Electronic alert outpatient protocol improves the quality of care for the risk of postcontrast acute kidney injury following computed tomography

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Background: Prevention and diagnosis of postcontrast acute kidney injury (AKI) after contrast-enhanced computed tomography is burdensome in outpatient department. We investigated whether an electronic alert system could improve prevention and diagnosis of postcontrast AKI.

Methods: In March 2018, we launched an electronic alert system that automatically identifies patients with a baseline estimated glomerular filtration rate of <45 mL/min/1.73 m², provides a prescription of fluid regimen, and recommends a follow-up for serum creatinine measurement. Participants prescribed contrast-enhanced computed tomography at outpatient department before and after the launch of the system were categorized as historical and alert group, respectively. Propensity for the surveillance of postcontrast AKI was compared using logistic regression. Risks of AKI, admission, mortality, and renal replacement therapy were analyzed.

Results: The historical and alert groups included 289 and 309 participants, respectively. The alert group was more likely to be men and take diuretics. The most frequent volume of prophylactic fluid in historical and alert group was 1,000 and 750 mL, respectively. Follow-up for AKI was more common in the alert group (adjusted odds ratio, 6.00; p < 0.001). Among them, incidence of postcontrast AKI was not statistically different. The two groups did not differ in risks of admission, mortality, or renal replacement therapy.

Conclusion: The electronic alert system could assist in the detection of high-risk patients, prevention with reduced fluid volume, and proper diagnosis of postcontrast AKI, while limiting the prescribing clinicians’ burden. Whether the system can improve long-term outcomes remains unclear.

Keywords: Acute kidney injury, Automation, Contrast media, Electronic prescription, Quality of health care
**Introduction**

Broader use of intravenous contrast media during contrast-enhanced computed tomography (CECT) can increase the incidence of postcontrast acute kidney injury (PCAKI), particularly in patients with known risk factors. Not only is PCAKI after CECT associated with long-term mortality [1, 2], but recurrent exposure to contrast may lead to more kidney failure in patients with diminished baseline renal function [3]. In populations where repeated CECT is an integral part of management, such as patients with cancer, appropriate measures to prevent and diagnose PCAKI are required to avoid adverse clinical outcomes, including the progression of chronic kidney disease (CKD), which prevents optimal evaluation and treatment of primary diseases [4].

Although the reported incidences of PCAKI vary widely depending on the specific study results, up to 36.5% is reported in moderate-to-severe CKD and diabetes [5–7]. In the absence of specific treatment, the European Society of Urogenital Radiology 2018 and the American College of Radiology 2018 guideline suggest that preventive hydration is a practical prevention strategy in high-risk patients with reduced estimated glomerular filtration rate (GFR) [8]. However, identification of patients indicated for prophylaxis is often difficult in outpatient settings at tertiary hospitals because attending clinicians ordering CECT, who may not be specialized in the pertinent field (i.e., nephrology or radiology), should be aware of the risk criteria and recommended regimen for intravenous volume administration. Absence of historical records of baseline renal function may also prohibit adequate assessment. Moreover, since the actual examination date of CECT is usually arranged on a different day from the date of order, time/place/personnel for intravenous fluid administration should be planned to match the schedule. Finally, the detection of PCAKI necessitates the measurement of serum creatinine (sCr) and follow-up visits to confirm the cases, which causes considerable inconvenience in outpatient clinics. These obstacles frequently cause insufficient hydration and missed PCAKI diagnosis [9].

With the advancement of artificial intelligence and information technology, clinical decision support systems are being actively developed and applied in various medical fields [10]. Automated alert systems incorporated into hospital information systems can help clinicians avoid inadvertent mistakes and promote multidisciplinary practices. In our hospital, we previously adopted an automated electronic alert system to detect in-hospital acute kidney injury (AKI) and proved that the system along with prompt intervention by nephrologists can help recover from AKI [11].

In this study, we leveraged an electronic alert system for the automatic identification of high-risk patients at the instance of CECT prescription in the outpatient department based on previous records of eGFRs. In addition, the protocolized order of the intravenous fluid replacement regimen was automatically provided to the prescribing clinician. We assessed the quality improvement of practices regarding PCAKI, namely, appropriate prevention, avoidance of underdiagnosis, and better clinical outcomes, after the launch of the system.

**Methods**

**Ethics statement**

The study was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (No. B-1804-468-306). The requirement for informed consent was waived by the IRB.

**Study design and population**

This was a retrospective cohort study that compared the two time periods, namely before and after the launch of the electronic alert system on March 1, 2018. CECTs performed in the outpatient department from March 1, 2017, to February 28, 2020, were initially collected. Patients were then categorized into historical or alert cohorts based on the date of prescription. Because the study group categorization should depend on whether the system was working on the date of prescription, the historical and alert cohorts included the CECT prescribed from March 14, 2014, to February 28, 2018, and from March 1, 2018, to February 28, 2020, respectively. Exclusion criteria were as follows (Fig. 1): 1) second prescription or thereafter in cases with repeated prescription during the study period (only the first prescription was evaluated); 2) participants without available baseline sCr values within 6 months; 3) under renal
replacement therapy (RRT); 4) baseline eGFR of more than 45 mL/min/1.73 m$^2$; 5) heart diseases defined as ventricular hypertrophy, ischemia, or infarct at the last electrocardiography before the index prescription; and 6) previous history of partial or total nephrectomy. Baseline eGFR was calculated from the minimum sCr within 3 or 6 months (6 months, if sCr was unavailable within 3 months) from the date of computed tomography (CT) examination using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [12].

**Electronic alert system**

The alert system consisted of three main features: 1) identification of high-risk patients; 2) recommendation of fluid prescriptions; and 3) detection and follow-up management of PCAKI (Fig. 2).

**Identification**

When CECT is prescribed, the system opens a pop-up window automatically (Supplementary Fig. 1, available online).
if the patient is undergoing RRT or the baseline eGFR is less than 45 mL/min/1.73 m² [13]. This window alerts clinicians regarding the risk of PCAKI. The doctor should choose one of the four options provided to proceed: 1) consultation with the nephrologist; 2) prescription of a pre-set order for prophylactic intravenous fluid and follow-up measurement of sCr; 3) typing in the reason why prophylaxis should be skipped; and 4) canceling the order of CECT.  

**Prescription**  
Once the doctor decides to conduct prophylaxis, the order set consisting of following lines is automatically provided, which can be revised depending on the patient’s status and the doctor’s clinical decision: 1) normal saline of 250 mL intravenously or 30 minutes to 1 hour (before CECT); 2) normal saline of 500 mL intravenously for 1 to 2 hours (after CECT); 3) sCr, which is to be sampled within 2 to 7 days after CECT; 4) (optional) acetylcysteine 1,200 mg twice a day for 2 days, starting from the afternoon prior to the day when CECT is being scheduled.

**Postcontrast acute kidney injury detection and follow-up**  
The patients are instructed to visit centers for blood sampling nearest to the residence, 2 to 7 days after CECT. However, we considered that sampling within 2 weeks of CECT was acceptable for the surveillance of PCAKI for patients’ convenience. The samples are delivered and analyzed in our hospital. The results of sCr determination and PCAKI diagnosis are transmitted to the patient via mobile phone. If the diagnosis of PCAKI is met, patients are further recommended to make another appointment with a nephrologist in our hospital, in addition to the doctor who prescribed CECT. PCAKI was defined as increase in sCr from baseline of more than 0.3 mg/dL or 50%, for this purpose [14].

**Data collection**  
Baseline characteristics such as demographic data, department where the index prescription was made, comorbidities, medications, and baseline laboratory values were collected from electronic medical records. Baseline laboratory
values were the most recent measurements taken within 6 months from the date of CT examination. Comorbidities at the time of the index prescription were identified from all available electronic health records using diagnostic codes from the International Classification of Diseases.

Outcomes

The primary outcome was the frequency and odds ratio (OR) of follow-up measurement of sCr within 2 weeks, which we considered representative of surveillance for PCAKI. Secondary outcomes were the development and severity of PCAKI, admission within 6 months after CECT, mortality, and RRT. Mortality and RRT were monitored until the time of the event or June 30, 2020, whichever occurred first.

Statistical analyses

Baseline characteristics were compared using the chi-square test or Fisher exact test, as appropriate for categorical variables. Continuous variables were compared using the Mann-Whitney U test, as the variables showed a non-normal distribution, as they were tested using the Shapiro-Wilk test. Missing data, including blood urea nitrogen, hemoglobin, albumin, cholesterol, sodium, potassium, total CO₂, and spot urine protein-to-creatinine ratio were imputed by random forests algorithm, using missranger function in ‘missRanger’ package (version 2.1.3). At least five sets of imputed data were generated for multivariable regressions and the results were pooled using ‘mice’ package (version 3.14.0).

The efficacy of the alert protocol was assessed using logistic regression, where the follow-up measurement of sCr was an outcome variable. Univariable and multivariable regression models were constructed.

We determined the risks of PCAKI among the participants with sCr measurements depending on the implementation of the alert system, using logistic regression. Two different definitions of PCAKI were used: 1) at least 0.5 mg/dL or 25% increase in sCr [15]; and 2) at least 0.3 mg/dL or 50% increase in sCr [16]. Severe PCAKI was defined as an ≥50% increase in sCr from the baseline.

The long-term clinical outcomes of admission within 6 months after CECT, mortality, and RRT were investigated for all included participants. Cox regression analyses were performed for mortality and RRT since these were regarded as time-to-event variables.

Subgroup analyses were performed for baseline eGFR of 35 mL/min/1.73 m². The level of eGFR was chosen because the sample sizes of participants with baseline eGFR less than 30 mL/min/1.73 m² were only 37 and 42 for the historical and alert groups, respectively, which were too small to perform statistical testing.

Analyses were performed using the R software (version 4.1.2; R Foundation for Statistical Computing). Statistical significance was set at a two-sided p-value of <0.05.

Results

Study flow

Fig. 1 illustrates the flowchart of the study. Overall, 598 participants were included in this study. Among them, 291 had sCr values within 2 weeks after CECT, permitting the comparison of the incidence and severity of PCAKI.

Baseline characteristics

The baseline characteristics of the historical and alert groups are shown in Table 1. The median age was 76.0 years for both groups, and 32.9% of the participants had diabetes. Baseline eGFRs were 38.8 and 39.2 mL/min/1.73 m². Participants in the alert group were more likely to be male and using diuretics. Otherwise, the two groups showed no significant differences.

Volume of administered fluid

Among the four options on the alert window, when clinicians choose ‘Cancel the order’ option, we cannot identify such cases. For the remaining three options, the selection rates were 95.4%, 3.2%, and 1.4%, for ‘Prescribe protocolized prophylaxis regimen,’ ‘Proceed with the order after explaining specific reason,’ and ‘Consult with nephrology department, automatically,’ respectively. The volumes of prophylactic hydration are shown in Supplementary Table 1 (available online). Most participants in the alert group were administered 750 mL of isotonic fluid according to the default prescription of the pre-specified protocol, which is
Table 1. Baseline characteristics of the study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Historical</th>
<th>Alert</th>
<th>p-value</th>
<th>No. of cases with missing value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>289</td>
<td>309</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>76.0 (71.0–81.0)</td>
<td>76.0 (70.0–80.0)</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>168 (58.1)</td>
<td>209 (67.6)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Department</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal medicine</td>
<td>133 (46.0)</td>
<td>149 (48.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urology</td>
<td>83 (28.7)</td>
<td>82 (26.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic surgery</td>
<td>28 (9.7)</td>
<td>29 (9.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General surgery</td>
<td>28 (9.7)</td>
<td>23 (7.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>17 (5.9)</td>
<td>26 (8.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>55 (19.0)</td>
<td>45 (14.6)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>97 (33.6)</td>
<td>100 (32.4)</td>
<td>0.82</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>7 (2.4)</td>
<td>2 (0.6)</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>3 (1.0)</td>
<td>0 (0.0)</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>9 (3.1)</td>
<td>22 (7.1)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>22 (7.6)</td>
<td>29 (9.4)</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>27.1 (23.0–34.2)</td>
<td>27.5 (22.4–33.3)</td>
<td>0.72</td>
<td>21 (7.3) 77 (24.9)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.9 (9.9–12.3)</td>
<td>10.9 (9.9–12.5)</td>
<td>0.82</td>
<td>30 (10.4) 85 (27.5)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.8 (3.4–4.1)</td>
<td>3.7 (3.5–4.1)</td>
<td>0.97</td>
<td>27 (9.3) 79 (25.6)</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>148.0 (130.0–168.1)</td>
<td>146.0 (127.0–172.0)</td>
<td>0.67</td>
<td>26 (9.0) 92 (29.8)</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>139.6 (137.7–141.0)</td>
<td>139.8 (138.0–141.2)</td>
<td>0.17</td>
<td>46 (15.9) 99 (32.0)</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.5 (4.3–4.8)</td>
<td>4.5 (4.3–4.8)</td>
<td>0.85</td>
<td>46 (15.9) 99 (32.0)</td>
</tr>
<tr>
<td>Total CO₂ (mmol/L)</td>
<td>22.4 (20.0–25.0)</td>
<td>23.0 (21.0–25.0)</td>
<td>0.44</td>
<td>95 (32.9) 176 (57.0)</td>
</tr>
<tr>
<td>Spot UPCR (g/g)</td>
<td>0.3 (0.2–0.8)</td>
<td>0.3 (0.2–1.0)</td>
<td>0.95</td>
<td>166 (57.4) 202 (65.4)</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.6 (1.4–1.8)</td>
<td>1.6 (1.5–1.9)</td>
<td>0.048</td>
<td></td>
</tr>
<tr>
<td>Baseline eGFR (mL/min/1.73 m²)</td>
<td>38.8 (34.4–41.9)</td>
<td>39.2 (33.4–42.4)</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td></td>
<td></td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>65 (22.5)</td>
<td>78 (25.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–6</td>
<td>128 (44.3)</td>
<td>147 (47.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥7</td>
<td>96 (33.2)</td>
<td>84 (27.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as number only, median (interquartile range), or number (%).
NSAID, nonsteroidal anti-inflammatory drugs; BUN, blood urea nitrogen; UPCR, urine protein-to-creatinine; eGFR, estimated glomerular filtration rate.

in the range of the recommended volume per body weight for most patients [17]. In the historical cohort, 1,000 mL of isotonic fluid infusion was the most frequent prescription. The mean infusion volume was significantly lower in the alert group than in the historical group (793 mL vs. 948 mL; p < 0.001 by two-tailed Student t test).

Follow-up measurement of serum creatinine

We investigated whether the alert system could prevent the underdiagnosis of PCAKI using follow-up sCr measurement within 2 weeks as a surrogate outcome. After the launch of the system, the frequency of follow-ups dramatically increased from 29.4% to 66.7%. In multivariable analysis, the alert system led to a significant increase in follow-up measurements after multivariable adjustment (OR, 6.00; 95% confidence interval [CI], 4.00–8.98; p < 0.001).

Clinical outcomes

Among the 291 participants with follow-up sCr values, we determined the incidence of PCAKI according to two different criteria, one by the PCAKI-specific consensus guideline and the other adopted from the KDIGO guideline.
Table 2. Efficacy of alert system on follow-up measurements of serum creatinine in patients at risk for postcontrast acute kidney injury

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>No. of event (%)</th>
<th>Univariable</th>
<th>Multivariable*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Historical (n = 289)</td>
<td>Alert (n = 309)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Within 2 wk</td>
<td>85 (29.4)</td>
<td>206 (66.7)</td>
<td>4.80 (3.39–6.79)</td>
</tr>
</tbody>
</table>

CI, confidence interval; OR, odds ratio.
*Adjusted for all the baseline variables in Table 1 (i.e., age, sex, department, cardiovascular diseases, diabetes, lymphoma, multiple myeloma, diuretics, nonsteroidal anti-inflammatory drugs, blood urea nitrogen, hemoglobin, albumin, cholesterol, sodium, potassium, total CO₂, spot urine protein-to-creatinine ratio, baseline estimated glomerular filtration rate, and Charlson comorbidity index).

Table 3. Risks of postcontrast AKI in subpopulation with follow-up sCr within 2 weeks after contrast-enhanced computed tomography

<table>
<thead>
<tr>
<th>AKI criteria</th>
<th>No. of event (%)</th>
<th>Univariable</th>
<th>Multivariable*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Historical (n = 85)</td>
<td>Alert (n = 206)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>AKI criteria 1a</td>
<td>13 (15.3)</td>
<td>29 (14.1)</td>
<td>0.91 (0.45–1.85)</td>
</tr>
<tr>
<td>AKI criteria 1b</td>
<td>19 (22.4)</td>
<td>38 (18.4)</td>
<td>0.79 (0.42–1.46)</td>
</tr>
<tr>
<td>Severe AKIb</td>
<td>9 (10.6)</td>
<td>11 (5.3)</td>
<td>0.48 (0.19–1.20)</td>
</tr>
</tbody>
</table>

AKI, acute kidney injury; CI, confidence interval; OR, odds ratio; sCr, serum creatinine.
*aIncrease in sCr from baseline within 2 weeks after computed tomography by one of the following criteria: 1) 0.5 mg/dL or more, or 2) 25% or more.
*bIncrease in sCr from baseline within 2 weeks after computed tomography by one of the following criteria: 1) 0.3 mg/dL or more, or 2) 50% or more.
*cIncrease in sCr from baseline within 2 weeks after computed tomography by either one of the following criteria: 50% or more. dAdjusted for all the baseline variables in Table 1 (i.e., age, sex, department, cardiovascular diseases, diabetes, lymphoma, multiple myeloma, diuretics, nonsteroidal anti-inflammatory drugs, blood urea nitrogen, hemoglobin, albumin, cholesterol, sodium, potassium, total CO₂, spot urine protein-to-creatinine ratio, baseline estimated glomerular filtration rate, and Charlson comorbidity index).

Table 4. Risks of long-term clinical outcomes before and after the application of alert system

<table>
<thead>
<tr>
<th>No. of event (%)</th>
<th>Univariable</th>
<th>Multivariable*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Historical (n = 289)</td>
<td>Alert (n = 309)</td>
</tr>
<tr>
<td>Admission within 6 mo</td>
<td>106 (36.7)</td>
<td>110 (35.6)</td>
</tr>
<tr>
<td>Mortality</td>
<td>22 (7.6)</td>
<td>13 (4.2)</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>14 (4.8)</td>
<td>6 (1.9)</td>
</tr>
</tbody>
</table>

CI, confidence interval; HR, hazard ratio; OR, odds ratio.
*Analysis for any causes within 6 months after computed tomography. θORs and 95% 95% CIs were described for admission within 6 months. θHRs and 95% CIs were described for mortality and renal replacement therapy. Adjusted for all the baseline variables in Table 1 (i.e., age, sex, department, cardiovascular diseases, diabetes, lymphoma, multiple myeloma, diuretics, nonsteroidal anti-inflammatory drugs, blood urea nitrogen, hemoglobin, albumin, cholesterol, sodium, potassium, total CO₂, spot urine protein-to-creatinine ratio, baseline estimated glomerular filtration rate, and Charlson comorbidity index).

for general forms of AKI (Table 2). Incidences ranged from 15.3% to 22.4% in the historical group and from 14.1% to 18.4% in the alert group. Protocolized prevention with less fluid volume did not show significant differences in the risk of PCAKI using both criteria, when analyzed by univariable (criteria 1: OR, 0.91; 95% CI, 0.45–1.85; p = 0.79; criteria 2: OR, 0.79; 95% CI, 0.42–1.46; p = 0.446) and multivariable (criteria 1: OR, 0.90; 95% CI, 0.40–2.03; p = 0.81; criteria 2: OR, 0.72; 95% CI, 0.35–1.50; p = 0.38) regressions. Similarly, the risk of severe AKI in multivariable analysis was not significantly different between the two groups (OR, 0.44; 95% CI, 0.13–1.48; p = 0.18).

We investigated whether timely diagnosis and management of PCAKI after CECT could improve long-term clinical outcomes. Our protocol encouraged patients with elevated sCr levels fulfilling the PCAKI criteria to visit the nephrology department, where aggravating factors of AKI can be corrected. Since the alert system assisted in more diagnosis of PCAKI than before by facilitating follow-up (Table 2, 3), we tested the association of the alert system with admission, mortality, and RRT (Table 4). We reasoned that more detection and appropriate management might result in better long-term outcomes. Numerically, proportion of patients experiencing the three outcomes were
reduced in the alert group by 1.1%, 3.4%, and 2.9%, respectively, albeit not statistically significant by two-tailed proportion test (data not shown). In univariable Cox regression analyses, the alert system tended to reduce the risk/hazards of admission (OR, 0.95; 95% CI, 0.68–1.33; p = 0.78), mortality (hazard ratio [HR], 0.84; 95% CI, 0.40–1.75; p = 0.63), and RRT (HR, 0.66; 95% CI, 0.22–1.95; p = 0.43), but the difference was not statistically significant. The results were similar to those of the multivariable analyses (Table 4).

Subgroup analyses

Additional analyses showed that the alert system was effective in supporting follow-up of sCr for both subgroups, with <35 or ≥35 mL/min/1.73 m² of baseline eGFR (Supplementary Table 2, available online). Regardless of the baseline eGFR, the alert system did not demonstrate a statistically significant benefit in admission, mortality, and RRT.

Discussion

In this study, we implemented a one-click electronic alert for PCAKI, which runs through the detection of at-risk patients, support for prophylaxis prescription, diagnosis, and referral to nephrologists. The system was developed with the intent of aiding clinicians prescribing CECT in the outpatient department and other personnel at a tertiary hospital. Automated alerts could significantly alter clinicians’ behavior, as more patients underwent surveillance of PCAKI. A more restricted volume of fluid infusion resulted in equivalent PCAKI incidence, and we observed a trend toward lower risks of long-term outcomes with the alert system, although this was not formally proven by statistical analyses.

Alerts supporting clinical decisions are increasingly adopted in-hospital information systems [10]. Several alerts aimed at early detection of AKI have been introduced in inpatient settings, with mixed results regarding their effectiveness on long-term endpoints [11,18,19]. One explanation for those alerts that could not improve the hard endpoints in previous studies was the absence of a universal treatment for AKI after it had already developed. Moreover, those alerts typically detect sCr elevation or a decrease in urine output from any cause, resulting in a heterogeneous study population. In contrast, the alert system in this study involves screening high-risk patients and preventing the development of PCAKI. Although the specific type or volume of intravenous fluid may be individualized, we could also provide attending clinicians with a common protocol for PCAKI prophylaxis based on clinical guidelines [8,20]. This could reduce alert fatigues, which many contemporary hospital information systems accompanying diverse electronic alerts are faced with. Another strength of our study was that, unlike previous studies, we targeted the outpatient population, which is usually difficult to follow. The result was that approximately two-thirds of patients underwent surveillance for PCAKI, which was more than double the follow-up rate from the historical group, suggesting acceptable user accommodation.

Reported incidences of PCAKI after CECT range widely from 0% to 21% depending on study designs, where outpatient data are usually from studies with small sample sizes [4,21]. In our study, the incidence of PCAKI was approximately 15% and did not demonstrate significant differences between the groups. The alert system helped providing the true rate of PCAKI in the outpatient setting, where many cases could be otherwise undetected due to omitted follow-up. Notably, severe PCAKI showed a greater tendency toward a reduced OR in the alert group without statistical significance. Since incidences could be measured only among patients with follow-up sCr, the limited sample size may have reduced the statistical power. Alternatively, selection bias could have been present, as patients in the alert group were more willing to participate in the follow-up sampling.

Importantly, we successfully restricted the volume of prophylactic fluid with equivalent AKI outcomes. In the outpatient clinic, the fluid infusion should be completed in a relatively short time, so reducing the volume of several hundred milliliters can be a great help by saving several hours and avoiding adverse effects due to rapid infusion. Volume overload easily complicates AKI, and excessive amount of intravenous fluid may cause deleterious effect [22]. It is suspected that previous AKI alerts that failed to improve patient outcomes provoked indiscriminate prescription of intravenous fluid upon detection of AKI causing harmful effects [18,19]. Thus, a reduction in the infusion volume minimizes the potential harm incurred by the alert protocol. Optimal volume and infusion rate to prevent PCAKI in the outpatient setting needs further investigation.
The alert system did not ultimately improve long-term clinical outcomes, including admission within 6 months, mortality, and RRT. First, this might be due to insufficient sample size because all results of the regression analyses showed a propensity to lower risk in the alert group, although this is merely a speculation. Because of the retrospective nature of the study, we could not determine the sample size in advance. Second, although we recommended appointments with nephrologist for patients diagnosed with PCAKI, the proportion of patients who visited the nephrology department was not satisfactory because it incurred excess medical expenses and time for the patients. Third, the association between CECT and adverse long-term outcomes may not be present. This issue has been explored in previous studies with inconclusive results. Experience of PCAKI or more frequent CECT was a significant risk factor for mortality and kidney failure in some studies [3,5], but others reported no difference in 30-day mortality or RRT following CECT [23,24]. Lastly, incomplete follow-up in one-third of the participants, still high even after considerable improvement, in the alert group may have weakened the efficacy of the intervention.

This study has several limitations. First, since the time periods when CECTs were performed in the two groups were different, the effects of secular differences in clinical practice could be present. However, the volume expansion protocol for outpatients was published in 2010 [25], and other preventive strategies, such as acetylcysteine and statins, have not been proven effective. Thus, the paradigms of prevention and treatment of PCAKI did not change considerably during the study period [26]. Second, the time window used for the diagnosis of PCAKI was 2 weeks after CECT, considering the convenience of patients who should visit clinics for sampling. Thus, some PCAKI cases that spontaneously improved within a few days could have been missed if sampling was performed later, although the overall impact of these recovery cases on the long-term prognosis might be rather weak. Moreover, causality between increases in sCr and contrast exposure cannot be proven because changes in sCr could occur for other reasons [27]. Third, since the study was carried out in a tertiary hospital, the results may not be generalizable without further research, preferably with a larger sample size. Lastly, specific treatment for PCAKI is limited, so the utility of the alert with respect to early detection may be attenuated. Previous studies have showed that early intervention by nephrologists is associated with better outcomes in AKI [28,29], and is a key determinant of prognostic benefit in in-hospital AKI alerts [11]. Thus, future research may provide evidence that the management of PCAKI by specialists, such as volume expansion or discontinuation of nephrotoxic drugs, can improve patient outcomes.

In conclusion, electronic alerts for PCAKI can be useful in automatic screening of high-risk patients, convenient prescription of protocolized fluid regimens, and follow-up of PCAKI at the outpatient department. Effective prevention of PCAKI is possible with a reduced fluid volume and desirable user acceptance. The clinical benefits of preventing PCAKI development and its long-term adverse outcomes need to be clarified.

**Conflicts of interest**

All authors have no conflicts of interest to declare.

**Funding**

This research was supported by a grant of Patient-Centered Clinical Research Coordinating Center (PACEN) funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI19C0481, HC20C0054).

**Data sharing statement**

The data presented in this study are available on request from the corresponding author.

**Authors’ contributions**

Conceptualization: SK  
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