Can decision support systems work for acute kidney injury?

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The overall incidence of acute kidney injury (AKI) in the developed world is estimated to be ~2–3/1000 population, similar to that of acute myocardial infarction [1]. In the developing world, AKI rates may be even higher due to various infectious diseases that either directly affect the kidney or lead to severe dehydration [2]. However, because of the silent nature of the syndrome, this is likely an underestimate. Moreover, older individuals are disproportionately affected. Among Medicare patients aged 66–69, for example, the rate of AKI in 2011 was 14.9 per 1000 patients, increasing to 18.8, 26.4, 35.9 and 49.6, respectively, for ages 70–74, 75–79, 80–84 and 85 and older [3]. Unfortunately, AKI is harder to predict in older patients because common risk factors are less predictive in this population [4]. Recent evidence also suggests that much milder forms of AKI (less severe dysfunction and shorter duration) are also associated with increased risk of hospital mortality as well as long-term adverse outcomes [5]. Although the reasons for this increased mortality are not fully understood, these studies and many others make a compelling argument that patients who develop AKI are at an additional increased risk of death that is in some way due to AKI itself. Drug-induced AKI (D-AKI) is a leading cause of AKI with ~20–25% of AKI cases attributed to a drug [6, 7]. The negative outcomes of D-AKI are remarkable with up to 70% of patients having residual kidney damage following an episode [8].

A further challenge is that AKI affects not just the critically ill and has been shown to complicate non-ICU hospitalizations with significant worsening of short- and long-term outcomes as well. For example, we showed that AKI occurred in 25% of patients admitted with community-acquired pneumonia to a hospital bed outside the ICU [9]. Despite the low overall acuity, patients developing AKI had a >4-fold increased risk of death in-hospital (1.2 versus 5.1%), and nearly 2-fold increase at 1 year (19.7 versus 34.2%; P < 0.001). Even within the ICU, patients with lower severity defined by absence of circulatory or respiratory failure had just as great an absolute risk (and higher relative risk) of death associated with AKI [10]. 'Low-severity' patients may be at greater relative risk from AKI because of the perception that these patients are not severely ill.

These challenges make AKI formidable even for experts and yet early management of AKI cannot rely solely on subspecialists. Similar to chronic kidney disease (CKD), nephrologists are frequently not involved in the detection and initial management of patients with AKI. Equally, efforts to stem the tide of the AKI epidemic cannot rely solely on, nor require, nephrology referral for all patients. The numbers of cases are too great. Conversely, limiting subspecialty input to the most severe cases will too often miss an opportunity to intervene when treatment or management would be most effective. For ICU patients, we found that fewer than 23% had evidence of AKI at ICU admission while >60% ultimately manifest the condition [11]. Furthermore, of 1510 patients identified at Stage 1, 840 (55.6%) progressed. Similarly, of the 2273 identified at Stage 2, 837 (36.8%) progressed [11]. These cases present important opportunities to intervene, yet consultation of subspecialists or pharmacists does not usually occur at these earlier stages—and some have even questioned the value of nephrology referral at these stages at all [12, 13]. Any effort to intervene in the course of AKI prior to severe (and often irreversible) stages will therefore require techniques that can be deployed by front-line clinicians—including attention to nephrotoxic drugs and drug dosing (Figure 1).

Clinical decision support systems (CDSS) have been developed to fully and/or partially automate the detection of AKI in the hospital setting [15–19]. Studies using these systems have consistently shown that they have the capacity to improve detection of AKI. However, some studies have also tried to determine if CDSS itself can improve patient outcomes. Colpaert et al. [18] showed that a CDSS increased the timeliness of interventions (mainly fluids or diuretics) but did not improve
outcomes, while Wilson et al. [19] found neither any change in practice nor outcomes. Similarly, McCoy et al. [20] found that overlaying pharmacy surveillance on top of an electronic AKI alert had no effect on adverse drug events.

Assessing the value of diagnostics by examining patient outcomes is a perilous endeavor because making a diagnosis cannot affect outcomes on its own. Accepting this limitation, there are a number of possible explanations for why electronic alerts have yet to be shown to facilitate improvements in patient outcome.

Figure 1 begins not at Stage 1 but at ‘high risk’. Alerts (as opposed to real-time risk assessment) inform on the presence of AKI as early as possible but they do not forecast AKI risk. Most CDSS for AKI only examine serum creatinine, which is already a lagging indicator. Creatinine is both insensitive to structural damage in the kidney and slow to increase after injury. Even if alerts may offer lead time, the time they provide may not be sufficient and there may already be irreversible damage to the kidneys. The use of urine output [5] or novel biomarkers [21] as part of a CDSS could change this paradigm.

The expectation that earlier detection itself will improve outcomes may be unrealistic [19]. Conversely, making patient-specific recommendations lends itself to better physician acceptance and possibly better patient outcomes [22].

Randomized trials of fluid resuscitation [23] and diuretics [24] have failed to demonstrate improvements in renal outcomes. Thus, it is difficult to see how CDSS can improve outcomes if it only leads to implementation of these interventions [18]. Vasoactive drugs have been relentlessly investigated [25, 26] all spectacular failures [27]. Holding electronic detection systems to the standard of improving outcomes will require better therapies to couple these systems too.

The methods used to evaluate CDSS for AKI lack gold standards. Most studies have asked whether the electronic system can detect those cases that are otherwise captured by billing codes or procedures. Difficult cases may be missed entirely and it may be these cases that benefit most from CDSS. Similarly, there are >100 drugs that may be associated with AKI, evidence to support which drugs and drug combinations are most important are lacking.

Conversely, many studies have emphasized sensitivity over specificity, which could lead to a significant number of false-positive alerts. A high false-positive alert rate can result in alert burden or fatigue, which manifests as physicians not responding to important alerts because they receive too many [22, 28, 29]. Lastly, most CDSS for AKI have delivered alerts within electronic charting or order entry system interfaces at the prescribing stage, where research has shown that they are less likely to be effective [22].

Thus, given these potential limitations to CDSS, it is probably prudent to first evaluate and then improve the ability of the system to detect AKI. A recent study by Sawhney et al. [17] represents one of the largest studies to date, including >100 000 patients in the UK National Health System. These authors demonstrated that an alert based on the serum creatinine portion of the Kidney Disease Improving Global Outcomes (KDIGO) criteria [14] detected >91% of patients who ultimately received an ICD-10 code for AKI. One advantage to the CDSS is that it finds prior serum creatinine measurements and compares them with the current creatinine, thus avoiding the need for a physician to find prior results in the record. However, a baseline creatinine obtained just prior to the current illness would be ideal, but unfortunately patients rarely have the intuition to get their creatinine checked just before developing AKI. As such we are left with deciding between various less ideal baseline values or no value at all. Various studies have shown that even an old baseline (up to 1 year prior) is better than nothing [30, 31]. When multiple baseline values are available, particularly when no clear pattern is discernable, a median is probably the most representative [31]. However, even here, judgment can be important. In a patient whose last six serum

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**FIGURE 1:** KDIGO recommendations for AKI management [14].
creatinines (one each month for the last 6 months) have been slowly rising, the most recent creatinine is probably the best reference. Similarly, some prior baselines might have been in the setting of prior episodes of AKI and it might be possible to select a more representative value out of the series of prior values if the history is known. In other words, the best reference creatinine is the one that the clinician believes is most representative of the patient’s premorbid renal function. No CDSS for AKI we are aware of has this level of sophistication. Finally, for a patient presenting with a clinical history compatible with AKI and an abnormal creatinine with no evidence of CKD by history or exam, the best reference creatinine may be a derived one. Since a normal creatinine may vary by >2-fold based on demographics (especially age, race and sex), it is inappropriate to use a single normal value for all patients. Instead, the patient’s demographics can be fitted into the estimated glomerular filtration rate (eGFR) equations such as the Modification of Diet in Renal Disease equation using a GFR of 75 ml/min/1.73 m² [32]. This approach has been validated in multiple studies: one showing that [8].


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