Perioperative Acute Kidney Injury Leading to Chronic Kidney Disease Following Major Abdominal Surgery: A Propensity Score-Matched Analysis

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Abstract

It is unknown whether acute kidney injury (AKI) affects de novo chronic kidney disease (CKD). The aim of this study was to examine the relationship between de novo CKD and perioperative AKI after major abdominal surgery. We hypothesized that AKI after major abdominal surgery would induce de novo CKD and performed a retrospective observational analysis after adjusting for preoperative covariates with propensity score matching. A total of 347 patients with normal renal function, who underwent major abdominal surgery, were observed for 2 years postoperatively. The incidence of AKI within 7 days of surgery was 13.2%. During the 2-year observation period, de novo CKD occurred in 22% of patients with AKI and in 8% of patients with a non-acute kidney injury (NAKI) (p=0.007). Based on the propensity score-matched analysis, the incidence of CKD was 22% for AKI and 13% for NAKI (p=0.070). All-patient analysis revealed that the probability of being CKD-free was lower in AKI patients, compared to that in NAKI patients (p=0.002). This was not the case for the propensity score-matched analysis (p=0.166). The survival rate was lower in patients with AKI compared to those with NAKI in propensity score-matched analysis (p=0.033).

A Cox proportional hazard regression analysis did not identify any risk factors for de novo CKD after surgery. We found that AKI patients showed higher mortality than non-AKI patients during the 2-year observation period after major abdominal surgery. However, we could not demonstrate that AKI affects de novo CKD in patients without renal dysfunction. The early detection and diagnosis of postoperative AKI will be key to perioperative management for major abdominal surgery.

Key words
Acute kidney injury (AKI), chronic kidney disease (CKD), perioperative period, estimated glomerular filtration rate (eGFR)

Introduction

Acute kidney injury (AKI) during the perioperative period is a frequent complication. Perioperative AKI not only leads to a prolonged hospital stay but also increases perioperative mortality¹. Previously, due to the lack of unified diagnostic criteria for renal failure, no consensus could not be reached regarding the frequency and prevention strategy for perioperative acute renal failure. However, in the 2000s, specific diagnostic criteria were introduced worldwide²–⁴. As the diagnostic criteria for AKI have been accepted worldwide, research on perioperative renal failure has increased over the last two decades. The degree of renal injury was distinctly defined, which facilitated clear analysis of the data and study comparisons.

The kidney is exposed to a variety of risks during the perioperative period, such as renal ischemia, renal hypoxia, infection, etc., increasing the risk of postoperative AKI⁵. In addition, the renal function of patients with chronic kidney disease (CKD) may also deteriorate during the perioperative period. Several studies have reported that the incidence of periopera-
tive AKI, following cardiovascular surgery was between 8.9–42%\(^6,7\), and 13.5–31.0% after major vascular surgery\(^8\). The reported occurrence of AKI after major abdominal surgery was lower at 6.7–18.5%\(^8\).

The occurrence of AKI increases perioperative mortality 1.48-fold\(^7\).

Although it was thought that patients with AKI generally make a complete recovery, recent investigations have shown that AKI can develop into CKD\(^9\).

While several studies have indicated the development of CKD subsequent to AKI during the perioperative period following cardiovascular surgery, there are few reports on the development of CKD after AKI following major abdominal surgery. In a systemic review, the incidence of AKI after abdominal surgery was 13.4% (95% CI=10.9–16.4%). The mortality rate following AKI was 12.6-fold higher than that in patients with non-acute kidney injury (NAKI)\(^10\). Furthermore, the adverse renal outcome as well as the mortality rate after 4 years was shown to be significantly higher in the AKI group compared with the NAKI group\(^11\). These studies included patients with decreased preoperative renal function, therefore we could not confirm whether AKI affected postoperative de novo CKD.

In this study, we investigated the relationship between de novo CKD and perioperative AKI after major abdominal surgery. We conducted a retrospective observational study and analyzed the sample after adjusting for preoperative factors, with propensity score matching. We hypothesized that AKI after major abdominal surgery can cause CKD and that AKI increases postoperative mortality.

**Materials and Methods**

**Study design**

This was a single center-retrospective observational, case-control study. The research protocol was permitted by the St. Marianna Medical University’s Institutional Review Board (IRB #3510). This study was carried out after registration with UMIN Clinical Trial Registry (UMIN ID: UMIN000030004, Principal Investigator: Takeshi Tateda, Date of registration: November 20, 2017, http://www.umin.ac.jp/ctr/index/htm). The retrospective observational study was carried out using existing data; hence, the requirement of informed consent was waived by IRB. This manuscript adheres to the applicable STROBE guidelines.

**Selection criteria**

Patients who underwent major abdominal surgery between January 1, 2013, and December 31, 2015, at the Kawasaki Municipal Tama Hospital, were included in the study and observed postoperatively for 2 years.

**Exclusion criteria**

Patients diagnosed with CKD preoperatively and who underwent cholecystectomy, appendectomy, and inguinal hernia repair were excluded from the analysis. Patients were also excluded if their baseline estimated glomerular filtration rate (eGFR) was less than 60 ml/min.

**Definitions**

The eGFR was calculated from serum creatinine (SCr) levels and determined using a Japanese formula\(^12\).

AKI was defined using the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) criteria (increase in SCr by ≥0.3 mg/dl within 48 hours or increase in Scr to ≥1.5 times baseline). We diagnosed AKI according to the highest level of SCr during the 7 days after surgery. CKD was defined using the KDIGO 2012 criteria. We diagnosed CKD according to the decrease in eGFR (<60 ml/min/1.73m\(^2\)) over 3 months. CKD was staged for severity according to eGFR; G1: eGFR >90 ml/min/1.73m\(^2\), G2: eGFR between 60–89 ml/min/1.73m\(^2\), G3a: eGFR between 45–59 ml/min/1.73m\(^2\), and G3b: eGFR between 30–44 ml/min/1.73m\(^2\).

The following factors were extracted from the electronic health records of each patient.

1. **Preoperative factors**: age, sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA PS), preoperative eGFR (baseline level), preoperative SCr, preoperative hemoglobin levels, and any comorbidities, including ischemic heart disease, hypertension, chronic obstructive pulmonary disease, diabetes mellitus, and malignant tumors.
2. **Intraoperative factors**: duration of anesthesia, duration of surgery, fluid infusion volume, blood transfusion, surgical site (hepatobiliary pancreatic, upper gastrointestinal, lower gastrointestinal, or other), surgical approach (laparotomy, or endoscopic procedure), use of vasoactive drugs, colloids infusion volume, elective, emergency, or a re-operation.
3. **Post-operative factors**: postoperative and recovery eGFR, postoperative and recovery SCr, chemotherapy, postoperative complications such as pneumonia or sepsis, Sequential Organ Failure Assessment
(SOFA) score (sepsis-related), incidence of AKI and CKD, mortality.

The postoperative eGFR was calculated from the highest SCr during the 7 days after surgery. eGFR recovery was calculated from the lowest stable SCr levels, at least 3 months after surgery.

**Main outcomes calculated**

We calculated the incidence of postoperative AKI, 2-year incidence of CKD and survival rates of AKI and CKD.

**Statistical analysis**

The comparison between the AKI and NAKI groups and the CKD and non-chronic kidney disease (NCKD) groups were analyzed with either the Mann-Whitney U test or the Student’s t-test for numerical data and with the Chi-square test or the Fisher’s exact test for categorical data.

The changes in eGFR from the baseline level were analyzed using the Friedman test between AKI and NAKI patients, as well as CKD and NCKD patients, followed by the Bonferroni post hoc test. Assessment for differences in eGFR level between AKI and NAKI group and also between CKD and NCKD group were performed using the Kruskal-Wallis test followed by the Steel-Dwass post hoc test.

Both the CKD incidence and survival rate in the AKI and NAKI groups were analyzed with the Kaplan-Meier survival curve. A comparison between the AKI and NAKI on Kaplan-Meier survival curves was calculated using log-rank test. This process was repeated for the survival rate in the CKD and NCKD group. To investigate the risk factors for de novo CKD during the 2-year observation period, a Cox proportional hazard regression analysis was performed with the following 4 variables, age, sex, baseline eGFR, and AKI.

To reduce the effect that preoperative covariant differences had on our statistical results, and to reduce bias, a propensity score-matched analysis was performed. A multivariate logistic regression analysis was performed to calculate propensity scores. The involved preoperative characteristics in this logistical model were age, sex, BMI, baseline eGFR, and ASA PS. These confounders were thought to be independent risk factors for AKI based on clinical knowledge. Each AKI patient was matched with a NAKI patient using the nearest-neighbor matching method without a replacement. As the matching number did not change either with or without a caliper width of a 0.2 standard deviation of the propensity score logit, we applied exact matching. Non-matched patients were removed from the propensity score-matched analysis. After matching, we used the standardized mean difference (SMD) to check the balance of preoperative factors. Statistical analysis was performed using R. ver-3.4.1 (R Project for Statistical Computing, Vienna, Austria) and JMP. Ver13.0 (SAS Institute Inc, Cary, NC, USA).

**Results**

A total of 535 patients underwent major abdominal surgery at Kawasaki Municipal Tama Hospital between January 1, 2013 and December 31, 2015. Forty-four patients with CKD prior to their surgery were excluded from the analysis. Furthermore, we excluded 144 patients with a suspected low renal function, with a baseline eGFR of less than 60 ml/min. Finally, 347 patients with normal renal function were analyzed. Of these 347 patients with a preoperative normal renal function, 46 (13.2%) suffered AKI within 7 days after surgery (Table 1). Ten AKI patients and 24 NAKI developed CKD during the 2-year observation period (22% vs 8%, p=0.007), and 10 AKI patients and 36 NAKI died after surgery (21% vs 12%, p=0.098) (Table 2).

All-patient analysis revealed more males and a lower baseline SCr in AKI than in NAKI. But there was no significant difference in age, BMI, preoperative hemoglobin, baseline eGFR, ASA PS classification and comorbidities between the two groups (Table 1). Emergency procedures and CKD were more frequent, intraoperative colloid volume was larger and SOFA score was higher in AKI than in NAKI. There was no significant difference in surgical site and surgical approach, intraoperative fluid volume, frequency of blood transfusion, use of vasopressor, duration of surgery and anesthesia and death between the two groups (Table 2).

All AKI patients were matched to a similar NAKI patient in the propensity score-matched analysis. The SMD of the preoperative characteristics between AKI and NAKI decreased from 0.221 ± 0.083 to 0.031 ± 0.028, showing that the balance of preoperative characteristics was improved after group matching (Table 1). After propensity score matching, each of the 46 matched pairs, made up of an AKI and NAKI patient, were analyzed. In the propensity score-matched analysis, there was no significant difference in preoperative and intraoperative factor except intraoperative colloid volume between AKI and...
Table 1. Patient Demographics (Preoperative Factor)

|                      | NAKI (n=301) | AKI (n=46) | P value | SMD | NAKI (n=46) | AKI (n=46) | P value | SMD |
|----------------------|--------------|------------|---------|-----|-------------|------------|---------|-----|
| Age (yr)             | 68.0 [60.0-76.0] | 65.5 [53.0-72.5] | 0.103   | 0.222 | 66.0 [57.3-74.0] | 65.5 [53.0-72.5] | 0.47 | 0.061 |
| BMI (kg/m²)          | 21.9 (3.7) | 22.7 (3.8) | 0.164 | -0.223 | 22.6 (3.5) | 22.7 (3.8) | 0.901 | -0.027 |
| Sex                  | 0.003 | 0.322 | 0.7833 | 0.0577 |
| male (%)             | 189 (63%) | 39 (85%) | 39 (85%) | 39 (85%) |
| female (%)           | 113 (37%) | 7 (15%) | 7 (15%) | 7 (15%) |
| Hb (mg/dl)           | 12.6 (2.0) | 13.2 (2.2) | 0.061 | -0.298 | 13.1 (2.0) | 13.2 (2.2) | 0.944 | -0.014 |
| Baseline SCr (mg/dl) | 0.79 (0.14) | 0.78 (0.15) | 0.001 | -0.495 | 0.79 (0.13) | 0.78 (0.15) | 0.982 | 0.071 |
| Baseline eGFR (ml/min 1.73 m²) | 75.6 [67.6-86.4] | 71.7 [64.4-81.1] | 0.068 | 0.247 | 71.7 [65.9-79.6] | 71.7 [64.4-81.1] | 0.848 | -0.01 |

Table 2. Patient Demographics (Intraoperative and Postoperative Factor)

|                      | NAKI (n=301) | AKI (n=46) | P value | SMD | NAKI (n=46) | AKI (n=46) | P value | SMD |
|----------------------|--------------|------------|---------|-----|-------------|------------|---------|-----|
| Intraoperative factor |              |            |         |     |             |            |         |     |
| Surgical approach   |              |            |         |     |             |            |         |     |
| Laparotomy (%)      | 184 (61%) | 29 (63%) | 0.068 | -0.298 | 28 (61%) | 29 (63%) | 0.982 | 0.071 |
| Endoscopic-aid (%)  | 115 (38%) | 17 (37%) | 0.141 | -0.131 | 18 (39%) | 17 (37%) | 0.141 | -0.131 |
| Conversion (%)       | 0 (0%)   | 0 (0%)   | 0.001 | -0.495 | 0 (0%)   | 0 (0%)   | 0.001 | -0.495 |
| Emergency (%)        | 30 (10%) | 10 (22%) | 0.062 | -0.223 | 3 (7%)   | 2 (4%)   | 0.062 | -0.223 |
| Surgical site        |              |            |         |     |             |            |         |     |
| HBP (%)              | 44 (15%) | 4 (9%)   | 0.001 | -0.495 | 10 (22%) | 4 (9%)   | 0.001 | -0.495 |
| upper GI (%)         | 68 (23%) | 7 (15%)  | 0.141 | -0.131 | 11 (24%) | 7 (15%)  | 0.141 | -0.131 |
| lower GI (%)         | 185 (63%) | 33 (72%) | 0.141 | -0.131 | 24 (52%) | 33 (72%) | 0.141 | -0.131 |
| others (%)           | 4 (1%)   | 2 (4%)   | 0.001 | -0.495 | 1 (2%)   | 2 (4%)   | 0.001 | -0.495 |
| Fluids volume (ml)   | 2550 [1900-3400] | 2650 [2163-3725] | 0.329 | -0.304 | 2975 [2312-3862] | 2650 [2163-3725] | 0.384 | -0.09 |
| Collod volume (ml)   | 500 [0-900] | 575 [500-1000] | 0.001 | -0.495 | 500 [467] | 575 [500-1000] | 0.019 | -0.399 |
| Blood transfusion (%)| 52 (17%) | 13 (28%) | 0.105 | -0.174 | 6 (13%) | 13 (28%) | 0.121 | 0.389 |
| Use of vasopresor (%)| 229 (76%) | 35 (70%) | 0.141 | -0.131 | 36 (70%) | 35 (70%) | 0.141 | -0.131 |
| Duration of surgery (min) | 269 (120) | 276 (135) | 0.773 | -0.046 | 297 (124) | 276 (135) | 0.522 | 0.134 |
| Duration of anesthesia (min) | 33 (172) | 33 (172) | 0.773 | -0.046 | 34 (172) | 33 (172) | 0.773 | -0.046 |
| Postoperative factor |              |            |         |     |             |            |         |     |
| Chemotherapy (%)     | 111 (37%) | 16 (35%) | 0.515 | 0.069 | 22 (48%) | 16 (35%) | 0.459 | 0.41 |
| Pneumonia (%)        | 14 (5%) | 4 (9%) | 0.001 | -0.495 | 2 (4%) | 4 (9%) | 0.001 | -0.495 |
| Sepsis (%)           | 69 (24%) | 15 (33%) | 0.195 | 0.085 | 12 (26%) | 15 (33%) | 0.497 | 0.047 |
| SOFA score           | 0.89 (1.04) | 1.30 (2.18) | 0.016 | 0.382 | 0.90 (1.01) | 1.30 (2.18) | 0.107 | 0.388 |
| AKI stage 1 (%)      | NA | 39 (85%) | NA | NA | NA | 39 (85%) | NA | NA |
| stage 2 (%)          | NA | 7 (15%)  | NA | NA | NA | 7 (15%)  | NA | NA |
| CKD stage 1 (%)      | NA | 39 (85%) | NA | NA | NA | 39 (85%) | NA | NA |
| stage 2 (%)          | NA | 7 (15%)  | NA | NA | NA | 7 (15%)  | NA | NA |

NAKI: non-acute kidney injury, AKI: acute kidney injury, SMD: standardized mean differences, BMI: body mass index, Hb: hemoglobin, eGFR: ml/min/1.73m²

Table 2.

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NAKI. The incidence of de novo CKD during the 2-year observation period was 22% (10 patients) in the AKI group, and 13% (6 patients) in the NAKI group (p=0.070 and p=0.379, respectively, Table 2). The Kaplan-Meier analysis revealed that the probability of the remaining CKD-free patients during the 2-year observation period was 22% (10 patients) in the AKI group, and 13% (6 patients) in the NAKI group.
observational period was significantly lower in the all-patient study (p=0.002), but that was not statistically significant in the propensity score matching study (p=0.166 (Figure 1).

The survival rate of the patients in the AKI group showed a greater decrease than that of the NAKI group for the propensity score matching study (p=0.033) (Figure 2). However, there was no difference in survival rate between the CKD and NCKD group (all patients; p=0.746 and propensity-score matched patients; p=0.519) (Figure 2).

The Cox proportional hazard regression analysis indicated that AKI (adjusted hazard ratio=2.63, 95% confidence interval 1.26–5.73) and baseline eGFR (adjusted HR=0.93, 95% CI 0.89–0.97) were independent risk factors for de novo CKD after surgery, in the all-patient study. However, we were unable to deduce an independent risk factor for CKD from the propensity score in the propensity-matched study (Table 3).

In the AKI group, eGFR decreased after surgery depending on the severity of renal dysfunction but returned to nearly the baseline level during the recovery stage (Figure 3, Table 4). In the CKD group, the eGFR of patients in stage G3a and G3b kidney disease also decreased after surgery, and this decrease continued into the recovery period (Figure 3, Table 4). The change in eGFR was similar between the all-patient and propensity score-matched patient analyses.

Discussion

Our study indicates that AKI reduces the 2-year survival rate after major abdominal surgery, despite the fact that these patients had preoperative normal renal function. But we could not demonstrate that AKI affects the occurrence of de novo CKD.

AKI and CKD have been thought to differ in their pathophysiologies, because AKI is a transient disease and renal function recovers, whereas CKD is a progressive disease and renal function does not recover. Several reports have revealed that CKD is a risk factor for AKI and vice versa. Although our results with Cox proportional hazard analysis demonstrated that preoperative eGFR and AKI are independent risk factors for de novo CKD in all-patient study, the results with propensity score-matched analysis did not show statistically significance. Therefore, these results may indicate that both preoperative renal function and AKI, are related to postoperative renal dysfunction, which could result in CKD. But further study is needed to clarify this point.

There have been many investigations exploring the perioperative risk factors for AKI. Grams et al. demonstrated that cardiac surgery has a high risk resulting in AKI, with age, sex, high blood pressure, and an eGFR<60 ml/min being the main risk factors. A multiple logistic regression analysis revealed that sex, hypertension, previous CKD, and an ASA PS of IV were risk factors for AKI following major surgery.

Figure 1. Probability of CKD free after surgery

Left: all patient analysis, right: propensity score-matched patient analysis.

CKD: chronic kidney disease, AKI: acute kidney injury, NAKI: non-acute kidney injury.
Figure 2. Survival rate.

Upper left panel: AKI and NAKI all patient analysis, lower left panel: CKD and NCKD all patient analysis, upper right panel: AKI and NAKI propensity score-matched patient analysis, and lower right panel: CKD and NCKD propensity score-matched patient analysis.

AKI: acute kidney injury, NAKI: non-acute kidney injury, CKD: chronic kidney disease, NCKD: non-chronic kidney disease

Table 3. Cox Proportional Hazard Ratio

| Factor                              | Unadjusted HR | 95% CI      | P value | Adjusted HR | 95% CI      | P value |
|-------------------------------------|---------------|-------------|---------|-------------|-------------|---------|
| Preoperative                       |               |             |         |             |             |         |
| All patient analysis                | Age (yr)      | 1.03        | 0.99-1.07| 0.06        | 1.03        | 0.99-1.06| 0.14    |
|                                    | Sex           | 0.79        | 0.38-1.66| 0.53        | 0.84        | 0.40-1.79| 0.65    |
|                                    | Baseline eGFR| 0.92        | 0.89-0.96| 0.0001      | 0.93        | 0.89-0.97| 0.0005  |
| Postoperative                      | AKI           | 2.98        | 1.42-6.23| 0.004       | 2.63        | 1.26-5.73| 0.01    |
| Propensity score matched patient analysis | Age (yr)      | 1.03        | 0.99-1.08| 0.35        | 1.04        | 0.99-1.09| 0.13    |
|                                    | Baseline eGFR| 0.82        | 0.19-3.64| 0.8         | 0.55        | 0.12-2.58| 0.45    |
|                                    | Postoperative | 2.08        | 0.71-6.10| 0.18        | 2.1         | 0.72-6.15| 0.18    |

HR: hazard ratio, CI: confidence interval, AKI: acute kidney injury, eGFR: estimated glomerular filtration rate

abdominal surgery\(^\text{13}\). In contrast to the present study, these 2 studies included patients with preoperative renal dysfunction. In a study conducted by Kheterpal et al. before the KDIGO classification had been released, the following factors were considered a preoperative risk factor for acute renal failure: age>59, BMI>32, having a high-risk surgery, the need to undergo emergency surgery, peripheral vascular disease, liver disease, and chronic obstructive pulmonary disease\(^\text{14}\). Similar to our study, Kheterpal et al. did not include patients with preoperative renal dysfunction and reported that acute renal failure was associated with increased 30-day, 60-day, and 1-yr mortality. Therefore, our results agree that postoperative AKI...
increases mortality, even in patients without preoperative renal dysfunction. We were unable to find an intraoperative risk factor for CKD in the all-patient or propensity score-matched patient analysis, with logistic regression analysis, despite a Mann Whitney U test revealing that the intraoperative colloid infusion number was larger in the AKI group than in the NAKI group.

Gameiro et al. revealed that the use of contrast media, diuretics, vasoactive drugs, unstable hemodynamics, massive blood loss, and blood transfusion and the need for large volumes of colloid infusions appeared to be intraoperative risk factors for AKI\(^{17}\). Intraoperative hypotension or unstable hemodynamics during surgery could lead to AKI\(^{19}\), as well as prolonged hypotension of fewer than 65 mmHg\(^{19}\). However, we did not examine the intraoperative hemodynamics in detail. As there were no differences in use of vasoactive drugs, our results do not indicate that intraoperative hemodynamics was closely related to AKI.

We determined that preoperative eGFR and AKI are independent risk factors for de novo CKD with an all-patient analysis. However, we could not identify any risk factors for CKD after adjusting for preoperative variations. These results indicate that various perioperative factors and the extent of renal injury reflect the occurrence and progression of CKD\(^{20}\). Although the incidence of CKD was higher in AKI patients than in NAKI patients by the all-patient analysis, the propensity score-matched analysis showed no difference between the two groups in the Kaplan-Meier curve analysis. Our results are congruent with those of Mizota et al.\(^{21}\) who determined that

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**Figure 3.** Changes in eGFR

Upper left panel: AKI all patient analysis, lower left panel: CKD all patient analysis, upper right panel: AKI propensity score-matched patient analysis, and lower right panel: CKD propensity score-matched patient analysis.

Upper panels blue dots = NAKI, red dots = AKI stage 1, and green dots = AKI stage 2. Lower panels blue dots = CKD stage G1, red dots = CKD stage G2, and green dots = CKD stage G3a, and purple dots = CKD stage G3b.

The lines denote the median values. AKI: acute kidney injury, CKD: chronic kidney disease, G1: estimated glomerular filtration rate (eGFR) >90 ml/min/1.73m\(^2\), G2: eGFR between 60–89 ml/min/1.73m\(^2\), G3a: eGFR between 45–59 ml/min/1.73m\(^2\), and G3b: eGFR between 30–44 ml/min/1.73m\(^2\)
Table 4. The Change of eGFR. Upper table shows median value [interquartile range] and lower table shows p value.

| AKI stage | CKD stage |
|-----------|-----------|
| All patient analysis | n 301 39 7 69 244 30 4 |
| baseline | 75.6 [67.6 - 86.4] 69.6 [64.3 - 87.6] 80.3 [72.3 - 88.1] 89.0 [81.8 - 107.9] 73.1 [66.7 - 81.8] 67.2 [61.5 - 76.9] 64.4 [62.3 - 66.3] |
| post | 71.8 [62.6 - 83.5] 48.2 [44.4 - 53.9] 28.4 [27.3 - 36.8] 92.2 [79.3 - 102.8] 68.0 [58.8 - 76.8] 57.2 [49.8 - 64.0] 46.5 [39.8 - 51.6] |
| recovery | 78.7 [68.8 - 87.7] 66.1 [60.6 - 79.5] 63.6 [58.3 - 68.7] 99.8 [94.6 - 110.7] 75.3 [77.7 - 82.2] 34.5 [31.1 - 56.8] 42.3 [39.3 - 43.4] |

Propensity baseline | 71.7 [65.9 - 79.6] 69.6 [64.3 - 78.6] 80.3 [72.4 - 88.1] 108.6 [83.8 - 109.3] 70.9 [64.6 - 78.9] 73.7 [64.4 - 78.2] 65.7 [64.4 - 67.0] |
Post | 67.8 [58.5 - 75.3] 48.2 [44.4 - 53.9] 28.4 [27. - 36.8] 71.9 [65.2 - 74.7] 55.3 [47.2 - 69.2] 49.2 [45.5 - 54.7] 41.8 [37.8 - 47.4] |
Matched analysis recovery | 74.3 [64.6 - 80.9] 66.1 [60.6 - 79.5] 63.6 [58.3 - 68.7] 94.7 [92.0 - 103.3] 72.2 [64.7 - 78.4] 54.4 [50.6 - 57.0] 41.2 [37.3 - 42.4] |

| Time | Stage | All patient analysis | Propensity score |
|------|-------|---------------------|------------------|
| baseline | NAKI: AKI stage 1 | 0.062 | 0.803 |
| Propensity | baseline | G1:G2 | <0.0001 | 0.0037 |
| P value | NAKI: AKI stage 2 | 0.867 | 0.432 |
| AKI stage 1: stage 2 | 0.345 | 0.345 |
| AKI stage 1: stage 2 | <0.0001 | <0.0001 |
| AKI stage 1: stage 2 | 0.014 | 0.014 |
| AKI stage 1: stage 2 | 0.0005 | 0.308 |
| AKI stage 1: stage 2 | 0.012 | 0.097 |
| AKI stage 1: stage 2 | 0.542 | 0.542 |
| AKI stage 1: stage 2 | G1:G3a | G1:G3b | 0.006 | 0.147 |
| AKI stage 1: stage 2 | G2:G3a | 0.008 | 0.999 |
| AKI stage 1: stage 2 | G2:G3b | 0.092 | 0.559 |
| AKI stage 1: stage 2 | G3a:G3b | 0.78 | 0.662 |
| AKI stage 1: stage 2 | G1:G2 | <0.0001 | 0.0015 |
| AKI stage 1: stage 2 | G1:G3a | <0.0001 | 0.0192 |
| AKI stage 1: stage 2 | G1:G3b | 0.005 | 0.095 |
| AKI stage 1: stage 2 | G2:G3a | 0.001 | 0.506 |
| AKI stage 1: stage 2 | G2:G3b | 0.018 | 0.234 |
| AKI stage 1: stage 2 | G3a:G3b | 0.24 | 0.817 |
| AKI stage 1: stage 2 | G1:G2 | <0.0001 | 0.0001 |
| AKI stage 1: stage 2 | G1:G3a | <0.0001 | 0.0005 |
| AKI stage 1: stage 2 | G1:G3b | <0.0001 | 0.0005 |
| AKI stage 1: stage 2 | G2:G3a | <0.0001 | 0.0001 |
| AKI stage 1: stage 2 | G2:G3b | <0.0001 | 0.0001 |
| AKI stage 1: stage 2 | G3a:G3b | 0.007 | 0.0429 |

AKI, age, and preoperative eGFR are independent risk factors for CKD within 1 year of abdominal surgery.

The mechanism that causes AKI to progress to CKD has not been completely elucidated. Renal injury causes the destruction of endothelial cells that can lead to tissue hypoxia and ischemia. In cases of mild to moderate kidney injury, most of the nephron is regenerated and restored with adaptive repair. In cases of severe kidney injury, the nephron undergoes maladaptive repair. Maladaptive repair is a dysregulated process, with aberrant matrix remodeling, inducing fibrosis that causes a decrease in renal function. Finally, in situations where the severity of kidney injury delayed the recovery of renal function, follow-up of postoperative renal function is an important strategy to predict CKD.
our study, it was AKI and not CKD that reduced the 2-year survival rate. This result is similar to that obtained in a study by Bihorac et al.\textsuperscript{27} in which they investigated the survival rate of AKI patients after major surgery. They demonstrated that the 5-year and 10-year survival rate following major surgery was lower in the AKI group (64% and 45%, respectively) than in the NAKI group (78% and 65%, respectively).\textsuperscript{27} There was no difference in survival rates between the CKD and NCKD groups in our study. A similar study reported that the survival rate began to decrease after 4 years in CKD stage 3 patients and after 5 years in CKD stage 4 patients after surgery.\textsuperscript{28}

We could not clarify whether CKD affects the survival rate after major abdominal surgery because the follow-up period in our study was too short.

Our study did have limitations, including being conducted in an urban primary medical center; the number of major abdominal surgeries conducted each year was less than other larger medical centers.

We found that baseline eGFR is an independent risk factor of CKD with all-patient analysis, but there was no statistical significance with propensity score-matched analysis on Cox proportional hazard regression analysis. Baseline eGFR was included as confounder on multivariate logistic regression analysis to calculate propensity score. Therefore, this may have been the reason for the statistical inconsistency between all-patient and propensity-matched analysis.

On the other hand, we could not demonstrate that AKI is an independent risk factor for postoperative CKD on propensity-matched analysis. However, the sample size was smaller in the propensity score-matched analysis than in the all-patient analysis, which may have led to the inconsistency between these 2 analytical methods. We could not clarify that AKI does not affect CKD after abdominal surgery.

We limited the number of preoperative factors we examined, using logistic regression analysis, to 4 to predict AKI, and 5 to predict CKD. It may be necessary to not only consider preoperative factors but also intraoperative factors to predict AKI that can lead to CKD.\textsuperscript{29–31} We evaluated AKI by only measuring SCr, and not urinary volume. The evaluation of AKI using both SCr and urinary volume is more accurate than that using only one of these parameters alone to predict 1-year mortality in Intensive Care Unit patients.\textsuperscript{32} Furthermore, the level of SCr decreases with hemodilution as a result of infusion with fluids, and the production of creatinine will decrease after surgery; therefore, we may have underestimated the level of SCr and under-evaluated AKI.\textsuperscript{33}

We performed propensity score-matching using the nearest-neighbor matching method, without a caliper. This resulted in all the AKI patients being included in the analysis. Therefore, this analysis will predominantly reflect the AKI population and not the NAKI population in the preoperative state. In the future, the analysis of larger sample sizes will be necessary.

In conclusion, we found that it was AKI and not CKD that strongly influenced mortality during the 2-year observation period after major abdominal surgery. However, we could not demonstrate that AKI and preoperative eGFR affect de novo CKD in patients without renal dysfunction. A prevention strategy and treatment for AKI that can lead to CKD has not yet been established, but the early detection and diagnosis of both AKI and CKD will be key to improved outcomes.

Conflicts of Interest
The authors have nothing to disclose.

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