# Nomogram as a Predictor for Postoperative Acute Kidney Injury in Super-Elderly Patients Undergoing Noncardiac Surgery

Thadakorn Tantisarasart, M.D.\*, Sunisa Chartmongkolchart, M.D.\*, Rassamee Chotipanvithayakul, M.D.\*\*

\*Department of Anesthesiology, \*\*Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hatyai Songkhla 90110 Thailand.

#### **ABSTRACT**

**Objective:** There has been increase the incidence of postoperative acute kidney injury (AKI), especially among super-elderly patients. The study aimed to identify risk factors and develop a nomogram among super-elderly patients undergoing noncardiac surgery.

**Material and Methods:** A single-center retrospective cohort study of patients aged greater than or equal to 80 years that underwent non-cardiac surgery between January 2018 to December 2020. Acute kidney injury (AKI) was identified by Kidney Disease Improving Global Outcome (KDIGO) during seven days after surgery. Multivariate logistic regression was constructed from preoperative and intraoperative data with variables with P-value<0.2 included in the final model. The performance of model function was conducted by area under the receiver curve (AUC) and calibration curves.

**Results:** Eight hundred and twenty patients were included; 124 (15%) developed postoperative AKI. A multivariate logistic regression model consisting of COPD, ASA classification, part of surgery, propofol and Succinylated gelatin was displayed as the nomogram. The model showed good discrimination with an AUC 0.746. The cutoff point of 63, which had the highest Youden index, was chosen with sensitivity and specificity of 83% and 45%, respectively. The nomogram showed good performance by the Hosmer-Lameshow goodness-of-fit test ( $X^2 = 6.0697$  and P value = 0.6394).

**Conclusion:** The nomogram predicted model for predicting postoperative AKI among super-elderly patients showed moderate discrimination ability and was instituted. It can help physicians to detect high-risk patients early and promptly prevent episodes of AKI.

Keywords: Postoperative acute kidney injury; super-elderly patient; nomogram (Siriraj Med J 2022; 74: 114-125)

#### **INTRODUCTION**

Mortality due to surgery and anesthesia has been reduced from >25% to 19% among elderly aged >80 years.<sup>1</sup> This substantially increased surgery and anesthesia among them. AKI, a preventable condition, has been one of the leading cause of post-operative morbidity and mortality rates, especially among super-elderly patients. The incidence of acute kidney injury is highest in elderly about 16.98%<sup>2</sup>

and increase is age-dependent.<sup>3</sup> Therefore, Postoperative acute kidney injury was associated with 30-day unplanned readmission, postoperative renal failure, dialysis, risk of infection and prolonged mechanical ventilation.<sup>4-6</sup> Postoperative AKI is likely related to multifactorial factors including preoperative factor which is intractable, and intraoperative and postoperative factors which can be improved and are preventable.

Corresponding author: Thadakorn tantisarasart

E-mail: thadakorn.t@psu.ac.th

Received 1 November 2021 Revised 7 December 2021 Accepted 26 December 2021

ORCID ID: https://orcid.org/0000-0002-2448-3276

http://dx.doi.org/10.33192/Smj.2022.15



All material is licensed under terms of the Creative Commons Attribution 4.0 International (CC-BY-NC-ND 4.0) license unless otherwise stated. Previous literature has reported that baseline decrease in eGFR, renal artery involvement, radiocontrast media, intraoperative hypotension, operative time, surgical technique, intraoperative crystalloid use, low preoperative Hemoglobin (Hb), intraoperative blood loss, peripheral arterial disease, perioperative transfusion, amount of blood loss, preoperative hypoalbuminemia, general anesthesia and preoperative use of angiotensin-converting enzyme inhibitor(ACEI), angiotensin II receptor blockers (ARB) and diuretics are associated with acute kidney injury. The most important factors in early detection of high risk patients include enhanced invasive monitoring, maintain fluid balance and avoid nephrotoxic agent. 8-10

However, there are many predictive tools such as preoperative GFR, preoperative proteinuria and preoperative creatinine, but none of these tools are best validated for prediction of AKI the incidence, risk factor of postsurgical AKI. Studies documenting predictive score use in postoperative acute kidney injury among elderly people are rare. Therefore, this study aims to develop a predicting tool for postoperative acute kidney injury in super-elderly patients.

#### MATERIALS AND METHODS

## Ethical approval and reporting guidelines

The study was approved by the institutional review board (IRB) of Prince of Songkla University Hospital (IRB number: 63-408-8-1). The inform consent was waived due to the study being observational study without medical

intervention. The study comply with the transparent reporting of a prediction model for TRIPOD statement.<sup>13</sup>

## Study hospital and study designs

This retrospective cohort study was conducted in a tertiary medical center in Thailand from 1 January 2018 to 31 December 2020. A total 820 records of all patients aged ≥80 years who underwent non-cardiac surgery and received either general anesthesia or spinal anesthesia were included.

Exclusion criteria were patients who had preoperative end-stage renal disease requiring renal replacement therapy, diagnosed acute kidney injury since the time of admission to a day prior to the surgery, amputee<sup>12</sup>, bed-ridden, patients without baseline serum creatinine or follow-up serum creatinine levels to identify postoperative AKI and no urine output recorded. Eligible patients' data were retrieved from anesthetic records in the hospital information system (HIS) (Fig 1). An anesthesiologist reviewed patients' profiles and clinical data including ASA classification, vital signs, and urine outputs. Laboratory results, details of surgery and anesthesia, and clinical and hospital-related outcomes were also recorded.

## Outcome and definition of acute kidney injury (AKI)

Postoperative AKI was assessed within 7 days after surgery. According to Kidney Disease-Improving Global Outcomes (KDIGO) 2012 guideline<sup>14</sup>, AKI was defined as either one of the following 3 conditions a) serum

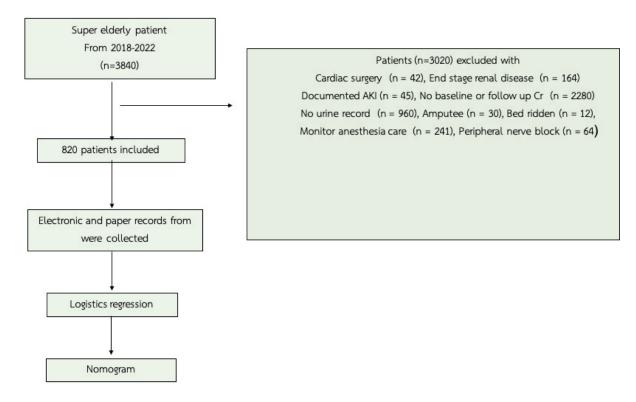


Fig 1. Study flow chart.

creatinine increased by more than 1.5-1.9 times of the baseline level, b) increase in serum creatinine level more than 0.3 mg/dL within 48 hours and c) urine output less than 0.5 mL/kg/h for 6 hours continuously.

The primary outcome was the 7-days AKI rate, according to KDIGO. Secondary outcomes were post-operative 30-day mortality rate, period of hospital stay, period of ICU stay and requirement of renal replacement therapy.

## Sample size determination

Estimated sample size estimated base on ability to detect association with exposure and outcome at odds ratio at least 1.5 with 80% power was 820. The statistical significance was set at P value  $\leq$  0.05.

# Statistical analysis

Statistical analysis was performed using R program version 4.0.2. <sup>15</sup> Categorical variables were presented as percentage and proportion such as gender, Body mass index (BMI), ASA classification, type of surgery, choice of anesthesia, part of surgery, and anesthetic drug use. The categorical parameters were compared between AKI group and non-AKI group by Student t-test or Wilcoxon Rank Sum test. In case of small size population, Chi-squared test or Fisher' exact test were used to compare the two groups. Continuous variables were presented as mean ± standard deviation (SD) and median ± interquartile range was used to describe normal and non-normal distribution, respectively. Categorical variables were analyzed using Chi-square test or Fisher' Exact test as appropriate.

## Predictors of postoperative acute kidney injury

Predictive factors included preoperative and perioperative data. Pre-operative factors included patient's profile, clinical condition, current medication, and laboratory variables including Hemoglobin and creatinine. Preoperative serum creatinine level was analyzed within 24-48 hours prior to surgery. Baseline creatinine clearance was computed by the standard Cockcroft Gault formula using age, lean body weight (kg), serum creatinine (mg/dL) and sex. Perioperative factors included anesthetic drugs, fluid resuscitation, use of vasopressors, estimated blood loss, duration of surgery, duration of hypotension and intraoperative urine output and intraoperative hemodynamic. (Supplement 1)

## Model development

Variables included in multivariate analysis were chosen from univariate analysis results that had p-value

< 0.2 (Tables 1 and 2). Multi-collinearity was tested by using variance inflation factor (VIF) > 5 criteria. Stepwise logistic regression method was used to get the final model (Table 3). The Hosmer-Lameshow goodness-of-fit test also displayed a good performance ( $X^2$ = 6.0697 and P value = 0.6394). The variable with p-value< 0.05 in multivariate logistic regression model was considered statistically significant.

#### Score derivation and validation

The prediction score variable was selected from multivariate analysis and weight adjustment was conducted by nomogram. For the final model, each predictor score was summarized in total postoperative acute kidney injury score. Youden's index was used to reveal maximize specificity and sensitivity cutoff values of prediction score.

#### **RESULTS**

A total 3840 patients who underwent non cardiac surgery were assessed for eligibility from 1 January 2018 to 31 December 2020. Eight hundred and twenty eligible patients were retrieved in this study. The incidence of postoperative acute kidney injury among super-elderly was 15%.

Table 1 shows clinical characteristics at preoperative period between patients with AKI (acute kidney injury) and non AKI with no statistically significant differences in demographic data such as age, sex, BMI, comorbidities and preoperative blood pressure among groups. The mean age of the super elderly was 87 years old and the average BMI was 21 kg/m². Generally, half of the AKI group underwent emergency surgery and had a higher proportion of ASA classification IV and V than non AKI group. No differences in part of surgery, choice of anesthesia and current medication were found between the two groups. Creatinine clearance among AKI group was significant lower than that in the non-AKI group.

Table 2 illustrates clinical characteristics in intraoperative period between AKI group and non-AKI group. According to induction agent, midazolam use was significantly higher among AKI group, while, Propofol use tended to lower incidence of AKI compared to others. Opioid drugs, muscle relaxant drugs and inhalation agents displayed no significant differences in the postoperative AKI. However, AKI group more frequently used vasopressors than non-AKI group. The incidence of postoperative acute kidney injury was higher among patients with duration of hypotension more than 15 minutes. The AKI group tended to use Succinylated gelatin for resuscitation more than non AKI group.

**Supplement 1.** Univariate analysis of risk factors for acute kidney injury.

| Variable                  | OR    | 95%CI        | P-value |
|---------------------------|-------|--------------|---------|
|                           |       |              |         |
| Age*                      | 1.04  | (1,1.09)     | 0.05    |
| Male*                     | 1.24  | (0.84,1.82)  | 0.28    |
| Comorbidities             |       |              |         |
| НТ                        | 1.37  | (0.9,2.07)   | 0.13    |
| DM                        | 1.36  | (0.85,2.18)  | 0.19    |
| COPD                      | 1.84  | (0.93,3.73)  | 0.09    |
| PVD                       | 1.12  | (0.13,9.7)   | 0.09    |
| CHF                       | 1.88  | (0.19,18.2)  | 0.58    |
| Type (ref=elective)       |       |              |         |
| Emergency                 | 1.92  | (1.3,2.82)   | <0.05   |
| Part (ref=Neuro)          |       |              |         |
| Abdomen                   | 1.9   | (0.92,3.95)  | 0.08    |
| Orthopedic                | 2.13  | (1,4.55)     | 0.05    |
| Urology                   | 3.93  | (1.48,10.39) | <0.05   |
| Vascular                  | 1.91  | (0.89,4.11)  | 0.09    |
| Others                    | 1.77  | (0.6,5.2)    | 0.30    |
| ASA (ref=II)              |       |              |         |
| III                       | 2.19  | (1.23,3.9)   | <0.05   |
| IV-V                      | 13.13 | (6.37,27.08) | < 0.05  |
| CrCl                      | 0.99  | (0.97,1)     | 0.04    |
| Hb                        | 0.93  | (0.84,1.02)  | 0.10    |
| Current medication        |       |              |         |
| ACEI                      | 0.76  | (0.38, 1.52) | 0.43    |
| ARB                       | 0.96  | (0.48,1.94)  | 0.92    |
| Choice (ref=spinal block) |       |              |         |
| General anesthesia        | 1.02  | (0.54,1.89)  | 0.96    |
| Induction                 |       |              |         |
| Propofol*                 | 0.38  | (0.25,0.56)  | <0.05   |
| Etomidate*                | 2.24  | (1.15,4.39)  | 0.01    |
| Ketamine*                 | 2.44  | (0.62,9.57)  | 0.02    |
| Midazolam*                | 1.98  | (1.34,2.92)  | <0.05   |
| Narcotic                  |       |              |         |
| Morphine*                 | 1.1   | (0.31,3.85)  | 0.88    |
| Fentanyl*                 | 4.96  | (0.67,36.83) | 0.11    |
|                           |       | ,            |         |

Supplement 1. Univariate analysis of risk factors for acute kidney injury. (Continue)

| Roccuronium*       0.78       (0.39,1.56)       0.00         Succinylcholine*       0.94       (0.48,1.83)       0.00         Inhalation (ref=no)       Compared to the properties of the properties   | value |
|--|-------|
| Roccuronium*       0.78       (0.39,1.56)       0.00         Succinylcholine*       0.94       (0.48,1.83)       0.00         Inhalation (ref=no)       0.84       (0.5,1.4)       0.00         Sevoflurane       0.55       (0.3,1)       0.00         Contrast media       0.78       (0.47,1.29)       0.00         Hypotension       (>= 30mins)       2.32       (1.52,3.52)       0.00         Duration of hypotension (>= 30mins)       2.32       (1.52,3.52)       0.00         Total urine output (ref>=2)       0.51-2       1.81       (1.05,3.12)       0.00         0.51-2       1.81       (1.05,3.12)       0.00         Diuretic use       1.24       (0.65,2.4)       0.00         Vasopressor use         Norepinephrine*       1.95       (1.33,2.88)       0.00         Ephedrine*       0.59       (0.39,0.89)       0.00         Epinephrine*       4.57       (1.67,12.5)       0.00         Dopamine*       9.58       (3.64,25.23)       0.00         Fluid         NSS*       1.74       (1.11,2.71)       0.00   |       |
| Succinylcholine*       0.94       (0.48,1.83)       0.00         Inhalation (ref=no)       0.84       (0.5,1.4)       0.00         Sevoflurane       0.84       (0.5,1.4)       0.00         Desflurane       0.75       (0.3,1)       0.00         Contrast media       0.78       (0.47,1.29)       0.00         Hypotension       1.52       (0.97,2.39)       0.00         Duration of hypotension (>= 30mins)       2.32       (1.52,3.52)       0.00         Total urine output (ref>=2)         <= 0.5  | 0.39  |
| Inhalation (ref=no)   Sevoflurane   0.84   (0.5,1.4)   Contrast media   0.78   (0.47,1.29)   Contrast media   0.78   (0.47,1.29)   Contrast media   0.78   (0.97,2.39)   Contrast media   0.78   (0.97,2.39)   Contrast media   0.55   (0.97,2.39)   Contrast media   0.55   (0.97,2.39)   Contrast media   0.52   (0.97,2.39)   Contrast media   0.55   (0.97,2.39)   Contrast media   0.55   (0.97,2.39)   Contrast media   0.55   (0.97,2.39)   Contrast media   0.51   (0.97,2.39)   Contrast medi | ).47  |
| Sevoflurane       0.84       (0.5,1.4)         Desflurane       0.55       (0.3,1)         Contrast media       0.78       (0.47,1.29)       0.70         Hypotension       1.52       (0.97,2.39)       0.70         Duration of hypotension (>= 30mins)       2.32       (1.52,3.52)       0.50         Total urine output (ref>=2)       (ref>=2)       0.51-2       1.81       (1.05,3.12)       0.70         Diuretic use       1.24       (0.65,2.4)       0.70       0.70         Vasopressor use         Norepinephrine*       1.95       (1.33,2.88)       0.50         Ephedrine*       0.59       (0.39,0.89)       0.70         Dopamine*       9.58       (3.64,25.23)       0.50         Fluid         NSS*       1.74       (1.11,2.71)       0.70  | ).84  |
| Desflurane       0.55       (0.3,1)         Contrast media       0.78       (0.47,1.29)       0.78         Hypotension       1.52       (0.97,2.39)       0.78         Duration of hypotension       (>= 30mins)       2.32       (1.52,3.52)       <  | 0.09  |
| Contrast media 0.78 (0.47,1.29) 0.78  Hypotension 1.52 (0.97,2.39) 0.79  Duration of hypotension (>= 30mins) 2.32 (1.52,3.52) 0.79  Total urine output (ref>=2) (1.51,3.52) 0.79  0.51-2 1.81 (1.05,3.12) 0.79  Diuretic use 1.24 (0.65,2.4) 0.79  Vasopressor use 1.95 (1.33,2.88) 0.79  Ephedrine* 0.59 (0.39,0.89) 0.79  Epinephrine* 4.57 (1.67,12.5) 0.79  Dopamine* 9.58 (3.64,25.23) 0.79  Fluid  NSS* 1.74 (1.11,2.71) 0.79  |       |
| Hypotension 1.52 (0.97,2.39) 0.00 Duration of hypotension (>= 30mins) 2.32 (1.52,3.52) 4.00  Total urine output (ref>=2)  <= 0.5 6.87 (3.8,12.42) 4.00 0.51-2 1.81 (1.05,3.12) 0.00 Diuretic use 1.24 (0.65,2.4) 0.00  Vasopressor use  Norepinephrine* 1.95 (1.33,2.88) 4.00 Ephedrine* 0.59 (0.39,0.89) 0.00 Epinephrine* 4.57 (1.67,12.5) 4.00 Dopamine* 9.58 (3.64,25.23) 4.00  Fluid  NSS* 1.74 (1.11,2.71) 0.00  |       |
| Duration of hypotension (>= 30mins)       2.32       (1.52,3.52)       <   | 0.33  |
| Total urine output (ref>=2)         <= 0.5   | 0.06  |
| <= 0.5   | 0.05  |
| 0.51-2       1.81       (1.05,3.12)       0.00         Diuretic use       1.24       (0.65,2.4)       0.00         Vasopressor use         Norepinephrine*       1.95       (1.33,2.88)       <  |       |
| Diuretic use       1.24       (0.65,2.4)       0.50         Vasopressor use         Norepinephrine*       1.95       (1.33,2.88)       <   | 0.05  |
| Vasopressor use         Norepinephrine*       1.95       (1.33,2.88)       <   | 0.03  |
| Norepinephrine*       1.95       (1.33,2.88)       <   | ).51  |
| Ephedrine*       0.59       (0.39,0.89)       0.50         Epinephrine*       4.57       (1.67,12.5)       <   |       |
| Epinephrine*       4.57       (1.67,12.5)       <  | 0.05  |
| Dopamine*       9.58       (3.64,25.23)       <  | 0.01  |
| Fluid NSS* 1.74 (1.11,2.71) 0  | 0.05  |
| NSS* 1.74 (1.11,2.71) 0  | 0.05  |
|  |       |
| Balanced salt solution* 0.51 (0.34 0.76) <   | 0.01  |
|  | 0.05  |
| Succinylated gelatin use* 2.55 (1.66,3.93)   | 0.05  |
| <b>Blood transfusion</b> 1.65 (1.12,2.42)  | 0.01  |
| RBC* 1.58 (1.07,2.34) 0  | 0.02  |
| FFP* 2.04 (1.25,3.34) <  | 0.05  |
| PC* 2.09 (1.07,4.05) C   | 0.03  |

**Abbreviations:** COPD: chronic obstructive lung disease, CHF: chronic heart failure, Hb: hemoglobin, Crcl: creatinine clearance, ACEI: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blockers, NSS: normal saline solution, PRC: packed red blood cell, FFP: fresh frozen plasma, PC: platelet count \*Continuous variables

**TABLE 1.** Clinical characteristics of preoperative period in super-elderly patients with and without Acute Kidney Injury (AKI) (N=820).

| Characteristics  | AKI group<br>(N=124)<br>N (%)  | Non-AKI group<br>(N=696)<br>N (%)  | P-value                      |
|--|--|--|------------------------------|
| Age (years) mean±SD  | 87.5 ±4.5  | 86.7±3.9   | 0.05                         |
| Gender Female Male BMI (kg/m²)*                                      | 53 (41.1)<br>71 (57.3)<br>21.9 (18.9,24.9)                             | 334 (48)<br>362 (52)<br>21.7 (19.1,24.2)                                     | 0.32                         |
| Comorbidities Diabetes Hypertension COPD Congestive heart failure    | 27 (21.8)<br>87 (70.2)<br>11 (8.9)<br>1 (0.8)                          | 118 (17.0)<br>440 (63.5)<br>35 (5)<br>3 (0.4)                                | 0.24<br>0.16<br>0.13<br>0.48 |
| Type of surgery Scheduled Emergency                                  | 59 (47.6)<br>65 (52.4)   | 442 (63.5)<br>254 (36.5)   | <0.05                        |
| ASA type  II  III  IV  V   | 15 (12.1)<br>78 (62.9)<br>28 (22.6)<br>3 (2.4)                         | 197 (28.3)<br>468 (67.2)<br>31 (4.5)<br>0 (0.0)                              | < 0.05                       |
| Preoperative Hb (g/dL)*  | 10 (9,11.2)  | 11 (9,12)  | 0.04                         |
| Preoperative Cr (mg/dL)*   | 1.1 (0.8,1.4)  | 0.9 (0.8,1.2)  | <0.05                        |
| Preoperative CrCl (mL/min)*  | 34.7 (26.8,44.9)   | 38.8 (29.6,49.7)   | <0.05                        |
| Part of surgery Abdomen Orthopedic Neurology Urology Vascular Others | 40 (32.3)<br>30 (24.2)<br>10 (8.1)<br>10 (8.1)<br>28 (22.6)<br>6 (4.8) | 223 (32.0)<br>149 (21.4)<br>106 (15.2)<br>27 (3.9)<br>155 (22.3)<br>36 (5.2) | 0.14                         |
| Current medication ACEI ARB  | 10 (8.1)<br>10 (8.1)   | 72 (10.3)<br>58 (8.3)  | 0.53<br>1                    |
| Choice of anesthesia General anesthesia Spinal block                 | 111 (89.5)<br>13 (10.5)  | 622 (89.4)<br>74 (10.6)  | 1                            |
| Preoperative blood pressure  SBP (mmHg)*  DBP (mmHg)*  MAP (mmHg)*   | 131 (115.8,146.2)<br>69 (60,77)<br>88.5 (81,98.2)                      | 130 (119,146.2)<br>70 (62,79)<br>90 (82,99)                                  | 0.72<br>0.18<br>0.47         |

Abbreviations: BMI: body mass index, COPD: chronic obstructive lung disease, CHF: chronic heart failure, Hb: hemoglobin, Cr: creatinine, Crcl: creatinine clearance, ACEI: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blockers, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure \*Continuous data were reported as median and IQR 1-3

**TABLE 2.** Clinical characteristics of intraoperative period in super-elderly patients with and without Acute Kidney Injury (AKI) (N=820).

| Characteristics  | AKI<br>(N=124)<br>N (%)                               | Non-AKI<br>(N=696)<br>N (%)                               | P-value                                 |
|--|---|---|---|
| Induction agent Propofol Thiopental Etomidate Ketamine Midazolam | 73 (58.9)<br>0 (0)<br>13 (11.5)<br>3 (2.4)<br>57 (46) | 551 (79.2)<br>12 (1.9)<br>35 (5.5)<br>7 (1.0)<br>209 (30) | <0.05<br>0.23<br><0.05<br>0.18<br><0.05 |
| Narcotic  Morphine  Fentanyl                                     | 120 (97.6)<br>123 (100)                               | 658 (97.8)<br>669 (99.4)                                  | 0.74<br>1                               |
| Muscle relaxant Succinylcholine Cisatracurium Rocuronium         | 11 (10.3)<br>97 (90.7)<br>10 (9.3)                    | 67 (10.9)<br>539 (87.8)<br>72 (11.7)                      | 0.98<br>0.49<br>0.58                    |
| Inhalation Sevoflurane Desflurane No                             | 72 (58.1)<br>29 (23.4)<br>23 (18.5)                   | 371 (53.3)<br>226 (32.5)<br>99 (14.2)                     | 0.37<br>0.05<br>0.26                    |
| Vasopressor Ephedrine Epinephrine Norepinephrine                 | 38 (30.6)<br>7 (5.6)<br>71 (57.3)                     | 298 (42.8)<br>9 (1.3)<br>283 (40.7)                       | 0.01<br><0.05<br><0.05                  |
| Duration of surgery (minutes) mean ± SD                          | 177.5 (135, 256.3)                                    | 180 (135, 256.2)  | 0.88                                    |
| Intraoperative hypotension                                       | 96 (77.4)   | 482 (69.3)  | 0.08                                    |
| Duration of hypotension (minutes)*                               | 15 (5,82.5)   | 10 (0,20)   | <0.05                                   |
| Contrast media use   | 21 (16.9)   | 144 (20.7)  | 0.39                                    |
| Diuretic use   | 12 (9.7)  | 55 (7.9)  | 0.63                                    |
| Fluid intake (mL)*   | 1150 (500 ,2000)                                      | 1100 (700, 1675)  | 0.63                                    |
| Balanced salt solution (mL)*                                     | 1000 (500, 1450)                                      | 1000 (700, 1500)  | 0.56                                    |
| NSS (mL)*  | 500 (100, 1212.5)                                     | 500 (0, 1000)   | 0.07                                    |
| Succinylated gelatin*  | 500 (450, 675)  | 500 (300, 500)  | 0.02                                    |
| Blood transfusion PRC FFP PC                                     | 54 (43.5)<br>26 (21)<br>13 (10.5)                     | 228 (32.8)<br>80 (11.5)<br>37 (5.3)                       | 0.01<br>0.02<br><0.05<br>0.04           |
| Intraoperative blood loss (mL)*                                  | 150 (50,412.5)  | 100 (50,300)  | 0.06                                    |
| Intraoperative urine output (mL/kg/hr)<br>≤0.5<br>0.51-2<br>>2   | 46 (37.1)<br>59 (47.6)<br>19 (15.3)                   | 80 (11.5)<br>389 (55.9)<br>227 (32.6)                     | <0.05                                   |

**Abbreviations:** NSS: normal saline solution, PRC: packed red blood cell, FFP: fresh frozen plasma, PC: platelet count \*Continuous data were reported as median and IQR 1-3

**TABLE 3.** Best predictive score revealed by multivariate logistic regression.

| Risk factor          | Ref       | Crude OR (95%CI)   | Adj.OR (95%CI)      | P (LR-test) | Risk Score |
|----------------------|-----------|--------------------|---------------------|-------------|------------|
| COPD                 | No        | 1.84 (0.91, 373)   | 2.02 (0.93, 4.38)   | 0.07        | 24         |
| Туре                 | Scheduled |                    |                     |             |            |
| Emergency            |           | 1.92 (1.3, 2.82)   | 1.43(0.89, 2.31)    | 0.14        | 14         |
| ASA                  |           |                    |                     |             |            |
| II                   |           |                    |                     | < 0.05      |            |
| III                  |           | 2.19 (1.23, 3.9)   | 2.58 (1.41, 4.73)   |             | 37         |
| IV-V                 |           | 13.13 (6.37,27.08) | 13.73 (5.94, 31.76) |             | 100        |
| Part of surgery      | Neuro     |                    |                     | <0.05       |            |
| Abdomen              |           | 1.9 (0.92,3.95)    | 2.85 (1.27,6.38)    | <0.05       | 42         |
| Orthopedic           |           | 2.13 (1,4.55)      | 3.22 (1.4,7.4)      | <0.05       | 48         |
| Urology              |           | 3.93 (1.48,10.39)  | 8.31 (2.86,24.12)   | <0.05       | 90         |
| Vascular             |           | 1.91 (0.89,4.11)   | 1.8 (0.78,4.12)     | 0.16        | 25         |
| Others               |           | 1.77 (0.6,5.2)     | 2.35 (0.73,7.57)    | 0.15        | 35         |
| Propofol             | Yes       | 2.65 (1.78,3.97)   | 1.63 (1,2.66)       | <0.05       | 19         |
| Succinylated gelatin | no        | 2.55 (1.66,3.93)   | 1.94 (1.2,3.14)     | <0.05       | 26         |

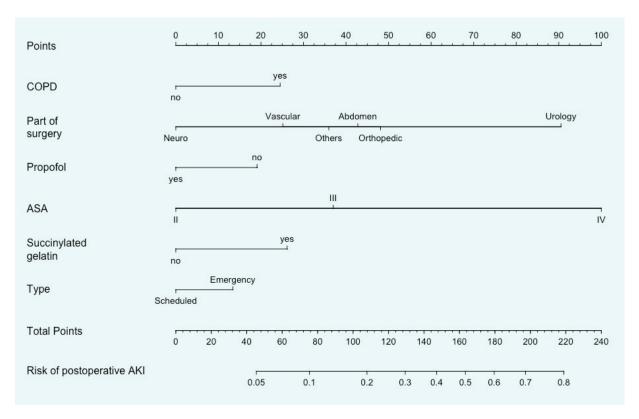
Nonetheless, Blood transfusion consists of red blood cells, fresh frozen plasma and platelet concentrate that were used in AKI group more than others. Intraoperative urine output less than 5 mL/kg occurred in 75% of AKI group, while an intraoperative output less than 5 mL/kg were found a higher risk in AKI group than non-AKI group (P-value<0.05). Other independent variables were not statistically different.

Table 3 presents multivariate logistic regression model adjusted for patient's status and anesthetic drug. Independent variables significantly associated with postoperative AKI were COPD, ASA classification, part of surgery, Propofol and Succinylated gelatin. There was greater frequency of AKI with higher ASA classification with ASA III and ASA IV with V [OR 2.58 (1.41,4.73), OR 13.73 (5.94,31.76), P-value <0.05], respectively. Part of surgery differed significantly between AKI and non-AKI group (P-value <0.05). The risk of AKI was associated with abdominal surgery, orthopedic surgery and urology surgery [OR 2.85 (1.27,6.38), OR 3.22(1.4,7.4), OR 8.31(2.86,24.12)], respectively, excluding patients that underwent vascular surgery. In contrast, Propofol conserved renal function

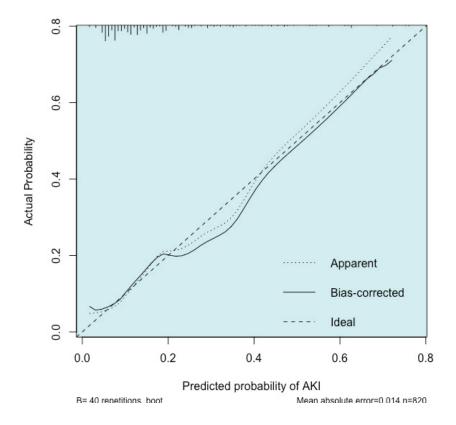
[OR 1.95 (1.21,3.16), P-value<0.05]. There was a statistically significant risk for AKI with Succinylated gelatin use [(OR 1.94(1.2,3.14), P-value <0.05)].

The nomogram comprised of COPD, ASA classification, Part of surgery, Type of surgery, Propofol and Succinylated gelatin (Fig 2). The score ranged from 20 to 100. The nomogram has a good discriminative ability to identify patients with postoperative AKI with AUC 0.746. The calibrate curve shows that the apparent value is almost the same as bias-corrected value; mean squared error = 0.00043 (Fig 3). Cutoff point at 63 was chosen, which had the highest Youden index. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the prediction score was 83, 45, 33, and 89%, respectively.

The rate of renal replacement was higher in patients with postoperative AKI compared with patients without AKI (P-value<0.05). Period of ICU stay and hospital stay was significantly longer in AKI group than other groups (P-value<0.05). Furthermore, 30-day mortality was significantly greater in AKI group (P-value <0.05).



**Fig 2.** The nomogram explicated by logistic regression. Each predictor variable is presented by a line in the figure. The prediction scores ranged from 0 to 100. The variables were gathered with point and paired with the probability of postoperative AKI. A drawing from was made from each variable to the "Points" axis to indicate the points of the variable. The scores for all variables were summed and placed on the "Total score" line. The predicted risk of postoperative AKI ranged from 5 to 80%.



**Fig 3.** The AKI nomogram and its performance. The Apparent value has a closer fit to Bias-corrected value, which means the nomogram had a good performance. Mean absolute error=0.014 Mean squared error=0.00036 Quantile of absolute error=0.03.

**TABLE 4.** Postoperative consequence in patients with and without Acute Kidney Injury (AKI).

| Characteristics            | AKI           | Non-AKI   | P-value |
|----------------------------|---------------|-----------|---------|
|                            | (N=124)       | (N=696)   |         |
| Renal replacement n (%)    | 15 (12.1)     | 1 (0.1)   | <0.05   |
| Period of ICU stay (days)* | 2.5 (0,12)    | 0 (0,1)   | <0.05   |
| Period of hospital (days)* | 14.5 (8.8,28) | 10 (7,18) |         |
| Death 30 n (%)             | 30 (24.2)     | 11 (1.6)  | <0.05   |

<sup>\*</sup>Continuous data were reported as median and IQR 1-3

#### **DISCUSSION**

Nowadays, there is no effective equipment to identify the probability of postoperative AKI in surgical patients, particularly in super-elderly patients. AKI is a serious consequence after surgery. A prior study demonstrated that approximately 6.8% of patients undergoing abdominal surgery developed an episode of AKI.<sup>16</sup> In the present study, almost 15% of AKI among super-elderly and 24.2% with AKI died in 30 days. The incidence of acute kidney injury is highest in elderly and increases with age.<sup>3,17</sup> There are many reasons for the comparatively high probability of AKI in super elderly patients, for instance, comorbidities that produce AKI, comorbidities that need intervention, medication or surgery that disarrange kidney function, and structure and function that alter with time.<sup>3,9</sup> According to meta-analysis, elderly patients fail to recover from AKI and develop to chronic kidney disease.18

The risk of postoperative acute kidney injury is associated with patient factors as age, type of surgery, emergency surgery, part of surgery, ASA classification, preoperative hemoglobin (Hb), preoperative creatinine, preoperative creatinine clearance, and medical comorbidities such as chronic obstructive lung disease (COPD). It is not surprising that emergency surgery was found as a part of the AKI prediction score, as in this study. A US national study revealed that not only cardiac surgery, but also urology, thoracic, orthopedic and malignancy were associated with AKI. In patients following non-cardiac surgery, ASA classification III and IV were shown to comprise a higher proportion of AKI than those with ASA classification I and II.

Other preoperative laboratory data, preoperative anemia<sup>7</sup> high creatinine<sup>20</sup>, low creatinine clearance<sup>6</sup> and

low eGFR² were shown to be similar with previous studies. In cardiac surgery, preoperative anemia increased AKI rate from 1.8% to 3.2%. Meanwhile, patients receiving blood transfusion had relative risk of AKI more than two times compared without transfusion. The mechanism of blood transfusion that could cause AKI is still unclear. Although, It was suggested that pathophysiology can aggravate tissue oxygen delivery and stimulate inflammatory process and oxidative stress. Previous study showed that higher baseline preoperative creatinine was significant risk factor for AKI. Apart from urine output, Mizota T et al. found perioperative urine output less than 0.3 mL/kg/h increased probability of AKI. Even if perioperative urine output was defined differently, the result remains the same.

Neither the univariate analysis nor the nomogram of the study found a significant difference with diuretic use, which is a known AKI stimulator. It is probably due to the reason that we are not given in lower creatinine clearance patient. Nonetheless, The use of diuretic, particularly furosemide has been demonstrated deleterious in prevention and treatment of AKI. 28,29

In this study, the use of norepinephrine and epinephrine was essential factor. Norepinephrine, is frequently used to restore MAP from 60 to 75 mmHg and increase renal oxygen delivery (RDO<sub>2</sub>), Glomerular filtration rate (GFR) and renal oxygenation.<sup>30</sup> On the other hand, It has been shown that norepinephrine decreases renal blood flow (RBF) and renal oxygen delivery, which provoke renal ischemia.<sup>31</sup> Epinephrine has the same efficacy as norepinephrine, but also causes hyperglycemia, hyperlactatemia and acidosis.<sup>31</sup> Based on current evidence, norepinephrine should be used to restore blood pressure within autoregulatory values

in hypotensive vasodilated patients with acute kidney injury.<sup>31</sup> According to previous knowledge, propofol is down regulated by nitric oxidase synthase to preserve renal function<sup>32</sup> and protect renal tissue via peroxidation of lipid membrane.<sup>33</sup> Lee et al. reported that propofol reduced the new onset of chronic kidney disease after nephrectomy.<sup>34</sup> Therefore, the anti-inflammatory effect of propofol might be significant in the use of TIVA technique, whereas propofol in this study was used as a sole induction agent.

Resuscitation fluid, such as Succinylated gelatin another factor which impacts postoperative acute kidney injury. Recent guidelines suggest avoiding the use of gelatin, as systemic colloids gather in proximal renal tubules and disturb renal function, increasing the risk of anaphylaxis, mortality, renal failure and bleeding.<sup>35</sup>

AKI Predictor in surgical super-elderly patients consist of baseline characteristics and perioperative data. We have found a relationship AKI: COPD, type of surgery, ASA classification, part of surgery and Succinylated gelatin. Propofol was used as a defensive factor in this study. Prior study on AKI prediction score in a different setting, displayed a good discrimination which AUC range above 0.7. For instance, for the eGFRpreSurg as a predictive role among very elderly patients, AUC was at 0.703.2 This represented eGFRpreSurg at cut off point 70mL/min/1.73 m<sup>2</sup> as a risk factor of postoperative AKI. Another study by Hong et al. reported the relationship between HUGE formula and mortality in elderly patients from hip fracture surgery with highest AUC of 0.78 (95%CI 0.667-0.892).<sup>26</sup> However, both of the predictors were in super-elderly patient settings and the score obtained from only preoperative data.

This nomogram score in the study is easily understood and handly to adopt in preoperative period. Accordingly, AKI is a preventable condition, nomogram may help physicians to early detect AKI and handle it in proper time. According to resource-limited countries such as Thailand, invasive monitoring in every case might be impossible. The most effective prevention is early detection in high risk, special monitoring, optimal fluid administration and nephrotoxic agent avoidance. From the research principle, it is expected that the nomogram will effectively assist in selection high risk AKI patients for prevention and aggressive intervention.

## Strength and limitation

The incidence of AKI might be precise because AKI in this study was determined by both urine output and serum creatinine. The result may be in indubitable in the occurrence of AKI.

There are some limitations of this study. Firstly, although all super-elderly patients who underwent surgery in the study period were retrieved to reduce selection bias, patient bias was unavoidable due to retrospective study. Secondly, this study could not analyze the cause of AKI categorized into three groups: prerenal, renal and postrenal due to lack of information in our electronic hospital system. The rate of renal replacement therapy was compared between AKI and non-AKI patients; nonetheless there was a lack of information to identify the reason for renal replacement therapy.

Finally, due to the lack of external validation of the scoring system since this is a single center study and there could have been sampling bias. Future studies performed on the scoring system using data of multiple centers can validate it.

# **CONCLUSION**

This study found an increase incidence of postoperative AKI among super-elderly patients and relationship between AKI and morbidity and mortality. Despite, AKI prediction score not being a definitive tool for observation and monitoring, it can help physicians consider various clinical risk factors in evaluating the chance of AKI. This nomogram can help clinical physicians improve the prognosis among super-elderly patients undergoing surgery.

#### REFERENCE

- Khan-Kheil AM, Khan HN. Surgical mortality in patients more than 80 years of age. Ann R Coll Surg Engl 2016 Mar;98(3):177-90
- 2. Wu Q, Yang H, Bo H, Fu M, Zhong X, Liang G, et al. Predictive role of estimated glomerular filtration rate prior to surgery in postsurgical acute kidney injury among very elderly patients: a retrospective cohort study. Ren Fail. 2019 Nov;41(1):866-74.
- 3. Coca SG. Acute kidney injury in elderly persons. Am J Kidney Dis Off J Natl Kidney Found. 2010 Jul;56(1):122-31.
- 4. Li N, Qiao H, Guo J-F, Yang H-Y, Li X-Y, Li S-L, et al. Preoperative hypoalbuminemia was associated with acute kidney injury in high-risk patients following non-cardiac surgery: a retrospective cohort study. BMC Anesthesiol. 2019 Sep 2;19(1):171.
- 5. Kim H-J, Koh W-U, Kim S-G, Park H-S, Song J-G, Ro Y-J, et al. Early postoperative albumin level following total knee arthroplasty is associated with acute kidney injury: A retrospective analysis of 1309 consecutive patients based on kidney disease improving global outcomes criteria. Medicine (Baltimore). 2016 Aug;95(31): e4489.
- Noyez L, Plesiewicz I, Verheugt FWA. Estimated creatinine clearance instead of plasma creatinine level as prognostic test for postoperative renal function in patients undergoing coronary artery bypass surgery. Eur J Cardio-Thorac Surg. 2006 Apr;29(4): 461-5.
- Jang WY, Jung J-K, Lee DK, Han S-B. Intraoperative hypotension is a risk factor for postoperative acute kidney injury after femoral

- neck fracture surgery: a retrospective study. BMC Musculoskelet Disord. 2019 Mar 27;20(1):131.
- 8. An Y, Shen K, Ye Y. Risk factors for and the prevention of acute kidney injury after abdominal surgery. Surg Today. 2018 Jun;48(6):573-83.
- Chaudery H, MacDonald N, Ahmad T, Chandra S, Tantri A, Sivasakthi V, et al. Acute Kidney Injury and Risk of Death After Elective Surgery: Prospective Analysis of Data From an International Cohort Study. Anesth Analg. 2019 May;128(5): 1022-9
- Kang W, Wu X. Pre-, Intra-, and Post-Operative Factors for Kidney Injury of Patients Underwent Cardiac Surgery: A Retrospective Cohort Study. Med Sci Monit Int Med J Exp Clin Res. 2019 Aug 6;25:5841-9.
- Swedko PJ, Clark HD, Paramsothy K, Akbari A. Serum Creatinine
  Is an Inadequate Screening Test for Renal Failure in Elderly
  Patients. Arch Intern Med. 2003 Feb 10;163(3):35-60.
- McPherson RA, Pincus MR, editors. Henry's clinical diagnosis and management by laboratory methods. 23<sup>rd</sup> edition. St. Louis, Missouri: Elsevier; 2017. 1565 p.
- Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD Statement. BMC Med [Internet]. 2015 Jan 6;13(1):1.
- Kellum JA, Lameire N. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care Lond Engl. 2013 Feb 4;17(1):204.
- R Core Team [Internet]. Vienna; 2020. Available from: https:// www.R-project.org/
- Long TE, Helgason D, Helgadottir S, Palsson R, Gudbjartsson T, Sigurdsson GH, et al. Acute Kidney Injury After Abdominal Surgery: Incidence, Risk Factors, and Outcome. Anesth Analg. 2016 Jun;122(6):1912-20.
- Sirikun J. Does Acute Kidney Injury Condition Affect Revised BAUX Score in Predicting Mortality in Major Burn Patients? Siriraj Med J. 2019 Apr 4;71(2):150-7.
- Schmitt R, Coca S, Kanbay M, Tinetti ME, Cantley LG, Parikh CR. Recovery of kidney function after acute kidney injury in the elderly: a systematic review and meta-analysis. Am J Kidney Dis Off J Natl Kidney Found. 2008 Aug;52(2):262-71.
- 19. Kheterpal S, Tremper KK, Heung M, Rosenberg AL, Englesbe M, Shanks AM, 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 Mar 1;110(3):505-15. Available from: https://doi.org/10.1097/ALN.0b013e3181979440
- Chen EY, Michel G, Zhou B, Dai F, Akhtar S, Schonberger RB. An Analysis of Anesthesia Induction Dosing in Female Older Adults. Drugs Aging. 2020 Jun;37(6):435-46.
- Karkouti K, Grocott HP, Hall R, Jessen ME, Kruger C, Lerner AB, et al. Interrelationship of preoperative anemia, intraoperative

- anemia, and red blood cell transfusion as potentially modifiable risk factors for acute kidney injury in cardiac surgery: a historical multicentre cohort study. Can J Anaesth. 2015 Apr;62(4):377-84.
- 22. Karkouti K, Wijeysundera DN, Yau TM, McCluskey SA, Chan CT, Wong P-Y, et al. Influence of erythrocyte transfusion on the risk of acute kidney injury after cardiac surgery differs in anemic and nonanemic patients. Anesthesiology. 2011 Sep;115(3): 523-30.
- 23. James SL, Castle CD, Dingels ZV, Fox JT, Hamilton EB, Liu Z, et al. Global injury morbidity and mortality from 1990 to 2017: results from the Global Burden of Disease Study 2017. Inj Prev. 2020 Oct;26(Supp 1):i96-i114.
- **24.** Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16(1):31-41.
- 25. Funk I, Seibert E, Markau S, Girndt M. Clinical Course of Acute Kidney Injury in Elderly Individuals Above 80 Years. Kidney Blood Press Res. 2016;41(6):947-55.
- 26. Hong SE, Kim T-Y, Yoo J-H, Kim J-K, Kim SG, Kim HJ, et al. Acute kidney injury can predict in-hospital and long-term mortality in elderly patients undergoing hip fracture surgery. PloS One. 2017 Apr 20;12(4):e0176259–e0176259.
- 27. Mizota T, Yamamoto Y, Hamada M, Matsukawa S, Shimizu S, Kai S. Intraoperative oliguria predicts acute kidney injury after major abdominal surgery. Br J Anaesth. 2017 Dec 1;119(6): 1127-34.
- 28. Zhang Y, Jiang L, Wang B, Xi X. Epidemiological characteristics of and risk factors for patients with postoperative acute kidney injury: a multicenter prospective study in 30 Chinese intensive care units. Int Urol Nephrol. 2018 Jul;50(7):1319-28.
- **29.** Ejaz AA, Mohandas R. Are diuretics harmful in the management of acute kidney injury? Curr Opin Nephrol Hypertens. 2014 Mar; 23(2):155-60.
- **30.** Redfors B, Bragadottir G, Sellgren J, Swärd K, Ricksten S-E. Effects of norepinephrine on renal perfusion, filtration and oxygenation in vasodilatory shock and acute kidney injury. Intensive Care Med. 2011 Jan;37(1):60-7.
- 31. Bellomo R, Wan L, May C. Vasoactive drugs and acute kidney injury. Crit Care Med. 2008 Apr;36(4 Suppl):S179-186.
- 32. Dikmen B, Yagmurdur H, Akgul T, Astarci M, Ustun H, Germiyanoglu C. Preventive effects of propofol and ketamine on renal injury in unilateral ureteral obstruction. J Anesth. 2010 Feb;24(1):73-80.
- **33.** Li H, Weng Y, Yuan S, Liu W, Yu H, Yu W. Effect of sevoflurane and propofol on acute kidney injury in pediatric living donor liver transplantation. Ann Transl Med. 2019 Jul;7(14):340.
- 34. Lee H-J, Bae J, Kwon Y, Jang HS, Yoo S, Jeong CW, et al. General Anesthetic Agents and Renal Function after Nephrectomy. J Clin Med. 2019 Sep 24;8(10).
- 35. Brown RM, Semler MW. Fluid Management in Sepsis. J Intensive Care Med. 2019 May;34(5):364-73.