Impact of Electronic Acute Kidney Injury (AKI) Alerts With Automated Nephrologist Consultation on Detection and Severity of AKI: A Quality Improvement Study

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Background: Several electronic alert systems for acute kidney injury (AKI) have been introduced. However, their clinical benefits require further investigation.

Study Design: Before-and-after quality improvement study.

Setting & Participants: A tertiary teaching hospital in Korea, which adopted an AKI alert system on June 1, 2014. Before and after launch of the alert system, 1,884 and 1,309 patients with AKI were included in the usual-care and alert groups, respectively.

Quality Improvement Plan: Implementation of an AKI alert system through which clinicians could generate automated consultations to the nephrology division for all hospitalized patients.

Outcomes: Primary outcomes included overlooked AKI events, defined as not measuring the follow-up creatinine value, and the consultation pattern of clinicians. Secondary outcomes were severe AKI events; AKI recovery, defined based on the creatinine-based criterion; and patient mortality.

Measurements: ORs for events of overlooked AKI, early consultation, and severe AKI were calculated with logistic regression. AKI recovery rate and patient mortality were assessed using Cox regression.

Results: After introduction of the alert system, the odds of overlooked AKI events were significantly lower (adjusted OR, 0.40; 95% CI, 0.30-0.52), and the odds of an early consultation with a nephrologist were greater (adjusted OR, 6.13; 95% CI, 4.80-7.82). The odds of a severe AKI event was reduced after implementation of the alerts (adjusted OR, 0.75; 95% CI, 0.64-0.89). Furthermore, the likelihood of AKI recovery was improved in the alert group (adjusted HR, 1.70; 95% CI, 1.53-1.88). Mortality was not affected by the AKI alert system (adjusted HR, 1.07; 95% CI, 0.68-1.68).

Limitations: Possible unreported differences between the alert and usual-care groups.

Conclusions: Implementation of the AKI alert system was associated with beneficial effects in terms of an improved rate of recovery from AKI. Therefore, widespread adoption of such systems could be considered in general hospitals.

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Acute kidney injury (AKI) is closely associated with deterioration of kidney function and increased mortality.[1-3] Many studies have addressed the necessity of improving AKI outcomes, and its risk factors and prognosis have been widely investigated.[4-6] Although several therapeutic and preventive interventions for AKI have been developed, universal treatment for AKI has not been established.[7-9] Instead, an individualized approach with optimal fluid balance and avoidance of nephrotoxic events is suggested.[10-12] There is a consensus that early detection of AKI events is crucial to improving patients' outcomes.[13,14] The role of a nephrologist has also been previously highlighted.[14-16]

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Mainly, AKI is defined by serum creatinine (Scr)-based criteria.[17,18] Because Scr is widely tested and can be quickly reported using comprehensible numeric values, there have been attempts to build an efficient surveillance system for AKI, also known as an AKI alert.[19-22] However, the only published randomized controlled trial of AKI alerts that we are aware of showed negative results,[22] and other studies identified several limitations despite promising preliminary outcomes.[20,21,23] In previous studies, change in clinicians' behavior was commonly suggested to be crucial for the success of an alert system.[23]

We implemented an AKI alert system in our hospital in 2014. An important difference between our system and those previously reported is that the attending clinicians could easily generate automatic direct consultation with the nephrology division. Here, we assessed the impact of the system by comparing outcomes of patients who had AKI events before and after launch of the system.

Methods

Ethics Considerations

The Food and Drug Administration of Korea approved the development and launch of the AKI alert system (KCT0002010). The Institutional Review Board (IRB) of Seoul National University Bundang Hospital approved the study (IRB number: B-1402/238-006) and waived the need for informed consents. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Study Design and Study Population

This before-and-after study was conducted at a tertiary referral hospital in Korea with more than 1,000 general admission beds. After approval by the hospital's leadership for the quality improvement activity, an AKI alert system was launched on June 1, 2014. No other major AKI-related activities or laboratory changes were implemented.

In the study cohort, we included index admission cases of adult patients with Scr measured during hospitalization in the first year after the system was introduced. The historical cohort consisted of index admission cases with the same criteria that were admitted from January 1 to December 31, 2013, before introduction of the alert system. Patients who had AKI in the study cohort were included in the alert group, and those with AKI events in the historical cohort, identified based on the same criteria used for the alert group, were included in the usual-care group.

Exclusion criteria were as follows: (1) ongoing renal replacement therapy, (2) impending end-stage renal disease (baseline estimated glomerular filtration rate < 15 mL/min/1.73 m^2), (3) admission to the nephrology division because these patients were already receiving care from the attending nephrologists, (4) death events on the day of AKI development were also excluded because these cases were beyond the reach of our system because the alerts were generated around midnight and reported to clinicians on the following day, and (5) patients who were already enrolled in the historical cohort were excluded from the alert group.

AKI Alert System With Automatically Generated Nephrology Consultation

The AKI alert system used the minimum Scr concentration within 2 weeks before the admission date as the baseline Scr concentration. When an earlier laboratory value was not available, the first Scr concentration measured during hospitalization was used as the baseline value. To minimize the information-processing burden of a real-time system, our system screened AKI events every midnight, defining AKI events as Scr concentration elevation of at least 1.5-fold or 0.3 mg/dL from baseline.[17,24] When physicians opened the patient's electronic medical record (EMR) the following morning, a pop-up window (screenshot in Fig S1, available as online supplementary material) displayed with the following message: "(Mild/Moderate/Severe) acute kidney injury (stage X). Do you want to send a consultation request to nephrology division?". An explanatory note is provided below the notification, reading "As the patient is diagnosed with acute kidney injury according to the international clinical practice guidelines, we ask the nephrology division for further evaluation and treatment." The clinician could choose either "yes" or "no" on the display, and if he or she clicked "yes," the following nephrology consultation was generated automatically (Fig S2): "We ask the nephrology division for further evaluation and treatment plan as the patient is suspected to have acute kidney injury, relative to the baseline serum creatinine level measured within 2 weeks before admission or sampled for the first time after hospitalization." The clinicians could also click the "no" button and request a consultation with a more detailed description, request a consultation later, or not consult the nephrology division at all. The board-certified nephrologists at our hospital were encouraged to answer all requests within 1 day.

Data Collection

The following demographic data were collected from the study and historical cohorts: age, sex, and baseline body mass index at the time of admission. The last laboratory values for hemoglobin and albumin before the AKI event were defined as the baseline levels. Anemia was defined as hemoglobin concentration < 11 g/dL, and hypoalbuminemia was defined as baseline albumin concentration < 3.0 g/dL. Comorbid conditions of hypertension, diabetes mellitus, ischemic heart disease, heart failure, and cancer were reviewed by the designated *International Classification of Diseases, Tenth Revision* diagnostic codes and the use of relevant medications. Information for medication use within 2 weeks before the AKI event was collected, including the use of renin-angiotensin-aldosterone system blockers, diuretics, and nonsteroidal anti-inflammatory drugs (NSAIDs).[4] The admitting department at the time of AKI development and any surgeries during hospitalization were recorded. Community-acquired AKI events were defined by the first Scr concentration measured after admission fulfilling the criteria for AKI. The study and historical cohorts were collected over 1 year, and the year was further divided into quarters in order to examine a possible time-phase variation in outcomes. Dates of consultations to the nephrology division were collected. Follow-up Scr concentrations and patient mortality within 30 days after the AKI event were also recorded to further assess clinical outcomes. Estimated glomerular filtration rates were calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) creatinine equation.[25]

Clinical Outcomes and Their Definitions

The first category of outcomes was change in clinicians' behavior, including instances of overlooked AKI and clinicians' consultation patterns. Overlooked AKI was defined as the absence of a follow-up Scr measurement within 2 weeks after AKI. Consultation to the nephrology division was classified into the following 3 outcomes: no consultation, early consultation, and late consultation. Early consultation was defined as consultation within 3 days from the AKI event. Consults issued more than 3 days after the AKI were considered late consultations.

The second category of outcomes aimed to assess AKI characteristics, including AKI recovery and the severity of Scr concentration elevation. Among several criteria used to define AKI recovery,[26-28] we chose a conservative criterion of return of Scr to <1.2 times the baseline level. We found that among patients with high baseline Scr concentrations

with AKI stage 1, events defined only by the criterion of ≥0.3-mg/dL elevation from baseline could be simultaneously included in the recovery of AKI events (eg, Scr elevation from 3.0 mg/dL to 3.5 mg/dL). Therefore, when the criterion of ≥0.3-mg/dL elevation was the only fulfilled criterion for AKI, the return of Scr concentrations to <0.2 mg/dL elevation from baseline was used to define AKI recovery. AKI recovery from zero to 30 days after AKI was analyzed and events with missing follow-up Scr measurements were censored at the last day of the Scr test.[22,26,27] Next, the degree of peak Scr concentration elevation was defined according to AKI stage,[17] and AKI stage 2 or 3 events were classified as severe AKI.[26]

Next, we assessed patient survival. Because a non-negligible portion of patients died outside the hospital, we collected mortality information from a national database maintained by a government organization that tracks all deaths in the country, following approval of the Ministry of the Interior of Korea.

Statistical Analysis

Data were presented as frequency and percentage for categorical variables and were compared between the usual-care and alert groups using χ^2 tests. Because the Shapiro-Wilk normality test indicated non-normal distribution of all continuous variables in our study population, continuous variables were expressed as median and interquartile range, and the difference between the usual-care and alert groups was analyzed using Mann-Whitney U test. We used logistic regression test to calculate odds ratios (ORs) for analyses of overlooked AKI, consultation pattern, and severe AKI outcomes. The Cox proportional hazards model was used to assess AKI recovery and patient mortality. In addition to univariable analyses, we performed multivariable complete-case analyses and analyses of the data set with multiple imputations for missing values. In complete-case analyses, models were adjusted for age (categorical: <50, 50-70, and >70 years); sex; baseline estimated glomerular filtration rate (categorical, <30, 30-60, and >60 mL/min/1.73 m^2); admitting department (categorical, surgical, and nonsurgical); whether the AKI was identified as community-acquired; history of cancer, hypertension, diabetes mellitus, ischemic heart disease, or heart failure; use of diuretics, NSAIDs, or renin-angiotensin-aldosterone system blockers; and AKI stages (1, 2, and 3). Anemia (hemoglobin < 11 g/dL) and hypoalbuminemia (albumin < 3.0 g/L) were also added to the adjustment variables in analyses with imputed datasets. AKI stages were not adjusted for when evaluating severe AKI outcomes because severe AKI itself was defined according to AKI stages. To account for missing hemoglobin

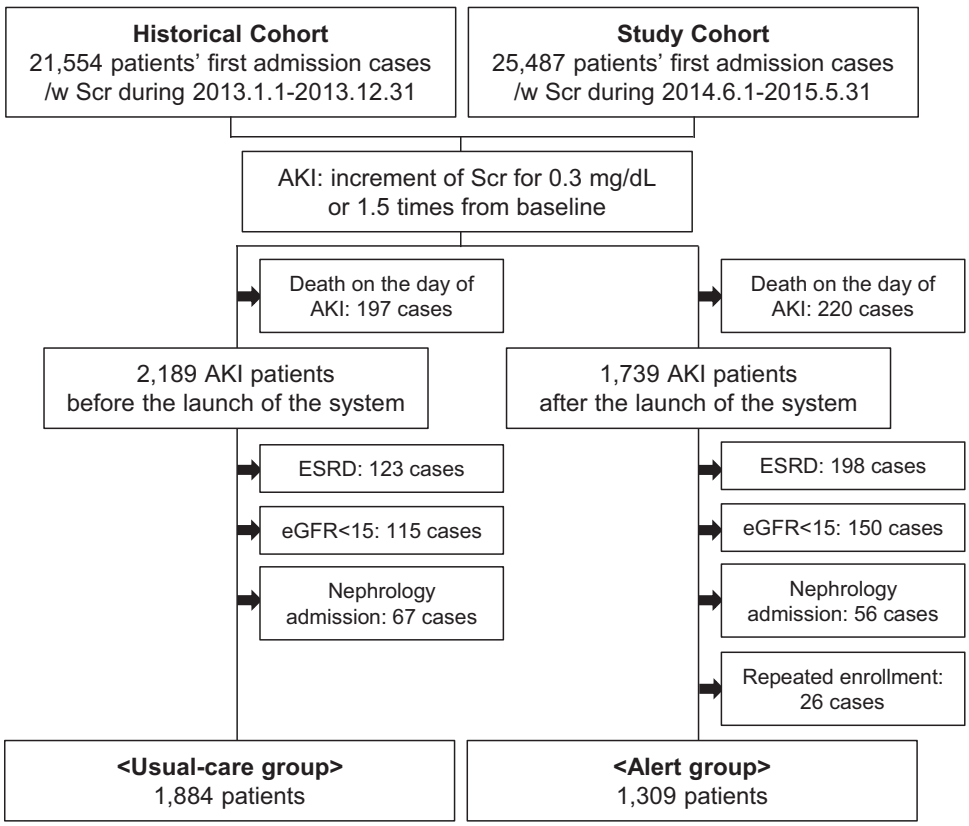

Figure 1. Flow chart of the study population. Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; Scr, serum creatinine.

Table 1. Patients' Baseline Characteristics at the Time of AKI

	Usual-care (n = 1,884)	Alert (n = 1,309)	*P*
Age, y	64 [50-74]	68 [54-77]	<0.001
Age category			<0.001
<50 y	450 (23.9%)	254 (19.4%)	
50-70 y	755 (40.1%)	456 (34.8%)	
>70 y	679 (36.0%)	599 (45.8%)	
Male sex	916 (48.6%)	761 (58.1%)	<0.001
BMI, kg/m^2	23.4 [21.1-25.8]	23.6 [21.1-26.1]	0.2
Surgery during hospitalization	887 (47.1%)	767 (58.6%)	<0.001
Laboratory values			
Baseline Scr, mg/dL	0.56 [0.39-0.87]	0.84 [0.59-1.13]	<0.001
Baseline eGFR, mL/min/1.73 m^2	105.6 [83.6-122.9]	86.8 [60.3-104.3]	<0.001
Baseline eGFR category			
>60 mL/min/1.73 m^2	1,619 (85.9%)	987 (75.4%)	
30-60 mL/min/1.73 m^2	189 (10.0%)	250 (19.1%)	
<30 mL/min/1.73 m^2	76 (4.0%)	72 (5.5%)	
Hemoglobin, g/dL	11.8 [10.3-13.2]	11.5 [10.0-13.1]	0.002
Anemia: <11 g/dL	653 (34.7%)	522 (39.9%)	0.003
Albumin, g/dL	3.6 [3.2-3.9]	3.4 [2.9-3.8]	<0.001
Hypoalbuminemia: <3.0 g/dL	213 (15.4%)	272 (29.2%)	<0.001
Medical history			
Hypertension	915 (48.6%)	721 (55.1%)	<0.001
Diabetes mellitus	507 (26.9%)	488 (37.3%)	<0.001
Ischemic heart disease	179 (9.5%)	172 (13.1%)	0.001
Heart failure	87 (4.6%)	111 (8.5%)	<0.001
Cancer	569 (30.2%)	437 (33.4%)	0.06
Medication use			
RAAS blockers	383 (20.3%)	283 (21.6%)	0.4
Diuretics	570 (30.3%)	609 (46.5%)	<0.001
NSAIDs	668 (35.5%)	370 (28.3%)	<0.001
Department			<0.001
Nonsurgical			
Internal medicine	659 (35.0%)	478 (36.5%)	
Neurology	170 (9.0%)	84 (6.4%)	
Rehabilitation	25 (1.3%)	5 (0.4%)	
Psychiatry	15 (0.8%)	6 (0.5%)	
Other nonsurgical	5 (0.3%)	14 (1.1%)	
Surgical			
General surgery	241 (12.8%)	162 (12.4%)	
Orthopedics	399 (21.2%)	174 (13.3%)	
Neurosurgery	57 (3.0%)	23 (1.8%)	
Otorhinolaryngology	14 (0.7%)	11 (0.8%)	
Thoracic surgery	165 (8.8%)	160 (12.2%)	
Urology	84 (4.5%)	154 (11.6%)	
Obstetrics & gynecology	41 (2.2%)	25 (1.9%)	
Plastic surgery	7 (0.4%)	5 (0.4%)	
Ophthalmology	2 (0.1%)	4 (0.3%)	
Other surgical	0 (0.0%)	4 (0.3%)	
Duration of hospitalization, d			
Total admission duration	11 [7-21]	12 [8-23]	0.002
From admission to AKI	3 [2-7]	2 [1-5]	<0.001
From AKI to discharge	7 [3-14]	8 [5-17]	<0.001

(Continued)

Table 1 (Cont'd). Patients' Baseline Characteristics at the Time of AKI

	Usual-care (n = 1,884)	Alert (n = 1,309)	*P*
Time of year			0.8
First quarter	487 (25.8%)	348 (26.6%)	
Second quarter	485 (25.7%)	317 (24.2%)	
Third quarter	409 (21.7%)	290 (22.2%)	
Fourth quarter	503 (26.7%)	354 (27.0%)	

Note: Values for categorical variables are given as number (percentage); for continuous variables, as median [interquartile range]. Serum albumin concentrations were available for 2,314 (72.5%) cases. One case had a missing baseline hemoglobin value. There were no other missing records for other variables shown in the table. Conversion factor for Scr in mg/dL to μmol/L, ×88.4.
Abbreviations: AKI, acute kidney injury; BMI, body mass index; eGFR, estimated glomerular filtration rate; NSAID, nonsteroidal anti-inflammatory drug; RAAS, renin-angiotensin-aldosterone system; Scr, serum creatinine.

and albumin values, multiple imputations using the "mice" package in R software (version 3.2.5; R Foundation for Statistical Computing) using the CART (classification and regression trees) method was performed, 5 imputed data sets were called, and combined results using the "pool" function were presented. Patients with overlooked AKI were excluded in the analysis of AKI recovery outcomes. Additional sensitivity analyses were performed: (1) assuming that patients with missing Scr follow-up either all had AKI recovery or (2) none recovered from their AKI events; (3) limiting the analysis to patients hospitalized during the follow-up period; (4) with another criterion, return to 1.5 times the baseline Scr concentration, to redefine AKI recovery; and (5) limiting follow-up duration to 7 days to assess the short-term effect. The number of patients needed to treat was calculated by inversion of absolute risk reduction of a cumulative incidence of AKI nonrecovery until 30 days. In addition, we divided the usual-care and alert groups into 4 subgroups according to whether patients were referred to nephrologists early and analyzed the clinical outcomes using patients in the usual-care group who did not receive early consultation as the reference group. All statistical analyses were performed using R software. Two-sided $P < 0.05$ was considered statistically significant.

Results

Study Population

Figure 1 shows the study flow diagram. There were 21,554 and 25,487 index admission cases in the historical and study cohorts, respectively. After excluding cases of death on the day of AKI, 1,739 patients had AKI events after the launch of the alert, and following the same criteria, 2,189 patients were identified as having AKI events in the historical cohort. Finally, after additional exclusion, we included 1,884 patients in the usual-care group and 1,309 patients in the alert group.

Baseline Characteristics

There were significant differences in baseline characteristics between the 2 groups (Table 1). Patients in the alert

Table 2. Comparison of Clinical Outcomes Between the Usual-Care and Alert Groups

			Univariable Analysis		Multivariable Analysis[a]	
	Usual-care (n = 1,884)	Alert (n = 1,309)	OR[b] (95% CI)	*P*	OR[b] (95% CI)	*P*
Clinicians' behavior						
Overlooked AKI[c]	340 (18.1%)	77 (5.9%)	0.28 (0.22-0.37)	<0.001	0.40 (0.30-0.52)	<0.001
Consultation pattern						
No consultation	1,685 (89.4%)	890 (68.0%)	0.25 (0.21-0.30)	<0.001	0.23 (0.19-0.29)	<0.001
Early consultation	123 (6.5%)	365 (27.9%)	5.54 (4.46-6.91)	<0.001	6.13 (4.80-7.82)	<0.001
Late consultation	76 (4.0%)	54 (4.1%)	1.02 (0.71-1.46)	0.9	0.72 (0.48-1.06)	0.09
AKI characteristics						
Severe AKI[d]	595 (31.6%)	355 (27.1%)	0.81 (0.69-0.94)	0.007	0.75 (0.64-0.89)	<0.001
AKI recovery[e]	858 (55.6%)	989 (80.3%)	2.04[e] (1.86-2.23)	<0.001	1.70[e] (1.53-1.88)	<0.001

Note: Values in group columns are given as number of patients with an event (percentage).
Abbreviations: AKI, acute kidney injury; CI, confidence interval; OR, odds ratio; Scr, serum creatinine.
[a]Adjusted for age (categorical: <50, 50-70, and >70 years); sex; baseline estimated glomerular filtration rate (categorical: <30, 30-60, and >60 mL/min/1.73 m^2); admitting department (categorical: surgical, and nonsurgical); whether the AKI was identified as community acquired; history of cancer, hypertension, diabetes mellitus, ischemic heart disease, or heart failure; use of diuretics, nonsteroidal anti-inflammatory drugs, or renin-angiotensin-aldosterone system blockers; presence of anemia (hemoglobin < 11 g/dL) and hypoalbuminemia (albumin < 3.0 g/dL); and AKI stage (1, 2, and 3). Missing data imputation was performed for hemoglobin and albumin data, using the CART (classification and regression trees) method.
[b]Unless otherwise indicated.
[c]Overlooked AKI was defined as absence of follow-up Scr measurement within 2 weeks from the AKI event.
[d]Stages 2 and 3 AKI events were defined as severe AKI. AKI stage was not adjusted for the outcome because the AKI stage itself was used to define the severe AKI events.
[e]Hazard ratios were calculated by Cox proportional hazards modeling. AKI recovery was defined as a return of Scr concentration to less than 1.2 times baseline. When the criterion of ≥0.3-mg/dL Scr concentration elevation was the only fulfilled criterion of AKI, the return of Scr concentration to <0.2 mg/dL elevation from baseline was used to define recovery. The overlooked AKI cases, 340 cases in usual-care group and 77 cases in alert group, were not included.

group were older and more likely to be men and to have had surgery during hospitalization (all $P < 0.001$). They also had poorer baseline kidney function than the usual-care group ($P < 0.001$) and lower hemoglobin ($P = 0.002$) and albumin ($P < 0.001$) concentrations. This tendency toward less favorable baseline characteristics in the alert group was also shown in the medical history review; histories of hypertension ($P < 0.001$), diabetes mellitus ($P < 0.001$), ischemic heart disease ($P = 0.001$), and heart failure ($P < 0.001$) were more common in patients who received AKI alerts. Diuretic use ($P < 0.001$) was more frequent in the alert group; in contrast, NSAIDs were more widely used in the usual-care group ($P < 0.001$). AKI developed earlier in the alert group ($P < 0.001$), and these patients were hospitalized longer after the AKI event ($P < 0.001$). Significant differences in several characteristics were also shown in patients without AKI in the entire study population (Table S1).

Change in Clinicians' Behavior

First, we investigated whether the AKI alerts changed clinicians' practice patterns (Table 2). The odds of an overlooked AKI event significantly decreased after implementation of the alerts (adjusted OR, 0.40; 95% confidence interval [CI], 0.30-0.52; $P < 0.001$). This change was also apparent when we assessed the outcomes with different criteria (Table S2). Furthermore, there was a marked reduction in the odds of an AKI case not receiving a nephrologist consultation (adjusted OR, 0.23; 95% CI, 0.19-0.29; $P < 0.001$), although the odds of late consultations (>3 days from AKI) was similar in both groups (adjusted OR, 0.72; 95% CI, 0.48-1.06; $P = 0.09$). Thus, the rate of early consultation increased more than 4-fold, with an adjusted OR for early consultation of 6.13 (95% CI, 4.80-7.82; $P < 0.001$). This increased rate of nephrology consultation was not observed in patients without AKI (Table S1) or mortality cases on the day of AKI occurrence (Table S3), which were beyond the reach of the alert system.

AKI Recovery and AKI Severity

Next, we assessed AKI characteristics (Table 2). Patients in the alert group had lesser odds of a severe AKI event (adjusted OR, 0.75; 95% CI, 0.64-0.89; $P < 0.001$) than those under usual-care. Moreover, patients in the alert group demonstrated an improved recovery rate compared to the usual-care group (Table 2; Fig 2), and the calculated number needed to treat was 4.03. The effect remained significant in our sensitivity analyses (Table S4) and results using the complete case analysis method (Table S5). We observed significant interactions between the effect of the alert system and the presence of decreased kidney function (estimated glomerular filtration rate < 60 mL/min/1.73 m^2; $P < 0.001$), sex ($P = 0.002$), admission to a surgical department ($P = 0.007$), and medical history of cancer ($P < 0.001$). Although the alert system was associated with facilitation of AKI recovery in every subgroup we tested (Fig 3), the benefit was greater in patients with relatively preserved kidney function, admission to nonsurgical departments, and no history of cancer, as well as in women.

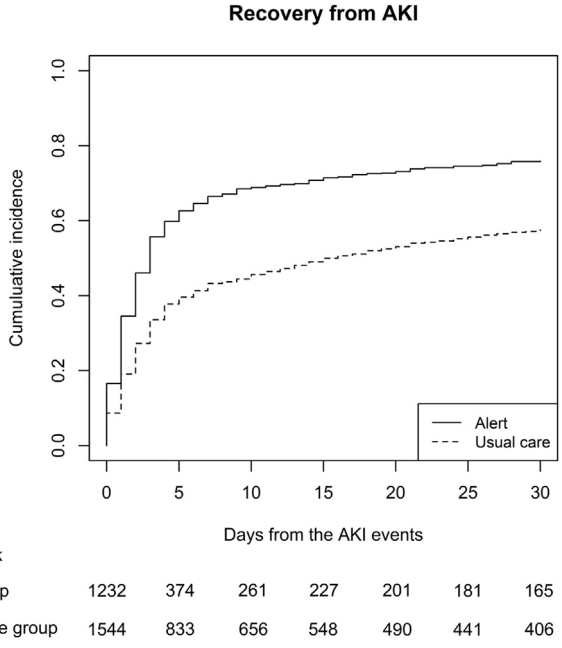

Figure 2. Adjusted survival curves from Cox proportional hazard models show acute kidney injury (AKI) recovery in the study population. Solid line indicates the adjusted survival curve of the alert group, and dashed line indicates the survival curve of the usual-care group. The x-axis shows days from the AKI event, and the y-axis shows adjusted cumulative incidence. The Cox proportional hazard model was adjusted for age (categorical, <50, 50-70, and >70 years); sex; baseline eGFR (categorical, <30, 30-60, and >60 mL/min/1.73 m^2); admitting department (categorical, surgical, and nonsurgical); whether the AKI was identified as community acquired; history of cancer, hypertension, diabetes mellitus, ischemic heart disease, or heart failure; use of diuretics, nonsteroidal anti-inflammatory drugs, or renin angiotensin aldosterone system blockers; and AKI stage (1, 2, and 3). The overlooked AKI cases were not included.

Patient Survival

In the study population, after the exclusion of mortality cases on the day of AKI, 83 patients died during the 30-day follow-up period, but no significant alteration of survival rate was observed across the study population (adjusted hazard ratio, 1.07; 95% CI, 0.68-1.68; $P = 0.8$). Characteristics associated with 30-day patient mortality in the study population were age 70 years or older, admission to surgical departments, AKI stage 2, and pre-existing cancer history (Fig 4). The absence of the effect of AKI alerts on patient mortality was also shown in subgroup analyses (Fig S3).

Effect of Time Phases in Each Study Group

The effect of time period did not show significant interaction with the effects of implementation of the alert ($P = 0.1$). Also, AKI recovery rate alert was not significantly

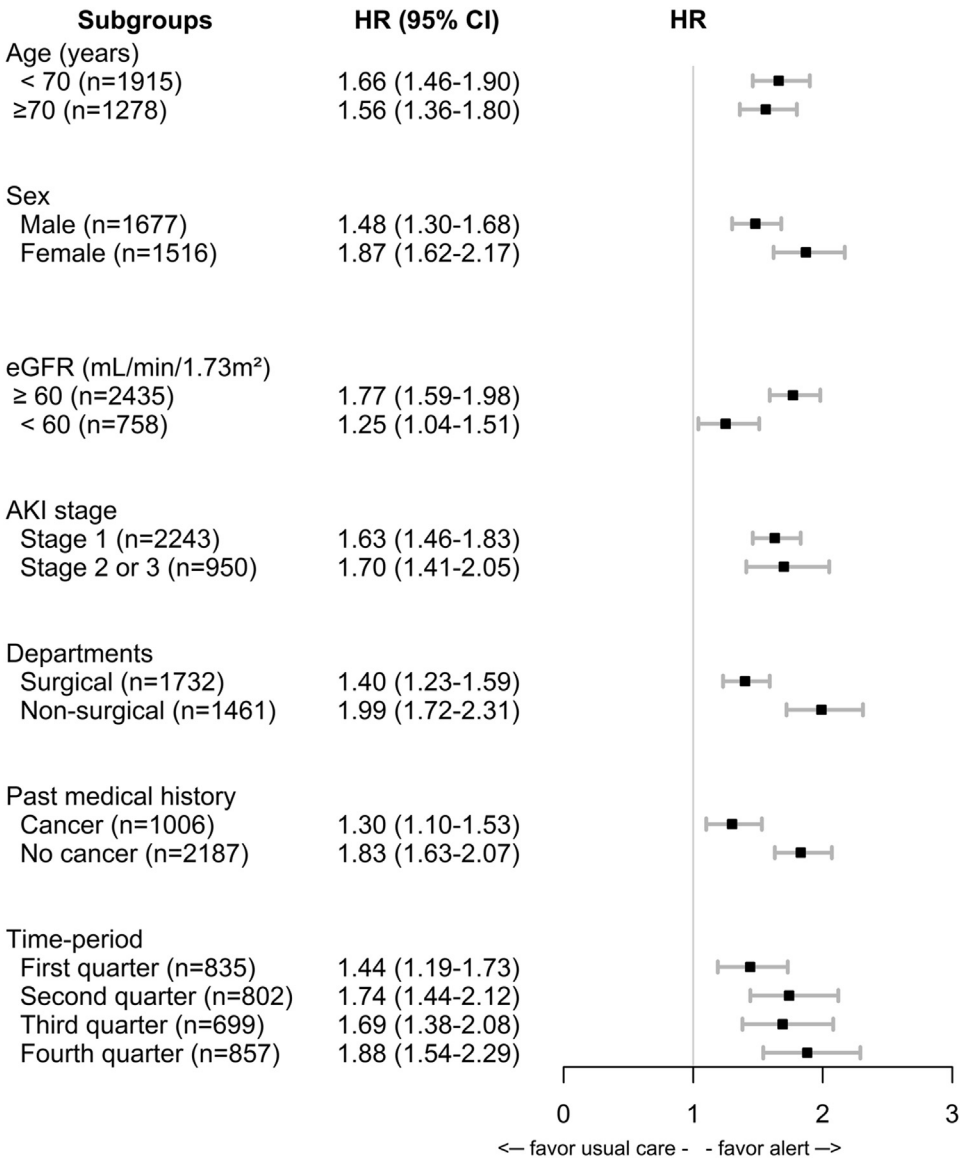

Figure 3. The impact of introduction of the acute kidney injury (AKI) alert system on AKI recovery within 30 days in the various subgroups. Boxes indicate hazard ratio (HR), and horizontal gray lines crossing the boxes indicate 95% confidence interval (CI). The Cox proportional hazard model was adjusted for age (categorical, <50, 50-70, and >70 years); sex; baseline estimated glomerular filtration rate (eGFR; categorical, <30, 30-60, and >60 mL/min/1.73 m^2); admitting department (categorical, surgical vs nonsurgical); whether the AKI was identified as community acquired; history of cancer, hypertension, diabetes mellitus, ischemic heart disease, or heart failure; use of diuretics, nonsteroidal anti-inflammatory drugs, or renin angiotensin aldosterone system blockers; and AKI stage (1, 2, and 3). The overlooked AKI cases were not considered.

different according to quarter-years in both the usual-care ($P = 0.1$) and alert ($P = 0.08$) groups.

Clinical Outcomes of Patients Who Had Early Consultation

We additionally assessed clinical outcomes of all those with early consultation, regardless of the study group (Table 3). These patients were significantly less likely to have their AKI events overlooked (adjusted OR, 0.17; 95% CI, 0.08-0.34; $P < 0.001$). Although they were more likely to have severe AKI events (adjusted OR, 1.76; 95% CI, 1.42-2.19; $P < 0.001$), they had better prognoses in terms of AKI recovery than those who did not have early consultation.

Furthermore, patients in the alert group who were not referred to nephrologists within 3 days were also less likely to have overlooked events (adjusted OR, 0.45; 95% CI, 0.34-0.60; $P < 0.001$) than the reference group (usual-care patients who did not receive early consultation), although the OR for overlooked events was higher than that for patients with early consultation (Table 4). Patients with early consultations, regardless of being in the

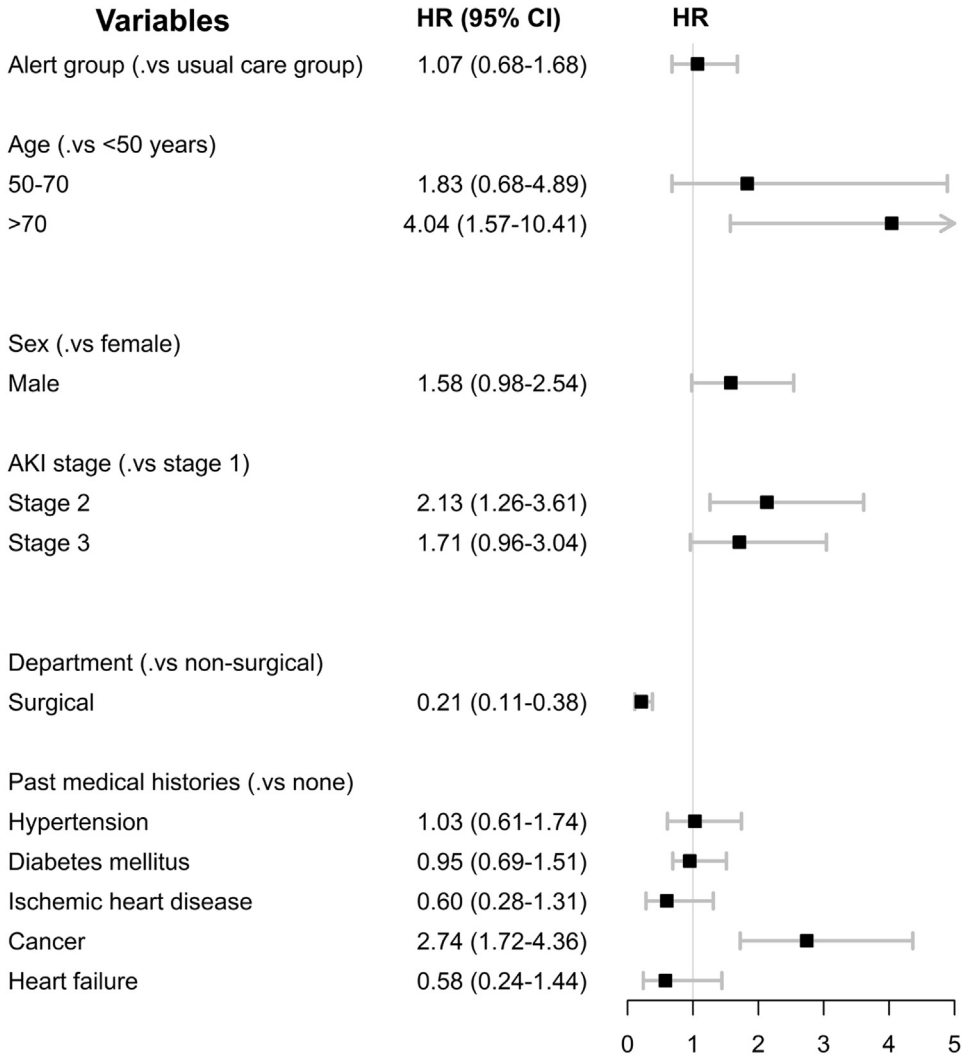

Figure 4. Risk factors for 30-day patient mortality in the study population. The impact of each characteristic on 30-day patient mortality is shown in the forest plot. Boxes indicate hazard ratio (HR) of characteristics, and horizontal gray lines crossing the boxes indicate 95% confidence interval (CI). The Cox proportional hazard model was adjusted for age (categorical, <50, 50-70, and >70 years); sex; baseline estimated glomerular filtration rate (eGFR; categorical, <30, 30-60, and >60 mL/min/1.73 m^2); admitting department (categorical, surgical vs nonsurgical); whether the acute kidney injury (AKI) was identified as community acquired; history of cancer, hypertension, diabetes mellitus, ischemic heart disease, or heart failure; use of diuretics, nonsteroidal anti-inflammatory drugs, or renin angiotensin aldosterone system blockers; and AKI stage (1, 2, and 3).

usual-care or alert group, had a better AKI recovery rate than the reference group. Patients who had early consultation after the AKI event despite the absence of the alerts were the most likely to have a severe AKI event (adjusted OR, 2.35; 95% CI, 1.57-3.50; $P < 0.001$). In contrast, those who were not referred to nephrologists early, although the attending clinicians received the alerts, were the least likely to have severe AKI (adjusted OR, 0.70; 95% CI, 0.58-0.84; $P < 0.001$).

Discussion

In our hospital, we launched an electronic AKI alert system, which linked a surveillance system to direct intervention by nephrologists. After the system was introduced, clinicians were more likely to monitor patients with AKI events and earlier involvement by nephrologists was observed. Moreover, we observed a significant improvement in AKI recovery rate and reduction of severe AKI events. Our study is the first to demonstrate an association of improved clinical outcomes with use of an electronic AKI alert system in hospitalized patients.

In previous studies, electronic AKI alerts showed benefits of early detection of AKI events, but most past studies did not detect improved clinical outcomes.[19-23] Considering that a large proportion of alert messages were sent to clinicians who were not internal medicine specialists, alerts alone

Table 3. Comparison of Clinical Outcomes Between Patients With and Without Early Consultation With Nephrology Division

	With Early Consultation (n = 488)	Without Early Consultation (n = 2,705)	Univariable Analysis		Multivariable Analysis[a]	
			OR[b] (95% CI)	*P*	OR[b] (95% CI)	*P*
Clinicians' behavior						
Overlooked AKI[c]	8 (1.6%)	409 (15.1%)	0.09 (0.04-0.18)	<0.001	0.17 (0.08-0.34)	<0.001
AKI characteristics						
Severe AKI[d]	186 (38.1%)	764 (28.2%)	1.56 (1.28-1.91)	<0.001	1.76 (1.42-2.19)	<0.001
AKI recovery[e]	393 (81.9%)	1454 (63.3%)	1.51[e] (1.35-1.68)	<0.001	1.25[e] (1.09-1.42)	0.001

Note: Values in group columns are given as number of patients with an event (percentage). Unless otherwise indicated, values in other columns are OR (95% CI).
Abbreviations: AKI, acute kidney injury; CI, confidence interval; OR, odds ratio; Scr, serum creatinine.
[a]Adjusted for age (categorical: <50, 50-70, and >70 years); sex; baseline estimated glomerular filtration rate (categorical: <30, 30-60, and >60 mL/min/1.73 m^2); admitting department (categorical: surgical, and nonsurgical); whether the AKI was identified as community acquired; history of cancer, hypertension, diabetes mellitus, ischemic heart disease, or heart failure; use of diuretics, nonsteroidal anti-inflammatory drugs, or renin-angiotensin-aldosterone system blockers; presence of anemia (hemoglobin < 11 g/dL) and hypoalbuminemia (albumin < 3.0 g/dL); and AKI stage (1, 2, and 3). Missing data imputation was performed for hemoglobin and albumin data, using the CART (classification and regression trees) method.
[b]Except as indicated.
[c]Overlooked AKI was defined as the absence of a follow-up Scr measurement within 2 weeks from the AKI event.
[d]Stages 2 and 3 AKI events were defined as severe AKI. AKI stage was not adjusted for the outcome because the AKI stage itself was used to define severe AKI events.
[e]Hazard ratios were calculated by Cox proportional hazards modeling. AKI recovery was defined as a return of Scr concentration to less than 1.2 times baseline. When the criterion of ≥0.3-mg/dL Scr concentration elevation was the only fulfilled criterion of AKI, the return of Scr concentration to <0.2 mg/dL elevation from baseline was used to define recovery. The 417 overlooked AKI cases were not included in analysis.

might be insufficient to improve patient management. A major strength of our alert system is that clinicians could easily request specialist consultation using a pop-up window in a daily-accessed EMR system. Therefore, attending clinicians were more likely to contact specialists earlier for AKI management. Early intervention by nephrologists beneficially affects the outcomes of patients with AKI events,[14,16] and in our study, even patients who were not under surveillance by the alert system had better AKI recovery outcomes if they were referred to the nephrology division early. Therefore, alteration of the behavior of attending clinicians and earlier specialized management might be a major reason for the improved AKI outcomes after implementation of the alert system. Additionally, the benefit of the pop-up window–based alert on its own should be considered because even patients in the alert group who were not early consulted had fewer overlooked AKI events and a better AKI recovery rate than the usual-care group without early consultation.

All subgroup analyses indicated improved AKI recovery after the alert system was introduced. Furthermore, the impact of the alert system was even more prominent in patients with preserved kidney function, women, and patients with no underlying cancer. Because these characteristics are related to better patient prognosis,[29,30] low-risk patients might more easily regain their underlying kidney function after an AKI event. By contrast, although the alert system was effective, there might be a subset of patients unable to recover from AKI despite early recognition of the event.

However, no significant change in patient mortality was observed in our study, and several possible reasons for this finding should be considered. First, our AKI alerts were not issued in real time. Most deaths occurred on the day of AKI and thus were beyond the reach of the system. Therefore, only a small proportion of acute death events were included in the current study. Second, our study cohort mostly consisted of index admission cases in general

Table 4. Clinical Outcomes of Subgroups, Divided According to Early Consultation and AKI Alerts

	Overlooked AKI[a]		Severe AKI[b]		AKI Recovery[c]	
	OR[d] (95% CI)	*P*	OR[d] (95% CI)	*P*	HR[c,d] (95% CI)	*P*
Usual-care group						
Without early consultation (n = 1,761)	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
With early consultation (n = 123)	0.24 (0.04-0.78)	0.04	2.35 (1.57-3.50)	<0.001	1.27 (1.01-1.60)	0.04
Alert group						
Without early consultation (n = 944)	0.45 (0.34-0.60)	<0.001	0.70 (0.58-0.84)	<0.001	1.73 (1.55-1.93)	<0.001
With early consultation (n = 365)	0.12 (0.05-0.24)	<0.001	1.39 (1.08-1.79)	0.01	1.74 (1.55-1.93)	<0.001

Abbreviations: AKI, acute kidney injury; CI, confidence interval; HR, hazard ratio; OR, odds ratio; Scr, serum creatinine.
[a]Overlooked AKI was defined as absence of follow-up Scr measurement within 2 weeks from the AKI event.
[b]Stages 2 and 3 AKI events were defined as severe AKI. AKI stage was not adjusted for the outcome because AKI stage itself was used to define the severe AKI events.
[c]HRs were calculated by Cox proportional hazards modeling. AKI recovery was defined as a return of Scr concentration to <1.2 times baseline. When the criterion of ≥0.3-mg/dL Scr concentration elevation was only fulfilled criterion of AKI, the return of Scr concentration to <0.2 mg/dL elevation from baseline was used to define recovery. The overlooked AKI cases, 340 cases in the usual-care group and 77 cases in the alert group, were not included.
[d]Adjusted for age (categorical: <50, 50-70, and >70 years); sex; baseline estimated glomerular filtration rate (categorical: <30, 30-60, and >60 mL/min/1.73 m^2); admitting department (categorical: surgical, and nonsurgical); whether the AKI was identified as community acquired; history of cancer, hypertension, diabetes mellitus, ischemic heart disease, or heart failure; use of diuretics, nonsteroidal anti-inflammatory drugs, or renin-angiotensin-aldosterone system blockers; presence of anemia (hemoglobin < 11 g/dL) and hypoalbuminemia (albumin < 3.0 g/dL); and AKI stage (1, 2, and 3). Missing data imputation was performed for hemoglobin and albumin data, using the CART (classification and regression trees) method.

wards, which further minimized the proportion of patients at risk for death in our study population. Overall, the AKI recovery rate was high and the survival rate might have been less affected by AKI management than by the patients' underlying medical conditions.

Our study had several limitations. First, this was not a randomized clinical trial; therefore, innate differences between the usual-care and alert groups existed. Although we adjusted several clinical variables and made some investigations of the effect of time phases, hidden confounders may be present. There were also differences in the characteristics and incidence of AKI between the study and historical cohorts, which further suggests that the study groups were not identical. However, the better clinical outcomes in the alert group, despite their less favorable baseline characteristics, support the conclusion that the system had benefit. Second, as mentioned, our AKI alert system could not report AKI events in real time, and there was a possible 1-day delay. A more efficient real-time alert system encouraging nephrology intervention might show superior results, including potential improvements in patient survival. Third, criteria for baseline Scr concentrations have not been established. Including Scr concentrations only within 2 weeks before admission might not efficiently detect community-acquired AKI events and their recovery because there could be patients without Scr information before hospitalization whose peak Scr concentration occurred on admission. Moreover, our AKI criteria might have included some patients with benign Scr concentration changes rather than AKI events because time-period criteria were not identically applied according to the suggested guideline.[17] Fourth, because the alert group was admitted for longer periods and had worse baseline characteristics, possible selection bias might exist because patients with a more complicated course were more likely to have a follow-up Scr. Last, our study results might not be transferrable to other hospitals, depending on the size or location of the hospital, because our study was performed in a single center. Also, an ~20% increase in consultation burden to the nephrology division should be considered.

In conclusion, our EMR-based AKI alert system altered the behavior of clinicians, increased the involvement of specialists, and improved AKI outcomes. Therefore, adoption of an AKI alert system linked to early nephrology intervention could be considered in hospitals to improve patient prognosis.

Supplementary Material

Figure S1: Screenshot of electronic AKI alert that appeared in EMR system.

Figure S2: Screenshot of automatically generated consult note that appeared in EMR system.

Figure S3: Impact of implementation of alert system on mortality in subgroups.

Table S1: Baseline characteristics and nephrology consultation of patients without AKI.

Table S2: Results of analysis when different criteria were used to define overlooked AKIs.

Table S3: Characteristics and delivery of care of mortality cases on day of AKI.

Table S4: Results of sensitivity analyses for AKI recovery.

Table S5: Results using complete case analysis method.

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