adults (age, ≥18 years) from January 2006 to December 2015 at a tertiary referral hospital in Korea using an electrical medical record database. As shown in Figure 1, we included the first index surgery of each patient in this study (n = 82,512). Operative procedures performed by non-surgical departments (e.g., colonoscopy procedures or radiologic interventions) were not considered. To exclude the effect of multiple surgeries within a short period, patients who underwent additional surgeries within 1 month from the index operation were excluded (n = 7911). We also excluded patients with previous end-stage renal disease (n = 77). The remaining patients were included in the study.

Patients who underwent surgeries under GA and non-GA (including local, spinal, and other [e.g., monitored anesthesia care] types of anesthesia) were separately grouped to investigate the characteristics of non-GA and GA operations. As we intended to assess the characteristics, prognosis, and clinical awareness of postoperative AKI after non-GA surgeries, the analysis was performed in multiple levels. We first investigated clinical management pattern in the entire cohort, and the characteristics and prognosis of postoperative AKI were assessed within those who had their perioperative renal function measurement

2.3. Investigations for clinical awareness regarding AKI

Firstly, we assessed clinicians' behavior of perioperative management regarding AKI, as we hypothesized that patients under non-GA surgeries would less likely to be paid attention for the risk of AKI. This investigation was performed in the entire cohort (n = 74,524, Fig. 1), with the following outcomes. First, missing measurements of baseline or follow-up sCr were collected. Baseline sCr was the lowest sCr within 3 months before the surgery, and missing measurements were recorded. Follow-up sCr measurement from a certain event defined as either surgery or AKI was considered present when a sCr value was recorded within 2 weeks after the event. Next, outcomes of perioperative nephrology division consultation were collected. When a consultation note to the nephrology division of our hospital was present within 3 months presurgery or 2 weeks post the AKI, we considered the patient as having been referred to the nephrology department in the according period.

2.4. Investigations for characteristics and prognosis of AKI

Next, those with missing baseline or follow-up sCr values were not considered in the analyses to study the risk factors and prognoses of AKI, as AKI itself was undefinable (Fig. 1). We also excluded patients who met the AKI criteria before surgery and those with preexisting impending kidney failure defined by a baseline sCr value >4 mg/dL to analyze kidney function deterioration in the postoperative period. The remaining patients, 41,996 in GA group and 11,488 in non-GA group, were included in the group to assess risk factors of AKI and prognoses. In these group of patients, AKI events were identified and staged according to the international Kidney Disease: Improving Global Outcome guidelines; sCr increased by 0.3 mg/dL within 48 hours or increase in sCr to 1.5 times baseline.[15] As sCr follow-up timing was heterogeneous, we used sCr values within 2 weeks post-surgery to identify AKI events, and peak sCr levels to stage AKI.[16,17] The prognostic outcomes included postoperative mortality and initiation of maintenance dialysis within 3 years post-surgery. We reviewed the national mortality database after acquisition of government approval as a considerable portion of

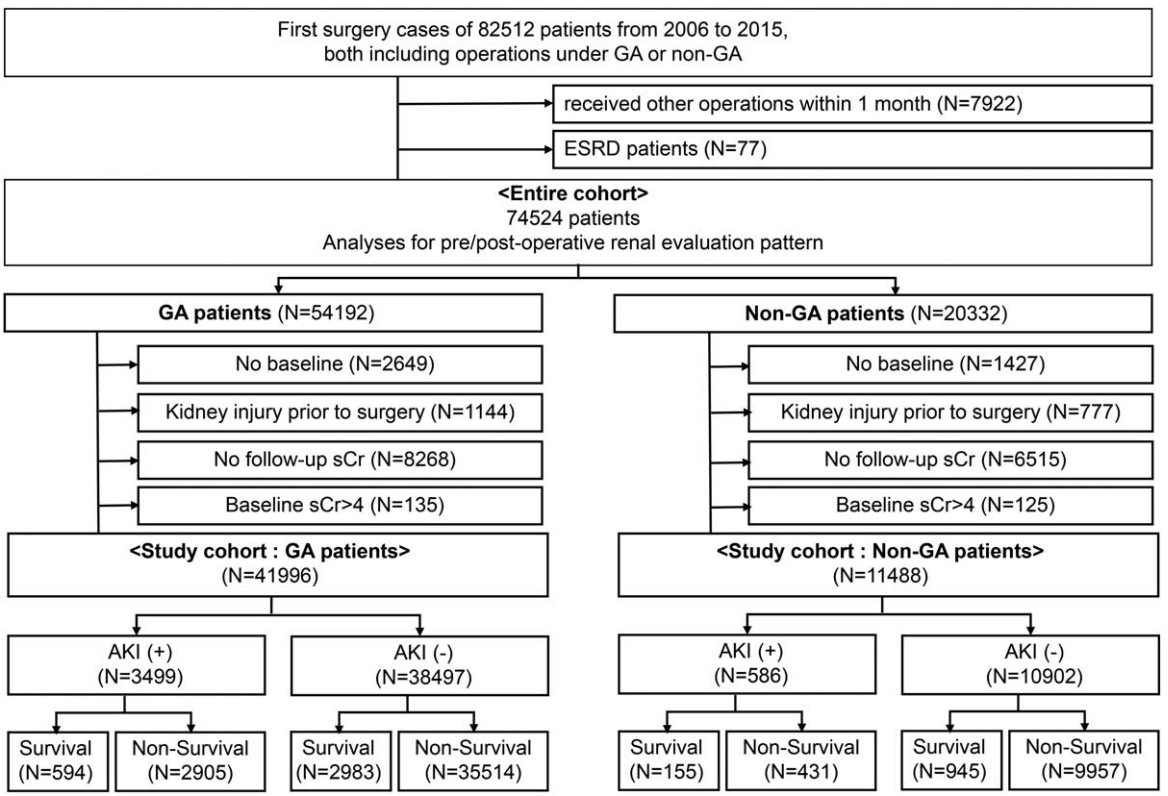

Figure 1. Flow diagram of the study population.

deaths occurred outside of the hospital. Also, we collected events indicating either doubling of sCr or halving of estimated glomerular filtration rate levels compared to baseline at 3, 6, and 12 months post-surgery, within a 2-month window period to analyze sCr-based outcomes.

2.5. Data collection

We collected data of the patients' age, sex, and baseline body mass index before surgery. The last laboratory values within 3 months before the operation were considered baseline[18]; collected laboratory examinations included sCr levels, estimated glomerular filtration rate (eGFR) as calculated by the Chronic Kidney Disease-Epidemiology Collaboration sCr method,[19] hemoglobin levels, serum albumin levels, and dipstick albuminuria results. Patients with baseline hemoglobin levels $\leq$11 g/dL were considered having anemia, and those with serum albumin levels $\leq$3 g/dL were considered having hypoalbuminemia.[20] Underlying comorbidities such as hypertension, diabetes mellitus, and cancer were identified by their designated International Classification of Disease-10 diagnostic codes[21] and relevant medication usage.

We reviewed the perioperative usage of the following medications: renin-angiotensin-aldosterone-system blockers, diuretics, and nonsteroidal-anti-inflammatory drugs.[22] The following surgery- or anesthesia- related characteristics were also reviewed: type of anesthesia, whether the surgery was an emergency operation, duration of surgery and anesthesia, preoperative American Society of Anesthesiologists (ASA) class,[23] and the main department caring for the patient.

2.6. Statistical analysis

Categorical variables are shown as frequencies (percentages) and were compared using the χ^2 test. We confirmed that all continuous variables in our study population were non-normally distributed using the Shapiro-Wilk normality test. Therefore, the variables are shown as median scores (25 percentile–75 percentile) and compared with the Mann–Whitney *U* test.

The patterns of nephrological evaluations were assessed through logistic regression analysis using the GA group as the reference. To analyze the risk factors for AKI, multivariable logistic regression analysis that was adjusted for clinical characteristics was performed. A survival curve was plotted using the Kaplan-Meier method to analyze the postoperative prognosis of patients with AKI; *P* values were calculated using the log-rank method. In the multivariable analysis, a Cox regression hazard model was used to assess the progression to end-stage renal disease and patient mortality. The sCr-based outcomes were analyzed using a logistic regression.

In multivariable analysis for evaluation for nephrological evaluation pattern, following variables were adjusted: age (continuous, years), sex, ASA physical state class (categorical, 1 class increment), and comorbidity of hypertension or diabetes mellitus. For post-AKI nephrological assessment, presence of baseline reduced kidney function (categorical, whether eGFR $<$60 mL/min/1.73 m^2 or not) and the stage of AKI (categorical, stage 1, 2, and 3) were added to the multivariable model, as patients with higher AKI stages or preoperative chronic kidney disease (CKD) were more likely to be followed up.[15,24] Next, in logistic regression analysis for AKI risk factor investigation, following variables were adjusted: age (continuous); sex; body mass index (BMI) (continuous); comorbidities of hypertension, diabetes mellitus, or cancer; surgery department (categorical, cardiovascular surgery, pulmonary surgery, general surgery, orthopedic surgery, urologic surgery and others); operation time; ASA physical state class (categorical, 1 class increment); presence of baseline reduced kidney function categorical, whether eGFR $<$60 mL/min/1.73 m^2 or not); baseline albuminuria (categorical, presence or absence); anemia (hemoglobin $<$11 g/dL); hypoalbuminemia (serum albumin $<$3.0 g/dL); and perioperative medication use including RAAS blockers, diuretic agents, and NSAIDs. For patient mortality and renal prognosis assessment, Cox proportional hazard model and logistic regression analysis was

Table 1

Baseline characteristics of the entire cohort.

	G surgery (n = 54,192)	Non-GA surgery (n = 20,332)	*P*
Demographic characteristics			
Age, y	57 (45–68)	60 (40–71)	<.01
Male sex	29,045 (53.6)	9403 (46.3)	<.01
Body mass index, kg/m^2	23.9 (21.7–26.1)	24.2 (21.9–26.6)	<.01
Obesity (body mass index ≥30)	1470 (4.6)	893 (6.9)	<.01
Comorbidities			
Hypertension	26,179 (48.3)	7132 (35.1)	<.01
Diabetes mellitus	4210 (7.8)	2375 (11.7)	<.01
Cancer	16,932 (31.2)	1796 (8.8)	<.01
Available baseline laboratory findings			
sCr, mg/dL	0.86 (0.70–1.00)	0.89 (0.70–1.06)	<.01
eGFR, mL/min/1.73 m^2	88.9 (74.1–101.5)	86.0 (67.7–100.8)	<.01
eGFR <60	4761 (9.2)	3173 (16.8)	<.01
Hemoglobin, g/dL	13.6 (12.4–14.8)	13.3 (12.1–14.6)	<.01
Anemia (hemoglobin <11 g/dL)	4842 (9.4)	2316 (12.2)	<.01
Albumin, g/dL	4.3 (4.0–4.6)	4.3 (3.9–4.5)	<.01
Hypoalbuminemia (albumin <3.0 g/dL)	1033 (2.0)	2316 (12.2)	<.01
Baseline urine albuminuria (dipstick)			<.01
(−)	36,515 (91.5)	12,225 (87.8)	
1+	1925 (4.8)	718 (5.2)	
2+	1114 (2.8)	545 (3.9)	
3+	374 (0.9)	432 (3.1)	
Perioperative medication use			
RAAS blockade	4661 (8.6)	1852 (9.1)	.03
Diuretics	8948 (16.5)	2380 (11.7)	<.01
NSAID	26,255 (48.5)	10,345 (50.9)	<.01
Surgery or anesthesia related characteristics			
Emergency operation	4453 (8.2)	1728 (8.5)	.22
Surgical time,h	2.2 (1.2–3.5)	1.2 (0.7–1.8)	<.01
Anesthesia time, h	3.0 (1.8–4.3)	1.8 (1.2–2.6)	<.01
ASA class			<.01
1–2	47,339 (90.7)	15,909 (91.2)	
3–4	4796 (9.2)	1533 (8.8)	
5–6	79 (0.2)	1 (0.0)	
Department			<.01
Orthopedic surgery	10,655 (19.7)	10,598 (52.1)	
Neurosurgery	4975 (9.2)	577 (2.8)	
Urology surgery	5780 (10.7)	1938 (9.5)	
Obstetrics and gynecology	2338 (4.3)	2170 (10.7)	
Plastic surgery	711 (1.3)	340 (1.7)	
General surgery	22,344 (41.2)	1703 (8.4)	
Cardiovascular surgery	2404 (4.44)	201 (1.0)	
Pulmonary surgery	2246 (4.1)	796 (3.9)	
Ophthalmology	393 (0.7)	1820 (9.0)	
Otorhinolaryngology	2346 (4.3)	189 (0.9)	

eGFR = estimated glomerular filtration rate, GA = general anesthesia surgery, NSAID = non-steroidal anti-inflammatory drug, RAAS = renin-angiotensin-aldosterone-system, sCr = serum creatinine.
Continuous variables were shown as median (interquartile ranges) scores. Categorical variables were reported as number (%)
The proportions of missing values in the entire cohort were as shown: baseline body mass index (n = 29,436, 39.5%), ASA physical state class (n = 4867, 6.5%), surgical time (n = 4936, 6.6%), baseline hemoglobin (n = 3900, 5.2%), serum albumin (n = 4556, 6.1%), and dipstick albuminuria results (n = 20,676, 27.7%).

adjusted with following variables: age (continuous, years); sex; comorbidities of hypertension, diabetes mellitus, or cancer; perioperative use of diuretic agents; surgical time (continuous, hours); ASA physical state class (categorical, 1 class increment); attending department (thoracic surgery-cardiovascular, thoracic surgery-pulmonary, general surgery, orthopedic surgery, urology, and others); baseline eGFR (continuous, mL/min/1.73 m^2); presence of hypoalbuminemia (serum albumin <3.0 g/dL) or anemia (hemoglobin < 11 g/dL); and presence of albuminuria (categorical, presence or absence) in urinalysis. Surgery departments were not included in the multivariable survival analyses for end-stage renal disease as there were departments without the events.

For missing values in our dataset, multiple imputations were performed with the "mice" package of the R software (version 3.2.5; The R Foundation) using the classification and regression trees method, calling 6 multiple imputed datasets and presenting the combined results with the "pool" function. The following variables were imputed when included in the analyses and the proportions of missing values in the entire cohort were as shown: baseline body mass index (n = 29,436, 39.5%), American Society of Anesthesiologists physical state class (n = 4867, 6.5%), surgical duration (n = 4936, 6.6%), baseline hemoglobin levels (n = 3900, 5.2%), serum albumin levels (n = 4556, 6.1%), and dipstick albuminuria results (n = 20,676, 27.7%). Missing values were identified to occur in a random manner.

All statistical analyses were performed using the R software. Two-sided *P* values <.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics

We detected significant differences in perioperative characteristics between the GA and non-GA groups in the entire cohort (Table 1). Patients of the GA group tended to be older ($P < .01$) and less obese ($P < .01$) compared to the non-GA group. Hypertension ($P < .01$) and cancer ($P < .01$) were more frequent in the GA group, whereas diabetes mellitus was more common ($P < .01$) in the non-GA group. Laboratory findings were also significantly different, and the GA group was generally had worse laboratory characteristics. We also observed differences in the attending department of surgery between the 2 groups ($P < .01$). The number of patients receiving specific types of anesthesia according to the attending department is shown in Supplemental Table 1, http://links.lww.com/MD/C416.

3.2. Clinical awareness regarding postoperative AKI in the non-GA group

The results regarding comparison between the GA and non-GA surgeries for their clinical assessment pattern for postoperative AKI are shown in Table 2. Patients of the non-GA group had their baseline sCr and follow-up sCr levels less frequently than those of the GA group. This result was significant for majority of surgery departments except the orthopedics department at which follow-up renal function was more frequently assessed in the non-GA than in the GA group. Preoperative consultation of the

Table 2

Perioperative nephrological evaluation pattern of the entire cohort.

			*Univariate analysis		*Multivariable analysis	
	GA surgery (n = 54,192)	Non-GA surgery (n = 20,332)	OR (95% CI)	*P*	†Adjusted OR (95% CI)	*P*
Measurement of baseline sCr	51,543 (95.1)	18,905 (93.0)	0.68 (0.64–0.73)	<.01	0.68 (0.63–0.72)	<.01
Cardiovascular surgery (n = 2605)	2235 (93.0)	194 (96.5)	2.10 (1.04–4.99)	.05	1.67 (0.72–3.91)	.23
Pulmonary surgery (n = 3040)	2153 (95.9)	768 (96.5)	1.18 (0.78–1.85)	.44	0.75 (0.45–1.25)	.27
General surgery (n = 24,047)	21,117 (94.5)	1523 (89.4)	0.49 (0.42–0.58)	<.01	0.42 (0.35–0.49)	<.01
Orthopedic surgery (n = 21,253)	10,430 (97.9)	10,276 (97.0)	0.69 (0.58–0.82)	<.01	0.72 (0.60–0.86)	<.01
Urologic surgery (n = 7718)	5696 (98.5)	1848 (95.4)	0.30 (0.22–0.41)	<.01	0.31 (0.23–0.42)	<.01
Neurosurgery (n = 5552)	4552 (91.5)	453 (78.5)	0.34 (0.27–0.43)	<.01	0.38 (0.30–0.48)	<.01
Obstetrics and gynecology surgery (n = 4508)	2106 (90.1)	1798 (82.9)	0.53 (0.45–0.63)	<.01	0.68 (0.57–0.82)	<.01
Others (n = 5799)	3254 (94.3)	2045 (87.1)	0.41 (0.34–0.49)	<.01	0.28 (0.23–0.35)	<.01
Measurement of follow-up sCr	45,422 (83.8)	12,795 (62.9)	0.33 (0.32–0.34)	<.01	0.34 (0.33–0.36)	<.01
Cardiovascular surgery (n = 2605)	2362 (98.3)	145 (72.1)	0.05 (0.03–0.08)	<.01	0.06 (0.04–0.10)	<.01
Pulmonary surgery (n = 3040)	2197 (97.8)	404 (50.8)	0.02 (0.02–0.03)	<.01	0.02 (0.01–0.03)	<.01
General surgery (n = 24,047)	20,009 (89.5)	938 (55.1)	0.14 (0.13–0.16)	<.01	0.10 (0.09–0.11)	<.01
Orthopedic surgery (n = 21,253)	9149 (85.9)	9289 (87.6)	1.17 (1.08–1.26)	<.01	1.21 (1.12–1.31)	<.01
Urologic surgery (n = 7718)	5148 (89.1)	1029 (53.1)	0.14 (0.12–0.16)	<.01	0.15 (0.13–0.17)	<.01
Neurosurgery (n = 5552)	4302 (86.5)	395 (68.5)	0.34 (0.28–0.41)	<.01	0.33 (0.27–0.40)	<.01
Obstetrics and gynecology surgery (n = 4508)	1008 (43.1)	331 (15.3)	0.24 (0.21–0.27)	<.01	0.27 (0.23–0.32)	<.01
Others (n = 5799)	1247 (36.1)	264 (11.2)	0.22 (0.19–0.26)	<.01	0.20 (0.17–0.23)	<.01
Preoperative nephrology consult	1244 (2.3)	455 (2.2)	0.97 (0.87–1.09)	.64	0.97 (0.87–1.09)	.63
Cardiovascular surgery (n = 2605)	52 (2.2)	6 (3.0)	1.39 (0.53–3.03)	.45	1.45 (0.60–3.55)	.41
Pulmonary surgery (n = 3040)	55 (2.4)	22 (2.8)	1.13 (0.67–1.84)	.63	1.16 (0.65–2.04)	.62
General surgery (n = 24,047)	522 (2.3)	24 (1.4)	0.60 (0.39–0.88)	.01	0.61 (0.41–0.93)	.02
Orthopedic surgery (n = 21,253)	242 (2.3)	257 (2.4)	1.07 (0.90–1.28)	.46	1.10 (0.91–1.31)	.32
Urologic surgery (n = 7718)	119 (2.1)	35 (1.8)	0.87 (0.59–1.27)	.49	0.92 (0.62–1.36)	.68
Neurosurgery (n = 5,552)	117 (2.4)	12 (2.1)	0.88 (0.46–1.54)	.68	0.88 (0.48–1.63)	.69
Obstetrics and gynecology surgery (n = 4508)	56 (2.4)	53 (2.4)	1.02 (0.70–1.49)	.92	0.97 (0.66–1.44)	.89
Others (n = 5799)	81 (2.3)	46 (2.0)	0.83 (0.57–1.19)	.32	0.71 (0.48–1.05)	.09

CI = confidence interval, GA = general anesthesia, OR = odds ratio, sCr = serum creatinine.

* The logistic regression analysis was used to calculate the odds ratios, with the patients undergoing general anesthesia surgery as the reference group.

† Adjusted with age (continuous, years), sex, ASA physical state class (categorical, 1 class increment), and comorbidity of hypertension or diabetes mellitus. Missing values for ASA classifications were imputed using multiple imputation with the chain equation with classification and regression trees.

nephrology department was requested in similar frequency in 2 groups, except for the general surgery department in which preoperative nephrology referral was less commonly requested in non-GA than in GA surgeries.

3.3. Postoperative AKI risk factors for AKI in the non-GA group

Among the patients in the study cohort with perioperative sCr measurements, 7.6% (n=4085) developed postoperative AKI. The incidences of identifiable AKI were 8.3% (n=3499) and 5.1% (n=586) in the GA and non-GA groups. In the multivariable analysis, within those with available perioperative sCr levels, patients who underwent non-GA surgery had similar odds for postoperative AKI as those underwent GA surgeries (adjusted odds ratio, 1.05; 95% confidence interval, 0.94–1.17; $P=.42$).

As shown in Table 3, the clinical characteristics associated with postoperative AKI included diabetes mellitus and cancer. The attended surgical department showed differences in their postoperative AKI risks and several other risk factors were also identified. Moreover, the clinical characteristics associated with postoperative AKI were similar between the GA and non-GA groups, although following variables were not associated with the risk of AKI in surgeries under non-GA; male sex, renin-angiotensin-aldosterone system blocker usage, baseline hypoalbuminemia, longer surgical duration, were not significantly associated with the development of postoperative AKI in patients undergoing non-GA surgeries.

3.4. Postoperative prognosis of patients with AKI

We identified 4677 cases of mortality and 55 cases of progression to end-stage renal disease in the study cohort. As shown in Fig. 2 and Table 4, postoperative AKI was associated with worse postoperative prognosis, inferred by both mortality and end-stage renal disease progression. Particularly in patients undergoing non-GA surgery, the risks of death, and renal failure were increased after AKI, which were comparable to the worse prognosis of AKI after GA surgeries. The above comparable

Table 3

Risk factors for acute kidney injury in the study cohort.

	In total study cohort (n=53,484) with 4085 acute kidney injury events		In GA surgery patients (n=41,996) with 3499 acute kidney injury events		In non-GA surgery patients (n=11,488) with 586 acute kidney injury events	
	*Adjusted OR (95% CI)	P	*Adjusted OR (95% CI)	P	*Adjusted OR (95% CI)	P
Demographic factors						
Age, ye	1.00 (0.99–1.00)	.03	0.99 (0.99–1.00)	<.01	1.01 (1.00–1.46)	.03
Male sex	1.22 (1.13–1.32)	<.01	1.27 (1.17–1.39)	<.01	1.20 (0.99–1.46)	.07
Body mass index, kg/m^2	1.00 (0.99–1.02)	.76	1.00 (0.99–1.02)	.81	1.01 (0.98–1.03)	.52
Comorbidities						
Hypertension	1.01 (0.93–1.09)	.86	0.99 (0.90–1.08)	.80	0.99 (0.81–1.21)	.92
Diabetes mellitus	1.20 (1.07–1.34)	.001	1.26 (0.99–1.28)	.06	1.49 (1.18–1.89)	<.01
Cancer	1.11 (1.01–1.21)	.02	0.97 (0.88–1.07)	.52	0.99 (0.72–1.35)	.95
Surgery department or organ						
Cardiovascular surgery	2.78 (2.20–3.52)	<.01	2.83 (2.18–3.66)	<.01	3.55 (1.78–7.10)	<.01
Pulmonary surgery	1.40 (1.08–1.82)	.01	1.36 (1.01–1.83)	.04	1.92 (1.03–3.60)	.04
General surgery	0.91 (0.73–1.13)	.38	0.99 (0.77–1.26)	.91	1.49 (0.81–2.74)	.20
Orthopedic surgery	0.70 (0.56–0.88)	.002	0.55 (0.42–0.72)	<.01	1.05 (0.62–1.79)	.84
Urologic surgery	4.02 (3.21–5.02)	<.01	5.31 (4.14–6.81)	<.01	1.26 (0.71–2.24)	.42
Neurosurgery	0.55 (0.43–0.72)	<.01	0.49 (0.36–0.65)	<.01	2.06 (1.07–3.96)	.03
Obstetrics and gynecology surgery	1.01 (0.72–1.41)	.96	1.07 (0.69–1.50)	.93	1.99 (0.97–4.09)	.06
Other	Reference		Reference		Reference	
Surgery characteristics						
Surgical time (1-h increment)	1.16 (1.13–1.18)	<.01	1.18 (1.16–1.21)	<.01	0.97 (0.85–1.10)	.59
ASA class (1 class increment)	1.38 (1.29–1.47)	<.01	1.34 (1.25–1.44)	<.01	1.61 (1.37–1.89)	<.01
Laboratory findings						
eGFR <60 mL/min/1.73 m^2	1.40 (1.26–1.55)	<.01	1.46 (1.30–1.64)	<.01	1.31 (1.04–1.65)	.02
Urine albuminuria	1.82 (1.53–2.17)	<.01	1.39 (1.24–1.56)	<.01	1.58 (1.15–2.19)	.007
Anemia (Hb <11 g/dL)	1.52 (1.36–1.69)	<.01	1.51 (1.33–1.71)	<.01	1.60 (1.26–2.03)	<.01
Hypoalbuminemia (albumin <3.0 g/dL)	1.82 (1.53–2.17)	<.01	2.27 (1.86–2.77)	<.01	1.21 (0.85–1.71)	.29
Perioperative medication use						
RAAS blockade	1.11 (1.00–1.23)	.06	1.14 (1.02–1.29)	.02	0.97 (0.75–1.27)	.85
Diuretic agent	2.89 (2.66–3.14)	<.01	2.97 (2.71–3.25)	<.01	2.41 (1.96–2.96)	<.01
NSAID	1.07 (0.93–1.09)	.86	1.01 (0.93–1.10)	.75	1.03 (0.84–1.25)	.80

BMI = body mass index, CI = confidence interval, eGFR = estimated glomerular filtration rate, GA = general anesthesia, Hb = hemoglobin, NSAID = non-steroidal anti-inflammatory drug, OR = odds ratio, RAAS = renin-angiotensin-aldosterone system.

* All variables in the table were adjusted in the multivariable logistic regression analysis, including: age (continuous); sex; BMI (continuous); comorbidities of hypertension, diabetes mellitus, or cancer; surgery department (categorical, cardiovascular surgery, pulmonary surgery, general surgery, orthopedic surgery, urologic surgery and others); operation time; ASA physical state class (categorical, 1 class increment); presence of baseline reduced kidney function categorical, whether eGFR <60 mL/min/1.73 m^2 or not); baseline albuminuria (categorical, presence or absence); anemia (hemoglobin <11 g/dL); hypoalbuminemia (serum albumin <3.0 g/dL); and perioperative medication use including RAAS blockers, diuretic agents, and NSAIDs. The adjusted odds ratio of each characteristic was shown in each row. Existing missing values for baseline obesity, ASA physical state class, surgical time record, anemia and hypoalbuminemia were imputed using multiple imputations with the chain equation with classification and regression trees.

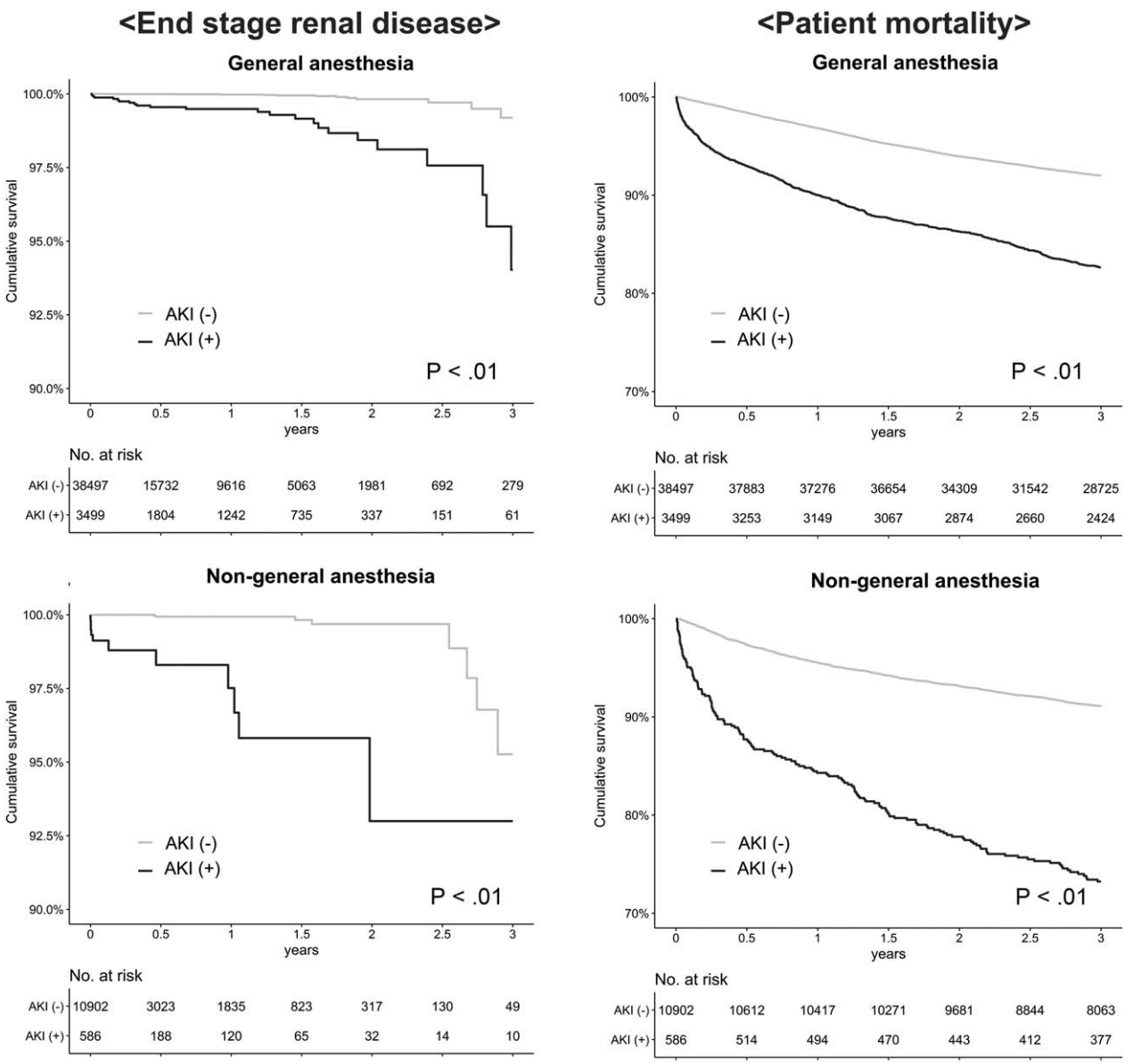

Figure 2. Kaplan-Meier survival curve showing the patient prognosis of the study cohort. The left graphs used progression to end-stage renal disease as an outcome and the right graphs used patient mortality as an outcome. The upper graphs show the survival curves of patients with surgeries under general anesthesia, and the lower graphs show the survival curves of those who underwent operations under non-general anesthesia. The black lines are the survival curve of patients with postoperative AKI events, and the gray lines with those without the AKI. The *y*-axes show the cumulative patient survival, and *x*-axes indicate the time (years) from operation. *P* values by the log-rank method and tables containing number of patients at risk are shown in each graph. AKI = acute kidney injury.

worse prognosis of AKI patients under GA or non-GA was similarly identified regarding sCr-based outcomes.

3.5. Patterns of nephrological evaluation in patients with postoperative AKIs

When we analyzed the patterns of clinical management after AKI among patients with postoperative AKI (Table 5), we found that clinicians were less likely to order follow-up sCr measurements in the non-GA group compared to the GA group. However, the overall odds of obtaining a nephrology consultation did not show a significant difference between 2 groups. Clinical management of postoperative AKI varied widely depending on surgery departments, with surgeries performed by the pulmonary department having even higher odds of measuring post-AKI sCr values than others. In the multivariable analyses, the odds of ordering post-AKI sCr were significantly lower for surgeries performed by the urology department as were the odds of obtaining nephrology referral after AKI for surgeries performed by general surgery department.

4. Discussion

In this study, we identified that postoperative AKI after non-GA surgeries had similar characteristics and significant association with postoperative prognosis as that after GA surgeries. In addition, we showed that despite the clinical significance, renal function measurement was less commonly performed in non-GA

Table 4

Postoperative prognosis of AKI in the study cohort.

	Total study cohort		GA surgery patients		Non-GA surgery patients	
	*Adjusted OR/HR (95% CI)	*P*	*Adjusted OR/HR (95% CI)	*P*	*Adjusted OR/HR (95% CI)	*P*
3-y Mortality	1.44 (1.32–1.57)	<.01	1.43 (1.30–1.58)	<.01	1.54 (1.28–1.85)	<.01
3-y ESRD	4.69 (2.99–7.35)	<.01	5.93 (2.72–12.93)	<.01	4.37 (1.48–12.89)	<.01
Long-term sCr/eGFR outcomes						
Doubling of sCr						
At 3±2 mo postop	6.02 (4.92–7.38)	<.01	6.41 (5.08–8.07)	<.01	5.46 (3.47–8.58)	<.01
At 6±2 mo postop	5.63 (4.38–7.24)	<.01	6.07 (4.56–8.06)	<.01	4.13 (2.32–7.35)	<.01
At 12±2 mo postop	6.18 (4.44–8.60)	<.01	6.19 (4.23–9.06)	<.01	6.60 (3.16–13.79)	<.01
eGFR halving						
At 3±2 mo postop	3.89 (3.16–4.80)	<.01	4.39 (3.46–5.56)	<.01	2.54 (1.53–4.24)	<.01
At 6±2 mo postop	3.46 (2.66–4.50)	<.01	3.89 (2.89–5.23)	<.01	2.20 (1.18–4.11)	.01
At 12±2 mo postop	3.84 (2.73–5.38)	<.01	3.69 (2.50–5.45)	<.01	4.19 (2.04–8.61)	<.01

GA = general anesthesia, OR = odds ratio, HR = hazard ratio, CI = confidence interval, ESRD = end stage renal disease, sCr = serum creatinine, eGFR = estimated glomerular filtration rate.

* The Cox regression test was used to calculate hazard ratios for mortality and ESRD outcomes, and the logistic regression test was used to obtain the odds ratios for the sCr-based outcomes. Multivariable models were adjusted for following variables: age (continuous, years); sex; comorbidities of hypertension, diabetes mellitus, or cancer; perioperative use of diuretic agents; surgical time (continuous, hours); ASA physical state class (categorical, 1 class increment); attending department (thoracic surgery-cardiovascular, thoracic surgery-pulmonary, general surgery, orthopedic surgery, urology, and others); baseline eGFR (continuous, mL/min/1.73 m^2); presence of hypoalbuminemia (serum albumin <3.0 g/dL) or anemia (hemoglobin <11 g/dL); and presence of albuminuria (categorical, presence or absence) in urine analysis. Surgery departments were not included in the multivariable survival analyses for ESRD as there were departments without the events.

operations than in surgeries under GA. Therefore, our study could serve as a retrospective evidence showing that additional attention to the postoperative AKI after non-GA surgery is warranted.

The main strengths of our study are that we analyzed large number of patients and focused on the characteristics, prognosis, and clinical awareness of AKI in non-GA surgeries, which was scarcely done before. Numerous studies demonstrated that postoperative AKI adversely affects surgery outcomes, including patient mortality and renal failure.[12,25,26] Clinicians do recognize the importance of postoperative AKI; however, whether this clinical awareness was similarly necessary and secured regarding AKI after non-GA surgery was not investigated before. In our study, as suspected, the patients of the non-GA group were less likely to have their perioperative kidney function measured, which is crucial to detect AKI.[15] This practice pattern might be acceptable if AKI prognosis was substantially better or incidences were lower after non-GA than the GA surgeries, but we identified that the incidence of AKI in the non-GA group was comparable to that of the GA group. In addition, AKI after non-GA surgery was also critically associated with patients' prognosis. Therefore, clinicians should consider additional attention for AKI risks in surgeries performed under non-GA.

The possible mechanisms of AKI after non-GA surgery in our study should be considered. Previously, perioperative hemodynamic instability and the use of nephrotoxic agents are

Table 5

Post-AKI nephrologic assessment and prognosis in patients who underwent non-GA surgery.

			Univariable analyses		Multivariable analysis	
	GA surgery	Non-GA surgery	OR (95% CI)	*P*	*Adjusted OR (95% CI)	*P*
Follow-up sCr measurement after AKI	1673 (47.8)	217 (37.0)	0.64 (0.54–0.77)	<.01	0.68 (0.50–0.74)	<.01
Cardiovascular surgery	414/776 (53.4)	17/26 (65.4)	1.65 (0.74–3.92)	.23	1.14 (0.44–2.89)	.79
Pulmonary surgery	24/136 (17.7)	19/41 (46.3)	4.03 (1.89–8.65)	<.01	2.44 (0.93–6.41)	.07
General surgery	400/947 (42.2)	17/37 (46.0)	1.16 (0.59–2.25)	.65	0.45 (0.19–1.04)	.06
Orthopedic surgery	93/251 (37.1)	116/351 (33.1)	0.84 (0.60–1.18)	.31	0.69 (0.43–1.11)	.13
Urologic surgery	616/1108 (55.6)	22/63 (34.9)	0.43 (0.25–0.72)	.002	0.47 (0.27–0.83)	.009
Neurosurgery	70/143 (49.0)	13/28 (46.4)	0.90 (0.40–2.04)	.81	1.02 (0.39–2.68)	.97
Obstetrics and gynecology surgery	9/45 (20.0)	5/20 (25.0)	1.33 (0.36–4.56)	.65	N/A	
Other	47/93 (50.5)	8/20 (40.0)	0.65 (0.24–1.72)	.39	N/A	
Post-AKI referral to nephrology division	359 (10.3)	81 (13.8)	1.40 (1.08–1.81)	.01	1.24 (0.93–1.65)	.14
Cardiovascular surgery	42/776 (5.4)	1/26 (3.9)	0.69 (0.04–3.42)	.73	0.16 (0.02–1.56)	.11
Pulmonary surgery	6/136 (4.4)	2/41 (4.9)	1.11 (0.16–5.05)	.9	0.74 (0.12–4.64)	.75
General surgery	130/947 (13.7)	4/37 (10.8)	0.76 (0.22–1.95)	.61	0.13 (0.04–0.46)	.002
Orthopedic surgery	53/251 (21.1)	60/351 (17.1)	0.77 (0.51–1.16)	.21	0.70 (0.44–1.11)	.13
Urologic surgery	83/1108 (7.5)	7/63 (11.1)	1.54 (0.62–3.28)	.30	0.81 (0.55–1.18)	.27
Neurosurgery	29/143 (20.3)	3/28 (10.7)	0.47 (0.11–1.47)	.24	0.41 (0.10–1.64)	.21
Obstetrics and gynecology surgery	4/45 (8.9)	2/20 (10.0)	1.14 (0.15–6.40)	.89	N/A	
Other	12/93 (12.9)	2/20 (10.0)	0.75 (0.11–3.07)	.72	N/A	

AKI = acute kidney injury, GA = general anesthesia, OR = odds ratio, CI = confidence interval, sCr = serum creatinine.

* Adjusted with age (continuous, years), sex, ASA physical state class (categorical, 1 class increment), and comorbidity of hypertension or diabetes mellitus, stage of AKI and presence of baseline reduced kidney function (eGFR <60 mL/min/1.73 m^2). Missing values for ASA classifications were imputed using multiple imputations with the chain equation with classification and regression trees.

considered the major causes of postoperative AKI.[25,27] In our study, the risk factors associated with AKI were similarly identified in GA and non-GA surgeries. This implies that the underlying mechanism of AKI and worsening of renal prognosis after the event may be similar in GA and non-GA surgeries. Attending clinicians should give additional attention to potential occurrence of AKI in patients with these traditional risk factors regardless of the performed anesthesia method.

Next, our result showing the differences between surgical departments needs to be noted. In our study hospitals, clinical management patterns after postoperative AKI varied widely between surgical departments. Patients who underwent non-GA surgery in the pulmonary department had higher odds of having follow-up sCr measurements; this might be because of the inclusion of patients who were critically ill or received intensive care. General surgery department showed a tendency to less frequently monitor follow-up AKI events or refer patients to the nephrology division, and patients underwent surgeries at the urology department had significantly lower odds of having follow-up sCr measurements. Additional study investigating the department-specific post-AKI management pattern is warranted to demonstrate more detailed results. In addition, these overall differences in post-AKI management across departments, not only after non-GA but also after GA surgeries, suggest that a systematic hospital-based approach may be necessary to establish guidelines for postoperative AKI management.

The following limitations should be considered in our study. First, possible selection bias was present. In the perioperative periods, the non-GA group was less likely to measure sCr values, and this was a common situation in those without comorbidities. Therefore, the actual incidence of postoperative AKI might be lower in non-GA patients, as low-risk patients are less likely to have follow-up sCr measurement. In addition, the lack of standardized follow-up measurement of sCr might also be associated with partial inclusion of non-surgery related AKI events, although this was hard to overcome because of the study's innate nature of being a retrospective study. Second, including all surgeries during a relatively long duration resulted in a heterogeneous study population. However, this approach was necessary to compare specific subgroups and to show differences or similarity between the GA and non-GA surgery cases. Third, as this was a single-center study and we mostly analyzed patterns of clinical management, our results might not be generalizable to other hospitals. Last, owing to its retrospective nature, possible hidden confounder might have been present, but was unidentifiable as individual risk factors associated with poor outcomes highly varied among the included patients. In addition, our study could not directly show whether strict AKI risk evaluation may really improve patients' prognosis after non-GA surgeries.

In conclusion, postoperative AKI was significantly associated with worse prognosis in patients undergoing non-GA surgeries and their incidence and impact of AKI was comparable to that of under GA operations. Despite this clinical importance, perioperative renal function assessment was less performed in non-GA surgery field. Additional attention to AKI risks in patients who undergo non-GA surgery is warranted.

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References

[1] Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol 2005;16:3365–70.
[2] Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA 2005;294:813–8.
[3] Yang L, Xing G, Wang L, et al. Acute kidney injury in China: a cross-sectional survey. Lancet 2015;386:1465–71.
[4] Hou SH, Bushinsky DA, Wish JB, et al. Hospital-acquired renal insufficiency: a prospective study. Am J Med 1983;74:243–8.
[5] Thiele RH, Isbell JM, Rosner MH. AKI associated with cardiac surgery. Clin J Am Soc Nephrol 2015;10:500–14.
[6] O'Connor ME, Kirwan CJ, Pearse RM, et al. Incidence and associations of acute kidney injury after major abdominal surgery. Intensive Care Med 2016;42:521–30.
[7] Masoomi H, Carmichael JC, Dolich M, et al. Predictive factors of acute renal failure in colon and rectal surgery. Am Surg 2012;78:1019–23.
[8] Thakar CV, Kharat V, Blanck S, et al. Acute kidney injury after gastric bypass surgery. Clin J Am Soc Nephrol 2007;2:426–30.
[9] Tomozawa A, Ishikawa S, Shiota N, et al. Perioperative risk factors for acute kidney injury after liver resection surgery: an historical cohort study. Can J Anaesth 2015;62:753–61.
[10] Lassnigg A, Schmidlin D, Mouhieddine M, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. J Am Soc Nephrol 2004;15:1597–605.
[11] Chertow GM, Levy EM, Hammermeister KE, et al. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med 1998;104:343–8.
[12] Bihorac A, Yavas S, Subbiah S, et al. Long-term risk of mortality and acute kidney injury during hospitalization after major surgery. Ann Surg 2009;249:851–8.
[13] Lee J, Baek SH, Ahn SY, et al. Pre-stage acute kidney injury can predict mortality and medical costs in hospitalized patients. PLoS One 2016;11: e0167038.
[14] Kheterpal S, Tremper KK, Heung M, et al. Development and validation of an acute kidney injury risk index for patients undergoing general surgery: results from a national data set. Anesthesiology 2009;110:505–15.
[15] Kidney Disease: Improving Global Outcomes (KDIGO) Work Group-KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl 2012;2:1–38.
[16] Mizuguchi KA, Mitani A, Waikar SS, et al. Use of postoperative creatinine to predict sustained kidney injury in patients undergoing mesothelioma surgery. Clin J Am Soc Nephrol 2012;7:1071–8.
[17] Wehbe E, Brock R, Budev M, et al. Short-term and long-term outcomes of acute kidney injury after lung transplantation. J Heart Lung Transplant 2012;31:244–51.
[18] Wong F, O'Leary JG, Reddy KR, et al. Acute kidney injury in cirrhosis: baseline serum creatinine predicts patient outcomes. Am J Gastroenterol 2017;112:1103–10.
[19] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.

[20] Park BS, Ahn S, Lee KH, et al. Impact of electronic acute kidney injury (AKI) alerts with automated nephrologist consultation on detection and severity of AKI: a quality improvement study. Am j Kidney Dis 2017.
[21] Intetnational classification of diseases, 10th revision: World Health Organization; 1990.
[22] Lapi F, Azoulay L, Yin H, et al. Concurrent use of diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers with non-steroidal anti-inflammatory drugs and risk of acute kidney injury: nested case-control study. BMJ 2013;346:e8525.
[23] Wannamethee SG, Shaper AG, Lennon L, et al. Metabolic syndrome vs Framingham Risk Score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. Arch Intern Med 2005; 165:2644–50.
[24] KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2013;3:1–50.
[25] Romagnoli S, Ricci Z. Postoperative acute kidney injury. Minerva Anestesiol 2015;81:684–96.
[26] Kheterpal S, Tremper KK, Englesbe MJ, et al. Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. Anesthesiology 2007;107:892–902.
[27] Carmichael P, Carmichael AR. Acute renal failure in the surgical setting. ANZ J Surg 2003;73:144–53.