Use of Electronic Results Reporting to Diagnose and Monitor AKI in Hospitalized Patients

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Summary

Background and objectives Many patients with AKI are cared for by non-nephrologists. This can result in variable standards of care that contribute to poor outcomes.

Design, setting, participants, & measurements To improve AKI recognition, a real-time, hospital-wide, electronic reporting system was designed based on current Acute Kidney Injury Network criteria. This system allowed prospective data collection on AKI incidence and outcomes such as mortality rate, length of hospital stay, and renal recovery. The setting was a 1139-bed teaching hospital with a tertiary referral nephrology unit.

Results An electronic reporting system was successfully introduced into clinical practice (false positive rate, 1.7%; false negative rate, 0.2%). The results showed that there were 3202 AKI episodes in 2619 patients during the 9-month study period (5.4% of hospital admissions). The in-hospital mortality rate was 23.8% and increased with more severe AKI (16.1% for stage 1 AKI versus 36.1% for stage 3) (P<0.001). More severe AKI was associated with longer length of hospital stay for stage 1 (8 days; interquartile range, 13) versus 11 days for stage 3 (interquartile range, 16) (P<0.001) and reduced chance of renal recovery (80.0% in stage 1 AKI versus 58.8% in stage 3) (P<0.001). Utility of the Acute Kidney Injury Network criteria was reduced in those with pre-existing CKD.

Conclusions AKI is common in hospitalized patients and is associated with very poor outcomes. The successful implementation of electronic alert systems to aid early recognition of AKI across all acute specialties is one strategy that may help raise standards of care.


Introduction

AKI is an important condition affecting 3.2%–18.3% of hospitalized patients (1–4). There now exist consensus criteria that provide a method of diagnosing and describing the severity of AKI. The Acute Kidney Injury Network (AKIN) diagnostic criteria are the most current (5), refining several aspects of the earlier RIFLE (risk, injury, failure, loss, ESRD) classification (6). These criteria have been shown to predict patient outcomes in many different clinical settings and have emphasized the high mortality rates associated with AKI (3,4,7–10). The AKIN criteria recognize that even a small decline in renal function is associated with poor outcomes (11). AKI therefore encompasses a wide spectrum of illness in a large number of patients, from an abrupt increase in serum creatinine of only 26 μmol/L (0.3 g/dl) through to critically unwell patients requiring renal replacement therapy (RRT). Although the AKI diagnostic criteria have been shown to be robust when applied retrospectively, they have proven more difficult to systematically apply in routine clinical practice.

Attempts to develop specific therapies for AKI have been unsuccessful; thus, management focuses on supportive aspects such as careful fluid balance, avoidance of nephrotoxic medications, and appropriate diagnostic investigations (12). If these are performed meticulously, the course of AKI can be improved (13). However, studies have reported that routine clinical practice can often be deficient in these areas (14,15); this is reflected in the worse outcomes seen with AKI occurring over a weekend (16). Similar deficiencies in care were reported in a UK National Confidential Inquiry into Patient Outcome and Death in AKI that also demonstrated that the majority of patients with AKI are cared for by non-nephrologists, emphasizing the relevance to all acute specialties (17).

We aimed to develop the first real-time, hospital-wide, electronic reporting system for AKI based on the AKIN diagnostic criteria (5). The primary aim of this project was to introduce an alert system for use in routine clinical practice to aid the early diagnosis of AKI in non-specialist areas. Using this system, we were also able to prospectively capture observational data for all cases of AKI at our center. This article reports the results of the first 9 months of the system’s introduction.

Materials and Methods

Setting

The Royal Derby Hospital is a 1139-bed teaching hospital that provides all major medical and surgical...
specialties (except neuro- and cardiothoracic surgery). The renal unit is a tertiary referral center, serving a population of 700,000. There is a central chemical pathology laboratory for all inpatient and outpatient samples, covering approximately 144 primary care practices. A compensated kinetic Jaffe method with an interassay coefficient of variance of 2.3% at 96 μmol/L (Roche P-analyzer; Roche Diagnostics, West Sussex, UK) was used to measure all serum creatinine values throughout the study period (normal creatinine range, 70–120 μmol/L).

Development of Electronic Reporting System

Development of an electronic AKI reporting system has to overcome the difficulties of finding an information technology solution to prospectively apply the AKIN diagnostic criteria. Problems arise because many of the currently available pathology software systems cannot easily be programmed to accurately identify an individual’s baseline creatinine. Our solution utilizes a combination of information technology and human algorithms and is based on serum creatinine criteria only.

Our system is summarized in Figure 1. All serum creatinine measurements sent from inpatient locations are included, with the exception of those from the renal dialysis unit and renal inpatient ward. We chose to exclude these areas to prevent a significant number of dialysis patients from being wrongly classified as having AKI. This does not result in the significant exclusion of patients with AKI under the care of nephrologists; these patients are identified from prior blood samples collected in the emergency department, admissions unit, or other inpatient location. The pathology computer system (iLab 5.8.1001; iSoft) automatically compares all measured creatinine values on an individual patient basis against an estimated baseline creatinine. This estimated baseline value is reverse calculated from the Modified Diet in Renal Disease (MDRD) equation assuming a GFR of 75 ml/min per 1.73 m² (18). All measured creatinine values that are 50% greater than (1.5 ×) the individual’s estimated baseline value are flagged internally within iLab. These results are then reviewed by a clinical chemist, who selects the real baseline creatinine for each patient using previous creatinine results (accepting the estimated baseline from reverse MDRD calculation in those cases in which there are no previous creatinine measurements available). The AKIN diagnostic criteria are then applied using a calculator designed in Excel 2003 (Microsoft Corporation). For each acute elevation in creatinine consistent with AKI, a report is issued in the hospital results reporting system (Clinical Manager 1.5; iSoft) that specifies AKI stage, value and date of baseline creatinine utilized, an intranet link to local AKI clinical guidelines, and a reminder of the AKIN diagnostic criteria. If AKI is not present, then no report is issued.

Using the AKIN diagnostic criteria in clinical practice, we made some practical decisions with respect to their application. Most importantly, we have chosen to include baseline values from the previous 12 months, disregarding the time constraint of 48 hours (2). The lowest stable creatinine value from this period is used; if possible, a baseline from the last 3 months is preferred. Disregarding the 48-hour time constraint avoids inaccurate classification of the large number of patients that have AKI on presentation to the hospital (19).

Data Collection

This system allows prospective data collection for all cases of AKI at our center. A daily electronic report of all
AKI episodes is automatically generated that details patient location (community versus hospital acquired), patient age, and baseline creatinine. These data are supplemented by peak serum creatinine (which allows calculation of highest AKI stage), last serum creatinine before discharge (to assess renal recovery), length of hospital stay, and whether the patient survived to hospital discharge. The requirement for RRT was obtained by cross-referencing with renal and intensive care databases (both prospective clinical data collection). Approval to use anonymized data in this way was obtained from the National Information Governance Board.

Validation
The diagnostic accuracy of this system was determined in two ways. First, the baseline creatinine value was manually checked for every AKI result by a nephrologist (N.M.S.) and the AKI stage recalculated, which allowed determination of the false positive rate. For the purposes of this analysis, all measurements that used the reverse estimated GFR method to calculate the baseline were assumed to be correct; the accuracy of this method was assessed separately. Second, every serum creatinine result over three randomly selected 24-hour periods was manually examined to detect cases of AKI not identified by the electronic reporting system; this generated a false negative rate.

Statistical Analyses
Parametric data are presented as mean ± SD and non-parametric data as median (interquartile range [IQR]). Fisher’s test was used to compare categorical data and the t test or Mann–Whitney test was used to compare continuous data depending on whether data were parametric or nonparametric. Binary logistic regression was used to test significant univariate associations with mortality. The patient was used as the unit of observation (as opposed to the AKI episode) except where stated. P values <0.05 were considered significant. All analyses were performed using SPSS software (version 15.0).

Results
Between June 1, 2010 and February 28, 2011, we observed 3202 AKI episodes in 2619 patients, which represented 5.4% of hospital admissions (both elective and nonelective). Of these patients, 435 had 1 episode of AKI and 1970 (61.5%) episodes were classified as stage 1 AKI, with similar numbers in stage 2 (638; 19.9%) and stage 3 (594; 18.6%). The median age of the population was 80 years (IQR, 16) and the distribution of cases across different specialties is shown in Figure 2, demonstrating that a minority of patients (7.5%) was directly cared for by nephrologists.

In terms of diagnostic accuracy, a false negative rate of 0.2% was observed with four missed cases in 1702 patients.
The false positive rate was 1.7% (103 creatinine results); a further 3.2% (194 creatinine results) received an incorrect AKIN stage.

**Association of AKI and Mortality**

The in-hospital mortality rate for the entire AKI population was 23.8% (624 patients). As a contextual reference, the unadjusted hospital-wide mortality rate for nonelective admissions during the same period was 3.2%. The mortality rate for stage 2 AKI was significantly higher than stage 1 (33.0% versus 16.3%; \(P<0.001\)). However, mortality rates in stage 3 were similar to those observed in stage 2 (36.1%; \(P=0.31\)). These data are summarized in Figure 3.

Because of the unexpected similarity in mortality between AKI stages 2 and 3, we compared mortality rates by AKI stage in those with and without abnormal baseline serum creatinine (defined as \(\geq 120\) μmol/L). In the 2010 patients with a baseline creatinine <120 μmol/L, mortality rates progressively rose as AKI became more severe (as shown in Figure 4A). In this group, we observed the expected reduction in patient numbers in higher AKI stages. However, in the 609 patients with acute on chronic decline in renal function (baseline serum creatinine \(\geq 120\) μmol/L), we observed an unexpected spread of patient numbers across the AKI stages, with a small number of patients with stage 2 AKI (Figure 4B). In this group, increasing AKI stage did not associate with higher mortality, with the highest rates observed in stage 2 AKI and no significant difference in mortality between stages 1 and 3 (Figure 4B).

In contrast to 1025 patients (39.1%) who sustained AKI during their hospital stay (hospital-acquired AKI), 1594 patients (60.9%) had AKI on hospital admission (community-acquired AKI). We observed significantly higher mortality rates in those with hospital-acquired AKI: 28.9% compared with 20.6% in those with community-acquired AKI (\(P<0.001\)).

Binary logistic regression including all important univariate associations revealed that increasing AKI stage was the strongest independent predictor of mortality and remained so after accounting for the effect of patient age (Nagelkerke \(R^2 = 0.12\); Hosmer and Lemeshow test for goodness of fit, \(P=0.27\)). The full results of this model are displayed in Table 1.

**RRT**

Proportionally, very few patients required RRT, with only 90 (3.4%) receiving RRT during the 9-month study period. There was a suggestion that baseline creatinine \(\geq 120\) μmol/L increased the risk of requiring dialysis although this difference was not statistically significant (4.3% of abnormal baseline group versus 2.8% of those with normal baseline; \(P=0.08\)).

Figure 3. | Proportion of patients who died before discharge in each AKI stage. Hospital-wide nonelective mortality is provided to give context, but direct comparisons between this group and those with AKI are not appropriate.
Figure 4. Stacked bar charts showing the number of patients in each AKI stage in those with normal and abnormal baseline creatinine values. The nonshaded areas denote the proportion of in-hospital mortality in each AKI stage; absolute numbers and proportion of in-hospital mortality are presented above each column. There was no difference between groups with (A) normal and (B) abnormal baseline creatinine values comparing in-hospital mortality. (A) Mortality rates were significantly higher with each step up in AKI stage. \( P < 0.001 \) for each for comparison of stage 1 AKI with stages 2 and 3. \( P = 0.04 \) for comparison of stage 2 AKI with stage 3 AKI. (B) The only significant difference in mortality rates was found in a comparison of stage 1 and stage 2 (\( P = 0.006 \)). Other differences did not reach significance (stage 1 versus stage 3, \( P = 0.06 \); stage 2 versus stage 3, \( P = 0.24 \)).
whereas 167 (59.2%) episodes had at least stage 1 AKI. In patient based on the degree of subsequent creatinine change (each equated to 282 episodes of AKI (8.8%) that occurred patients with Estimated Baseline Creatinine of AKI stages 2 and 3; longer hospital stays. The median length of stay was 8 days (IQR, 13), and higher AKI stages were associated with survived to discharge. Median length of stay was 9 days (IQR, 13) for stage 1 AKI, 190 (69.9%) in stage 2, and 159 (58.8%) in stage 3 (P<0.001 for all comparisons). Of the 43 patients who required acute RRT and survived to discharge, 22 (51.2%) had achieved a complete renal recovery by the time of discharge. Mean creatinine at discharge was 127.7±78 μmol/L; this value was significantly higher than mean baseline creatinine of 109.6±48 μmol/L (P<0.001).

The proportion of patients with renal recovery progressively decreased as AKI stage increased, with 760 (80.0%) achieving this in stage 1 AKI, 190 (69.9%) in stage 2, and 159 (58.8%) in stage 3 (P<0.001 for comparisons of the 43 patients who required acute RRT and survived to discharge, 22 (51.2%) had achieved a complete renal recovery by the time of discharge.

Length of Stay
Length of stay data were analyzed for those patients who survived to discharge. Median length of stay was 9 days (IQR, 13), and higher AKI stages were associated with longer hospital stays. The median length of stay was 8 days (IQR, 13) for stage 1, 9 days (IQR, 16) for stage 2, and 11 days (IQR, 16) for stage 3 (P<0.001 for comparisons of stage 1 AKI with stages 2 and 3; P=0.03 for comparisons of AKI stages 2 and 3).

Patients with Estimated Baseline Creatinine
Overall, from a total of 6037 blood samples classified as AKI, an estimated baseline was used in 426 (7.1%). This equated to 282 episodes of AKI (8.8%) that occurred without a previous creatinine result. In these cases, the presence or absence of AKI was determined retrospectively based on the degree of subsequent creatinine change (each patient’s results manually reviewed). Forty-three (15.2%) episodes were subsequently deemed not to represent AKI, whereas 167 (59.2%) episodes had at least stage 1 AKI. In the remaining 72 episodes, the accuracy of the estimated baseline could not be assessed.

Discussion
We describe a real-time electronic results reporting system for AKI based on the current AKIN diagnostic criteria. This system has been successfully introduced into routine clinical practice to aid early recognition of AKI. This system also allows prospective data collection to determine current incidence and outcomes of AKI across a general hospitalized population, providing a resource to monitor trends in these variables over time.

AKI is both common and associated with poor outcomes (1–4,20). Our prospective study adds to the relatively small number of those examining heterogeneous, hospitalized populations (1,4,9,20) and confirms the high incidence of AKI in this setting. Because we included both elective and nonelective admissions, the incidence of AKI in those admitted as an emergency is likely to be higher. As previously reported, AKI is particularly common in elderly persons (17). Not only does aging increase the risk of sustaining AKI, but additional challenges in management may also be introduced by extreme age or the presence of multiple comorbidities.

We also observed high mortality rates, in line with previous studies with similar populations that reported mortality rates of 19.7%–24.5% (1,4). Mortality was significantly higher in those with more severe AKI (stages 2 and 3) and, importantly, this association held true after adjustment for age and pre-existing CKD. In addition, hospital length of stay was increased and the chances of renal recovery progressively decreased with more severe AKI. These latter observations emphasize the large health-related costs that are associated with this condition. In the face of these poor outcomes, it must be acknowledged that current standards of care for patients with AKI are not universally good (14,15,17). A UK National Confidential Inquiry into Patient Outcome and Death report in AKI found deficiencies in care in more than half of cases, many resulting from delays in diagnosis (17). Our results also confirm that most patients with AKI are cared for by non-nephrologists. On the basis of this background, the development of electronic alert systems to aid early recognition of AKI is an important step in addressing the current status quo. At our center, we have combined this with other

<table>
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<th>Variable</th>
<th>Hazard Ratio for In-Hospital Mortality</th>
<th>95% Confidence Interval</th>
<th>P Value</th>
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<td>Stage 2 AKI</td>
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<td>2.3–3.6</td>
<td>&lt;0.001</td>
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<tr>
<td>Stage 3 AKI</td>
<td>3.6</td>
<td>2.8–4.6</td>
<td>&lt;0.001</td>
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<td>Renal replacement therapy</td>
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<td>1.1–2.8</td>
<td>0.02</td>
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<td>Hospital-acquired AKI</td>
<td>1.8</td>
<td>1.5–2.2</td>
<td>&lt;0.001</td>
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<tr>
<td>Age (per 5-yr increase)</td>
<td>1.2</td>
<td>1.1–1.2</td>
<td>&lt;0.001</td>
</tr>
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</table>

Variables with significant associations with mortality were tested. For AKI stage, stage 1 was taken as the reference category (in the absence of a control group without AKI). Hospital-acquired AKI was compared with community-acquired AKI that was used as the reference category. Baseline renal function and multiple AKI episodes did not enter the model.

Table 1. Binary logistic regression model with in-hospital mortality as the dependent factor
interventions designed to improve the basic aspects of care. These include a sustained program of cross-discipline education aimed at both medical and nursing staff, the publication of easily available clinical guidelines on the hospital intranet that are linked to the AKI reporting system, and an improved mechanism for nephrology referral.

Despite the potential efficacy of electronic alert systems in improving clinical outcomes (21), there have been relatively few attempts at introducing electronic reporting for AKI. Our system is therefore the first to provide a robust, practical solution to prospectively apply the AKIN criteria on a hospital-wide basis. The value of electronic alerts was shown in patients taking nephrotoxic drugs, in whom an email alert resulted in a 55% risk reduction of AKI (this study predated the current AKIN definition) (22). In a similar, more recent study, interruptive electronic alerts were also shown to improve medicines management in those with AKI (23). However, the alert system prompted responses in only 52% of cases and passive alerts were less effective. It has proved possible to set up a system to apply the RIFLE criteria within the confined setting of a single intensive care unit (24). The only hospital-wide alert system previously described did not use AKIN/RIFLE definitions; rather, it identified patients with a 75% increase in creatinine over their most recent value. This inability to reference creatinine change to an individual’s true baseline reduced accuracy (25). In comparison, our solution is both accurate and sustainable, although it does depend on 40 minutes to 1 hour of chemical pathology reporting time every day. Although this may limit uptake in some centers, introducing human judgment when deciding baseline creatinine has been a significant contributor to the system’s accuracy. Importantly, this obviates reliance on a nadir creatinine, an approach that may overestimate AKI (26).

Although the AKIN criteria performed well in patients with normal baseline creatinine values, their value was reduced in those with pre-existing CKD. Although the effect of CKD on the performance of diagnostic criteria for AKI was previously reported, it remains under-recognized (2). Pre-existing CKD can also reduce the utility of biomarkers of AKI (27). This effect of CKD has implications for clinical practice with respect to interpreting AKI in this group, and also suggests that current diagnostic criteria need further refinement. The issue of how to define an individual’s baseline creatinine is also of high importance when applying diagnostic criteria. Using the stringent 48-hour time constraint as specified in the AKIN definition ensures that creatinine changes are acute but will result in over-reliance on estimated baseline values. Using estimated baseline values leads to overclassification of AKI in those with pre-existing CKD (18,26), a trend that was also seen in our study. By accepting baseline creatinine results from the previous 12 months, <10% of our population had to rely on estimated values. There is a wide variety in the way in which baseline creatinine is currently defined, which has a significant effect on the diagnostic threshold for AKI (2). This variation is likely to pervade independent development of new electronic alert systems, and there is a clear need to have widespread consensus on how best to define baseline creatinine.

There are some limitations to our study. We did not have complete patient-level data, which prevents statistical adjustment for important confounders such as comorbid conditions or severity of acute illness. This must be taken into account when interpreting the associations between AKI and mortality or length of hospital stay, although our results are in accordance with many other studies that did adjust for these factors (1,3,4). We also acknowledge that by excluding blood samples from the nephrology ward, a small number of patients who develop in-hospital AKI after admission may be missed; this also has relevance if patients are directly admitted to the nephrology ward. It would have been preferable if we were able to report 30-day mortality as opposed to in-hospital mortality rates. In addition, we had to use an estimated baseline creatinine value in a significant proportion (8.8%) of cases, which can result in an overestimation of AKI in those with pre-existing CKD. Finally, our follow-up period was short, limited to the duration of hospital stay.

In this study, we report an effective method for real-time, hospital-wide electronic reporting of AKI. We confirm the high incidence of AKI in hospitalized patients and its association with high mortality rates, longer length of stay, and incomplete renal recovery. Electronic reporting may be a key measure in improving the management of AKI in combination with additional strategies to raise standards of care across all acute specialties.

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Disclosures
None.

References


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