Information Technology and Acute Kidney Injury: Alerts, Alarms, Bells, and Whistles

F. Perry Wilson

The goal of this review is to describe the rationale for alerting systems for acute kidney injury, the challenges associated with alert implementation, and the efficacy (or lack thereof) of acute kidney injury alerts to date.
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INTRODUCTION

That acute kidney injury (AKI) is a common, costly, and devastating condition is well known to nephrologists.[1-5] Yet, despite efforts by the nephrology community to bring AKI awareness and AKI research into the limelight,[6] nonnephrologist clinicians do not appear to have embraced the importance of the syndrome.

While lack of awareness of the definitions and outcomes of AKI may be to blame, it may equally be the result of a therapeutic nihilism that permeates AKI discussions, even among nephrologists. That there are "no treatments for AKI" is a common refrain parroted from the wards to medical conferences. While true in a narrow sense, there are no drug-based therapies that have been broadly shown to affect clinical outcomes across the spectrum of AKI that there is "nothing to be done" when AKI develops is patently false.

Guidelines from the Kidney Disease: Improving Global Outcomes group, the UK National Institute for Health and Care Excellence, and the European Renal Association provide concrete recommendations for physicians faced with AKI (Table 1).[7,8] While these recommendations are often dismissed as merely supportive, the optimization of hemodynamics, avoidance of nephrotoxins, and attention to relevant diagnostic tests are broadly supported. While we lack clinical trial data suggesting that, for example, cessation of NSAIDs truly modifies the course of AKI, this is largely due to the perception that such a trial would be unethical, rather than due to lack of interest.

Acute Kidney Injury Recognition

That something can and should be done for patients with AKI is clear. It is also clear that nothing can be done for these patients if AKI goes unnoticed. Several lines of research suggest that AKI is frequently "missed" by clinicians. First are studies that compare the documentation rate (usually assessed by billing codes) of AKI. These studies universally find low rates of diagnostic coding for AKI, often at levels lower than 50%.[9-11] A study by Grams and others examined 1970 hospitalizations with AKI as defined by change in creatinine. Only 361 (18%) of those had evidence of AKI documentation based upon administrative coding.[12] While lack of diagnostic coding is not a perfect proxy for AKI recognition (clinicians may recognize and yet fail to document AKI), it is likely that a large number of patients with AKI may simply fly under the radar.

Further evidence supporting the hypothesis that some AKI events are "missed" can be found by examining the behavior of physicians in the setting of AKI with and without evidence of documentation. In a study of over 6000 patients with a doubling of creatinine, physicians who documented AKI in the medical record were more likely to discontinue nephrotoxic medications and engage in diagnostic testing compared to physicians who did not document AKI.[13] Beyond increasing the rate of appropriate clinical behaviors in the setting of AKI, the study demonstrated that, after adjustment for AKI severity, individuals with AKI who also had formal documentation of AKI had a lower inpatient mortality than those individuals without formal documentation of AKI. Taken together, these lines of evidence suggest that a significant proportion of AKI goes unrecognized, that the opportunity for therapeutic actions is missed, and that these factors may contribute to poor outcomes.

Against this backdrop, the rationale for electronic alerting of AKI is clear. One hopes that alerts increase recognition, recognition changes management, and proper management improves outcomes. AKI alerts have proliferated in recent years,[14-19] in large part due to the widespread adoption of the Electronic Health Record. In addition, given that AKI can be defined by the change in a single variable (creatinine), AKI alerts are "low-hanging fruit" compared to more complicated alert systems (such as those for sepsis).[20-23] Far from a limitation, it seems imperative that nephrologists take the lead on rigorous evaluation of these alerts as they may not be entirely without harm.

Acute Kidney Injury Alert Challenges

Despite the relative simplicity of detecting AKI via a change in creatinine, alerts can range from the very simple to quite complex. Urine output data have rarely been used in AKI alert studies,[24] owing largely to the lack of rigorous standards of collection, though novel measurement

From the Program of Applied Translational Research, Yale University School of Medicine, New Haven, CT; and Veterans Affairs Medical Center, West Haven, CT.

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Address correspondence to F. Perry Wilson, Veterans Affairs Medical Center, Yale University School of Medicine, 60 Temple St, Suite 6C, New Haven, CT 06510. E-mail: Francis.p.wilson@yale.edu

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devices for catheterized patients are being tested (clinicaltrials.gov NCT02195713).

Even if hospital systems adopt alerts based solely on changes in creatinine, several factors must be considered. Should alerts be generated for modest changes in creatinine (such as 0.3 mg/dL) which may include patients without "true" AKI? We previously demonstrated that, due to laboratory and eGFR-independent biological variation in creatinine, a significant portion of patients may be diagnosed with AKI due to random fluctuations in creatinine, rather than true injury.[25] This is particularly true for patients with higher baseline creatinine. For patients with a baseline creatinine of 3.0 mg/dL, we found that after four creatinine measurements, roughly 50% would be diagnosed with AKI even with a completely stable GFR.

Additionally, while the KDIGO-specified time frame for changes in creatinine ranges from 48 hours (for a 0.3 mg/dL change) to 7 days (for a 50% change), "rolling windows" may be difficult to program in the Electronic Health Record, leading some alerts to adopt a "nadir-to-peak" approach which may increase the rate of alerting among those with longer lengths of stay.

Finally, how should prehospitalization creatinine concentrations be integrated? For those without a prehospitalization creatinine measurement, several studies have imputed a creatinine as if the patient had an eGFR of 75 mL/min/1.73 m^2.[26] In the alert setting, such an imputation would dramatically increase the alerts among those with chronic kidney disease—a group already at risk for "false-positive" alerts as described above.

CLINICAL SUMMARY

- Electronic alerts for acute kidney injury and other conditions are relatively feasible to implement but have unclear evidence of clinical benefit.
- Some possibility of harm associated with alerting exists.
- Clinical trials are the best mechanism to evaluate alerts, and alerts found not to improve patient outcomes should be abandoned.
- Alert targeting may help to both improve alert efficacy and decrease alert fatigue.

Decisions about alert triggers are, as is the case with all diagnostic tests, a tradeoff between sensitivity and specificity. This tradeoff is particularly problematic in the AKI alert paradigm, as more sensitive systems may be necessary to capture individuals with "subtle" AKI—those that might be missed clinically. At the same time, more sensitive systems create a greater number of false-positive alerts, which can be very frustrating for providers.

Once an alert is triggered, how should it be presented to the provider? Again, designers are faced with a tradeoff: this time between alert intrusiveness and potential effectiveness. In terms of pure effectiveness, "hard stop" alerts seem the natural choice. In the AKI framework, a hard stop alert would prevent a provider from, for example, ordering a contrast study while a patient has AKI. Providers would be forced to appeal through some mechanism to obtain the needed study. While an alert of this type would no doubt reduce the rate of contrast administration in AKI, it might engender revolt from providers who feel it too aggressively impedes their workflow. On the flip side, "soft" alerts, such as in-basket messages (that may or may not be read), hardly hinder workflow at all but may not lead to substantive change in provider behavior. Striking the balance between these extremes is critical and should be done with direct feedback from those who are likely to receive alerts. To date, there are no studies in AKI that have varied alert intrusiveness to elucidate the "sweet spot" between workflow impediment and patient benefit.

Acute Kidney Injury Alert Effectiveness

Several studies have evaluated the effectiveness of alerts for AKI. Broadly speaking, the studies have shown that alerts change provider behaviors. A smaller subset of studies have suggested that alerts improve patient outcomes. A summary of studies, outcomes, and effects appears as Table 2.

To date, only one randomized trial—performed by our group—has evaluated the efficacy of AKI alerts and failed to show a difference in the rates of change in creatinine, dialysis, or death.[29] While this may imply a true lack of efficacy, it should be noted that in this study, alerts were sent only once per patient, required no

Table 1. Guideline-Based Management of AKI

KDIGO	NICE	UK Kidney Association
Adjust drug dosing	Urinalysis	Adjust drug dosing
Fluids if volume depleted	Consider ultrasound	Urinalysis
Pressors if shock	Relieve urological obstruction	Contrast precautions
Protocolized hemodynamic management	Avoid diuretics	Avoid diuretics
Insulin therapy in critically ill	Consider kidney replacement therapy	
Nutritional support	Consider referral to nephrology	
Avoid diuretics		
Avoid nephrotoxins		
Monitor creatinine, urine output		
Avoid subclavian catheters		

Abbreviations: AKI, acute kidney injury; KDIGO, Kidney Disease Improving Global Outcomes; NICE, National Institute for Health and Care Excellence.

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