Incidence, Outcomes, and Risk Factors of Community-Acquired and Hospital-Acquired Acute Kidney Injury

A Retrospective Cohort Study

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Abstract: The disease burden and outcomes of community-acquired (CA-) and hospital-acquired acute kidney injury (HA-AKI) are not well understood. The aim of the study was to investigate the incidence, outcomes, and risk factors of AKI in a large Taiwanese adult cohort. This retrospective cohort study examined 734,340 hospital admissions from a group of hospitals within an organization in Taiwan between January 1, 2010 and December 31, 2014. Patients with AKI at discharge were classified as either CA- or HA-AKI based on the RIFLE (risk, injury, failure, loss of function, end stage of kidney disease) classification criteria. Outcomes were in-hospital mortality, dialysis, recovery of renal function, and length of stay. Risks of developing AKI were determined using multivariate logistic regression based on demographic and baseline clinical characteristics and nephrotoxin use before admission.

AKI occurred in 1.68% to 2% hospital discharges among adults without and with preexisting chronic kidney disease (CKD), respectively. The incidence of CA-AKI was 17.25 and HA-AKI was 8.14 per 1000 admissions. The annual rate of CA-AKI increased from 12.43 to 19.96 per 1000 people, but the change in HA-AKI was insignificant. Comparing to CA-AKI, those with HA-AKI had higher levels of in-hospital mortality (26.07% vs 51.58%), mean length of stay (21.25 ± 22.35 vs 35.84 ± 34.62 days), and dialysis during hospitalization (1.45% vs 2.06%). Preexisting systemic diseases, including CKD, were associated with increased risks of CA-AKI, and nephrotoxic polypharmacy increased risk of both CA- and HA-AKI.

Patients with HA-AKI had more severe outcomes than patients with CA-AKI, and demonstrated different spectrum of risk factors. Although patients with CA-AKI with better outcomes, the incidence increased over time. It is also clear that optimal preventive and management strategies of HA- and CA-AKI are urgently needed to limit the risks in susceptible individuals.

Introduction

Hospital-acquired acute kidney injury (HA-AKI) is a widely recognized disorder that carries a substantially increased risk of mortality for many hospitalized patients.1–3 Studies have shown that causes of HA-AKI include sepsis, critical illness, surgery, and use of contrast media and aminoglycosides during hospitalization.4,5 Few data have been published on the group of patients presenting at hospital with an existing acute increase in serum creatinine (SCr) level, or community-acquired AKI (CA-AKI).5–11 Studies have reported that the incidence of CA-AKI was 2 to 3 times higher than HA-AKI, but has the same prognostic significance as HA-AKI on mortality, longer length of stay (LOS) and higher healthcare costs.1,3,10

Recent literature reviews have suggested that there are etiological and geographical differences in characteristics of AKI in different regions of the world.12,13 For instance, in some countries, CA-AKI is more likely to be associated with chronic kidney disease (CKD), other chronic kidney diseases (liver, heart, lung),8,10,14 and polypharmacy with nephrotoxic drugs.15 In other countries, CA-AKI occurs most frequently in young, previously healthy individuals or in the context of one particular predisposing disease.13 More information on the burden and consequences of AKI will therefore facilitate better prevention and management.

A set of criteria for analyzing the severity of AKI, known as RIFLE (risk, injury, failure, loss of function, end stage of kidney disease), has been widely adopted. It has been used to flag the likelihood of developing AKI, particularly CA-AKI, but its utility in a Taiwanese adult cohort is less clear. CKD and dialysis are widespread in Taiwan, so it is important to characterize variability in risk among groups of patients, to facilitate early identification and prevention of disease. The aim of this...
study is therefore to investigate the incidence, severity, and outcomes of AKI in Taiwan. We also examined the potential risk factors for AKI associated with hospital admission in a large adult cohort.

METHODS

The study was approved by the Institutional Review Board and the Ethics Committee of Chang Gung Medical Foundation (CGMF), Taiyuan, Taiwan.

Study Design, Setting, and Sources of Data

The cohort study was conducted using electronic medical records (EMRs) for the period from January 1, 2010 to December 31, 2014 from CgmF. CgMF is the largest group of hospitals within an organization in Taiwan, and in 2013, it provided approximately 11% of the total Taiwan National Health Insurance (NHI) program-reimbursed healthcare services, including emergency, outpatient, and inpatient care. The Taiwan NHI program is a compulsory, nationwide health insurance program, which covers more than 95% of contracted hospitals in Taiwan and 99% of the 23 million persons enrolled in the program. CgMF maintains comprehensive, centralised patient-level EMRs for the hospitals located from the North to South of Taiwan, so the study participants are considered generalizable to the Taiwan general population.

AKI Cohort

The study included all patients hospitalized between January 1, 2010 and December 31, 2014 with a discharge diagnosis of International Classification of Diseases, Ninth Revision (ICD-9) code of 584, for AKI. The first admission for AKI during the study period was defined as the index admission. AKI events were further categorized by RIFLE (risk, injury, failure, loss of function, and end stage) stage (risk, injury and failure) according to the ratio 1.5 to 2.0, 2.0 to 3.0, and >3.0. When the index SCR at admission was 4.0 mg/dL or more, the episode was categorized as failure stage. Using 2 methods to identify the presence of AKI, ICD-9 codes for discharge diagnosis and the RIFLE (risk, injury, failure, loss, and end-stage kidney disease) definition, provided additional confirmation of a correct diagnosis. Patients diagnosed as AKI by a discharge diagnosis of AKI but not met with RIFLE classification stage 1 criteria were classified as non-RIFLE AKI group.

SCR laboratory evaluations at index admission, previous year (baseline) and during hospitalization were examined. For CA-AKI, baseline SCR was defined as the lowest measured SCR within the 12 months before the index SCR at admission. If there was more than one laboratory result in the baseline period, the lowest value was used. For CA-AKI, only index SCR performed in the emergency department of outpatient clinics of the patient’s hospitalization were included to classify as CA-AKI related hospitalization. The HA-AKI group of patients was those for whom the highest measured SCR during hospitalization increased at least 1.5 times above admission value (peak/index SCR > 1.5). Patients who met the criteria of CA-AKI were excluded from the assessment of AKI developed during hospitalization.

Only patients aged >18 years at index admission were enrolled in the study. Exclusion criteria included patients who had undergone renal replacement therapy, including dialysis or renal transplant, within 12 months before the index admission, and absence of valid SCR laboratory results at index, baseline, and at least one follow-up point.

Outcomes

The incidence of AKI was calculated by dividing the number of cases by the total number of hospitalizations in each calendar year. Patient-level outcomes included mortality, LOS, and dialysis during the index hospital admission. Recovery of renal function at the time of discharge was classified by eGFR improvement ≥50% (≥1.5-fold reduction from the index eGFR) or ≥60 mL/min/1.73 m². The measure of eGFR was based on the Modification of Diet in Renal Disease equation, which is routinely used in the study setting.

Baseline Risk Factor Assessment

Demographic information, clinical condition, and medical history for the 12 months before the index admission were retrieved for all study patients. Quan–Charlson comorbidity Index score was used to categorize degree of severity of baseline clinical conditions. Information about use of medicines concerned in patients with impaired renal function was retrieved from the outpatient pharmacy dispensing records for all study patients. Exposure to medicines with nephrotoxic potential initially was defined as ever/never use of study drugs within the 3-month risk window before admission. In a second step, cumulative exposure was identified by the sum of all types of different nephrotoxic medicines identified within the 3-month risk window. Medication use with renal dysfunction concerns (Supplemental Table 1, http://links.lww.com/MD/A966) were categorized into 19 classes by pharmacological mechanism and modified using the potentially inappropriate medication list for the elderly in Taiwan.

Statistical Analysis

Continuous data are presented as mean (standard deviation, SD) or median (interquartile range, IQR, 25th–75th percentile), and categorical data as number and percentages. Means of baseline characteristics were compared using unpaired Student t tests for continuous variables and Chi-square tests for categorical variables. To identify any trends in incidence of CA- and HA-AKI, annual changes over the study period were examined using the Cochran–Armitage test for binomial outcome. A primary multivariable logistic regression model was employed to determine the ORs and 95% confidence intervals (CIs) to predict the occurrence of AKI based on all baseline characteristics. A secondary multivariable logistic regression model was used to identify the OR for developing CA- or HA-AKI based on all baseline characteristics. All analyses were carried out using SAS version 5.1 (Stata Corp, College Station, TX).

RESULTS

The study cohort included 395,219 adults with a total of 734,340 hospitalizations between January 1, 2010 and December 31, 2014. The average age at admission was 57.48 (±17.25) years old and 64.7% were male patients. The mean LOS was 11.90 (±19.63) days.

Incidence of AKI

During 2010 to 2014, 14,684 (2%) hospital discharges with a diagnosis of AKI were identified, using the International Classification of Diseases Version 9 (ICD9-CM), code 584. The overall AKI-associated hospitalization was 20.21 per 1000 admissions (±0.97). The incidence of AKI according to the RIFLE definition complicated with 11,542 patients, of whom there were 6,287 with CA-AKI (17.25 ± 3.86 per 1000 people),
3104 with HA-AKI (8.14 ± 1.68 per 1000 people), and 2151 with non-RIFLE AKI (5.76 ± 1.35 per 1000 people). The agreement on the presence of AKI between disease codes and the RIFLE definition was 81.36% [(6287 + 3104)/11,542] among patients with more than 2 SCr measures. Excluding patients with baseline CKD (n = 2568 admissions, 17.5%), from the study cohort, the rate of AKI was 1.68% hospital discharges.

FIGURE 1. Incidence of discharges with a diagnosis of AKI and mortality rate, 2010–2014; AKI = acute kidney injury.

FIGURE 2. Incidence rate of RIFLE-based AKI, by calendar year and severity. Data are presented as mean cases per 1000 hospitalized adults. AKI = acute kidney injury, CA-AKI = community-acquired AKI, HA-AKI = hospital-acquired AKI, RIFLE = risk, injury, failure, loss of function, and end stage of renal disease.
Changes in Trends in AKI Incidence

Over the study period, the annual rate of discharge with a diagnosis of AKI increased from 18.44 to 21.24 cases per 1000 admissions (Figure 1). The annual rate (mean) for the failure stage was high for both HA- and CA-AKI, and increased over time in CA-AKI (from 8.2 to 11.62 per 1000 people) (Figure 2B). The annual rate for the risk stage was low, but increased in both groups (HA from 1.20 to 1.63 cases and CA from 2.15 to 3.89 cases per 1000 people) (Figure 2D). There was an increase in the injury stage in CA-AKI (from 2.0 to 4.25 cases per 1000 people), but no change in HA-AKI (Figure 2C).

Table 1 shows the baseline characteristics of patients by RIFE definition of AKI. There were consistently more male patients in all groups, in a ratio of 3:2. On average, patients were 68.02 (±15.33) years old for CA-AKI, 66.61 (±16.23) for HA-AKI, and 68.37 (±16.24) for non-RIFE AKI. Patients in the CA-AKI group generally had more Quan–Charlson comorbid conditions than other groups. The most common preexisting comorbid conditions among patients with AKI were diabetes with/without complications (34.01%), CKD (17.67%), and tumors, including metastatic solid tumors (23.27%).

AKI Outcomes

In-Hospital Mortality

The overall in-hospital mortality was 30.71% in patients with AKI diagnosis at discharge, compared with 3.33% for patients without AKI. The annual mortality rate associated with AKI steadily declined from 32.73% in 2010 to 23.46% in 2014.

**Table 1.** Demographic and Clinical Characteristics of Study Cohort by Type of AKI

|                         | Overall (n = 11,542) | CA-AKI (n = 6287) | HA-AKI (n = 3104) | Non-RIFE AKI (n = 2151) | P       |
|------------------------|----------------------|-------------------|-------------------|------------------------|---------|
| Gender, n, %           |                      |                   |                   |                        | <0.0001 |
| Male                   | 6985 (60.52)         | 3688 (58.66)      | 2021 (65.11)      | 1276 (59.32)           |         |
| Age, y                 | 67.7 ± 15.76         | 68.02 ± 15.33     | 66.61 ± 16.23     | 68.37 ± 16.24          | <0.0001 |
| Age, y                 |                      |                   |                   | <0.0001                |         |
| 18 to <30              | 244 (2.11)           | 106 (1.69)        | 84 (2.71)         | 54 (2.51)              |         |
| 30 to <45              | 825 (7.15)           | 426 (6.78)        | 243 (7.83)        | 156 (7.25)             |         |
| 45 to <60              | 2352 (20.38)         | 1266 (20.14)      | 685 (22.07)       | 401 (18.64)            |         |
| 60 to <75              | 3709 (32.13)         | 2086 (33.18)      | 973 (31.35)       | 650 (30.22)            |         |
| ≥75                    | 4412 (38.23)         | 2403 (38.22)      | 1119 (36.05)      | 890 (41.38)            |         |
| Quan–CCI score         | 1.72 ± 1.86          | 2.08 ± 1.94       | 1.31 ± 1.67       | 1.24 ± 1.61            | <0.0001 |
| MI                     | 159 (1.38)           | 110 (1.75)        | 26 (0.84)         | 23 (1.07)              |         |
| CHF                    | 640 (5.54)           | 430 (6.84)        | 117 (3.77)        | 93 (4.32)              |         |
| Peripheral vascular disease | 149 (1.29)    | 107 (1.7)         | 34 (1.1)          | 8 (0.37)               |         |
| CVD                    | 1017 (8.81)          | 677 (10.77)       | 197 (6.35)        | 143 (6.65)             |         |
| Dementia               | 313 (2.71)           | 214 (3.4)         | 51 (1.64)         | 48 (2.23)              |         |
| CPD                    | 799 (6.92)           | 496 (7.89)        | 191 (6.15)        | 112 (5.21)             |         |
| Rheumatologic disease  | 107 (0.93)           | 72 (1.15)         | 25 (0.81)         | 10 (0.46)              |         |
| Peptic ulcer bleeding  | 937 (8.12)           | 650 (10.34)       | 171 (5.51)        | 116 (5.39)             |         |
| Liver diseases          | 1131 (9.80)          | 817 (13.0)        | 205 (6.60)        | 109 (5.07)             |         |
| DM without complications| 3201 (27.73)         | 2035 (32.37)      | 653 (21.04)       | 513 (23.85)            |         |
| DM with complications   | 725 (6.28)           | 560 (8.91)        | 85 (2.74)         | 80 (3.72)              |         |
| Hemiplegia or paraplegia| 42 (0.36)            | 28 (0.45)         | 7 (0.23)          | 7 (0.33)               |         |
| CKD                    | 2039 (17.67)         | 1369 (21.78)      | 390 (12.56)       | 280 (13.02)            |         |
| Tumors                 | 2686 (23.27)         | 1643 (26.13)      | 685 (22.07)       | 358 (16.64)            |         |
| HIV/AIDS               | 4 (0.03)             | 4 (0.06)          | 0                 | 0                      |         |
| Prior nephrotoxic medicine use |            |                   |                   |                        |         |
| None                   | 3658 (31.69)         | 1758 (27.96)      | 1115 (35.92)      | 785 (36.49)            | <0.0001 |
| 1 to <3 categories     | 3200 (27.72)         | 1603 (25.5)       | 907 (29.22)       | 690 (32.08)            |         |
| ≥3 categories          | 4684 (40.58)         | 2926 (46.54)      | 1082 (34.86)      | 676 (31.43)            |         |
| Number of drug categories | 2.19 ± 2.08         | 2.43 ± 2.13       | 1.96 ± 2.04       | 1.79 ± 1.91            | <0.0001 |

Data are shown as the mean (standard deviation, SD) for age and Quan–CCI (Quan–Charlson Comorbidity Index) score, and number of nephrotoxic drug categories, and number (percent of group) of patients in each group.

Liver diseases include mild, moderate, and severe; tumors include any malignancy and metastatic solid tumor.

AKI = acute kidney injury, CA-AKI = community-acquired AKI, CHF = congestive heart failure, CKD = chronic kidney disease, CPD = chronic pulmonary disease, CVD = cerebrovascular disease, DM = diabetes mellitus, HA-AKI = hospital-acquired AKI, HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome, MI = myocardial infarction, non-RIFLE AKI = patients discharged with a diagnosis of AKI but not meeting the RIFE criteria (i.e., Scr changes < 1.5 times), RIFE = risk injury failure loss and end stage of renal disease.

*P-value calculated using ANOVA.
acquired acute kidney injury, NA

(i.e., SCr changes loss and end stage of renal disease.

AKI (22.65–50.96).

eGFR recovery RIFLE stage 0.14

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TABLE 3. Severity of AKI and Recovery of Renal Function

| Renal Function at Admission | Overall (n = 11,542) | CA-AKI (n = 6287) | HA-AKI (n = 3104) | Non-RIFLE AKI (n = 2151) | P |
|-----------------------------|---------------------|------------------|------------------|--------------------------|---|
| SCr (mg/dL)                 | 3.58 ± 3.26         | 4.66 ± 3.63      | 2.56 ± 2.66      | 1.92 ± 0.85              | <0.0001 |
| eGFR (mL/min/1.73 m²)       | 34.32 ± 35.75       | 21.56 ± 20.29    | 55.26 ± 51.36    | 41.38 ± 26.26            | <0.0001 |
| eGFR ≥ 60 (mL/min/1.73 m²)  | 1818 (15.75)        | 276 (4.39)       | 1181 (38.05)     | 361 (16.78)              | <0.0001 |
| RIFLE stage                 |                     |                  |                  |                          | 0.141 |
| Risk                        | 1719 (18.3)         | 1174 (18.67)     | 545 (17.56)      | NA                       |     |
| Injury                      | 1896 (20.19)        | 1237 (19.68)     | 659 (21.23)      | NA                       |     |
| Failure                     | 5776 (61.51)        | 3876 (61.65)     | 1900 (61.21)     | NA                       |     |
| Renal Function at Discharge |                     |                  |                  |                          |     |
| Overall (n = 1199)          | 2.94 ± 2.55         | 3.25 ± 2.79      | 3.45 ± 2.5       | 1.36 ± 0.85              | <0.0001 |
| eGFR ≥ 60 (mL/min/1.73 m²)  | 2420 (26.31)        | 1078 (24.34)     | 445 (15.06)      | 897 (49.39)              | <0.0001 |
| eGFR recovery ≥ 50%         | 2414 (26.24)        | 2531 (57.15)     | 475 (16.08)      | 899 (49.5)               | <0.0001 |

Data are shown as the mean (± standard deviation, SD) for length of stay, and number (percent of group) of patients in each group; renal function recovery was defined using the last eGFR measure during hospitalization, as the presence of eGFR ≥ 60 mL/min/1.73 m², or return to at least 50% of index value (at admission).

AKI = acute kidney injury, CA-AKI = community-acquired acute kidney injury, eGFR = estimated glomerular filtration rate, HA-AKI = hospital-acquired acute kidney injury, NA = not applicable, non-RIFLE AKI = patients discharged with a diagnosis of AKI but not meeting the RIFLE criteria (i.e., SCr changes < 1.5 times), RIFLE = risk injury failure loss and end stage of renal disease, SCr = serum creatinine.

1SCr at baseline (median, 25th–75th quartile): CA-AKI: 3.66 (2.01–6.10); HA-AKI: 1.43 (0.9–3.27); non-RIFLE AKI: 1.70 (1.28–2.48).

2eGFR at baseline (median, 25th–75th quartile): CA-AKI: 41.74 (8.04–29.79); HA-AKI: 45.34 (16.64–78.56); non-RIFLE AKI: 35.82 (22.65–50.96).

P-value calculated using Chi-square test for CA- and HA-AKI.
1.03 – 1.10) and having a cancer history (aOR, 1.25; 95% CI, 1.07 – 1.46) were associated with an increased risk of developing HA-AKI (Figure 3B).

More than 70% of AKI patients had used at least one prescription with renal dysfunction concern before developing AKI (72.04% for CA-AKI, 64.08% for HA-AKI, and 63.51% for non-RIFLE AKI). The proportion of patients exposed to more nephrotoxic medicines was higher for CA- than HA-AKI (Cochran–Armitage test, Z = 6.52, 1-sided P < 0.001). The baseline renal function was worse in the CA-AKI group (Table 2). We also examined the association between number of nephrotoxic medicines and AKI severity. Figure 4B shows the distribution of number of nephrotoxic medicines previously used by RIFLE stages. Compared with patients at the risk stage of AKI, those who were exposed to more types of nephrotoxic medication before admission were more likely to develop severe stage AKI (Cochran–Armitage test supports the trend, Z = –6.52, 1-sided P < 0.001).
association between number of drug categories used and the injury stage was not significant (Cochran–Armitage test supports the trend, \( Z = 0.70, 1\text{-sided } P = 0.24 \)). The most common nephrotoxic medicines used before AKI admission were antihypertension agents (e.g., aldosterone antagonists, angiotensin II-converting enzyme inhibitors/angiotensin receptor blockers, calcium channel blockers), antithrombotic agents, and nonsteroidal antiinflammatory drugs (NSAIDs) (see Supplemental Table 3, http://links.lww.com/MD/A966). It is possible that health professionals are now more aware of AKI in hospitalized patients, as the decline in in-hospital mortality in this study was consistent with previous results.14,31 The impact of prior polypharmacy with nephrotoxic drugs on AKI development has also been highlighted in recent observational studies.12,32 One study using RIFLE criteria in a population-based case–control study suggested that NSAIDs used in combination with rennin–angiotensin system inhibitors (RASIs) and/or diuretics increased the risk of CA-AKI by 64%.15 We found that NSAIDs, RASIs, and diuretics were used frequently in the three months before admission for CA-AKI, which is consistent with a complex background of chronic conditions in the study cohort, and suggests these patients were likely to have unstable or severely impaired renal function.

The agreement on presence of AKI between diagnostic code at discharge and SCr changes in the study was considered high (82%) among patients with more than 2 SCr measures. A large discharge cohort study suggested that using hospital discharge code would lead to substantial underestimation of AKI incidence, as milder changes or rapidly reversible SCr results may not coded as AKI.33 RIFLE classification, however, relies on having at least 2 measures of renal function, which depends on the frequency of SCr testing in the relevant practice setting. AKI may therefore go undetected because of insufficient SCr testing. As the diagnostic code is unable to differentiate severity of kidney injury, greater RIFLE AKI severity revealed a link to higher mortality and longer LOS, which showed good discrimination for patient outcomes of the RIFLE stages in the study cohort. The 18% of patients who had an AKI diagnosis at discharge code but did not reach the threshold for RIFLE stages in the study cohort, and suggests these patients were likely to have unstable or severely impaired renal function.

**DISCUSSION**

This large, cohort study of hospitalized adults confirmed the findings from previous studies in different practice settings that CA-AKI was more common than HA-AKI.8,10,25 Both CA- and HA-AKI increased risk of mortality, but in-hospital mortality and LOS were worse in HA-AKI than CA-AKI.8,10,25 One of the major findings of this study was that CA-AKI increased steadily over time,12,26 which suggests that it could have a significant impact on the quality of patient care and healthcare resource utilization.

The study results demonstrated that the risk profile was different for CA- and HA-AKI, with CA-AKI being more common in patients with preexisting chronic diseases, including diabetes, rheumatologic diseases, CKD, liver disease, chronic pulmonary disease, peptic ulcer disease, cerebrovascular disease, congestive heart failure, and tumor (Figure 3). In contrast, baseline comorbid conditions were not linked to HA-AKI, indicating that the causes and etiology of AKI developed during hospitalization differed from those in patients admitted with existing renal dysfunction. Several single-setting studies have reported that prevalence of HA-AKI varied by inpatient setting (e.g., medical or surgical wards, and intensive care) and was linked to common hospital-related factors including heart failure, sepsis, cardiac catheterization, use of aminoglycosides and radiographic contrast media and acute organ system dysfunction.29–30 The distribution of common discharge diagnoses was broad and varied between patients with CA- and HA-AKI (Supplemental Table 3, http://links.lww.com/MD/A966). It is possible that health professionals are now more aware of AKI in hospitalized patients, as the decline in in-hospital mortality in this study was consistent with previous results.14,31

The medicines should be used with caution in patients with impaired renal function was prevalent in the study cohort. Prior target medications exposure was linked to both CA- and HA-AKI, after adjusting for patient demographic characteristics and preexisting chronic conditions. Exposure to more nephrotoxic medicines was associated with more severe AKI. The impact of prior polypharmacy with nephrotoxic drugs on AKI development has also been highlighted in recent observational studies.12,32 One study using RIFLE criteria in a population-based case–control study suggested that NSAIDs used in combination with rennin–angiotensin system inhibitors (RASIs) and/or diuretics increased the risk of CA-AKI by 64%.15 We found that NSAIDs, RASIs, and diuretics were used frequently in the three months before admission for CA-AKI, which is consistent with a complex background of chronic conditions in the study cohort, and suggests these patients were likely to have unstable or severely impaired renal function.

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The major strength of this study is the availability of SCr laboratory results from a large cohort of hospitalized adults, which allowed us to use the up-to-date consensus RIFLE criteria to identify AKI, in particular CA-AKI, and to differentiate degrees of severity of AKI in the study cohort. The differences
in comorbid conditions, prior nephrotoxic polypharmacy and baseline SCr level between HA- and CA-AKI will help to identify patients who are particularly vulnerable to different forms of AKI. The study results also revealed new information about trends in HA- and CA-AKI, supporting development of strategies to limit the risks of CA-AKI.

The study did, however, have some limitations. First, although possible misdiagnosis of AKI (ICD-9-CM codes have a positive predictive value of 47.9% for AKI) was avoided by using the RIFLE definitions, the true incidence of AKI may be underestimated. The baseline incidence of RIFLE AKI that does not result in hospitalization is unknown. Patients with a spuriously high or low SCr value may have received a misclassification of AKI incidence or severity stage. This study was performed at a tertiary medical center, and the epidemiological features and risk factors of AKI found in the study population may therefore not be generalizable to patients in lower level hospitals.

The findings have important implications for research and patient care. We found an increasing incidence of CA-AKI among hospitalized adults and its risk profile underscored the need to increase awareness of AKI among policy makers and health professionals, to support the development of effective strategies for early identification and prevention of AKI. Further research into the longer-term outcomes of AKI is warranted.

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