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Early detection of acute kidney injury and the application of automated electronic alert systems

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Abstract

Acute kidney injury (AKI) is a common and serious medical condition associated with high rates of mortality. Early diagnosis and timely institution of remedial measures can help improve the adverse clinical outcomes associated with AKI. The diagnostic criteria for AKI have changed recently following the publication of evidence suggesting that even small changes in serum creatinine levels predict poor outcomes. Awareness of risk factors for development of AKI and familiarity with the new diagnostic criteria are essential in the management of acutely ill patients; both in community and hospital settings. Computerised algorithms, built within the laboratory software, can now automatically create electronic alerts (e-Alerts) for AKI if changes in serum creatinine meet AKI diagnostic thresholds. This innovation can be a useful tool in helping with early detection of AKI; however, users need to be aware of its various applications and limitations.

A rapid deterioration in renal function in any patient, irrespective of the underlying cause, predicts adverse clinical outcomes and should alert care providers of the need to institute remedial measures without delay.

Acute kidney injury (AKI), a term used when increases in serum creatinine (SCr) reach certain thresholds or when there has been a sustained decrease in urine output, frequently develops in association with acute illnesses; its early recognition and prompt management is critical if clinical outcomes are to be improved.

AKI occurs in approximately 5-7 % of patients admitted to hospitals in the United Kingdom (UK).[1,2] There is a graded increase in risk of mortality, duration of hospitalisation and incidence of chronic kidney disease (CKD) with increasing severity of AKI.[3] The AKI diagnostic and staging criteria are presented in ***tables 1*** and ***2*** *page 16*. Patients who are admitted to the Hull and East Yorkshire Hospitals (HEY) NHS Trust with AKI have a 30-day mortality rate of 31% whereas the average length of stay in hospital for patients with AKI stages 1, 2 and 3 at our hospital is 9.1, 10.7 and 16.2 days respectively.[4] Treating stage 3 AKI puts a significantly greater burden of costs on the healthcare system compared with lower stages. Data from a hospital in our region shows that the current estimated cost of treating a patient with AKI stage 3 is approximately £4200 GBP

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compared to £3200 GBP, the average cost of treatment for patients with AKI stage 1.5 These observations highlight the critical importance of detecting AKI at an early stage when its potential harmful effects may be reversible using simple interventions such as intravenous fluids and cessation of nephrotoxic medications; once renal dysfunction is established, treatment options are limited other than renal replacement therapies (e.g. haemodialysis).

Recognising AKI during its early stages requires a high index of clinical suspicion (i.e. awareness of risk factors for the development of AKI) and a familiarity with current diagnostic criteria. On the latter issue, it should be noted that AKI diagnostic criteria have undergone several modification in recent years which the wider medical community, particularly non-specialist hospital and community practitioners, may not yet have fully appreciated. In a survey of hospital trainees in the Newcastle region,6 participants were given questionnaires to test their knowledge related to AKI. Of the 146 survey respondents, only 2% were able to define AKI accurately based on the Risk, Injury, Failure, Loss and End-stage (RIFLE)7 criteria; 73% were unable to detail even one of its components. The National Confidential Enquiry into Patient Outcome and Death (NCEPOD)[8] in 2009 also highlighted worrying problems in the management of patients with AKI; it suggested that deficiencies in the care of patients who died in hospital with AKI may be related to a lack of awareness of the risks, pathophysiology and principles of management related to this condition.

The criteria for diagnosis and staging of AKI proposed by Kidney Disease: Improving Global Outcome (KDIGO),[9] and endorsed by National Institute of Health and Clinical Excellence (NICE),[10] has now superseded all previous recommendations and should be used as the gold-standard to distinguish AKI in clinical practice (***tables 1*** and ***2*** *page 16*). The main driving forces behind recent changes in AKI diagnostic criteria have been to prioritise early recognition of AKI and promote appropriate responses to the risk categories defined by different AKI stages. The objective nature of the new criteria have led to new innovations in the designing of computer systems that can automatically detect changes in a patient's SCr and flag up possible AKIs. At Hull and East Yorkshire Hospitals NHS Trust (HEY Trust), such a system was first developed during 2012 and has been fully operational since September 2013. All blood samples received at the laboratory with SCr requests are automatically screened for AKI. The algorithm that enables our laboratory computers to perform this function was written locally. It compares patient's current SCr with both their most recent previous sample and their lowest result during the previous six months. If the increase in SCr is consistent with KDIGO criteria i.e. greater than 25 µmol/l or 1.5 times the baseline, then the result is flagged up as 'possible AKI' and is highlighted as such to the team looking after the patient through the results

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reporting system (Patient Centre). Our AKI electronic alert (e-alert) system is highly sensitive for detecting AKI (i.e. it will rarely miss patients with AKI); this is achieved by using the 'lowest' SCr of the previous six months as baseline. If patients have not had any blood tests during this interval then the program uses the lowest SCr of the previous 12 months as baseline. This approach does however result in a number of false positives (i.e. low positive predictive value). Another point worth considering is that HEY Trust e-alert system will not detect all AKIs. Firstly, patients who have not had any blood tests during previous 12 months, and therefore do not have a baseline SCr, will not be flagged up as AKI. Secondly, patients who do not exhibit significant changes in SCr can still have AKI if they meet the urine output criteria.

There are multiple other versions of the e-alert systems currently in use throughout hospitals in the UK. In a recent AKI conference[11] organised to discuss best practices in this field, thirty different hospitals presented their versions of AKI e-alert systems.[12] These systems were mostly developed independently of each other in accordance with local level requirements and limitations; there is therefore a wide variation in their design as well as output. Attempts to standardise the e-alert systems throughout UK are underway. A consensus conference convened by the Royal College of Physicians of Edinburgh in 2012 represented the first such attempt to build a national consensus towards this aim.[13] This meeting included representatives from leading centres in UK who had already implemented AKI e-alerts at their respective hospitals. Developing a nationally acceptable system however needed consideration of several practical and logistical issues. These included problems such the ability of computer algorithms to determine baseline SCr, software limitations related to laboratory computer systems and the communication of their output to clinical teams. Association for Clinical Biochemistry and Laboratory Medicine took the lead in resolving some of these issues[14] by involving the various stake-holders involved in implementing e-alerts in the NHS; these included renal physicians, software manufacturers and regulatory bodies. A new algorithm has now been agreed nationally for early detection of AKI based on KDIGO definition of AKI (***Figure 1*** *page 14*).[15] Through a recent patient safety alert,[16] NHS England has mandated all hospitals in the UK to implement AKI e-alert systems based on the agreed algorithm (***Figure 2*** *page 15*). To conform to this new guidance, the HEY e-alert system is changing soon to bring our practice in line with national standards. As a result of these changes, the end user may notice fewer AKI e-alerts (the new algorithm may not be as sensitive) and that the system will display AKI stages along with e-alerts (not currently performed by HEY Trust e-alert system).

The AKI e-alert system is not a diagnostic tool and has several limitations; it merely raises the possibility of AKI in patients to

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the clinician. It is not designed to replace the application of clinical judgement but rather to assist with it to optimise patient safety and care. Its design has not yet been perfected and there are ongoing controversies that need to be addressed. The most prominent issue has been the determination of baseline SCr. Most clinicians can 'eye ball' a patient's previous SCr results and estimate their pre-AKI baseline based on the most commonly found stable readings. It has not yet been possible to program a computer to replicate this due to the inherent complexity associated with this process. The nationally agreed algorithm proposes using the median of all SCr measurements from the previous year as baseline if no SCr measurements are available during the past 7 days (this applies to most new hospital admissions). This approach has no evidence base and studies to validate it are urgently needed. It can be argued that using median SCr as baseline will raise the baseline in those with recurrent episodes of AKI and those who present with prolonged duration of illness and have had multiple SCr checks during that period. It may therefore miss certain patients with AKI.

There are also ongoing discussions on the best strategy to handle the output from e-alert systems. A well-defined pathway on how to ensure that AKI e-alerts are acknowledged and acted on has not yet been agreed. A review of conference posters[12] presented at a recent meeting on this subject reveals that hospitals have implemented their own systems based on available resources and personnel. At Barking, Havering and Redbridge NHS Trust, all stage 3 AKI's are phoned through to the relevant ward by the laboratory staff whereas other alerts are simply reported as an additional note along with other test results. These alerts do not require end-user acknowledgement. At Barts Health NHS Trust, details of patients with AKI stage 2 and 3 are sent on a daily basis to a group email which includes renal, critical care outreach and intensive care teams. At some hospitals, the e-alerts are linked to hospital 'whiteboard' allowing users to identify patients on the ward with AKI in real time. In East Kent University Hospitals Trust, the critical care outreach team routinely reviews all AKIs stage 2 and above. At HEY Trust, e-alerts are currently displayed as a free-text comment and reported along with other biochemistry results (***Figure 3*** *page 15*). There is no obligation for clinicians to acknowledge results. There is limited evidence regarding the superiority of one solution over others and hospitals will continue to implement their own solutions based on available resources, local needs and incidence of AKI. The use of a telephonic notification system has been linked with earlier intervention and improved outcomes in a cohort of patients in intensive care settings.[17]

The early recognition of AKI is only useful if it can be shown to impact on patient outcomes. In a non-randomised interventional study[18] from the United States

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researchers identified hospitalised patients who had developed AKI as in-patients and checked their daily SCr. All these patients received routine care (control group). Two months later, they repeated the same process but this time, patients with AKI were reviewed early and within 18 hours of onset of AKI (intervention group). They showed that early nephrology review reduced the chances of AKI progression from 12.9% to 3.3% (AKI progression was defined as 2.5 fold increase in creatinine from admission). In a retrospective observational study[19] from Switzerland involving 4296 patients with AKI, early for nephrology review (within 5 days of diagnosis) was associated with lower mortality rates and duration of hospitalisation, and better renal outcomes (i.e. need for emergency dialysis and requirement for dialysis at discharge). There are no randomised controlled trials on the impact of early intervention on patient outcomes in AKI; it can therefore not be said with certainty whether the beneficial effects of early intervention are due to nephrologists' involvement or other factors e.g. increased awareness of AKI during non-randomised interventional studies or harmful effects of late intervention in retrospective studies. Data cited above however certainly point towards improved patient outcomes associated with early intervention regardless of which specific factor plays the most important role.

AKI e-alert systems also enable us to study the epidemiology and outcomes of AKIs in new ways. Previous studies would have underestimated the incidence, prevalence and impact of AKIs due to problems with the ascertainment of AKI cases. For example, reliance on referrals to nephrology[20] or the application of clinical coding data[21] in order to detect AKIs would have missed a large number of cases. The e-alerts allow us to screen large number of blood samples for presence of AKI and follow patients prospectively. This should enable the study of full burden of AKI and its outcomes and help with healthcare planning as well as resource allocation. Preliminary data locally indicates that in the six months between 1st November 2013 and 30th April 2014, a total of 1294 patients were admitted to HEY Trust with AKI. Given that our hospital covers a catchment area with a population of 427,082 persons over the age of 15 years,[22] the annualised incidence of AKI in our region is approximately 606 per 100,000 persons.

In summary, AKI is a common both in the community and among hospitalised patients. It is associated with high rates of mortality. In patients who survive, it can have serious long-term implications such as CKD and its associated complications. AKI can be prevented and its progression to higher stages halted. Studies have shown that taking simple early steps such as:

1. stopping nephrotoxic medications
2. assessing fluid status
3. monitoring urine output
4. checking for sepsis
5. ruling out obstruction

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The above measures can reduce patients' chances of developing more severe AKI. The e-alert system is a relatively new tool in helping clinicians with diagnosing AKI at an early stage which should enable them to take preventative measures sooner. The design of e-alerts has not yet been perfected; nonetheless, the presence of an e-alert in any patient should be taken seriously and confirmed through manually looking in to patients previous results. Once confirmed, corrective measures should be taken without delay. Most hospitals, including ours, has an AKI management pathway (available through our hospital's intranet page); it is recommended that non-specialists familiarise themselves with it so that patients could be managed appropriately and referred to renal services early if indicated.

Practice points

1. Early detection of AKI requires a high index of clinical suspicion (i.e. awareness of risk factors for AKI) and knowledge of new AKI diagnostic and staging criteria.
2. AKI e-Alert systems are already active in clinical areas and can aid with early detection of AKI.
3. In its early stages, the harmful effects of AKI may be reversible using simple measures such as stopping nephrotoxic medications, assessing fluid status, checking for sepsis and ruling out urinary tract obstruction.

Supplementary box: Methods

Medline was searched using key words 'Acute kidney injury' AND 'alert$ OR warning OR "early detection" OR computer$ OR electronic OR "real-time"'. Articles were restricted to those published in English language since 2005. Titles of the 378 citations obtained using this strategy were read and 20 were selected for further review. References within these 20 papers were also reviewed for any further resources. We have aimed to include original and review articles that describe the use of automated and/or real-time system for early detection of acute kidney injury (AKI). We have prioritised those articles that describe an intervention or outcome.

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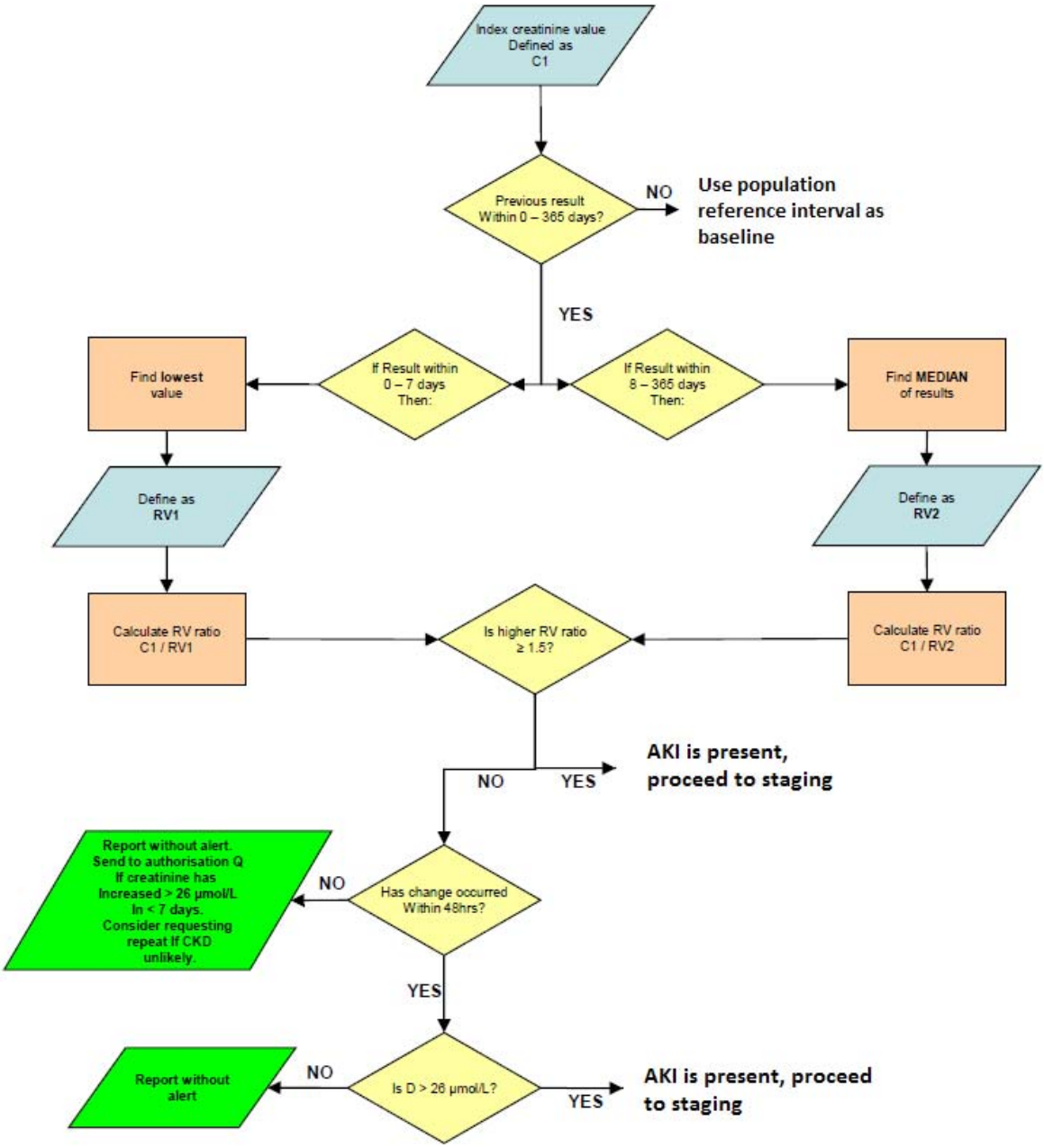

***Fig.1:* Simplified algorithm for early detection of acute kidney injury (AKI)**

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Patient Safety Alert

Stage Three: Directive

Standardising the early identification of Acute Kidney Injury

9 June 2014

Alert reference number: NHS/PSA/D/2014/010

Alert stage: Three - Directive

"A national algorithm, standardising the definition of AKI has now been agreed...This algorithm has been endorsed by NHS England and it is recommended that the algorithm is implemented across the NHS."

When: By 9 March 2015

***Fig.2:* 2 A Level 3 ('Directive') patient safety alert was issued by NHS England in June 2014 advising all NHS Acute and Foundation Trusts providing pathology services to implement the nationally agreed algorithm for early detection of acute kidney injury.**

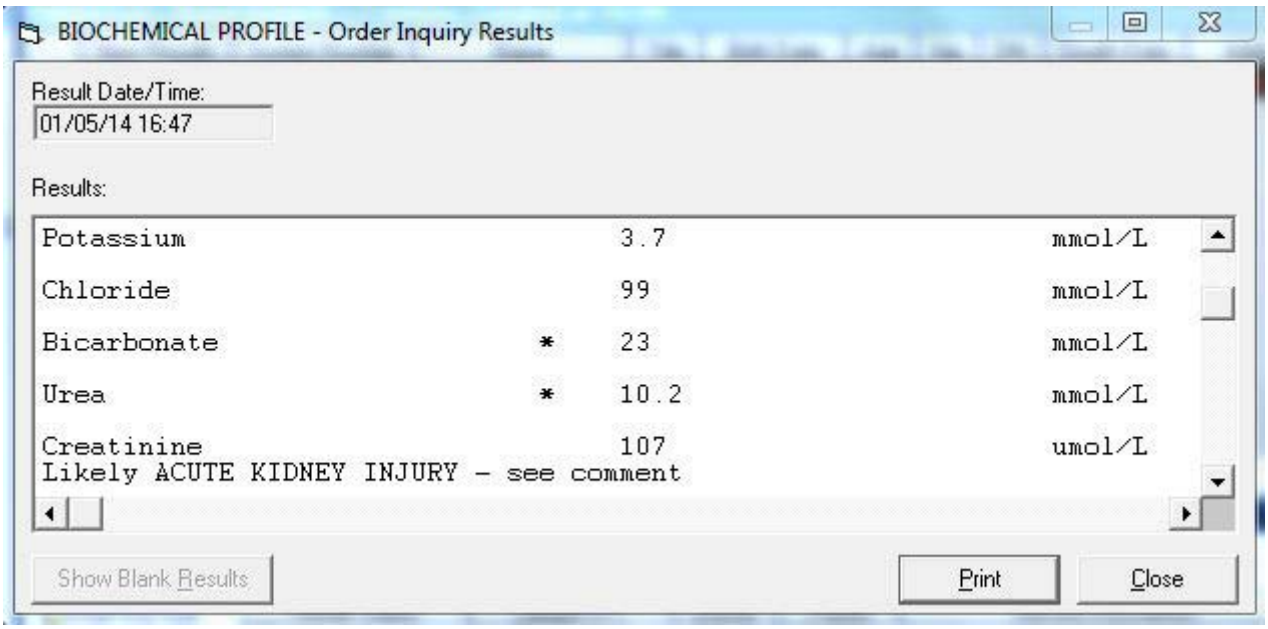

***Fig.3:* 3 Notification of possible AKI identified through e-alert system at Hull and East Yorkshire Hospitals NHS Trust**

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Table.1: Diagnosis of Acute Kidney Injury based on Kidney Disease: Improving Global Outcomes (KDIGO) criteria

If the answer to any of the following is yes, then patient has AKI

1. In the past 6 hours: has patient passed less than 0.5 ml/kg/h of urine?
2. In the past 48 hours: has SCr risen by at least 26 μmol/l?
3. In the past 7 days: has SCr risen by 1.5 times (use the lowest SCr during the past 7 days as baseline)?*

* If no SCr in the past 7 days, then use previous stable SCr measurements as baseline

Table.2: Staging of Acute Kidney Injury based on Kidney Disease: Improving Global Outcomes (KDIGO) criteria

	Serum creatinine criteria	Urine output criteria
Stage 1	1.5–1.9 times baseline in the past 7 days OR ≥26 μmol/l increase in the past 48 hours	< 0.5 ml/kg/h for 6–12 hours
Stage 2	2.0–2.9 times baseline in the past 7 days	< 0.5 ml/kg/h for ≥12 hours
Stage 3	≥3.0 times baseline in the past 7 days OR Increase in SCr to ≥354 μmol/l OR Initiation of renal replacement therapy	< 0.3 ml/kg/h for ≥24 hours OR Anuria for ≥12 hours

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