

ACUTE KIDNEY INJURY
UK CONSENSUS CONFERENCE

**Management of acute kidney injury:
*the role of fluids, e-alerts and
biomarkers***

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The full RCPE UK Consensus Conference on acute kidney injury supplement is available at:
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Foreword

It is not just the name that has changed over recent years. It was always known to the older among us as acute renal failure; the new name, acute kidney injury (AKI), reflects our new understanding that even small decrements in renal function in acutely ill people are associated with a significant negative impact on clinical outcomes.

Acute kidney injury is often not well managed by non-specialists in the UK. A report from the National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) in 2009 provided a wake-up call: 20-30% of cases of AKI are avoidable and better management of AKI may save up to 12,000 lives each year. Recent international guidelines (Kidney Disease Improving Global Outcomes – KDIGO) have been widely welcomed and guidance from the National Institute for Health and Clinical Excellence (NICE) is imminent. However the Royal College of Physicians of Edinburgh identified three important areas where there remains real uncertainty in the management of AKI: namely the role of fluids, the use of e-alerts and the role of biomarkers. The well-established process of a consensus conference was an ideal method to address them.

Of these three areas, the assessment of fluid volume status and its appropriate correction excited the most debate. While there was agreement that clinical assessment is far from ideal, there was disappointment

that there are still no readily available non-invasive tools that the clinician can utilise 'on the spot'. Perhaps when ultrasound becomes as familiar to clinicians as the palpating hand, this will change. There was more positive news over the appropriate type of fluid for routine correction of hypovolaemia, and balanced salt solutions won the day. E-alerts were welcomed, but there are still considerable technical issues in correctly identifying those whose results should be flagged and ensuring that the necessary clinician receives the information promptly. They are already being introduced in several parts of the country and agreement on the principles and organisation of such e-alerts is urgently needed. Biomarkers have real potential as early markers of kidney injury, but in clinical practice the bottom line is 'not yet'.

We would like to thank the staff of the RCPE for their wonderful support in delivering both excellent preparatory material and a splendid conference. The quality of the submitted papers and posters was high and the discussion throughout pertinent and perceptive. We hope the undoubted benefits of the exercise for all of those involved will, through this publication, spread widely and improve patient care.

Ian Gilmore
John Feehally
November 2012

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RCPE UK Consensus Conference

Management of acute kidney injury: the role of fluids, e-alerts and biomarkers

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INTRODUCTION

Acute kidney injury (AKI) is a common, life-threatening condition associated with poor outcomes. Current NHS expenditure on AKI and its consequences is greater than for prostate, bowel and lung cancer combined. There is evidence that many patients are not well managed and 20–30% of cases are potentially avoidable. Optimal care could save up to 12,000 lives a year and produce substantial financial savings. Clear clinical guidelines on the early identification and management of patients with AKI will help to inform the effective commissioning of care for these patients.

AKI may present in primary care or as acute admissions to hospital, but may also develop during hospital admission. Only a minority of AKI cases will reach specialist nephrology care. Many people with AKI are frail and elderly with complex co-morbidity, and present with acute illness.

Care of patients can be improved by doing the basics well. This includes:

- Early recognition of those at risk of AKI
- Informing patients at risk of AKI and their carers when to temporarily discontinue ACE inhibitors (ACEi) angiotensin receptor blockers (ARB), diuretics and non-steroidal anti-inflammatory drugs (NSAID) during acute illness.
- Improved training and education of clinical teams responsible for their care
- Hospitals must provide adequate systems and staffing to deliver high quality care, ensuring continuity of care and appropriate escalation to senior medical staff for assessment of complex cases
- Agreed referral criteria for specialist nephrology input
- Assessment of risk factors for AKI in all acutely ill patients. Risk scores, already in use in some patient groups at risk of AKI, need to be developed and validated for wider use.
- All patients admitted non-electively into hospital and all acutely ill patients in primary care will require assessment of their volume status, urinalysis

and a medicines review. ACEi/ARB, NSAID should be withheld pending senior review within 12 hours.

- All patients admitted non-electively into hospital should also have baseline measurement of serum creatinine and electrolytes (including chloride), repeated within 24 hours. Urinalysis will help to identify the minority with intrinsic kidney disease that require early specialist assessment.

An international clinical practice guideline on AKI has recently been published (*Kidney Disease Improving Global Outcomes – KDIGO*). In the UK, NICE guidance on AKI is in preparation. This consensus statement makes recommendations on three aspects of AKI care which are not a major focus of the KDIGO and NICE work.

What is the role of fluid therapy in AKI?

Summary: Fluid therapy should be guided by repeated evaluation of volume status. A balanced salt solution should be the usual fluid for volume replacement.

- All hospitals must have fluid therapy guidelines for resuscitation, replacement and maintenance which will inform the timeliness of intervention, choice of fluid, and frequency of reassessment
- Patients with AKI receiving intravenous (IV) fluid therapy require regular re-evaluation of volume status, daily weights, and regular monitoring of creatinine and electrolytes (including chloride and bicarbonate).
- Evaluation of volume status should be based on history, cumulative fluid balance and clinical examination (including pulse, blood pressure (BP), jugular venous pressure, capillary refilling, weight and postural change in pulse and BP).
- Clinical assessment of volume status is difficult and should be a focus for education and training of clinical staff.
- Central venous pressure (CVP) measurement does not have a role in the routine assessment of volume status in the ill patient at risk of AKI.
- Choice and prescription of maintenance IV fluids must be guided by a daily assessment of the patient's water and electrolyte requirements.

- Crystalloid solutions are preferred to colloid
- Balanced salt solutions should be the standard IV fluids for the correction of hypovolaemia
- Research is required to evaluate and validate new techniques to assist with the clinical assessment of volume status

What is the role of E-alerts in AKI?

Summary: Identification of AKI in both primary and secondary care should be facilitated through introduction of e-alert systems

- If early identification of AKI, defined by changes in serum creatinine concentration, is to be achieved and early treatment facilitated, e-alerts should prove valuable tools in primary and secondary care
- E-alert systems should be introduced in the context of e-guidance on management of AKI, continuing education of clinical teams, and agreed care bundles.
- At present systems are being developed ad hoc. A national group should be established to develop agreed standards for e-alert systems recognising the need for some system-dependent local flexibility. Components of the system should include an agreed definition of AKI based on the KDIGO classification and a standardised methodology for derivation of baseline serum creatinine. We recommend use of an enzymatic serum creatinine assay with an IDMS-traceable calibration to enable standardisation.
- Healthcare providers employing e-alert systems must have robust arrangements to ensure appropriate and prompt responses with clear lines of accountability.
- We recommend audit and research to confirm that in addition to identification of AKI the use of e-alert systems improves outcomes.

What is the role of biomarkers in AKI?

Summary: It is premature to recommend the use of novel biomarkers of AKI in current clinical practice

- Identification of accurate and early biomarkers may be a key to improving outcomes in AKI
- Serum creatinine is an index of glomerular filtration and is therefore not an ideal biomarker for AKI.
- The ideal biomarker for AKI should provide timely diagnosis, have high diagnostic and prognostic accuracy, and allow assessment of response to treatment. Measurement of biomarkers should be affordable and reproducible.
- Novel markers of early kidney damage are being developed and evaluated, but their exact role in diagnosis and management in AKI remains unproven.
- Further research should evaluate the role of novel biomarkers in multicentre clinical intervention studies throughout the patient pathway. Future studies require better integration between laboratory scientists and clinicians.

What is the role of intravenous fluids in acute kidney injury?

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ABSTRACT Over recent years there has been an increased awareness that even moderately small rises in serum creatinine are associated with worse patient outcomes. This knowledge has been translated into newly proposed definitions for acute kidney injury (AKI) which are based on rises in serum creatinine and/or reductions in urine output. These definitions have been developed by international experts from different organisations which include the Acute Dialysis Quality Initiative (RIFLE definition), Acute Kidney Injury Network (AKIN definition) and most recently Kidney Disease: Improving Global Outcomes (KDIGO definition). There are many different causes of AKI with the most common form being hypovolaemia (often in the setting of sepsis), resulting in hypotension and ischaemic injury to the kidneys. Prevention of AKI remains essential and necessitates the identification of patients at risk and optimising their volume status which may require intravenous (IV) fluids. Treatment is limited to rapid resuscitation with IV fluids and restoration of haemodynamic stability, which may also require the use of vasopressors. Fluid resuscitation with IV fluids may become complicated, particularly in patients with oliguric AKI, when volume overload can occur if oliguria is used in isolation to determine the need for continued fluid administration. For many years it has been common practice to use 0.9% sodium chloride as the fluid of choice, but evidence now demonstrates that this is associated with significant adverse effects. More recently a number of publications have raised concerns regarding the use of hydroxylethyl starch (HES) solutions in acutely ill patients because of an increased risk of AKI. It is therefore important that both undergraduate and postgraduate training programmes include teaching on the clinical evaluation of volume status and the prescription of appropriate IV fluids. The complexity of volume assessment and management in this clinical context requires that the person most likely to prescribe (usually the most junior member of the team) is adequately trained in this area. Delivering this in an effective manner presents a challenge and needs to be assessed in 'high stakes' examinations.

KEYWORDS Acute kidney injury, AKI, volume status, intravenous fluids

DECLARATION OF INTERESTS Dr Lewington has received an honorarium from Baxter for a lecture and an educational grant from BBraun for an IV fluids book.

INTRODUCTION

There has been a significant degree of progress over recent years in understanding and raising awareness of AKI.¹ Much of this work has been stimulated by the proposal of new definitions of AKI by a number of different organisations.²⁻⁴ The new definitions are based upon rises in serum creatinine or reductions in urine output (oliguria). This has provided important data that confirm that patients who experience relatively small rises in serum creatinine have worse outcomes.^{5,6} In 2009 the National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) reported that only 50% of AKI patients received good care.⁷ The sequelae of AKI have now been characterised more clearly, with a recognition that the severity and duration of AKI predicts progression to chronic kidney disease (CKD).⁸ Hypovolaemia, often in the setting of sepsis, remains one

of the most common causes of AKI, resulting in hypotension and hypoperfusion of the kidneys, requiring rapid fluid resuscitation to restore haemodynamic stability. Prevention of AKI includes optimisation of volume status with the prescription of an appropriate fluid. The clinical practice surrounding the administration of IV fluids requires an appreciation of the nature of the fluid deficit, an understanding of the constituents of the available fluids and the clinical skills to assess the volume status and response to treatment. Recent publications have raised significant concerns regarding the prescription of excessive volumes of 0.9% sodium chloride, while the use of HES in critically ill patients has been reported to be associated with an increased risk of AKI.⁹⁻¹¹ There is therefore an ongoing need to improve education surrounding the role of IV fluids in both prevention and treatment of AKI.

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DEFINITIONS OF AKI

Acute kidney injury is a result of a rapid fall in glomerular filtration rate occurring over hours or days and can be oliguric or non-oliguric. The consequences include a failure to regulate fluid and electrolyte balance and a failure to excrete metabolic waste products and drugs. Advances in understanding the epidemiology and prognosis of AKI has been hampered by the lack of a universal definition. The Acute Dialysis Quality Initiative (ADQI) proposed the RIFLE definition and staging system to provide an opportunity to standardise the collection of data and raise awareness that there are different severities of injury.² With the increasing recognition that even moderately small rises in serum creatinine are associated with worse patient outcomes, this definition and staging system was further refined by the Acute Kidney Injury Network (AKIN), which included a rise of 26 $\mu\text{mol/L}$ within 48 hours in the definition criteria.³ Most recently the Kidney Disease: Improving Global Outcomes (KDIGO) international guideline group⁴ has harmonised both of these definitions such that AKI is defined by:⁴

- Serum creatinine rises by $\geq 26 \mu\text{mol/L}$ within 48 hours or
- Serum creatinine rises ≥ 1.5 fold from a baseline value measured within the previous week or
- Urine output is $< 0.5 \text{ ml/kg/h}$ for > 6 consecutive hours

If serum creatinine concentration has not been measured in the previous week, the most recent creatinine concentration measured within the last three months can be used. It is important to establish the aetiology of the AKI, with the most common cause being hypovolaemia and/or sepsis resulting in hypotension and ischaemic injury to the kidneys.

HYPOVOLAEMIA AND AKI

Acute kidney injury is commonly secondary to hypovolaemia in the setting of sepsis which results in hypotension and decreased perfusion of the kidneys. Depending on the severity and duration of the hypotension, the patient may initially develop pre-renal AKI (a functional process, which is potentially reversible), but may progress to ischaemic damage of the kidney parenchyma known as intrinsic AKI. If kidney damage occurs there is a higher risk that the patient will develop kidney failure requiring renal replacement therapy (RRT). If AKI develops, the kidneys lose the ability to auto-regulate blood flow and become vulnerable to further ischaemic injury. It is therefore essential to restore haemodynamic stability by correcting the hypovolaemia as quickly as possible with an intravenous infusion of appropriate fluids. This will be dependent upon accurate clinical assessment of volume status and a documented

management plan, which requires regular review and defined endpoints. Patients who develop oliguric AKI are particularly at risk of developing fluid overload if the clinical response to fluids is not carefully monitored and correctly interpreted.

ASSESSMENT OF VOLUME STATUS

The assessment of a patient's volume status is an essential component of safe and effective prescribing of IV fluids and the correction of hypovolaemia. A comprehensive assessment of volume status requires a physical examination, review of the fluid balance chart (to include daily weights) and the medication chart (antibiotics may be made up in significant volumes of fluid). See Table 1 for the recommended components of a volume status assessment.

TABLE 1 Recommended components of a volume status evaluation

Capillary refill time
Pulse rate (beta blockers/diltiazem prevents tachycardia in response to hypovolaemia)
Blood pressure (lying and standing if able)
Jugular venous pressure
Skin turgor (over clavicle)
Lungs (pulmonary oedema)
Heart sounds (gallop rhythm – hypervolaemia)
Oedema (peripheral/sacral)
Urine output
Weight change to assess water balance

Acute kidney injury secondary to hypovolaemia and hypotension is associated with oliguria, defined as a urine output $< 0.5 \text{ ml/kg/h}$. Oliguria must not be looked at in isolation as it can be a physiological response to uncomplicated surgery in the first 48 hours to conserve salt and water in an attempt to maintain intravascular volume.¹² The key clinical question is whether or not the oliguria is secondary to significant intravascular hypovolaemia requiring treatment. Invasive monitoring may be required intra-operatively to guide optimal treatment. A failure to recognise this physiological response and incorrectly consider the oliguria in isolation as indicating hypovolaemia may result in excessive administration of IV fluid (commonly 0.9% sodium chloride) that not only expands the blood volume excessively but also over-expands the interstitial fluid volume, causing oedema and weight gain. The metabolic response to surgery impairs the patient's ability to excrete the additional salt and water fluid load, making interstitial oedema worse, compromising organ function and increasing the risk of morbidity and mortality.¹³

PREVENTION OF AKI

There have been recent advances in the processes around surgery such as the enhanced recovery from surgery programme which have been introduced widely.¹⁴ It is anticipated that this programme will improve patient recovery and reduce complications such as excessive prescription of 0.9% sodium chloride, which has been well-described in the literature.¹⁵ It is recommended that any patient admitted to hospital who is acutely ill or undergoing major surgery that has been identified as at risk of developing AKI should have a daily volume status evaluation as outlined in Table 1, and an appropriate fluid therapy management plan.

There are certain specific clinical contexts that merit further discussion with respect to the prevention of AKI around which there still remains a degree of debate. Contrast-induced AKI is rare in patients with normal kidney function but can occur in patients with risk factors following the receipt of iodinated contrast.¹⁶ Patients at high risk are more elderly patients (>75 years), who are acutely ill with a history of CKD (eGFR<60 ml/min/1.73 m²) and receiving intra-arterial iodinated contrast. It is recommended that such patients should be discussed with the radiologists with respect to their risk factors and alternative imaging considered.¹⁷ If it is determined that the imaging is required then following volume status evaluation, patients should receive intravenous fluid at 1 ml/kg/hour 12 hours prior to and 12 hours following the procedure (caution if cardiac failure) selecting either 0.9% sodium chloride or isotonic (1.4%) sodium bicarbonate solution with the urea, creatinine and electrolytes monitored for 3–5 days.⁴

Patients who develop rhabdomyolysis (crush injury) are at risk of developing AKI as the myoglobin is freely filtered by the kidneys and is directly toxic to the tubular epithelial cells, particularly in the setting of hypovolaemia and acidosis. The principles of management are prompt correction of hypovolaemia and establishment of a good urine output (>100 ml/hr) with rapid fluid resuscitation. Initially IV 0.9% sodium chloride solution is recommended at a rate of 10–15 ml/kg/hour.¹⁸ There is additional weak evidence supporting the alkalinisation of the urine to reduce the precipitation of myoglobin which may be achieved by intravenous 1.4% sodium bicarbonate at 50 ml/hr to maintain a urinary pH >6.5. Careful monitoring is required as large volumes of rapidly infused 0.9% sodium chloride can lead to a hyperchloraemic metabolic acidosis.

TREATMENT OF AKI

Treatment of AKI involves the identification and correction of the underlying cause (not all AKI will be secondary to hypovolaemia and/or sepsis). If the patient is deemed to be hypovolaemic following a volume status assessment, resuscitation with IV fluid should be

commenced immediately. The aim is to restore blood pressure and perfusion to the kidneys thereby minimising any ischaemic damage. This can be commenced with an IV fluid bolus of 500 ml (250 ml if cardiac failure) of a balanced crystalloid solution such as Hartmann's (0.9% sodium chloride if rhabdomyolysis or hyperkalaemia) or colloid (not HES).¹² The insertion of a central venous pressure (CVP) line and urinary catheter (not mandatory and could introduce infection) can be considered to aid with the assessment of volume status. The patient's clinical response to fluid should be assessed and if there is none and no pulmonary oedema, a further 500 ml bolus of crystalloid should be administered with continued clinical reassessment. Continued excessive administration of 0.9% sodium chloride should be avoided due to the risk of hyperchloraemic metabolic acidosis. If the patient develops oliguric AKI (<0.5 ml/kg/24 hrs) despite adequate fluid resuscitation, this should be considered to be volume-unresponsive AKI. Further excessive fluid resuscitation may result in pulmonary oedema. If the patient has volume-unresponsive AKI, continue with IV fluid cautiously, matching urine output and monitoring for signs of respiratory distress (rising respiratory rate, pulmonary oedema or falling oxygen saturations).

The first sign of recovery from oliguric AKI may be an increase in urine output. Alternatively, recovery may be heralded by a reduction in the rise in the daily serum creatinine followed by a plateau in its value prior to a fall. Recovery from AKI can result in a polyuric state in some patients with the production of large urine volumes until the capacity of the renal tubule to concentrate urine returns. There must therefore be careful attention to the patient's volume status and fluid requirements, which can be overlooked. Patients can be at risk of developing a free water deficit which manifests as hypernatraemia and requires an increased intake of water (intravenous 5% dextrose if unable to take water orally). Failure to address the free water deficit promptly will not only slow renal recovery but will also put the patient at risk of neurological complications. Another potential complication is the development of hypokalaemia, which requires appropriate therapy due to the risk of cardiac arrhythmias and ileus. A balanced crystalloid containing potassium is recommended in this clinical context, but if the hypokalaemia persists, then 5% dextrose/0.18% sodium chloride solution with higher concentrations of added potassium chloride should be prescribed.

THE RELATIONSHIP BETWEEN THE TYPE OF FLUID USED IN RESUSCITATION AND AKI

The type of fluid that should be used in the resuscitation phase of hypovolaemia remains controversial and the debate as to whether crystalloids or colloids are preferable continues. However there are now an increasing number of studies that provide more guidance.

A Lewington, DN Lobo

The SAFE study demonstrated that 0.9% sodium chloride was as effective as 4% human albumin for fluid resuscitation in critically ill patients.¹⁹ The SAFE study demonstrated that there was no difference in renal outcome based on the need for and duration of RRT. The KDIGO working group has suggested that isotonic crystalloids (0.9% sodium chloride) rather than colloids (albumin, HES) should be used during initial resuscitation but that colloids may still have a role in patients requiring additional fluid.⁴ It is intuitive to believe that balanced crystalloid solutions such as Hartmann's (or Ringer's lactate) are less likely to cause acid-base disturbances than 0.9% sodium chloride but outcome studies in this area were lacking until relatively recently.^{20,21} A study in patients undergoing renal transplantation showed that renal function was more likely to be compromised in patients receiving 0.9% sodium chloride rather than Ringer's acetate and that the former group of patients had a greater risk of developing hyperkalaemia and metabolic acidosis than the latter.²² Intraoperative bleeding and requirement of blood products and the need to administer bicarbonate to correct metabolic acidosis was greater in patients receiving 0.9% sodium chloride after abdominal aortic aneurysm repair than those receiving Ringer's lactate.²³ A more recent propensity analysis also demonstrated that post-operative complications were greater in patients receiving 0.9% sodium chloride on the day of surgery than those receiving a balanced solution (plasmalyte 148/plasmalyte A) and that patients receiving 0.9% sodium chloride were five times more likely to need dialysis than those receiving the balanced solution.²⁴

Sodium chloride (0.9%) solutions are excreted much more slowly in comparison to solutions with a lower sodium and chloride content and result in prolonged dilution of the haematocrit and albumin. Retention of fluid can result in weight gain which persists in comparison with solutions of more balanced electrolyte composition, which generally are diuresed more rapidly. While animal studies have demonstrated that hyperchloraemia can result in renal arteriolar constriction, reduced renal blood flow and decreased glomerular filtration rate, this phenomenon was until recently not demonstrated in humans.^{25,26} A recent study using magnetic resonance imaging (MRI) has shown that even in healthy human volunteers, the hyperchloraemic acidosis caused by 0.9% sodium chloride infusion is associated with renal oedema and a fall in renal blood flow velocity and cortical tissue perfusion when compared with a balanced crystalloid.²⁷ These changes may be explained by the fact that high chloride content of the glomerular filtrate results in decreased proximal chloride resorption and an increase in the delivery of chloride to the distal nephron. An increased concentration of chloride in the renal tubule causes entry of chloride into the macula densa, depolarisation of the basement membrane and release of adenosine, which in turn increases afferent arteriolar resistance and decreases GFR. Another recent study has

shown that decreasing the amount of chloride delivered to critically ill patients resulted in a lower increase of the mean serum creatinine concentration, a decrease in the incidence of injury and failure class of RIFLE-defined AKI and the need for RRT. However, there were no differences in hospital mortality, hospital or ICU length of stay, or need for RRT after hospital discharge.²⁸ All these studies show that 0.9% sodium chloride is neither normal nor physiological and that it is associated with several adverse consequences, especially on renal function.²⁹ Hence, balanced crystalloids should be preferred to 0.9% sodium chloride.

There have been a number of publications recently that have investigated the use of the colloid HES in the treatment of hypovolaemia. It has been hypothesised that renal tubular injury can result either from direct effects or secondary to an elevated oncotic pressure. The VISEP study demonstrated that patients with severe sepsis who received a high molecular weight HES solution (MW >200 kDa) had an increased risk of AKI.⁹ This prompted a more recent study, which demonstrated that patients with severe sepsis who received fluid resuscitation with a lower molecular weight HES (MW =130 kDa) had an increased risk of death and were more likely to require renal replacement therapy as compared to patients receiving a balanced crystalloid solution, Ringer's acetate.¹⁰ Most recently, critically ill patients who received a low molecular weight HES (MW =130 kDa) for fluid resuscitation in the intensive care unit were demonstrated to have an increased requirement for renal replacement therapy.¹¹ While the jury is out it would seem advisable to avoid using HES solutions for fluid resuscitation in critically ill patients. As with prescribing of any fluid it is important it is based on sound principles.³⁰

CONCLUSIONS

Acute kidney injury is associated with a significant degree of morbidity and mortality. There has been a greater appreciation of this over recent years with the development of new definitions to improve earlier recognition of the disease. The mortality associated with AKI has remained unchanged for the last 40 years despite advances in modern medicine. The longer term consequences following an episode of AKI have been characterised more clearly, with the demonstration that the severity and duration of an episode of AKI predicts progression to CKD. Acute kidney injury is most commonly secondary to hypovolaemia, often in the setting of sepsis. Prevention of AKI is essential and necessitates the identification of patients at risk with the optimisation of volume status. There remains no specific therapeutic intervention other than supportive measures with the prompt treatment of sepsis and correction of hypovolaemia to re-establish haemodynamic stability. There is still much debate regarding the type of fluid

(crystalloid or colloid) to be preferred for the early phase of resuscitation. However there have been a number of publications that have highlighted significant concerns regarding the excessive use of 0.9% sodium chloride as a resuscitation fluid in surgical patients. Significant concerns now surround the use of HES solutions in critically ill patients due to an increased incidence of AKI requiring RRT. It would therefore seem prudent to avoid using such fluids in this clinical context. The prescription of IV fluids has been marginalised for

too long. It depends upon clinical evaluation of the patient's volume status, recognition of the nature of the fluid deficit and prescription of the appropriate fluid with regular review and defined endpoints. The inappropriate prescription of IV fluids may have significant consequences, leading to electrolyte abnormalities and fluid overload. It is important that undergraduate and postgraduate education undertakes the task of improving the appreciation of all of the clinical components of safe and effective IV fluid prescribing.

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What is the role of e-alerts in acute kidney injury?

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ABSTRACT Acute kidney injury (AKI) is common, harmful and often preventable, yet standards of clinical practice are variable. A significant contributor to reported deficiencies in care is the delay or even failure to diagnose AKI. There is therefore considerable interest in developing electronic systems to report the presence of AKI and alert the clinician to its occurrence with the aim of triggering earlier, more effective intervention. However, there are considerable technical complexities in developing such systems when the current diagnostic criteria for AKI are employed. This paper will review the studies published in this area that have attempted to tackle this problem, as well as discussing the challenges and potential solutions.

KEYWORDS Acute kidney injury, AKI, e-alert, electronic alert, electronic reporting

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INTRODUCTION

Acute kidney injury (AKI) is common, occurring in up to 22% of hospital admissions and is associated with poor outcomes.¹ These include prolonged admissions, elevated mortality rates, accelerated progression of chronic kidney disease (CKD) and significantly increased healthcare costs.^{2,3} These poor outcomes are due in part to variable standards of care, highlighted in a National Confidential Enquiry into Patient Outcome and Death (NCEPOD)⁴ and other reports.⁵⁻⁷ A significant contributor to these poor standards was the delay in diagnosis or failure to recognise AKI, sometimes attributable to the fact that many patients with AKI are cared for by non-nephrologists.⁴ Despite an absence of specific treatments for AKI, early intervention focusing on the basic elements of care (fluid balance, haemodynamic observations, medication review, appropriate investigation) can improve outcomes.⁸

There is therefore an urgent need to improve early recognition and treatment of AKI and the development of electronic alert systems (e-alerts) would seem to be an effective way of doing this. The aims of such systems are to automatically and systematically identify all AKI episodes, notify the responsible clinician and therefore trigger earlier intervention. E-alerts can be influential on patient outcomes,⁹ but to date there have been few attempts at introducing such systems for AKI. This may be due in part to the relatively short period of time since the widespread acceptance of the risk, injury, failure, loss, end-stage renal disease (RIFLE) and subsequent acute kidney injury network (AKIN) criteria. Furthermore, these criteria are based on a relative change in serum creatinine with respect to an individual's

baseline creatinine level, which presents a significant challenge to the use of current pathology software for their prospective application in clinical practice. This issue of prospective application is highlighted in the recent *Kidney Disease: Improving Global Outcomes (KDIGO)* guidelines that, for the first time, specifically discuss recommendations for using these criteria in 'real life' clinical practice.¹⁰ The development of e-alert systems for AKI therefore remains in its early stages. This paper will summarise current knowledge as well as discussing the technical challenges and potential solutions in this area.

PUBLISHED STUDIES ON E-ALERTS IN AKI

Currently available studies were identified by a systematic search of the following databases: Medline/Pubmed, Embase, Cochrane Library, NHS Evidence, Health Business Elite, Health Management Information Consortium, UptoDate and are summarised in Table 1. The first study to describe a successful alert focused on the management of medicines in AKI and predated current diagnostic criteria.¹¹ Rind et al. developed an email alert for patients prescribed nephrotoxic or renally excreted medicines and who developed AKI (defined as an acute rise in serum creatinine level of >44 µmol/L for nephrotoxic medications and >50% rise for renally excreted drugs). The authors studied 922 patients using a time series study design and found a significant reduction in the time it took to adjust the medication during the intervention period (97.5 hours vs 75.9 hours). Despite this improvement, the length of time to medication adjustment remained more than three days even after the intervention was introduced. The main beneficial effect of alerts was seen with patients on renally excreted drugs that

required dose adjustment. Risk of developing 'serious' renal impairment (a two-fold increase in serum creatinine level to $>177 \mu\text{mol/L}$) was halved during the intervention period, although the event rate was low (22 cases of serious renal impairment in the control period vs nine during the intervention). There was no impact on mortality or hospital length of stay (LoS).

A similar time series study was reported by McCoy et al. who also limited their method to patients prescribed nephrotoxic or renally excreted drugs and used a similar definition of AKI (rise in serum creatinine level of $>44 \mu\text{mol/L}$ within 48 hours).¹² They describe an electronic order entry system with custom-built passive alerts for AKI, alongside a second interruptive alert requiring physician acknowledgment when a nephrotoxic prescription had not been altered in response to the initial alert. This study also demonstrated that e-alerts could alter physician behaviour with an increase in the proportion of medication adjustments within 24 hours of the onset of AKI (33.9% during the control period vs 59.5% during the intervention) and a significant reduction in response times. Again, response rates remained below the ideal even after the introduction of e-alerts. This may reflect the observation that interruptive alerts had the most impact while passive alerts were not effective at changing physician response compared with the baseline. This may also suggest that e-alert systems should not be introduced in isolation, but in conjunction with other service improvement measures (e.g. AKI guidelines, education programmes, care bundles) to maximise impact.

Colpaert et al. reported the first e-alert system based on current diagnostic criteria.¹³ Their system was confined to a single, 56-bed intensive care unit (only 36 beds were included in the subsequent study) and was based on urine output and serum creatinine components of the RIFLE criteria. Deterioration in either parameter triggered an automatic message that was sent to a cordless telephone carried by the relevant doctor. Although the alert was generated automatically, the system depended on manual entry of the baseline creatinine level to use as a reference value as well as two-hourly data entry by the nursing staff for urine output measurements. A second study from this group assessed the efficacy of this system on physician behaviour and clinical outcomes in 951 patients, again employing a time series design with control periods before and after the intervention period.¹⁴ In this case, over 90% of the alerts generated were based on reduced urine output. There was a significant increase in the proportion of patients receiving therapeutic intervention for AKI within 60 minutes (28.7% in the intervention period vs 7.9% and 10.4% in the control periods); this was mainly due to quicker administration of fluids or vasopressors. Despite this, there was no convincing evidence of an effect on patient outcomes including

mortality, intensive care unit (ICU) LoS, frequency of renal replacement therapy (RRT) and maximum AKI stage attained. The only patient variable positively affected by AKI alerts was that more patients with RIFLE-Risk (RIFLE-R) returned to the baseline level (i.e. no AKI) after therapy was administered (65.9% in the intervention group compared with 61.0% and 63.1% in the control groups, $p=0.048$). This mainly reflected an improvement in urine output and benefit was not observed in those with more severe AKI (RIFLE-Injury or RIFLE-Failure stages).

The first hospital-wide electronic alert system generated messages using a pathology software system that were sent to the attending physician.¹⁵ Alerts were automatically generated when the current serum creatinine level was $\geq 75\%$ greater than the last recorded value (the so-called delta check that is available on most pathology software systems). There was no time limit on the period between the current and last recorded creatinine values. Using this method, 463 patients were identified over a three-month study period. Diagnostic accuracy was limited however as 66% of patients who subsequently required RRT for AKI did not generate an alert (the daily creatinine change was $<75\%$ of its previous value or no previous results were available). Effects of e-alerts on therapeutic intervention rate or patient outcomes were not studied but the alert system was used to collect prospective data. Patients with AKI tended to be elderly with co-morbidities and the in-hospital mortality rate was high at 36%. Factors associated with mortality were also reported and tested with multivariable prediction models. The authors of the study estimated the potential workload using different percentage increases in creatinine levels and demonstrated an exponential rise in the number of alerts by lowering the threshold of the measurement in an attempt to improve sensitivity. This observation is supported by a retrospective study comparing a delta check method using a $>26 \mu\text{mol/L}$ rise in creatinine level as the alert threshold vs current diagnostic criteria.¹⁶ This much lower threshold produced a low false negative rate (2%) but compared with the AKIN criteria it had a false positive rate of 16%, demonstrating that increased sensitivity results in reduced specificity, unless more sophisticated algorithms are employed.

More recently, a hospital-wide electronic system based on current diagnostic criteria was reported by the Derby group.¹⁷ This system was introduced in April 2010 and continues to run successfully in routine clinical practice. Commercially available software is used and the system is based on the serum creatinine components of the AKIN criteria, disregarding the 48-hour time window when selecting the baseline creatinine level. All serum creatinine measurements sent from inpatient locations (excluding the renal unit) are automatically

TABLE 1 A summary of the currently available published studies of e-alerts for acute kidney injury

Author	Year	Participants and setting	Type of e-alert	IT requirements	Definition of AKI	Study design	Outcomes assessed	Main results
Rind et al. ¹¹	1994	Patients on nephrotoxic or renally excreted medications within Department of Medicine. 922 patients	Email sent to attending clinician	Email, pathology results, electronic prescribing all within a single system	Creatinine increase of 44 µmol/L (0.5 mg/dL) from baseline, no time limit	Time series design (control-intervention-control-intervention-control periods)	Time to medication adjustment, rise in creatinine level after alert (serious renal impairment defined as two-fold increase). LoS, mortality	Time to medication adjustment reduced (97.5 to 75.9 hours), less effect in nephrotoxic medications, 22 vs 9 patients with serious renal impairment, smaller rise in creatinine in intervention group, no difference on mortality/LoS. A total of 65% physicians wanted to keep alerts, 28% found them annoying. Smallest effect in most toxic medications
McCoy et al. ¹²	2010	Patients on nephrotoxic or renally excreted medications with eGFR >30 mL/min. 1,598 patients	Alert within e-prescribing order-entry system, both passive and interruptive components	In-house order-entry and electronic medical record system	Creatinine increase of 44 µmol/L (0.5 mg/dL) from baseline within 48 hours – consciously chose not to use RIFLE/AKIN	Time series design (control-intervention)	Effect on medication adjustment within 24 hours and time to medication adjustment	Medication adjustment in <24 hours increased (33.9 to 59.5 per 100 events), significant reduction in response times. Passive alerts did not change prescribing behaviour, interruptive alerts more effective
Colpaert et al. ¹³	2007	See below	See below	See below	See below	Initial description of technique	Nil	Nil (subsequently reported sensitivity of the system was 100% and specificity 96.8%)
Colpaert et al. ¹⁴	2012	Single intensive care unit (36 beds), 951 patients over six month study period	Alert message sent on DECT (cordless) phone	Commercially available electronic medical record for ICU with in-house programming for AKI calculation, linked to ICU monitors and pathology results, nurse input for UO/vitals. Personal computer at each bedside	RIFLE criteria, both creatinine and urine output. Baseline criteria manually selected and input	Time series design (control-intervention-control)	Proportion of treatments given within 60 minutes after alert, time to treatment, maximum RIFLE stage, RRT, length of ICU stay, mortality	A total of 92% of alerts were UO. More patients in alert group received treatment <60 minutes (28.7% vs 7.9%/10.4%). Fluid/vasopressor administration happened more quickly with alerts (19 vs 29 minutes). No difference in any patient outcome except greater percentage of patients in alert group with a return to baseline within eight hours in RIFLE class only, UO criteria only (65.9% vs 61%/63.1%)

TABLE 1 A summary of the currently available published studies of e-alerts for acute kidney injury (continued)

Author	Year	Participants and setting	Type of e-alert	IT requirements	Definition of AKI	Study design	Outcomes assessed	Main results
Thomas et al. ¹⁵	2011	Hospital-wide, 463 patients over three months	Alert message within integrated pathology software	Integrated clinical environment pathology software	≥75% increase in creatinine from last measured value	Observational study	AKI incidence, demographic data, mortality, RRT incidence, renal recovery, factors associated with mortality	AKI incidence 3% of admissions. Median age 75, co-morbidity common. For AKI that required RRT false negative rate was 66%. RRT rate 2.8%. In-hospital mortality 36%. 17% had progression of CKD after AKI. Factors associated with mortality reported. 85% patients no baseline within 48 hours, interval no effect on mortality analysis
Selby et al. ¹⁷	2012	Hospital-wide (excluding renal unit), 2,619 patients over nine months	Electronic results reporting of AKI stage	Commercially available laboratory and results reporting systems	AKIN criteria, serum creatinine only, 48-hour time constraint disregarded	Observational study	Diagnostic accuracy, AKI incidence, mortality, length of hospital stay, renal recovery	Diagnostic accuracy good (false positive 1.7%, false negative 0.2%). AKI incidence 5.4% of admissions. In-hospital mortality 23.8%. Severity of AKI associated with mortality, LoS and renal recovery rate. AKIN criteria performance reduced if pre-existing CKD. Only 7.1% required estimation of baseline creatinine

$\mu\text{mol/L}$ = micromoles per litre; **LoS**= length of stay; **mL/min**= millilitre per minute; **eGFR**= estimated glomerular filtration rate; **RIFLE**= risk, injury, failure, loss, end-stage renal disease; **AKIN**= acute kidney injury network; **UO**= urine output; **RRT**= renal replacement therapy; **ICU**= intensive care unit

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compared on an individual patient basis against an estimated baseline creatinine level that is reverse calculated from the modification of diet in renal disease (MDRD) equation using a glomerular filtration rate of 75 mL/min/1.73m². All measured creatinine values that are 50% greater (1.5 times) than the individual's estimated baseline value are flagged internally. These results are then reviewed by a clinical chemist, who selects the real baseline creatinine level for each patient using previous creatinine results (accepting the estimated baseline from reverse MDRD calculation when there are no previous creatinine measurements available). The AKIN diagnostic criteria are then applied using a calculator. For each acute elevation in creatinine level consistent with AKI a report is issued that specifies AKI stage, value and date of baseline creatinine level employed, 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. The diagnostic accuracy of this system is good, with a false negative rate of 0.2% and a false positive rate of 1.7% (a further 3.2% of true AKI episodes were assigned to an incorrect AKIN stage). This system can also be used to generate prospective observational data, showing that e-alert systems can be used to monitor trends in incidence and outcomes of AKI over time, on a hospital-wide basis. In the initial reported nine months, 3,202 AKI episodes in 2,619 patients were observed, which represented 5.4% of total admissions. In-hospital mortality was 23.8% and the severity of AKI was associated with increased mortality, longer LoS and lower renal recovery rate. Importantly, the use of AKIN criteria was less effective when patients had pre-existing CKD; in these cases the association between the higher AKI stage and increasing mortality was lost. By disregarding the 48-hour time limit when selecting the baseline creatinine value and extending this up to 12 months, only 7.1% of patients required the use of an estimated baseline.

In addition to published studies, there have been several conference abstract reports of electronic alert systems that have been introduced or trialled in the UK (summarised in Table 2). The AKI alert system at Nottingham University Hospitals NHS Trust (Bisset et al., Abstract SA PO2113, ASN 2011) has been operating since April 2011, but was tested in pilot form for a year prior to this. Of the established alerts based on RIFLE or AKIN criteria it was the first fully automated and real time system. It was developed using a combination of both RIFLE and AKIN staging criteria, reporting the higher stage in the event of a discrepancy between the two. The intention was to increase sensitivity but retain specificity. In effect, although implementation of the alert preceded publication of KDIGO guidelines, the algorithms applied are equivalent to KDIGO AKI criteria. The alert uses the lowest creatinine level up to a year prior to admission as baseline but uses a calculated

'theoretical' creatinine value (based on the MDRD equation, as described for the Derby alert) when an actual baseline is not available. The alert was developed within the Trust's in-house web based information system ('NotIS'), which provides a clinical access point for the Trust's patient administration systems (PAS), including electronic requesting and results reporting. Procedural Language/Structured Query Language (PL/SQL) code is executed automatically on the NotIS Oracle database whenever an electronic creatinine result is received for a current inpatient from the pathology laboratory system Winpath. This code checks the newly received result against both previous results and baseline creatinine values for the patient and it tags an alert comment on to the result if criteria for AKI are fulfilled. The alert comment includes AKI stage and reference to the Trust's AKI guidelines. A prospective database of AKI staging and outcome (including in-hospital mortality rate) is populated automatically. Patients with known end-stage renal disease are excluded from the AKI alert by identification of their attendance at a dialysis clinic on PAS, as the alert system will search outpatient clinic codes for all patients.

A system introduced in Gloucester Hospitals identifies patients with serum creatinine changes that fulfil the KDIGO criteria for the diagnosis of AKI (Penders et al., Abstract P115, RA 2012). The abstract did not delineate the specific methodology of this system, which was trialled over a two week period. Two systems using similar methodology to that of Thomas et al.¹⁵ have also been described, from Inverness (Gamble et al., Abstract P228, RA 2012) and from Antrim (Stirling et al., Abstract P227, RA 2012). These systems automatically generate an alert for acute rises in serum creatinine of >50% from baseline or of ≥ 30 $\mu\text{mol/L}$ respectively. For the Inverness system, the definition of baseline creatinine was not specifically stated whereas the Antrim system used the most recent serum creatinine from the last 30 days. Evaluation of the Inverness system was reported for the first 20 patients identified; the Antrim system was trialled for a 17-day period. Finally, the Royal Cornwall Hospital has developed a system that sends a list of all patients with serum creatinine results of >354 $\mu\text{mol/L}$ to the nephrology team on a daily basis, who then contact the supervising medical team to offer advice or a renal review if necessary (Bommaya et al., Abstract P1, BRS 2012). This system was described for the first year of its running. There has been considerable variation in the reported duration of observation to evaluate these systems. A meaningful period of assessment is likely to require several months of observation, ideally with a time-series design or between centre comparison.¹⁴ Equally the high incidence of AKI means that for hospital-wide systems, a large number of cases can be accrued over a period of 3–6 months.

What is the role of e-alerts in acute kidney injury?

TABLE 2 A summary of the studies of e-alerts for acute kidney injury available in conference abstract form

Author	Year	Participants and setting	Type of e-alert	IT requirements	Definition of AKI	Study design	Outcomes assessed	Main results
Bisset et al.	2011	Hospital-wide, initial report for first three months	Fully automated alert, reporting AKI stage real time with creatinine result	Code written into in-house hospital information system	Combination of RIFLE and AKIN criteria (equivalent to KDIGO)	Observational	Incidence of AKI stages	Description of method, 3,468 patients with AKI identified over initial three month period, AKI stages reported
Penders et al.	2012	Hospital-wide, report was of initial two-week trial	Automated flagging system, specifics of method not stated	Not stated	KDIGO criteria	Observational	Comparison of patients with AKI above and below age 80	A total of 273 samples identified with AKI. Elderly patients with AKI had worse outcomes and increased LoS
Gamble et al.	2012	Hospital-wide, excluding ICU, renal unit and paediatric patients.	Electronic alert message on results reporting system	Not stated	Acute rise in creatinine of >50% from baseline, baseline not defined	Observational	Description of first 20 patients identified, plus interview of ten hospital practitioners regarding utility	Patients were generally elderly and co-morbid, 72% on nephrotoxic drugs. One of the e-alerts prompted nephrology referral. Positive feedback from practitioners
Stirling et al.	2012	Hospital-wide, excluding ICU, renal unit and paediatric patients. Report was of initial 17-day trial	Automated alert message via pathology reporting system	Not stated	Acute rise in creatinine of ≥ 30 $\mu\text{mol/L}$ as compared to creatinine measurements in last 30 days	Observational	Practicality of method, mortality rates as per AKIN staging	A total of 137 patients identified over 17 days, 84% AKI stage one, 12% AKI stage two, 4% AKI stage three. Mortality increased with increasing AKI stage. Only 5% of patients identified were referred to nephrology
Bommaya et al.	2012	Hospital-wide, report over 12 months	Automated list sent to nephrology team who contacted attending medical team	Not stated	All creatinine values >354 $\mu\text{mol/L}$	Observational	Description of nephrology intervention patterns	A total of 750 patients identified, 628 already known to nephrology. Management altered by nephrology review in 22 cases

LoS= length of stay; eGFR= estimated glomerular filtration rate; RIFLE= risk, injury, failure, loss, end-stage renal disease; AKIN= acute kidney injury network; KDIGO= kidney disease: improving global outcomes; UO= urine output; RRT= renal replacement therapy; ICU= intensive care unit

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All of the currently published studies use serum creatinine level as the measure of renal function. Creatinine performs relatively poorly as a biomarker of AKI due to the non-linear relationship between serum creatinine level and glomerular filtration rate (GFR) as well as the delay between renal injury and the time at which the serum creatinine level begins to change. However, creatinine testing is unlikely to be replaced in the near future due to its low cost, widespread availability and lack of suitable alternatives. The only other studies in this area relate to automated risk prediction scores within electronic medical records to identify patients at increased risk of developing AKI.¹⁸ Although not directly pertaining to this topic, the use of such systems in clinical practice to prevent cases of AKI may be useful. Further evaluation is clearly required, but their utility in reducing contrast-induced nephropathy has recently been demonstrated.¹⁹

ALGORITHMS FOR AKI ALERT SYSTEMS

The first consideration when designing algorithms for an AKI e-alert is the definition of AKI to be used. Since the widespread adoption of RIFLE and AKIN criteria and the recent publication of KDIGO guidelines (summarised in Table 3), it seems logical that AKI alerts should incorporate one of these staging systems, which will also provide consistency between centres. For practical reasons, this usually comprises just the serum creatinine component; urine output criteria are less well validated and in most situations cannot be routinely measured unless patients have a urinary catheter. Simpler alert systems might be appropriate for some situations and would be easier to implement, although the trade-off between simplicity and diagnostic accuracy must be acknowledged e.g. a delta check highlighting all cases where the serum creatinine level has increased by a certain percentage could provide a crude alert.¹⁵

Even if alert algorithms are based on RIFLE, AKIN or KDIGO criteria, other issues are still problematic. When an alert is designed for hospitalised patients, the first question is how to assess the creatinine level on admission. An AKI alert based on the first measurement on admission is important in identifying 'community-acquired AKI' rather than 'hospital-acquired AKI'. The NCEPOD report⁴ recommends that all patients admitted acutely should have their creatinine level checked on admission, but in order for this to be useful it requires a reference (or baseline) creatinine level to act as a denominator. Other criteria (RIFLE and AKIN) require the baseline creatinine level to be taken within seven days or 48 hours respectively, while KDIGO criteria are a composite of both, depending on the magnitude of the rise in creatinine level. However, if these time frames were applied to the admission creatinine level, the reference measurement might be higher than the true

TABLE 3 A KDIGO staging of acute kidney injury.¹⁰ To diagnose AKI, the KDIGO guidelines suggest that a rise in creatinine of 1.5–1.9 times baseline occurs within seven days or a rise of ≥ 0.3 mg/dL ($27 \mu\text{mol/L}$) within 48 hours.

Stage	Serum creatinine level	Urine output
1	1.5–1.9 times baseline OR $\geq 0.3 \mu\text{mg/dL}$ ($\geq 26.5 \mu\text{mol/L}$) increase	<0.5 mL/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 mL/kg/h for ≥ 12 hours
3	3.0 times baseline OR Increase in serum creatinine to $\geq 4.0 \text{ mg/dL}$ ($\geq 353.6 \mu\text{mol/L}$) OR Initiation of renal replacement therapy OR In patients <18 years, decrease in eGFR to <35 mL/min per 1.73 m ²	<0.3 mL/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours

KDIGO= kidney disease: improving global outcomes;
eGFR= estimated glomerular filtration rate

level because the seven days or 48 hours might include a prodrome of the acute illness. Algorithms applying strict RIFLE or AKIN criteria might therefore lose sensitivity for detecting community-acquired AKI, which is important as up to two-thirds of AKI cases are community-acquired.¹⁷ Possibilities for selecting a suitable baseline for the assessment of the admission creatinine level include exclusion of baseline creatinine taken within seven days of admission, use of the lowest creatinine level recorded in a defined time prior to admission or use of average creatinine levels over a defined period. The time period in question might be three, six or 12 months prior to admission and changing this may also affect results.²⁰ However, some clarity on this issue has been provided by an important recent study, the first to systematically evaluate the different methods of selecting the baseline creatinine level against a consensus value selected by nephrologists as the gold standard.²¹ The method that performed best was an average of outpatient creatinine values over a period of seven to 365 days prior to hospitalisation as a baseline; these results may now provide standardisation in the approach to assessing relevant increases in the creatinine level. Where no qualifying baseline creatinine level exists, it would be inappropriate to exclude patients from the alert, as they might have a very high creatinine level on admission. The most widely accepted solution is to calculate a 'theoretical' baseline creatinine level by assuming a normal eGFR (usually 75 mL/min/1.73 m²) using the MDRD equation.²²

There are also difficulties and challenges in determining the creatinine levels during the patient's admission i.e. for detection of hospital acquired AKI. Again, the determination of baseline is crucial. For modern alert systems applying RIFLE or AKIN criteria, the baseline would generally be the lowest creatinine level in the preceding seven days or 48 hours, respectively. This approach however might miss the 'creeping creatinine' i.e. a slow rise in the creatinine level during an admission, where there is a >50% rise, but not within a seven day (or 48-hour) period. This is really a criticism of RIFLE and AKIN criteria rather than the alert system, but the detection of creeping creatinine could be achieved by using the same pre-admission baseline level as the denominator for all subsequent creatinine values. This would increase sensitivity but reduce specificity (with respect to RIFLE or AKIN based systems). Such an algorithm could be used in addition to the strict RIFLE and/or AKIN criteria, with an alert being triggered if any of the different AKI criteria were fulfilled.

The level of complexity of currently available alert systems is highly variable. It is likely to reflect the clinical priorities of the respective institutions, as well as technical factors such as the level of information and computer technology (ICT) support available and the suitability of the laboratory and hospital information systems for coding the alert. In general, pathology laboratories generate results (including the serum creatinine level) on their Laboratory Information Management System (LIMS). Code can be applied at this point, or later, after the result has been passed to the hospital information system. The interaction of the LIMS and other hospital information systems is likely to influence the ease and optimal point at which algorithms could be applied. A simple delta check might provide a crude alert system requiring very little ICT resource for set-up or maintenance, and could usually be applied using an existing system. At the other end of the spectrum, the Nottingham AKI alert requires access to more clinical parameters than are provided by LIMS (for example access to clinic codes which would identify a patient as having end-stage renal disease rather than AKI) and so operates within the Trust's patient administration systems. In some centres, a human authorisation step might be required to overcome software limitations and accurately apply current diagnostic criteria. The alert itself may be issued in a passive or active manner. Passive alert systems flag up AKI with a message along with the relevant creatinine level, leaving the clinician user with the responsibility for taking action. Active alert systems might comprise an automatic telephone call to the clinician, as happens in the Derby system for all patients with AKI stage three, or even trigger a patient visit from an AKI outreach team. The choice will depend on both clinical factors and resources, with active alerts likely to require greater financial commitment.

National Health Service (NHS) Trusts seeking to introduce an AKI e-alert system therefore have a number of options with respect to complexity and technical requirements. In time, it is likely that software packages containing ready-made alert systems will become available to hospitals with compatible LIMS or hospital information systems, but there are current options for most hospitals to implement a simple bespoke e-alert system. The choice of alert mechanism might depend on local factors, including budget. However, despite the practical issues that may dictate the development of different systems depending on local capabilities, there remains a strong argument for consistency in the diagnostic criteria used across the UK, as well as in the methodology used to select the baseline creatinine level. Only with such consistency will it be possible to compare trends between different centres or plan robust regional databases or national AKI registries.

CONCLUSIONS

To date, only a few electronic AKI alert systems have been described in the literature. These e-alerts and others in development vary in the diagnostic criteria that are applied and the complexity and mechanisms of issuing the alert. None has yet provided convincing evidence of an improvement in clinical outcome, the ultimate goal, although there are data supporting their effectiveness at altering physician behaviour. However, given the worrying inadequacies in timely detection and management of AKI highlighted by the NCEPOD, it seems likely that any means of improving reliability and timing of detection would be of benefit. This underpins the case for wider implementation of AKI e-alerts and testing of those systems in acute hospitals in the UK.

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The role of biomarkers in the diagnosis of acute kidney injury

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ABSTRACT Efforts over many decades to prevent or treat acute kidney injury (AKI) in high-risk patients have been hampered by the lack of time-sensitive and mechanism-specific markers for AKI to target early interventions. In AKI, serum creatinine (the generally accepted 'standard of care' test for the clinical diagnosis of AKI) may not increase until days after renal tubular injury has begun. Furthermore, because serum creatinine is primarily a functional marker of glomerular filtration, it is not optimally suited to diagnose AKI resulting from renal tubular injury, but rather serves to define the severity of the resulting loss of renal function. Thus, the use of serum creatinine increments for AKI case definition has led to the conduct of numerous unsuccessful clinical trials of putative therapies for AKI in patients with established acute tubular injury and a significantly elevated plasma creatinine; in contrast to the successful use of a wide variety of targeted AKI therapies administered prophylactically or in the period immediately following renal insults in experimental models.

Serum creatinine changes that define AKI by validated classification systems (RIFLE and AKIN), are currently the most useful biomarkers for AKI case identification and staging. Whichever functional criterion is used for AKI case definition (oliguria is another), appropriate differential diagnosis and prognostic assessment can be further improved by the use of traditional and novel biomarkers of renal tubular damage. These markers can be used to differentiate cases of acute tubular necrosis versus prerenal azotemia or chronic kidney disease, potentially leading to more accurate diagnosis, and improved triage and management. In tandem with increasingly timely, sensitive, and specific markers of kidney damage, more time-sensitive functional markers of acute GFR change may further improve the monitoring and diagnostic assessment of AKI in the future.

KEYWORDS Acute kidney injury, biomarker, diagnosis

DECLARATION OF INTERESTS No conflicts of interest declared.

INTRODUCTION

Acute kidney injury (AKI) is a common cause of increasing morbidity, mortality, management complexity and expense in modern healthcare. Over several decades, research to treat evolving AKI in high-risk patients has been hampered by the lack of timely diagnostic biomarkers to target early interventions in clinical trials.¹⁻⁹ A biomarker is defined as 'a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention'.³ In AKI, serum creatinine (the generally accepted 'standard of care' biomarker/lab test for the clinical diagnosis of AKI) is a functional biomarker that may not increase until days after renal tubular injury has begun, when the initiation and extension phases of acute tubular necrosis (ATN) have already occurred and kidney damage has resulted in a severe loss of excretory function.^{1-4, 6-8} Accordingly, because serum creatinine is primarily a functional marker of glomerular filtration, it is not optimally suited to diagnose AKI resulting from renal

tubular injury (damage), but rather serves to define the severity of the resulting loss of renal function. This approach has led to the conduct of numerous unsuccessful clinical trials of putative therapies for AKI in patients with established acute tubular injury and a significantly elevated plasma creatinine, in contrast to the successful use of a wide variety of targeted AKI therapies administered prophylactically or in the period immediately following renal insults in experimental models. Despite many discovery attempts, a reliable marker of early kidney injury in serum or urine has yet to be clinically validated and widely utilised, although significant progress has been made in recent years. Much has been made of the search for a 'renal troponin' to improve early diagnosis and outcomes in AKI, similar to the improvement in the outcomes of acute coronary syndromes (ACS) in recent years. Several candidate AKI biomarkers have been proposed and are in various stages of the development and validation process, although several barriers to widespread clinical implementation remain.

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BIOMARKERS AND AKI DIAGNOSIS

There are multiple potential uses for novel (and traditional) biomarkers in the diagnostic evaluation of AKI. In addition to making an early AKI diagnosis, novel biomarkers may be useful as prognostic biomarkers (defined as 'a baseline patient or disease characteristic that categorises patients by degree of risk for disease occurrence or progression; which informs about the natural history of the disorder in a particular patient in the absence of a therapeutic intervention') to inform the assessment and management of AKI.³ It is well established for example that serum creatinine or estimated glomerular filtration rate (eGFR) are prognostic biomarkers of AKI risk ('disease occurrence') following radiocontrast studies or cardiac surgery and preoperative estimation of renal function is used (along with other clinical variables) for risk assessment and to guide management. Similarly, the degree of elevation of the concentrations of several novel AKI biomarkers seems to be predictive of the severity of AKI (progression to higher stage of AKI, requirement for renal replacement therapy [RRT]). Accordingly, some of these novel biomarkers have apparent utility for the differential diagnostic and prognostic evaluation of AKI. However, in the absence of a proven successful intervention for AKI therapy, no AKI biomarker has been shown to fulfil the criteria required to guide therapy, as a predictive biomarker ('a baseline characteristic that categorises patients by their likelihood for response to a particular treatment'), or as a surrogate biomarker (substitute for a clinical endpoint).³ The vast majority of AKI biomarker studies published to date have been typical of the earlier phases of classical biomarker development:⁹ the earliest were proof-of-concept studies that established with cross-sectional or case-control designs (retrospectively, or in prospective cohorts) that biomarker concentrations differed between AKI cases and controls, consistent with utility to diagnose AKI. Subsequently, validation studies with prospective cohort or nested case control designs have linked AKI biomarker increments to clinical outcomes (AKI progression/stage, RRT, length of stay [LoS], mortality), consistent with utility as prognostic biomarkers. Fewer studies have determined the incremental diagnostic or prognostic value of novel AKI biomarkers in combination with known clinical predictors. Furthermore, it is a weakness of this evolving area of clinical investigation that many studies are single-centre and of inadequate size and the majority only measure one or a few candidate AKI biomarkers.⁹

Many of the most promising early studies of novel AKI biomarkers were conducted in cardiac surgery patients.⁵⁻¹⁵ Neutrophil gelatinase-associated lipocalin (NGAL), which is a 25-kD gelatinase-bound protein that was originally characterised in neutrophils, was among the earliest of these novel AKI biomarkers developed for

clinical use. In a landmark study, Mishra and colleagues found in a clinical trial of 71 children undergoing cardiac surgery that urinary NGAL increased within two hours of cardiopulmonary bypass to a level of greater than 50 µg/L in all 20 children who had an increase in serum creatinine of more than 50% (RIFLE-Risk), and in only one of the 51 children who did not meet the definition of AKI.¹⁰ Although the sensitivity and specificity to predict this level of kidney injury of 100% and 98%, respectively, is impressive, giving an area under the receiver operating characteristic (ROC) curve of 0.999, the clinical relevance of these urinary NGAL elevations was less certain, as none of the children manifesting this change in kidney function progressed to severe AKI or required RRT. Of course, even lower stages of AKI have been shown to result in acute distant organ injury, as well as later chronic kidney disease (CKD). Certainly, based upon early evidence and subsequent studies, commercial development of this biomarker continued, along with several others. Taken together, the results to date concerning the performance of plasma and/or urine NGAL to predict AKI in adults following cardiac surgery or in other patient populations have not been as impressive as the initial study by Mishra and colleagues.^{5-10,13,14} In particular, the results of the first large prospective multicentre study of AKI biomarkers in cardiac surgery were relatively disappointing.¹¹⁻¹⁴ The Translational Research Investigating Biomarker Endpoints in AKI study (TRIBE-AKI) prospectively studied serial biomarker profiles in 1,219 adults and 311 children undergoing cardiac surgery in six adult and three paediatric centres.¹¹⁻¹⁴ The investigators found that preoperative serum cystatin C concentrations were superior to serum creatinine and associated eGFR formulas for the prediction of perioperative AKI, with better performance in adults than in children.¹¹ Preoperative urinary albumin/creatinine ratios were also predictive of perioperative AKI in adults, but not in children.¹² In adults, post-operative urine interleukin-18 (IL-18, another novel AKI biomarker) and plasma NGAL levels peaked within six hours of intensive care unit (ICU) arrival, whereas serum creatinine increases did not occur before 24-72 hours.¹³ A clinical prediction model for AKI (including preoperative and operative variables) had an area under curve (AUC) of 0.69 for the diagnosis of AKI; this was improved to 0.76 by urine IL-18 and 0.75 by plasma NGAL. In this study, higher urine IL-18 and plasma NGAL levels were also associated with longer lengths of stay in ICU and hospital and higher risk of dialysis or death, but urine NGAL was not predictive of AKI or associated with adverse clinical outcomes. In the paediatric substudy, urine NGAL and urine IL-18, but not plasma NGAL, performed similarly to plasma NGAL and urine IL-18 in the adult study for the prediction of AKI and adverse clinical outcomes.¹⁴ Finally, these investigators found that higher levels of urine IL-18, urine albumin/creatinine ratio, or plasma

NGAL at the time of post-operative AKI diagnosis (by serum creatinine elevation to AKIN stage 1) in 380 patients were predictive of AKI progression to a higher stage (AKIN 2–3, in 45 patients), providing improved risk classification over a clinical model that included serum creatinine,¹⁵ confirming some prior single-centre findings in this setting.¹⁶

Results of prospective, single-centre studies evaluating the performance of novel AKI biomarkers in critically ill ICU patients have been mixed, with a generally moderate performance^{5–9, 17–22} and there has not been a large, multicentre prospective study in this setting. The most consistent performance of AKI biomarkers for the prediction of AKI and associated adverse clinical outcomes has been in the emergency room studies by Nickolas and colleagues.^{23,24} These investigators evaluated the sensitivity and specificity of a single emergency department measurement of urinary NGAL for diagnosing AKI.²³ Based on the premise that a single serum creatinine measurement cannot distinguish AKI from CKD or prerenal azotemia, the authors sought to test the sensitivity and specificity of a single measurement of urinary NGAL and other selected urinary proteins to detect AKI in a spectrum of patients. This prospective cohort study was conducted in the emergency department of a single urban medical center. A total of 635 patients were admitted to the hospital with AKI, prerenal azotemia, CKD, or normal kidney function. The diagnosis of AKI was based on the RIFLE criteria and assigned by researchers who were blinded to experimental measurements. Urinary NGAL, N-acetyl-beta-d-glucosaminidase (NAG), alpha 1-microglobulin and alpha 1-acid glycoprotein were measured along with serum creatinine, but only serum creatinine was available to treating physicians. Patients with AKI had a significantly elevated mean urinary NGAL level compared with the other kidney function groups (416 µg/g creatinine [standard deviation, 387]; $p=0.001$). At a cut-off value of 130 µg/g creatinine, sensitivity and specificity of NGAL for detecting AKI were 0.9 (95% confidence interval [CI], 0.73 to 0.98) and 0.995 (CI, 0.99 to 1.00), respectively, and positive and negative likelihood ratios were 181.5 (CI, 58.33 to 564.71) and 0.1 (CI, 0.03 to 0.29); these values were superior to those for NAG, alpha 1-microglobulin and alpha 1-acid glycoprotein, fractional excretion of sodium and serum creatinine. In multiple logistic regression, urinary NGAL level was highly predictive of clinical outcomes, including nephrology consultation, dialysis and admission to the ICU (odds ratio [OR] 24.71 [CI, 7.69 to 79.42]). The authors concluded that a single measurement of urinary NGAL helps to distinguish AKI from normal renal function, prerenal azotemia and CKD and predicts poor inpatient outcomes. Limitations of this study included the lack of a gold standard (such as kidney biopsy) to precisely establish a definitive diagnosis, which is a common

deficiency in AKI studies, in part overcome by blinded adjudication in this study; the fact that a single serum creatinine value >2.5 mg/dL also performed well as a predictor of clinical outcomes (though inferior to NGAL); and the non-specific elevation of urine NGAL in a variety of chronic renal diseases that could lead to adverse outcomes in the absence of AKI. Nonetheless, these data suggested the need for further evaluation of this test in the emergency room setting, which was recently published by these authors.²⁴ In a three-centre study of 1,635 unselected patients, concentrations of five biomarkers (NGAL, IL-18, cystatin C, kidney injury molecule-1 [KIM-1] and liver-type fatty acid binding protein) were obtained from urine samples taken at the time of admission from the emergency department to hospital. Urinary concentrations of all of these urinary biomarkers were elevated in intrinsic AKI (defined by blinded adjudication), compared to those with other forms of renal impairment (prerenal AKI, CKD) or those with normal kidney function, with urinary NGAL performing best (AUC 0.81) for the diagnosis of intrinsic AKI. Urinary NGAL and KIM-1 performed best for prediction of a clinical adverse composite outcome of RRT or death, improving the performance of a model that included serum creatinine at the time of enrolment. Finally, they confirmed that the subgroup with elevations of both serum creatinine and either urinary NGAL or urinary KIM-1 were at the highest risk for adverse clinical outcomes, compared to those with elevations of serum creatinine, urinary NGAL, or urinary KIM-1 alone (intermediate risk), or those with creatinine, NGAL, or KIM-1 levels all below a 75th percentile cut-off level (low risk). This latter phenomenon is similar to the findings of Haase and colleagues, who pooled data from ten studies of NGAL in 2,322 patients and found a graded relationship between clinical risk and elevation of biomarkers of kidney dysfunction (serum creatinine) and kidney damage (NGAL), with the highest risk in those with biomarker evidence of both AKI (defined by serum creatinine elevation) and kidney damage (NGAL elevation).²⁵ The potential combined use of serum creatinine with biomarkers of kidney damage to differentiate between causes of renal dysfunction (prerenal azotemia vs ATN vs CKD vs other) is further supported by several recent, single-centre studies, which have also consistently found that the higher levels of damage biomarkers are predictive of AKI progression to higher stages, requirement of RRT and other adverse clinical outcomes.^{15,16,21,26–28} In contrast, renal recovery will probably be predictable in future using other emerging biomarkers, including prompt declines (vs persistent elevation) of biomarkers of injury.^{29,30} In addition to increasing the precision of diagnostic assessment of AKI cases, the potential to improve the triage and management of such cases is clear, although this has yet to be proven by biomarker-guided clinical trials. It is important to note that the use of traditional semi-quantitative microscopic

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analysis of urinary sediment (scoring granular cast and renal tubular epithelial cell counts) has also been shown to perform well in differential diagnostic and prognostic assessments,^{31–34} comparable to novel AKI biomarkers in the most recent study.²⁸ Accordingly, our ability to distinguish reversible, prerenal AKI from other causes, including severe tubular damage with ATN (but perhaps not milder, rapidly reversible tubular injury),²⁷ is growing. Such accurate differential diagnostic and prognostic information is very valuable in the provision of evidence-based, personalised care to patients at risk of AKI. As newer, more sensitive and dynamic methods of monitoring GFR changes are developed, kidney damage biomarkers will facilitate the interpretation of the cause and prognosis of acute GFR loss. However, rather than regarding GFR measurement and changes as the gold standard to diagnose kidney injury, it should be recognised that acute GFR loss ('AKI') of similar severity can occur in the absence of kidney damage (prerenal azotemia) or as a very late marker of kidney damage (severe ATN), and optimal management strategies are likely to incorporate complementary use of these evolving indices of kidney function and damage.³⁵

CONCLUSION

Taken together, the available data suggest that the clinical use of novel biomarkers for early diagnosis of AKI is likely to remain limited until further prospective multicentre studies demonstrate utility. Similarly, the results of ongoing studies to clinically validate the results of pre-clinical data that suggest utility of a panel of biomarkers for the early diagnosis of nephrotoxic AKI are eagerly awaited, since the use of these tools to decrease harm rather than for initiation of specific therapy is another worthwhile concept. Currently, the most demonstrable utility of novel AKI biomarkers appears to be in differential diagnosis of AKI cases, as well as the prognostic evaluation of such cases. Although such information has the obvious potential for clinical utility by changing patient management, which is the next step in the clinical development and implementation of novel biomarkers, this is unproven in prospective trials using such information to guide assessment and change management (none of the above studies used real-time AKI biomarker measurements in patient care). Similarly, prospective trials in patients with increased renal risk profiles will be required to prove that such biomarker-guided interventions improve clinical outcomes and are cost-effective. Finally, only the pairing of novel AKI biomarkers that identify appropriate AKI cases with a therapeutic intervention that ameliorates AKI and its clinical outcomes can ultimately fulfil the promise suggested by the 'renal troponin' concept. In this regard, it should be noted that none of the definitions of AKI currently in use, based on fractional or absolute

increments of serum creatinine or urine output, are accepted by regulatory agencies as endpoints for the approval of drugs to prevent or treat AKI. For example, although many such interventions are widely adopted based upon the results of small clinical studies showing benefit in preventing radiocontrast nephropathy with previously approved medicines such as N-acetylcysteine or sodium bicarbonate, new pharmacotherapies would not be approved on this basis. Unfortunately, trials of drugs using clinical endpoints such as dialysis-free survival, most notable in the case of atrial natriuretic peptide for ATN therapy, have been unsuccessful. Accordingly, despite a wealth of evidence documenting the association of graded serum creatinine increases with decreased survival in several settings, it remains unproven that prevention of such creatinine increases by any intervention results in improved outcomes. Although the majority of clinical studies seeking to validate the performance of candidate AKI biomarkers for the prediction and risk stratification of AKI use creatinine-defined AKI as the clinical gold standard, this does not reflect the shortcomings of AKI definitions based on serum creatinine.³⁶ The real gold standard for the AKI biomarkers is whether or not they can be used to define and risk-stratify AKI and related complications, facilitating early diagnosis and inter-ventions to improve clinical outcomes. If novel AKI biomarkers can be proven superior for these purposes, they may even replace serum creatinine (or cystatin) changes and urine output as our primary clinical tools to diagnose AKI and monitor response to therapy. Currently however, in those countries where novel AKI biomarkers are available for clinical use, their function to inform assessments of differential diagnosis and prognostic assessment and associated management decisions (triage, RRT initiation, etc) is probably where initial adoption is most appropriate. For example, excessive volume challenge might be avoided in oliguric patients in whom extreme elevation of kidney damage biomarkers is found, whether or not serum creatinine is also increased. Where available, a combination of functional and damage marker assessments can define the absence of kidney injury (normal markers), 'subclinical' kidney damage with preserved function (e.g. early aminoglycoside toxicity), promptly reversible functional AKI without detectable damage ('prerenal azotaemia'), or severe AKI with evidence of kidney damage combined with loss of function (ATN). Even in this setting, the determination of appropriate reference ranges and cut-off levels of novel biomarkers for the diagnosis of AKI in patient subgroups (gender, age, presence of sepsis, etc) is work in progress.^{22,27,37} It is also unlikely that a single biomarker will be able to provide an accurate diagnostic assessment of all aspects of a complex, multifactorial process such as AKI and a panel or population-specific selection of biomarkers may be necessary for optimal performance in different clinical settings. However, this is a more

realistic short-term goal than the successful pairing of novel AKI therapies (with none yet proven) with early predictive biomarkers of AKI; a paradigm that has been the driving force behind the development of these biomarkers for several years.

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SESSION I – WHAT IS THE ROLE OF FLUID THERAPY IN AKI?

THE ECONOMIC IMPACT OF ACUTE KIDNEY INJURY

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Objective: To estimate the human and financial impact of acute kidney injury (AKI) in the NHS in England.

Methods: Hospital Episode Statistics (HES) data for the English NHS were examined to identify all hospital admissions in adults (aged ≥ 18) with a recorded diagnosis of AKI, (International Classification of Diseases ICD-10 codes N18 or N280) during 2010–11. Day cases were excluded. The findings were compared with laboratory data on the prevalence of AKI by AKIN stage in admissions at East Kent Hospitals University NHS Foundation Trust during a six-month period in 2009. Regression analyses were conducted to estimate the impact of AKI on length of stay and resource use. Costs were estimated for acute care and for long-term renal replacement therapy (RRT) after AKI.

Results: Acute kidney injury was recorded in 2.4% of admissions in HES. Multivariate regression analysis indicated that patients with a recorded AKI diagnosis stayed in hospital 10.54 (95% CI 10.22–10.86) days longer than those without AKI. A total of 18.0% of critical care bed days occurred in people with a record of AKI. In 28.5% of AKI admissions, the patient died before discharge

In data from East Kent, AKI prevalence was very much higher. After adjusting for age and gender to match the HES population, AKI prevalence was estimated at 13.2% (of admissions). AKI diagnosis increased both length of stay and critical care use, but to a lesser degree than in those with a recorded AKI diagnosis in HES.

The cost of acute admissions for AKI in 2010–11 is estimated at £424–£769 million. The cost of long-term RRT after AKI is estimated at more than £200 million a year.

Conclusion: Acute kidney injury entails a heavy human and financial burden. It would appear that AKI may be substantially under-recorded in hospital records and national datasets.

PREVENTING AKI IN SURGICAL PATIENTS: DOES IT MATTER WHAT TYPE OF FLUID IS USED?

Professor Dileep Lobo, HPB Surgeon, University of Nottingham

Traditional teaching has dictated that the surgical patient is at particular risk of acute kidney injury if underhydrated and it was thought that excessive volumes of intravenous fluids in the perioperative period helped protect the kidney and reduce the risk of acute kidney injury (AKI). Acute kidney injury secondary to hypovolaemia and hypotension is associated with oliguria, defined as a urine output <0.5 ml/kg/h. Oliguria must not be looked at in isolation as it can be a physiological response to uncomplicated surgery in the first 48 hours to conserve salt and water in an attempt to maintain intravascular volume. The key clinical question is whether or not the oliguria is secondary to significant intravascular hypovolaemia requiring treatment. Invasive monitoring may be required intra-operatively to guide optimal treatment. A failure to recognise this physiological response and incorrectly consider the oliguria in isolation as indicating hypovolaemia may result in excessive administration of IV fluid (commonly 0.9% sodium chloride) that not only expands the blood volume excessively but also over-expands the interstitial fluid volume, causing oedema and weight gain. The metabolic response to surgery impairs the patient's ability to excrete the additional salt and water fluid load, making interstitial oedema worse, compromising organ function and increasing the risk of morbidity and mortality.

The KDIGO working group has suggested that isotonic crystalloids (0.9% sodium chloride) rather than colloids (albumin, HES) should be used during initial resuscitation but that colloids may still have a role in patients requiring additional fluid. It is intuitive to believe that balanced crystalloid solutions such as Hartmann's (or Ringer's lactate) are less likely to cause acid-base disturbances than 0.9% sodium chloride but outcome studies in this area were lacking until relatively recently. The 0.9% sodium chloride solutions are excreted much more slowly in comparison to solutions with a lower sodium and chloride content and result in prolonged dilution of the haematocrit and albumin. Retention of fluid can result in weight gain which persists in comparison with solutions of more balanced electrolyte composition, which generally are diuresed more rapidly. While animal studies have demonstrated that hyperchloraemia can result in renal arteriolar constriction, reduced renal blood flow and decreased glomerular filtration rate, this phenomenon was until recently not demonstrated in humans. A recent study using magnetic resonance

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imaging has shown that even in healthy human volunteers, the hyperchloraemic acidosis caused by 0.9% sodium chloride infusion is associated with renal oedema and a fall in renal blood flow velocity and cortical tissue perfusion when compared with a balanced crystalloid. These changes may be explained by the fact that high chloride content of the glomerular filtrate results in decreased proximal chloride resorption and an increase in the delivery of chloride to the distal nephron. An increased concentration of chloride in the renal tubule causes entry of chloride into the macula densa, depolarisation of the basement membrane and release of adenosine, which in turn increases afferent arteriolar resistance and decreases GFR. Another recent study has

shown that decreasing the amount of chloride delivered to critically ill patients resulted in a lower increase of the mean serum creatinine concentration, a decrease in the incidence of injury and failure class of RIFLE-defined AKI and the need for renal replacement therapy (RRT). However, there were no differences in hospital mortality, hospital or ICU length of stay, or need for RRT after hospital discharge. All these studies show that 0.9% sodium chloride is neither normal nor physiological and that it is associated with several adverse consequences, especially on renal function. Hence, balanced crystalloids should be preferred to 0.9% sodium chloride.

SESSION 2 – WHAT IS THE ROLE OF FLUID THERAPY IN AKI?

NUTRITIONAL ASPECTS OF IV FLUID THERAPY

Professor J Powell-Tuck, Emeritus Professor of Clinical Nutrition, Barts, and the London School of Medicine and Dentistry

Fasting results in a shift of sodium into, and potassium out of, the cells. There is a loss of total body potassium, with a relative maintenance and retention of total body sodium.^{1,2} The extracellular space is expanded relative to the intracellular.³ Saline infusions are poorly tolerated. Refeeding results in a reversal of these processes, but as energy intake increases so sodium, potassium, phosphate and magnesium shifts can result in rapid and dangerous changes in plasma concentrations of these electrolytes, as well as intravascular expansion, oedema and heart failure – the so-called ‘refeeding syndrome’.⁴

Water soluble vitamins become depleted during fasting and may play a role among others in the mitochondrial energy dependent processes linked to cellular pump function.⁵ Sudden increase in energy provision without adequate vitamin replacement can result in acute deficiency and lactic acidosis.⁶

Management of critical illness seeks to prevent multiple organ, including renal, failure by maintaining organ membrane function and maintaining mitochondrial function. Not only is there interest in the place of providing safe, utilisable amounts of energy and protein but also in the use of specific nutrients used in pharmacological dosage such as glutamine and selenium. Glutamine may function through mitochondrial function and preservation of glutathione while selenium may preserve membrane integrity by providing antioxidant protection.

Nutrition thus has a profound effect on cell membrane integrity and pump function; as such it plays a major role in determining distribution of intracellular electrolytes and water.

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WHAT ARE THE CONSEQUENCES OF TOO MUCH FLUID?

Professor Ravi Mehta, Division of Nephrology, UCSD, USA

Fluid management in hospitalised patients is a complex process as aggressive fluid resuscitation is commonly utilized for initial hemodynamic support and fluid administration often contributes to fluid retention, particularly when there is impaired kidney function.¹ In order to recognise the consequences of fluid accumulation it is necessary to define how much is ‘too much’.² In previous studies, a cut-off of 10% or more has been associated with decreased survival.^{2–4} There are several consequences of fluid accumulation such as peripheral, tissue and organ edema, respiratory failure, hypertension, and increased cardiac demand, prolonged duration of mechanical ventilation as well as poor wound healing and delayed bowel recovery in the perioperative period.⁵ It is now fairly well established that the extent and duration of fluid overload are incrementally associated with a higher risk for mortality, morbidity and increased resource utilization. It is uncertain whether fluid retention

is simply a marker of the severity of organ failure or a mediator of events. Particularly it is unclear whether fluid accumulation contributes to the development and maintenance of acute kidney injury. The mechanisms by which fluid overload could influence outcomes have never been clearly demonstrated. Recent insights of the presence of the endothelial glycocalyx⁶ as a potential target has provided new information on potential mechanisms for the effects of fluid retention. However, there are considerable gaps in our knowledge and there is a great need for basic and clinical research to enhance our understanding of the effects of fluid therapy to improve patient management and outcomes.

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SESSION 3 – WHAT IS THE ROLE OF E-ALERTS IN AKI?

ELECTRONIC ALERTS FOR AKI – CAN THEY MAKE A DIFFERENCE?

THE DERBY EXPERIENCE

Dr Nicholas M Selby, Consultant Nephrologist, Royal Derby Hospital, Derby

Acute kidney injury (AKI) is common in hospitalised patients and is associated with poor outcomes. Patients with AKI are cared for by all acute specialities; delays in recognising AKI can result in variable standards of care. The implementation of electronic alert systems to aid early recognition of AKI is one strategy that may improve this.

To that end, we designed a real time, hospital-wide, electronic reporting system based on Acute Kidney Injury Network (AKIN) criteria that has been operational in clinical practice since April 2010. This system has been validated (false positive rate 1.7%, false negative rate 0.2%) and also allows prospective data collection on the incidence and outcomes of AKI.

Initial results demonstrated in-hospital mortality rates of 23.8% that increased with more severe AKI (16.1% for AKI stage 1 versus 36.1% in stage 3, $p < 0.001$). More severe AKI was associated with longer length of hospital stay (eight days [IQR 13] for stage 1 versus 11 days [IQR 16] for stage 3, $p < 0.001$) and reduced chance of renal recovery (80.0% in stage 1 AKI versus 58.8% in stage 3, $p < 0.001$). The utility of the AKIN criteria was reduced in those with pre-existing chronic kidney disease.

We have also evaluated the impact that the introduction of electronic alerts (alongside other quality improvement measures) has had on patient outcomes. Over an 18 month period, there was a progressive reduction in 30-day mortality rates, falling from 23.7% to 20.8% ($p = 0.022$). After accounting for the effects of age, co-morbidity, severity of AKI, baseline renal function and admission type (elective or non-elective) this improvement in survival was maintained. We also observed a trend towards a progressive reduction in the proportion of patients progressing to AKI stage 3. This was accompanied by audit data that suggested some improvements in standards of basic AKI management.

THE NOTTINGHAM EXPERIENCE

Dr Mark Devonald, Consultant Nephrologist, Nottingham University Hospitals NHS Trust and Honorary Consultant Lecturer, School of Clinical Sciences, Nottingham

Nottingham University Hospitals (NUH) is one of the largest NHS trusts in the UK. To improve identification and management of acute kidney injury (AKI), we developed an electronic alert system. Algorithms were designed to compare every inpatient serum creatinine with previous values for each patient. An alert accompanies the elevated creatinine result if AKIN or RIFLE criteria for AKI are fulfilled. AKI stage is reported and the clinician is referred to the Trust's AKI guidelines on the intranet. Where there is discrepancy between AKIN and RIFLE staging, the higher stage is reported. Reference creatinine, for comparison of the first inpatient result, is taken to be the lowest creatinine from 7–365 days prior to admission. Where no reference creatinine

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is available, a theoretical value is calculated from the MDRD equation, assuming eGFR of 75 mL/min.

The Nottingham AKI alert is fully automated, requiring no input or calculations by laboratory staff or clinicians. It works real time, with the alert accompanying the qualifying creatinine result. A prospective database is generated automatically which includes some demographic data and outcomes, such as in-hospital mortality and length of stay.

The alert system has been in operation since April 2011, but was tested in pilot form for a year prior to that. In the first 12 months of operation, 13,314 of 165,767 admissions (8%) generated at least one alert. A total of 73.3% of alerts were stage 1, 16.9% stage 2 and 9.8% stage 3. In-hospital mortality was 8%, 19% and 25% for stage 1, 2 and 3 AKI respectively.

The Nottingham AKI alert facilitates early detection of AKI in this large acute NHS Trust. It remains to be seen whether this will result in improved outcomes, which is the subject of ongoing research.

E-ALERTS – IS A NATIONAL APPROACH POSSIBLE?: A BIOCHEMIST'S PERSPECTIVE

Dr Rick Jones, Senior Lecturer, Yorkshire Centre of Health Informatics, University of Leeds

Though a single brand, the NHS is notoriously fragmented. Patient pathways traverse many organisations and despite many years of effort the barriers to data exchange are

still a major hindrance to holistic care. Pathology services almost all organisations involved in delivering care but historically has been located in the acute sector servicing GPs on an individual, bilateral basis. Furthermore, the IT landscape of primary care is itself fragmented with many thousands of individual databases servicing the 8,000 plus practices. Thus, it is rare for complete records of biochemical tests on individual patients to be held in coherent record sets. In identifying the onset of AKI from biochemical data, the need to identify trends and time-based changes is essential.

This talk will explore the current organisational, technical and scientific barriers to producing such coherent records and analysis tools but will demonstrate how a national service could be provided using existing technologies at affordable cost.

Further reading

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SESSION 4 – WHAT IS THE ROLE OF BIOMARKERS IN AKI?

THE ROLE OF BIOMARKERS IN THE DIAGNOSIS OF ACUTE KIDNEY INJURY

Professor Patrick Murray, Intensivist, Mater Misericordiae University Hospital, Dublin

Efforts over many decades to prevent or treat acute kidney injury (AKI) in high-risk patients have been hampered by the lack of time-sensitive and mechanism-specific markers for AKI to target early interventions.¹ In AKI, serum creatinine (the generally accepted 'standard of care' test for the clinical diagnosis of AKI) may not increase until days after renal tubular injury has begun.² Furthermore, because serum creatinine is primarily a functional marker of glomerular filtration, it is not optimally suited to diagnose AKI resulting from renal tubular injury, but rather serves to define the severity of the resulting loss of renal function. Thus, the use of serum creatinine increments for AKI case definition has led to

the conduct of numerous unsuccessful clinical trials of putative therapies for AKI in patients with established acute tubular injury and a significantly elevated plasma creatinine; in contrast to the successful use of a wide variety of targeted AKI therapies administered prophylactically or in the period immediately following renal insults in experimental models.¹

Serum creatinine changes that define AKI by validated classification systems (RIFLE and AKIN), are currently the most useful biomarkers for AKI case identification and staging.² Whichever functional criterion is used for AKI case definition (oliguria is another), appropriate differential diagnosis and prognostic assessment can be further improved by the use of traditional and novel biomarkers of renal tubular damage.^{3–6} These markers can be used to differentiate cases of acute tubular necrosis versus prerenal azotemia or chronic kidney disease, potentially leading to more accurate diagnosis, and improved triage

and management. In tandem with increasingly timely, sensitive, and specific markers of kidney damage, more time-sensitive markers of acute functional markers of GFR change may further improve the monitoring and diagnostic assessment of AKI in the future.

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DEVELOPING A BIOMARKER PIPELINE FOR AKI

Professor Rosamonde Banks, Professor of Biomedical Proteomics, Clinical & Biomedical Proteomics Group, Cancer Research UK Centre, Leeds Institute of Molecular Medicine, St James's University Hospital, Leeds

The need for new biomarkers to enable earlier detection of acute kidney injury (AKI) and to provide information about the underlying pathophysiology and prognosis is well acknowledged. With recent developments in genomic, transcriptomic and proteomic technologies, the numbers of studies focussing on novel biomarker discovery in all areas of medicine is increasing and potential novel biomarkers are being identified. However if the clinical potential of these is to be realised, it is essential that we review and start to put in place the various elements of the 'biomarker pipeline' to ensure a timely evaluation and evidence-based progression of such biomarkers into clinical practice. The various aspects of such a pipeline will be discussed in the context of AKI ranging from initial discovery study design, availability of high quality sample banks, assay development and validation, through to randomised controlled trials and health economic studies. Parallel studies examining the underlying biological mechanisms relating to emerging markers will not only provide further confidence in the rationale for their use but also may indicate opportunities for targeting specific pathways therapeutically. Many elements of this will be illustrated using neutrophil gelatinase-associated lipocalin

(NGAL) as an example and an ongoing NIHR-funded Biomarker Evaluation Programme which could form a template for AKI biomarker studies will be described.

Further reading

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WHERE ARE THE HORIZONS FOR BIOMARKERS

Dr Edmund Lamb, Consultant Clinical Scientist (Biochemistry) and Head of Clinical Biochemistry, East Kent Hospitals University NHS Foundation Trust

A biomarker has been defined as: 'a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathological processes, or pharmacological responses to a therapeutic intervention'.¹ As such, it encompasses old friends including serum creatinine and cystatin C and urinary albumin/total protein. But by 'biomarkers' we generally infer 'second generation' biomarkers; largely those uncovered as a result of a proteomic discovery process.² The number of biomarkers and the literature describing their application is expansive. Biomarkers may be used to diagnose, to predict prognosis and to predict or measure response to therapy. There is a need to focus on which application we are interested in and which marker we wish to use. Markers should be characterised and assays designed that detect a single defined protein, with transferable standardisation between manufacturers. Markers may be measured in blood or urine, at the point of care or in central laboratories, and their relative merits should be considered (practicality, stability, timing, correction for urinary dilution or not). To facilitate appropriate cut-points we need to understand the normal biological variation of biomarkers, including in people at risk of acute kidney injury (AKI), and factors that might influence these cut-points (age, gender, co-morbidity e.g. diabetes or UTI). Large studies of representative groups of patients

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reflecting the needs of our healthcare system should be undertaken including head-to-head comparisons of the diagnostic accuracy of biomarkers. Second generation markers should be directly compared to older (and cheaper) markers that are often overlooked (e.g. N-acetyl- β -D-glucosaminidase, α 1-microglobulin). Studies should include health economic analysis of biomarker impact and pressure should be brought to bear on diagnostic companies to reduce assay costs. Biomarkers have the potential to revolutionise nephrology practice. But it is essential that the basic science and commercial imperatives aren't allowed to run ahead of clinical science. It is noteworthy that nearly 30 years after initial data describing cystatin C as a GFR

marker,³ hardly any UK laboratories currently offer it as a routine test. We need to make sure that the Emperor really has got some clothes before we look to the horizons.

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SESSION 5 – AKI: THE PATIENT'S JOURNEY

AKI IN THE COMMUNITY

Dr Berenice Lopez, Consultant Chemical Pathologist (Metabolic Medicine), Harrogate District Foundation Trust

Acute kidney injury (AKI) is associated with significant morbidity, mortality and resource utilisation¹ and hospital-acquired AKI (h-AKI) is often preventable and avoidable.² However, little is known about community-acquired AKI (c-AKI).

An audit was conducted to examine the care of adults with c-AKI as defined by KDIGO.³ Patients admitted to Harrogate Hospital with AKI from July to December 2011 were identified using the laboratory information system (LIMS) but excluded if medical records were lost or admission was for palliation. C-AKI occurred in 23 (18.1%) patients and 15 patients (nine female, six male) were included. Patients had a mean age of 71.3 (44–89) years and three (2–6) risk factors for AKI.⁴ Using LIMS, previous episodes of c-AKI in these patients were identified and a total of 30 episodes of c-AKI were evaluated (15 stage 1 AKI, three stage 2 AKI, 12 stage 3 AKI).

Patients were admitted in 26 (86.7%) cases; three episodes of c-AKI stage 1 were unrecognised and one was referred. Hyperkalaemia (>6.0 mmol/L) complicated six admissions in association with potassium retaining drugs. Non recovery of baseline renal function post-AKI occurred in 13 (43.3%) cases – five new CKD (stages 1–4), eight progression of known CKD (stages 3A–5) – and seven patients died within 47.6 (9–139) days from admission.

GP input occurred in 24 (80%) cases prior to admission – mean 2.0 contacts (1–5) within 7.5 days (range 1–26) of admission. Fluid status, blood pressure, abdominal examination and urinalysis were recorded in one (4.2%), 20 (83.3%), nine (37.5%) and seven (29.2%) consultations respectively. Medications were reviewed in one case. Renal function was checked in 13 (54.2%) prompting

admission in nine (69.2%) cases. The commonest causes of c-AKI were hypovolaemia, sepsis and nephrotoxic drugs.

GP recognition and referral of c-AKI 2 and 3 was appropriate but cases of c-AKI 1 were missed. Improved risk assessment, renal function monitoring and targeting of modifiable risk factors including timely withdrawal of relevant drugs may have avoided or ameliorated the severity of c-AKI in 14 (58.3%) cases. However, unlike h-AKI, prevention and recognition of c-AKI is influenced by patient health seeking behaviour and improved clinician and patient awareness is required.

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ACUTE KIDNEY INJURY AT THE FRONT DOOR

Dr Sian Finlay, Acute Medical Unit, Dumfries & Galloway Royal Infirmary, Dumfries

Acute kidney injury (AKI) commonly occurs in hospitalised patients, but its true prevalence has been difficult to capture because of the lack of a universal definition. In recent years, new definitions have been proposed which have allowed a more universal approach,¹ and it has become apparent that AKI occurs not only in critical illness, but in 18–22% of the general hospital population.² There is also evidence that even relatively small rises in serum creatinine are associated with

adverse patient outcomes, including increases in length of hospital stay, mortality, and costs.³ AKI is not simply a marker of severe illness, but is an independent risk factor for mortality. Mortality estimates range from 10% in patients with uncomplicated AKI to 80% in those with multi-organ failure. In addition, an episode of AKI can have long-term consequences, with the severity and duration of an episode predicting the risk of progression to chronic kidney disease.⁴

It is important therefore that patients with AKI, or those at risk of developing it, are recognised at the earliest opportunity following hospital admission, and that early management is directed at minimising further injury or complications. Many patients respond to simple interventions which can be delivered by non-specialists. Published data suggest that up to 30% of AKI cases may be preventable with measures such as correction of hypovolaemia and cessation of nephrotoxic medications during intercurrent illness.⁵ Unfortunately there is evidence that this is not done reliably in UK hospitals. In 2009 the NCEPOD report identified widespread deficiencies in the recognition and management of AKI.⁶ Acute medicine is the fastest growing specialty in the UK, with acute medical units representing the hospital entry point for a large number of unscheduled admissions, many of whom are elderly and have multiple co-morbidities; it is clear that prevention and management of AKI in this setting is essential in order to address the deficiencies described in the NCEPOD report. Development of a robust risk assessment tool for AKI would be an important step in the right direction.

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THE PATIENT'S PERSPECTIVE

Mr Michael Wise, AKI survivor, specialist in restorative dentistry and oral surgery and visiting professor UCL

The experiences of Michael Wise, an AKI survivor will be described. They will be presented as a timeline commencing in 2009 when he was very fit and healthy, followed by sudden critical illness as a result of Strep B septicaemia leading to toxic shock and multi-organ failure, intensive care, dialysis, living donor kidney transplant in 2010 and recovery to today.

Michael has very vivid memories of his experiences and hopes that by presenting them he may assist clinicians in better understanding a patient's experience and thereby help others. As a patient he considers it essential that the clinician really listens to the patient. Having 'a foot in both camps' by spending his professional life as a clinician and then becoming a patient, he may have particularly valuable insight.

The best way to view a summary of this presentation is to go to the London Acute Kidney Network website and click on patients. There is a video presentation which is similar to the presentation which will be given at the meeting. Available from: <http://www.londonaki.net/patients>

SHORT, MEDIUM AND LONG TERM OUTCOMES OF PATIENTS WITH ACUTE AND ACUTE ON CHRONIC KIDNEY INJURY

Professor Chris Isles, Consultant Physician and Nephrologist, Dumfries & Galloway Infirmary, Dumfries

Acute kidney injury (AKI) requiring renal replacement therapy (RRT) is common, has multiple causes and continues to be associated with a hospital mortality of around 50% despite recent advances in therapy. The aims of our study were to determine the influence of ventilation as a marker of illness severity and underlying chronic kidney disease (CKD) as a marker of co-morbidity on short (<90 days), medium (one year) and long-term (five year) outcomes.

We conducted a prospective study of all patients requiring RRT for AKI in South West Scotland between 1 January 1994 and 31 December 2005. Survival of patients who were and were not ventilated and of those with and without underlying CKD was compared by odds ratio (OR) derived using a logistic regression model after adjusting for age and sex.

A total of 396 patients with AKI received RRT by haemodialysis or haemofiltration during the study period. Their average age was 69 (range 17–94) years; 236 (59%) were male, 176 (44%) were ventilated and 98 (25%) had underlying CKD. Contrasting patterns of survival emerged. Ventilation was associated with a significantly lower 90-day survival (OR 2.10, 95% confidence interval [CI] 1.34, 3.29) whereas the presence of underlying CKD

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did not predict such early outcome (OR 1.49, 95% CI, 0.89, 2.50). Survival curves for ventilation began to converge while those with patients with underlying CKD started to diverge at one year. At five years the predictive power for ventilation during the acute illness was no longer apparent (OR 1.51, 95% CI 0.89, 2.57) while the adverse effect of underlying CKD was statistically highly significant (OR 5.28, 95% CI 2.14, 13.1).

Our data show that in an unselected cohort of patients with AKI requiring RRT, patients with a life-threatening acute illness e.g. multi-organ failure due to pneumonia, may stand to do better in the long term provided they survive the acute event, than those who have chronic co-morbidity such as underlying CKD.

SESSION 7 – THAT'S CHALLENGING

CONTRAST-INDUCED ACUTE KIDNEY INJURY

Dr Mark Downes, Consultant Vascular/Interventional Radiologist

Contrast-induced acute kidney injury (CI-AKI) formerly known as 'contrast-induced nephropathy (CIN)' is a significant complication associated with the use of iodinated contrast media (CM) and as the demand for complex imaging and interventions and CT procedures continues to increase, CI-AKI remains a concern. Minimising the risk of CI-AKI in patients who have been identified as 'at-risk' is, therefore, an essential component of best clinical practice for radiologists and cardiologists who perform CM-enhanced procedures.

When a high-risk patient is identified, several strategies can be applied to minimise the occurrence of CI-AKI. Cessation of all nephrotoxic medications should be implemented if possible ≥ 24 hours before the contrast use.¹ Adequate pre-and post-procedural volume expansion is considered one of the most effective CI-AKI prevention measures.² Although the optimal hydration strategy is still debated, a peri-procedural, intravenous regimen using normal saline or bicarbonate is currently recommended.²

Prophylactic haemodialysis has not been shown to protect patients with chronic kidney disease against CI-AKI,² and the benefit of haemofiltration also remains inconclusive.³

Volume and type of CM used during the CT procedure may also influence the development of CI-AKI. In studies involving intra-arterial CM administration, CM volume has been shown to be an independent predictor of CIN, highlighting the importance of administering the lowest possible CM dose.⁴ With respect to CM type, there are numerous small, often poorly designed trials that have considered the impact of CM osmolality on nephrotoxicity

Further reading

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in at-risk populations. The precise benefit of iso-osmolality is controversial and remains hotly contested for commercial reasons. National and international guidelines have recognised this area of difficulty and give general guidance only.^{5,6}

This presentation will review management strategies to minimise the occurrence of CI-AKI in patients at risk and introduce rapidly developing new concepts of CM dose reduction with advanced CT technology.

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AKI IN PAEDIATRICS: LITTLE PEOPLE, LITTLE DATA, BIG PROBLEM

Dr Sally Feather, Consultant in Paediatric Nephrology, Leeds General Infirmary, Leeds

The incidence of acute kidney injury (pAKI) in paediatrics (pAKI) is rising.^{1,2} Furthermore, aetiologies of pAKI are changing from primary renal disease due to the survival of paediatric patients with significant systemic disease

(e.g. cardiac and oncological) particularly on paediatric intensive care units. The impact of management of these diseases on the kidney has led to a substantial increase in pAKI.¹⁻³

Recognising the need to identify and manage pAKI, attempts have been made to standardise definitions of pAKI and these include the paediatric RIFLE criteria (pRIFLE)⁴ and Acute Kidney Injury (AKIN) criteria. Studies have also looked at the use of pAKI urinary biomarkers.¹

Although there is UK data (UK Renal Registry) on the aetiology of paediatric established renal failure (largely due to congenital renal malformations), there is no data or even specific category for acute cortical necrosis or AKI. There is clearly a need to establish long term longitudinal studies of pAKI survivors to determine the extent to which pAKI will become a significant cause of chronic kidney disease (CKD).

Of concern, longer term follow up studies of paediatric patients with pAKI due to a range of diseases show that they are at increased long term risk of CKD.^{1,2} Since these patients are will survive for decades, long term monitoring with respect to CKD is of great importance and needs to be identified in transition to adult services.

In summary, pAKI is an increasing and important problem not just for paediatricians, as survivors will need to be followed up throughout adult life. It is essential that pAKI is included in the current investment in AKI as much research data is needed and currently lacking.

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AKI IN THE ICU OR GLOBAL PERSPECTIVES

Professor Ravi Mehta, Division of Nephrology, UCSD, USA

Acute kidney injury (AKI) is a common event in hospitalised patients associated with poor outcomes.¹ Even mild AKI, defined as AKI stage I in the RIFLE and AKIN classifications² has been increasingly recognised as a major contributor to morbidity and mortality.³ However, there is limited information on the epidemiology of mild to moderate AKI in critically ill patients throughout the world. Previous prospective

multicentre studies have generally included patients with severe AKI and have had limited information on the risk factors and concomitant events contributing to outcomes.⁴⁻⁶

In 2008, we initiated an ongoing multicentre prospective observational study on AKI (AKIN criteria) in critically ill patients around the world including both emerging and developed nations. Patients are screened for AKI within seven days from admission to the ICU.² Data were entered in a web-based system and included demographics, co-morbidities including chronic kidney disease (CKD), baseline risk factors, daily vital signs, labs and concomitant risk factors and outcomes including dialysis requirement, length of stay and survival. Over the last four years, 1,275 of 6,647 screened patients developed AKI (19%) and 1,038 (81%) were enrolled in our registry with data currently available for 745 patients. There are significant differences in risk factors, natural history and outcomes in developed and emerging countries. This registry provides a unique ongoing look at the changing face of AKI in the ICU setting across the world and provides opportunities for informing the design and conduct of clinical and translational research in AKI.

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POSTER BOARD	TITLE	AUTHORS	SESSION
PB01	Intravenous fluids in medical patients	J Richardson (1), E Clegg (2); (1) Flat 512, One Brewery Wharf, Waterloo Street, Leeds, LS10 1GY (2) St James' University Hospital, Leeds	Fluid therapy
PB02	Fluid therapy prescribing on the medical admissions unit, Sheffield	I Elsayed, W Dean, M James, S Mofidi; Northern General Hospital, Sheffield Teaching Hospitals	Fluid therapy
PB03	Fluid therapy administration in acute kidney injury – data from the Acute Medical Unit Optimising Kidney Care (AMUOKC) Study	N Stock (1), K Armitage (1), C Gibbins (2); (1) Acute Medicine Registrar, Wansbeck General Hospital, Ashington, NE63 9JJ (2) Acute Medical Registrar, Royal Victoria Infirmary, Newcastle, NE1 4LP	Fluid therapy
PB04	Prevention of contrast-induced nephropathy (CIN) according to local guidelines at University of North Staffordshire Hospital (UHNS)	I Nguyen, R Rana, J Pugh, P Rajran, I Britton, C Thompson; University Hospital of North Staffordshire NHS Trust, Royal Infirmary, Princes Road, Stoke-on-Trent, ST4 7LN	Fluid therapy
PB05	Advantages of an automated e-alert system for acute kidney injury	AM Yates (1), CJ Thompson (2); (1) Clinical Biochemistry (2) Department of Nephrology University Hospital of North Staffordshire NHS Trust, Stoke on Trent	E-alerts
PB06	An automated real time e-alert system to identify and stage acute kidney injury in a large NHS trust	I Juurlink, C Porter, L Bisset, R Bavakunji, J Lewis, M Devonald; Renal and Transplant Unit, Nottingham University Hospitals NHS Trust, City Campus, Nottingham, NG5 1PB	E-alerts
PB07	WINNER OF BEST POSTER A before and after evaluation of acute kidney injury outreach: extended follow up	M Thomas (1), J Baharani (1), A Sitch (2), G Dowswell (2); (1) Heart of England Foundation Trust, Birmingham (2) University of Birmingham	E-alerts
PB08	The effects of an e-alert warning in the management of patients with acute kidney injury	S Elmamoun, C Goldsmith, A Abraham, A Wooton, H Wodeyar; University Hospital Aintree NHS Foundation Trust, Liverpool, L9 7AL	E-alerts
PB09	Study on pattern of referral and treatment of patients with acute kidney injury in a single hospital	G Shivashankar (1), T Lightbody (2), R Roberts (2); (1) Specialist Registrar, (2) CMTI, (3) Consultant Nephrologist, Bradford Royal Infirmary	E-alerts
PB10	Could implementation of a computerised warning system for acute kidney injury improve survival of the patients?	S Shojai, P Boddana, R Penders, N Wood, A Babu, I Dasgupta; Renal Unit, Gloucester Royal Hospital, Gloucestershire Hospitals NHS Foundation Trust, Great Western Road, Gloucester, GL1 3NN	E-alerts
PB11	Acute kidney injury e-alerts improving care	F Akinlade, A James, P Ayling, I Bera, S Sajid, S de Freitas	E-alerts
PB12	The use of reference change value (RCV) in generating e-alerts for the early identification of acute kidney injury	A Khalid (1), M Cox (1), B Bartlett (2), S Bell (1); (1) Renal Unit (2) Dept of Biochemistry Ninewells Hospital, Dundee	E-alerts
PB13	Real time reporting of AKI: six month's experience	KR Wallace (1), A Mallard (2), J Stratton (1), PA Johnston (1), S Dickinson (1), RG Parry (1); (1) Renal Unit, (2) Clinical Chemistry Dept Royal Cornwall Hospital, Truro, Cornwall, TR1 3LJ	E-alerts
PB14	A potential role for e-alerts in the management of community-acquired AKI in primary care	AE Garner (1), SL Harding (2), MP Bosomworth (1), AJP Lewington (3); (1) Dept of Blood Sciences, Leeds General Infirmary, Leeds Teaching Hospitals Trust (2) Park Edge Practice, Leeds (3) Dept of Renal Medicine, St James's Hospital, Leeds Teaching Hospitals Trust	E-alerts
PB15	Acute kidney injury in the community: a brief feasibility study for the role of biochemical alerts	SL Harding (1), AE Garner (2), AJP Lewington (3), MP Bosomworth (2); (1) Park Edge Practice, Leeds PCT (2) Dept of Blood Sciences, Leeds General Infirmary, Leeds Teaching Hospitals Trust, (3) Dept of Renal Medicine, St James's University Hospital, Leeds Teaching Hospitals Trust	E-alerts

POSTER BOARD	TITLE	AUTHORS	SESSION
PB16	Staying alert: a simple e-alert for acute kidney injury	N Flynn, C Laing, A Dawnay; Depts of Clinical Biochemistry and Nephrology, University College London Hospitals and Royal Free Hospital NHS Foundation Trusts, London (London Acute Kidney Injury Network [LAKIN])	E-alerts
PB17	A study of natural history of acute kidney injury amongst hospitalised patients based on an 'elevated creatinine alert system' – single centre experience	GK Rajakaruna, D McNaughton, A Sharma, P West, D Jayasena; North Middlesex University Hospital, London	E-alerts
PB18	Markers of tubular injury in paediatric oncology patients receiving cisplatin and/or ifosfamide	C Barton, M Pirmohamed, B Pizer; Department of Paediatric Oncology, Alder Hey Children's Hospital, Eaton Road, Liverpool, L12 2AP	Bio-markers
PB19	Acute kidney injury in paediatric cancer patients receiving cisplatin	C Barton, A Oates, D Hawcutt, M Pirmohamed, B Pizer; Department of Paediatric Oncology, Alder Hey Children's Hospital, Liverpool, L12 2AP	Bio-markers
PB20	The effects of aprotinin withdrawal on transfusion rates and acute kidney injury in cardiac surgery: a single centre observational study	GJ Walkden (1) R Goudie (2), V Verheyden (1), GJ Murphy (1); (1) Bristol Heart Institute, University of Bristol, Bristol, BS8 1TH (2) School of Social & Community Medicine, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS	Other relevant issues
PB21	Timing of acute kidney injury – does it matter? A single centre experience	CL Pang, J Baharani	Other relevant issues
PB22	Renal outcomes in critically ill patients requiring sustained low efficiency dialysis (SLED) in the intensive care unit	PA Austin (1), C Tweedie (1), SL Crofts (1), J Joss (1), SJ Cole (1), S Bell (2); (1) Dept of Anaesthesia & Intensive Care Medicine, (2) Renal Unit, Ninewells Hospital, Dundee, DD1 9SY	Other relevant issues
PB23	Improving outcomes of acute kidney injury through education	G Xu, R Westacott, R Baines, N Selby, S Carr; University Hospitals of Leicester and Royal Derby Hospital, UK	Other relevant issues
PB24	Does sildenafil prevent post-cardiopulmonary bypass acute kidney injury via non-endothelial dependent mechanisms?	SH Qureshi (1), GI Welsh (2), RR Foster (2), SC Satchel (2) NN Patel (1), V Verheyden (1), GJ Murphy (1); (1) Bristol Health Institute, University of Bristol, Bristol Royal Infirmary, Upper Maudlin Street, Bristol, BS2 8HW (2) Academic Renal Unit, Learning and Research Bldg, Clinical Sciences North Bristol, University of Bristol, Southmead Hospital, Bristol, BS10 5NB	Other relevant issues
PB25	Acute kidney injury in stroke patients	R Durairajan (1), K Lund (1), T Kalra (1), A Sivaramakrishnan (1), T Loganathan (1), A Kundu (1), D Sinha (1), L Coward (1), A O'Brien (1), P Guylar (1), M Almond (2), A Kiley (3); (1) Acute Stroke Unit (2) Department of Nephrology (3) Department of Biochemistry Southend University Hospital	Other relevant issues
PB26	Multimodal approach to the reduction of acute kidney injury in orthopaedic patients	P Farquharson (1), K Norman (2), S Mcleod (3); (1) ST4 Anaesthesia (2) CTI Anaesthesia (3) Consultant Anaesthetist NHS Tayside	Other relevant issues
PB27	Outcomes following ITU admission with AKI – five-year single centre experience	A Rao (1, 2) K Slade (1), J Ruddy (1), D Pitcher (2), J Traynor (1); (1) Monklands Hospital, Airdrie, UK (2) UK Renal Registry, Bristol, UK	Other relevant issues
PB28	Using a multimedia approach to improve management of acute kidney injury in a busy district hospital	R Raj (1), G Gallagher (2), C Lakra (3); (1) Ealing Hospital, Uxbridge Road, Southall, UB1 3HW (2) Harefield Hospital, Hill End Road, Harefield, Uxbridge, UB9 (3) University College Hospital, 235 Euston Road, London, NW1 2BU	Other relevant issues

WHAT IS THE ROLE OF FLUID THERAPY IN AKI?

PB01 INTRAVENOUS FLUIDS IN MEDICAL PATIENTS

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Fluid therapy was assessed in 39 medical patients at a large teaching hospital. We assessed fluids prescribed, the quality of prescription and the use of biochemical markers. When commencing IV fluid therapy, seven of the patients had acute kidney injury (AKI). Of these, three had resolved and a further three patients developed AKI while receiving IV fluid therapy. Of the total number of patients, only 46% had daily biochemical monitoring; 95% of the patients had their biochemistry monitored at least once during therapy leaving 5% with no biochemical analysis for the audit period.

The patients who were found to have or had developed AKI were independently analysed; 29% had daily biochemical monitoring and 71% had monitoring at least once during therapy; 40% of which had biochemical analysis done only once.

Overall fluid balance monitoring was recorded in 29 of the total 119 days of prescribed fluids. Daily weights and fluid volume status were not assessed, which would be helpful for guiding the amount of IV fluid therapy required for each patient.

Our findings were: poorly documented evidence of fluid balance and sporadic biochemical testing. Recommendations for guidance to be provided by the Trust and the audit will be used to assess for any improvement following roll-out of Trust-wide fluid prescription charts.

Fluid therapy is commonly being used in secondary care to treat AKI and patients should be monitored appropriately during the period of therapy.

PB02 FLUID THERAPY PRESCRIBING ON THE MEDICAL ADMISSIONS UNIT, SHEFFIELD

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Acute kidney injury (AKI) is common in hospitalised patients and is associated with poor prognosis, where mortality can reach up to 50% in patients on ICU. The 2009 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) reported that good care was provided to only 50% of AKI patients. Among

key recommendations of the report is implementing early recognition and management of ill patients (NICE CG 50). The Renal Association guideline on management of AKI involves the importance of fluid status assessment and appropriate fluid therapy.

We collected prospective data on types of fluids prescribed to AKI patients on AMAU at NGH Sheffield, over the month of August 2012, the training grade of prescribing doctor and whether or not fluid status was documented.

We identified 18 patients using *Kidney Disease: Improving Global Outcomes (KDIGO)* criteria, of whom 82% were prescribed NaCl 0.9%, 9% got Hartmann's and 9% got a colloid as their initial fluid resuscitation, with similar prescriptions over the following two days. On day three 56% of patients received 0.9% NaCl, 18% received glucose 5%, 18% had their IV fluids stopped and none were given Hartmann's. A total of 28% of the fluids were prescribed by FY1 doctors and 72% by FY2-ST2 doctors. Fluid status was not documented in any of the patients' medical records.

An evidence base to favour a particular type of fluid therapy is not available, however understanding of physiological changes in the acutely ill patients shows a potential for hyperchloremic metabolic acidosis with excessive use of 0.9% NaCl and a risk of hyponatremia with excessive use of dextrose.

Education of junior doctors regarding the basis underpinning fluid therapy, importance of careful assessment of fluid status and assessment of response to treatment, are integral to providing good quality care to AKI patients.

PB03 FLUID THERAPY ADMINISTRATION IN ACUTE KIDNEY INJURY – DATA FROM THE ACUTE MEDICAL UNIT OPTIMISING KIDNEY CARE (AMUOKC) STUDY

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Introduction: The Acute Medical Unit Optimising Kidney Care (AMUOKC) study is a multi-site study carried out in the North East of England designed to test interventions that are practical and effective in the management of acute kidney injury (AKI). The pilot study provided a picture of current AKI management.

Methodology: A total of 153 patients across four sites were included in this analysis. Data were collected retrospectively from review of case notes.

Results: A total of 100, 36 and 18 patients had stage 1, 2 and 3 AKI respectively, as classified by the *Kidney Disease: Improving Global Outcomes (KDIGO)* criteria. On admission, 83 (54%) patients were hypovolaemic, 22 (14%) euvolaemic, 14 (9%) hypervolaemic. Fluid status was not recorded in 34 (23%) patients. Eighty-four patients received normal saline intravenous fluid therapy in the first 24 hours. Eight patients received Hartmann's solution, three patients 5% dextrose, 42 patients a mixture of fluid types. In 12 patients the fluid administered was not recorded. Volume of fluid administered for all AKI stages varied from 0 to 8,100 ml in the first 24 hours. In stage 1, 2, and 3 AKI the mean volume of fluid administered in the first 24 hours was 3,162 ml, 3,676 ml and 4,614 ml respectively. Volume of fluid administered did not correspond to recorded volume status. In-hospital mortality was 32%, 25% and 62% for stage 1, 2 and 3 AKI respectively.

Conclusions: The current volume and type of intravenous fluid therapy administered to patients with AKI varies considerably. Guidelines are needed to enhance the management of patients with AKI.

PB04 PREVENTION OF CONTRAST-INDUCED NEPHROPATHY ACCORDING TO LOCAL GUIDELINES AT UNIVERSITY OF NORTH STAFFORDSHIRE HOSPITAL

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Background: Contrast-induced nephropathy (CIN) is extremely important, and associated with prolonged hospital stay, risk of permanent renal impairment with increased risk of mortality.

Purpose: Audit patients attending for elective and acute computed tomography (CT) scans with contrast at University of North Staffordshire Hospital (UHNS), assessing incidence of chronic kidney disease (CKD) and acute renal impairment, and application of local guidelines to avoid CIN in patients with eGFR 30–60.

Method: Audit 1,001 consecutive patients attending for CT scan with contrast from 14 November to 11 December 2011. Patient's eGFR in the three months preceding the scan were assessed with post-scan eGFR obtained at 0–6 days. CIN was defined as a creatinine rise

of >44 μmol within 72 hours of contrast administration. Severity of AKI was assessed according to *Kidney Disease: Improving Global Outcomes (KDIGO)* classification. In patients in whom CIN was suspected, potentiating factors were examined. Compliance with guidelines was assessed by notes review in subsets.

Results: A total of 474 inpatients, 527 outpatients, aged 1–97 years, with median age 60–69 years. A total of 93% patients had pre-scan eGFR with the incidence of eGFR <60 of 13% (14.6% inpatients and 12.8% outpatients). Inpatients with impaired pre-scan renal function, 46% had post-scan eGFR, 3.3% having a creatinine rise of >44 μmol . Only 42% of subset reviewed with CKD 3 had fluid prophylaxis 0.9% saline 12 hours pre- and post-scan.

Conclusion: Renal impairment is present in 14.6% of inpatients and 12.8% of outpatients, justifying guidelines for risk stratification and prophylaxis for CIN, but this should be easily administered. CIN is multifactorial and in the CT population may be more a contrast-associated AKI.

WHAT IS THE ROLE OF E-ALERTS IN AKI?

PB05 ADVANTAGES OF AN AUTOMATED E-ALERT SYSTEM FOR ACUTE KIDNEY INJURY

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E-alerts are valuable tools highlighting clinical events; their value however is only if they are acted upon. In our institution an audit of the reporting of AKI to requesters using existing electronic and manual systems (automated comments, alert flags and telephone calls) in place via the biochemistry laboratory were not adequate in detecting and highlighting AKI in line with *Kidney Disease: Improving Global Outcomes (KDIGO)* guidelines.

Results: In March 2012, 375 patients were defined as having AKI stage 1 (76%), 2 (13%), or 3 (10%); of these cases, clinicians were alerted by telephone in only 61 cases. A total of 115 had an automatic comment added stating the creatinine had changed by 25%; 208 baseline creatinines had a concentration above the reference range and were therefore flagged as high. In addition, renal registrars recorded that only 19% of patients with AKI 2/3 were referred or discussed with the renal team.

AKI patients needed to be easily recognisable by teams with prompts for action; a new programme was developed on the Laboratory IT system, Pathmanager. This examines every patient's creatinine measured in the UHNS laboratory; the lowest creatinine value over the previous 28 days acts as a baseline. The creatinine change is then calculated as a percentage and absolute change, allowing all KDIGO AKI criteria to be screened. The twice daily report generated is then imported to UHNS clinical Information System portal (CIS). CIS highlights AKI stage next to the patient demographics with additional guidance in a comments field. Consultants/wards can see at a glance if any of their patients has AKI.

PB06 AN AUTOMATED REAL TIME E-ALERT SYSTEM TO IDENTIFY AND STAGE ACUTE KIDNEY INJURY IN A LARGE NHS TRUST

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Acute kidney injury (AKI) occurs in up to 22% of hospitalised patients and is associated with significant mortality and morbidity. The 2009 National Confidential Enquiry into Patient Outcome and Death (NCEPOD)

report highlighted deficiencies in detection and management of AKI in the UK. To improve detection in our large NHS Trust, we developed an automated, real time electronic alert which identifies and stages AKI. It has been active since April 2011 and was assessed in pilot form the preceding year.

Algorithms compare admission creatinines (SCr) with baseline SCr (lowest SCr from 7–365 days prior to admission). Where no baseline exists, SCr is calculated using MDRD formula, assuming GFR of 75 mL/min. Where RIFLE or AKIN criteria are fulfilled, an alert accompanies the SCr result, giving AKI stage (the higher of RIFLE/AKIN where there is discrepancy) and referring the clinician to an intranet-based AKI guideline. All subsequent inpatient SCr results are scrutinised and the alert revised.

Prospective data are collected automatically. For April 2011–April 2012, counting only highest stage alert per admission, there were 13,314 alerts from 165,767 admissions (8% of admissions). Of these, 9.8% were stage 3, 16.9% stage 2 and 73.3% stage 1. In-hospital mortality was 8%, 19% and 25% for stage 1–3 respectively. Mean length of stay was 12, 15 and 15 days for stage 1–3 (compared with five days for patients with no alert).

Our e-alert has facilitated detection of AKI using the same diagnostic criteria as those subsequently published by *Kidney Disease: Improving Global Outcomes (KDIGO)*. It remains to be seen whether the alert will lead to improved outcomes.

PB07 A BEFORE AND AFTER EVALUATION OF ACUTE KIDNEY INJURY OUTREACH: EXTENDED FOLLOW UP

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Background: There is considerable evidence that acute kidney injury (AKI) management is suboptimal. In 2008 we studied AKI 'alerts' and showed that their use was feasible.

Methods: In AKI outreach the care of patients identified by alerts is supplemented by early intervention from nephrology clinicians. Patients were identified by an alert issued for a $\geq 75\%$ rise in creatinine in the ICE laboratory information system (Sunquest Europe). In a four-week 'before' phase, alerts were collected but no intervention was made. In a consecutive seven week 'after' phase in

2009, the alerts were reviewed by a dedicated team of trained nephrology clinicians. They provided early advice on best care of the patient.

Results: There were 157 first alerts on patients in the before phase, and 251 first alerts during the after phase, with a total of 408 patients. Successful outreach calls were made for 88.5% of alerts. The interventions made during the calls will be presented: large numbers of drug and non-drug changes to management were suggested. Survival was better in the after phase by about 7%, compared to the before phase. We will present extended follow up of the study.

Conclusions: AKI outreach is feasible for a relatively high number of patients, even with only a modest number of nephrology clinician hours. The potential mechanism of the survival advantage remains to be determined. The clear suggestion of a survival benefit warrants further study. The design of a NIHR sponsored pilot study of AKI outreach (the AKORDD study) will be briefly discussed.

PB08 **THE EFFECTIVENESS OF AN E-ALERT WARNING IN THE MANAGEMENT OF PATIENTS WITH ACUTE KIDNEY INJURY**

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Introduction: The 2009 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report *Adding Insult to Injury* highlights the importance of early recognition of acute kidney injury (AKI).

Objectives: An electronic e-alert was introduced at University Hospital Aintree to detect patients who developed AKI and flag this to a parent team with a link to the Trust online AKI management algorithm.

Methods: The e-alert was piloted at our Trust from 24 May to 22 June 2012. Demographic data including co-morbidity, time to recognition of AKI, length of stay, outcomes and adherence to AKI management algorithm were collected.

Results: A total of 38 patients out of 58 were studied. Acidosis (five), pulmonary oedema (three) or hyperkalaemia (three) were uncommon. We analysed whether the appropriate general measures detailed in the online guide were performed. There was no statistically significant difference in overall management, or the proportion of patients referred appropriately to nephrology between those patients that had the e-alert acknowledged and those that didn't.

Conclusions: Overall AKI management was better than the NCEPOD report, however the e-alert system did not lead to any further improvements in patients overall management. However, 50% of AKIN 2 and 100% of AKIN 3 were referred to nephrology. Therefore, staging AKI in our alert system will link in closer with our current online AKI guidance.

PB09 **STUDY ON PATTERN OF REFERRAL AND TREATMENT OF PATIENTS WITH ACUTE KIDNEY INJURY IN A SINGLE HOSPITAL**

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Introduction: Acute kidney injury (AKI) is the commonest reversible organ injury in hospital settings, with prevalence of up to 7%. It carries a poor prognosis, with mortality between 10–80% depending on study population. The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) made several recommendations after identifying deficiencies in the treatment of AKI.

Methodology: We prospectively audited 50 consecutive patients with AKI using the NCEPOD audit tool. The data was collected over a four-month period including all admissions and referrals to the nephrology service.

Results: Thirty-one patients were male and half of all patients were in the age range of 60–80; 16/50 patients had at least chronic kidney disease (CKD) stage 3 on admission. Forty patients had AKI stage 3 on referral. Aetiologies included sepsis (15), multifactorial (16) and post-operative (seven). Case review suggested that better fluid status monitoring and/or avoiding nephrotoxics may have prevented AKI in 19 cases. There was at least a 24-hour delay in making a referral to nephrology in 12 cases. Eight patients needed ICU stay with 14 requiring renal replacement therapy (RRT) (four CVVH and ten HD). Thirty-eight patients recovered renal functions to baseline with eight requiring long term haemodialysis. Four patients died, with three deaths related to AKI.

Conclusion: These data suggest that measures leading to the earlier recognition of AKI (e-alerts, specific training, pathway development) could improve the outcome for a significant number of patients.

PB10 COULD IMPLEMENTATION OF A COMPUTERISED WARNING SYSTEM FOR ACUTE KIDNEY INJURY IMPROVE SURVIVAL OF THE PATIENTS?

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Background: Acute kidney injury (AKI) is a major risk factor for in-hospital mortality. We started an initiative in our two district acute general hospitals with a catchment population of 612,000. Two months after the implementation of the first phase of the initiative we conducted this cross-sectional study to assess the effect of the computerised warning system on overall survival of admitted patients across the non-nephrology disciplines.

Methods: A total of 181 patients in six consecutive weeks were admitted to hospital and were flagged by our validated computerised warning system as AKI using AKI Network criteria. We compared the survival of these patients with the survival of 61 similar cohort of patients admitted and flagged as AKI in two consecutive weeks three months prior to implementation of the warning system.

Results: Mean age of patients was 72.9 (SD 15.2) years and 76 (SD 13.7) years for the group prior to and after implementation of warning system respectively ($t=1.42$, $p=0.159$). Univariate log-rank Kaplan-Meier survival analysis also did not show any statistically significant difference in survival of two groups of patients ($X^2[2]=3.64$, $p=0.162$).

Conclusion: The implementation of a computerised warning system could aid early recognition of AKI which is an essential step, but not enough to improve the outcome of these patients. A cross-discipline AKI e-learning module, AKI management guideline linked to the warning system and an electronic nephrology referral system are complementary interventions we have introduced. Further research is required to assess the effect of the above measures on the outcome of this group of patients.

PB11 ACUTE KIDNEY INJURY E-ALERTS IMPROVING CARE

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Aims: To investigate whether automated acute kidney injury (AKI) alerts alongside biochemistry results can improve the recognition (earlier, more consistent) of AKI amongst clinicians and be a tool for quality improvement.

Methods: At Barking, Havering and Redbridge University Hospitals (BHRUT) NHS Trust we designed three computer algorithms linked to three alert messages explaining whether the patient has AKI (plus stage), is recovering from AKI, and lastly a less specific message (if no baseline creatinine is available) warning of AKI or chronic kidney disease (CKD). Using the Clinisys-Winpath Pathology Information System we implemented these algorithms in an innovative way that uses a dynamically adjusted baseline with subsequent blood tests. The clinical coding rate of AKI (N17) is used as a surrogate to determine whether recognition of AKI improves.

Results: After an in-house trial within a test system, the system was launched live within the Trust on 18 July 2012. From the highly specific algorithms alone, 761 cases of AKI were detected to date; 89 +/- 9 unique cases per week with 9% stage 3, 23% as stage 2 and 68% as stage 1. The variability in the coding rate is greater.

Future plans: The coding rate variability suggests recognition could improve but several months of data are required to establish whether a reduced 'recognition gap' has occurred with the implementation of e-alerts. A rapid review service for all AKI stage 3 patients independent of firm referral is now possible (one-third of our alerts occur from ED bloods) and we are able to audit AKI care with reduced bias.

PB12 THE USE OF REFERENCE CHANGE VALUE IN GENERATING E-ALERTS FOR THE EARLY IDENTIFICATION OF ACUTE KIDNEY INJURY

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The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report on acute kidney injury (AKI) highlighted the need for early recognition of developing AKI. We have identified that rates of AKI have been increasing within the orthopaedic wards at Ninewells Hospital. As part of an initiative aimed at reducing rates of AKI within these wards, we introduced a pilot of e-alerts to identify these patients early. Proposed criteria for the definition of AKI specify magnitude of change and rate of change in creatinine. The latter is often difficult to programme into conventional laboratory systems.

We have therefore studied the utility of assessment of results against reference change values (RCV) for serum creatinine. This enables an objective assessment of significance of change in serum creatinine based on knowledge of the inherent within subject biological variation in serum creatinine (CV= 6.3%) and the analytical variability (CV Circa 2%). At a probability of 0.95 and 0.99 the one tailed RCVs for a rise in creatinine are 14.3% and 20.2% respectively.

Report analysis rules were built into the Sunquest Ice electronic reporting system alerting the renal team of patients fitting the above criteria during a four-week pilot period within the four orthopaedic wards. During this period, 68 alerts were generated. Of these, 17 (25%) required intervention. None of these patients were referred by the orthopaedic team prior to contact by the renal team.

Reference change value is a potentially useful means of early identification of AKI using electronic laboratory alerts. However, the workload involved and who should receive these alerts pose challenging questions.

PBI3 REAL TIME REPORTING OF AKI: SIX MONTH'S EXPERIENCE

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Early intervention in the management of acute kidney injury (AKI) has been shown to improve outcomes. To facilitate early review we have introduced real time reporting for AKI.

Methods: An algorithm was implemented using the laboratory computer system to code and report AKI; AKI 2 and AKI 3 patients are phoned to the requesting location and/or the renal team.

Results: From last December to May there were 1,906 AKI reports; 56.3% (n=1,073) AKI 1, 26.9% (n=513) AKI 2 and 16.8% (n=320) AKI 3; an average of five AKI 1, 2–3 AKI 2 and 1–2 AKI 3 cases per day. There were 1,519 patient admissions with AKI, having a 51:49 male (n=773) to female (n=746) ratio and a mean age of 74.8 years. Of these cases, 62.6% were medical, 16.9% surgical, 6.9% orthopaedic, 5.3% from speciality wards and 8.3% from peripheral hospitals, with a mean length of stay (LOS) of 13.7 days. However, only 31% of patients with AKI reports were clinically coded for AKI. The mortality of patients with AKI was 36.4%; 12.3% (n=185) showed progression of AKI. In comparison, there were 65,529 admissions without AKI with a mean LOS of 1.8 days and mortality of 6.56%.

Discussion: The low proportion of patients coded for AKI suggests under-recognition of AKI by junior doctors and poor understanding of the significance of AKI on patient mortality and morbidity. The 12.3% of patients with progression of AKI may have benefitted from earlier renal intervention. These are both areas which can be targeted to improve patient mortality and impact on the tariff paid to the hospital.

PBI4 A POTENTIAL ROLE FOR E-ALERTS IN THE MANAGEMENT OF COMMUNITY-ACQUIRED AKI IN PRIMARY CARE

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Many clinical laboratories are implementing e-alerts to detect acute kidney injury (AKI). The majority of these alerts and associated literature have focussed on hospital patients rather than those presenting to primary care. The purpose of this study was to explore the application of an e-alert for community-acquired AKI (c-AKI) by investigating the incidence and management of c-AKI in patients presenting to their GP.

The Clinical Biochemistry database was used to gather all serum creatinine results from primary care over six months. Patients with a creatinine increase $\geq 50\%$ were selected and further searches conducted to exclude hospital-acquired AKI. From a total of 94,761 GP patients, 85 patients with c-AKI were identified. The number of patients with stage 1, 2 and 3 were 61 (72%), eight (9%) and 16 (19%) respectively, according to *Kidney Disease: Improving Global Outcomes (KDIGO)* definitions. During the AKI episode, 24 (28%) patients were admitted to hospital and the creatinine returned to baseline in 16 (67%). Of the 61 (72%) patients managed in primary care, only 27 (44%) returned to baseline creatinine and 21 (34%) had no further creatinine tests (within two months). Ten of the 16 patients with stage 3 were admitted to hospital where five (50%) returned to their baseline creatinine compared to one (17%) patient in primary care.

These results suggest there is a relatively low incidence of c-AKI presenting to primary care but management may be suboptimal. Therefore an e-alert providing guidance on referral and follow up could potentially improve outcomes without generating a large volume of alerts.

PB15 ACUTE KIDNEY INJURY IN THE COMMUNITY A BRIEF FEASIBILITY STUDY FOR THE ROLE OF BIOCHEMICAL ALERTS

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As part of a larger project relating to awareness of acute kidney injury (AKI) and appropriate management it was decided to investigate how a biochemical e-alert system may be implemented into general practice and how this may assist the earlier recognition of high-risk patients developing AKI.

We looked at a single practice in North East Leeds with a population of just over 5,200 patients. A retrospective search of urea/electrolyte results for the practice population was undertaken over a six-month time period. Any patient that had two or more readings within this time frame was included in the study population. The readings were then checked to see if patients had a diagnostic 1.5 time baseline increase in creatinine. We then looked in detail at these patient records to establish the risk factors present prior to renal deterioration. A total of 14 suitable patients were identified.

Five out of 14 patients had significant risks that, had e-alerts been available, may have anticipated the need for earlier review to reduce the risk of AKI.

It was felt from this small initial study that further awareness and education of risk factors for AKI in primary care was needed, especially given the devolution of follow up from secondary care into the primary care forum.

We propose to increase the study to include a larger general practice population, and also propose to undertake a GP awareness programme using the newly written *Acute Kidney Injury Map of Medicine* material to improve awareness of risk factors and appropriate early interventions.

PB16 STAYING ALERT: A SIMPLE E-ALERT FOR ACUTE KIDNEY INJURY

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An NHS kidney care survey identified IT issues and cost as barriers to using acute kidney injury (AKI) e-alerts. We describe an e-alert taking ten minutes to set up that we believe could be implemented on all laboratory IT systems.

A real time automated delta check flagged a >50% increase in creatinine from the most recent result within a 90-day period and automatically appended a comment '?AKI – creatinine increase >50% from previous' with a link to the LAKIN website. In addition, all creatinine results >300 µmol/L were retrospectively reviewed twice daily and phoned if AKI was suspected.

From 11,930 creatinine requests over 12 days, 91 (in 88 patients) triggered an alert for >50% increase to >50 µmol/L – six from ITU, 26 A&E and acute admissions, 29 other inpatients, 25 outpatients, four primary care and one unknown. *On Kidney Disease: Improving Global Outcomes (KDIGO)* staging the alerts were 64 AKI 1, 20 AKI 2 and seven AKI 3 with a mean creatinine increase of 69 µmol/L at a mean of 20 days from the most recent previous result. For each patient we reviewed pre-AKI creatinine results – one-quarter of alerts were deemed inappropriate due to the most recent previous creatinine being atypically low. There were 54 creatinine results (from 26 patients) >300 µmol/L of which one-third were due to chronic kidney disease (CKD) rather than AKI. There were no convincing episodes of AKI among 20 alerts where the trigger creatinine was <50 µmol/L.

This study shows that a simple approach under laboratory control can detect and flag AKI at little extra cost.

PB17 A STUDY OF NATURAL HISTORY OF ACUTE KIDNEY INJURY AMONGST HOSPITALISED PATIENTS BASED ON AN 'ELEVATED CREATININE ALERT SYSTEM' – SINGLE CENTRE EXPERIENCE

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Background: Multiple studies have shown that uncomplicated acute kidney injury (AKI) has a poor prognosis with mortality ranging from 10–80%. As a result, AKI is no longer considered an innocent complication causing morbidity in hospitalised patients.

Methods: In order to recognise patients with AKI early and offer nephrology input in accordance with Renal Association guidelines, an alert system based on abnormal creatinine was introduced at the North

Middlesex University Hospital. This was generated daily for patients with a serum creatinine > 300 µmol/L. The cut-off was targeted to capture patients with stage 3 AKI.

Results: A total of 333 alerts were received by this system for the year 2011. Mean age of the population was 70.2 with an age range of 21–92.

Conclusion: The highest prevalence of AKI was found amongst care of the elderly population and 60.5% had pre-existing chronic kidney disease. This system has provided us with the data to study the incidence, prevalence and natural history of AKI amongst our local population. It has also enabled us to identify the risk factors for AKI, assess the relationship between timing, severity and number of risk factors for AKI and the course of AKI. More importantly it has enabled the patients with AKI to receive early and timely nephrology input.

WHAT IS THE ROLE OF BIOMARKERS IN AKI?

PB18 MARKERS OF TUBULAR INJURY IN PAEDIATRIC ONCOLOGY PATIENTS RECEIVING CISPLATIN AND/OR IFOSFAMIDE

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Background: Children with cancer receiving nephrotoxic chemotherapeutic agents such as cisplatin and ifosfamide are at risk of both acute and chronic, and reversible and irreversible, kidney injury. Monitoring for changes in glomerular function is now routine, with biochemical markers of glomerular function such as serum creatinine (sCr), and the use of chromium 51-labelled ethylenediaminetetraacetate (51 Cr-EDTA) to measure glomerular filtration rate (GFR). Markers of tubular injury are however less well defined.

Objectives: A two-step systematic review was undertaken to determine which markers, if any, have been described in studies relating to children with cancer, and then specifically those receiving cisplatin and/or ifosfamide.

Search strategy: EMBASE, MEDLINE and CINAHL were searched via the NHS Evidence Portal. Search terms were independently matched to the thesaurus of each database. An initial search was conducted to generate a list of markers of renal tubular injury that had been identified or explored in either *in vitro* and or *in vivo* biological or clinical studies. Only biochemical, genetic, peptide, and microRNA markers were included. A second literature search was conducted to identify articles relating to renal injury in paediatric patients receiving cisplatin or ifosfamide. The two searches were cross-referenced.

Results: A total of 97 markers of tubular injury were identified from the defined search terms. Of these, 14 were cross-referenced to the defined population,

including fractional excretion of phosphate, cystatin C, interleukin-18 and variance in amino acid and metabolite profiles.

Conclusion: Current literature describes a wide range of biomarkers of tubular injury with the potential to find application in children receiving nephrotoxic chemotherapy, whether for clinical (e.g. surveillance or monitoring of AKI) or research (e.g. development of preventative strategies or surrogate markers in clinical trials). However, the clinical utility of identified biomarkers is currently limited by considerations such as small sample size in studies conducted, the requirement for specialist modalities (e.g. nuclear magnetic resonance spectroscopy), complexity of analysis (e.g. urine amino acid profiles) cost of assays (e.g. ELISA). Further work is needed to identify new biomarkers of tubular kidney injury arising from nephrotoxic chemotherapy, with studies in larger cohorts of patients to validate the utility, sensitivity and specificity of those already proposed.

PB19 ACUTE KIDNEY INJURY IN PAEDIATRIC CANCER PATIENTS RECEIVING CISPLATIN

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Paediatric cancer patients receiving cisplatin are at risk of developing acute kidney injury (AKI). Routine markers for monitoring transient and permanent changes in glomerular function (GF) include serum creatinine (sCr), and chromium 51-labelled ethylenediaminetetraacetate (51 Cr-EDTA) measurement of glomerular filtration rate (GFR). Markers of tubular injury are however less well defined, and none are routinely used in clinical practice. Using routine clinical data, the current study aimed to identify the incidence the of AKI in patients being treated within a tertiary paediatric oncology, and potential markers for future studies

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Method: Core data including sCr levels, gentamicin levels and magnesium supplementation were collated from the electronic and pharmacy records of 68 children who had received cisplatin. AKIN scores were given based on biochemical data alone.

Results: Complete data was available on 63 patients; 35/63 (56%) of patients had an AKIN score of 0, 21/63 (33%) had an AKIN score of I, and 7/63 (11%) had an AKIN score of II. No patients had an AKIN score of III.

A total of 71% of patients with AKIN II had received gentamicin (number of courses: range 1–12, mean 5.8) between commencing chemotherapy and data collection, compared with 33% of patients with AKIN I (range 1–8, mean 3.14).

A total of 86% of those patients with AKIN II required magnesium supplementation on treatment (vs 24% of AKIN I patients), with 71% of those patients with AKIN II requiring magnesium supplementation after treatment (vs 19% of AKIN I patients).

No patients who required magnesium supplementation off treatment had not previously had supplementation on treatment

Conclusion: Based on biochemical data alone 44% of patients had an AKIN score of I or II. Those patients with an AKIN score of II received a higher mean number of courses of aminoglycosides than other groups (AKIN I or 0), and were more likely to require magnesium supplementation, both on and off treatment. This suggests that cumulative aminoglycoside doses may have a role in the stratification of patients at risk of AKI for research and follow-up purposes, and that the utility of magnesium supplementation as a marker of AKI merits further investigation.

OTHER RELEVANT ISSUES

PB20 THE EFFECTS OF APROTININ WITHDRAWAL ON TRANSFUSION RATES AND ACUTE KIDNEY INJURY IN CARDIAC SURGERY: A SINGLE CENTRE OBSERVATIONAL STUDY

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Background: Coagulopathic haemorrhage remains a major cause of perioperative morbidity in cardiac surgery. The serine protease inhibitor aprotinin prevents coagulopathic haemorrhage but was withdrawn in 2008 after clinical studies raised significant safety concerns. After careful re-analysis, aprotinin has again been licensed for the prevention of coagulopathic haemorrhage. To better understand the risks and benefits of re-introducing aprotinin into practice, we aimed to determine the effect of aprotinin's withdrawal on transfusion, bleeding and acute kidney injury (AKI).

Methods: Adult patients having cardiac surgery between 5 September 2006 and 29 December 2010 at a single tertiary cardiac centre, and for whom clinical, haematology and blood bank data were available were included. Outcomes were compared between patients (n=2,932) operated on before aprotinin's withdrawal on 5 September 2008 and propensity-matched patients (n=2,932) immediately preceding this date. Outcomes are presented as adjusted odds ratios or hazard ratios

(95% confidence interval). Sensitivity analyses established the likely influence of regression, selection and time series bias on our results.

Results: Aprotinin withdrawal was associated with significant increases in exposure to allogenic red blood cells 1.23 (1.08–1.39), platelets 1.82 (1.54–2.16), fresh frozen plasma 1.41 (1.15–1.74) and cryoprecipitate 1.88 (0.99–3.68). Post-operative blood loss and re-sternotomies for bleeding were not significantly increased: odds ratio 1.30 (0.91–1.87) post-suspension. Aprotinin withdrawal was associated with a significant increase in AKI incidence: 1.67 (1.06–2.65), but had no effect on one-year mortality: hazard ratio 1.16 (0.90–1.51). The results of sensitivity analyses did not alter our conclusions.

Conclusion: Aprotinin's withdrawal resulted in increased allogenic blood component exposure and post-procedural AKI in cardiac surgery patients.

PB21 TIMING OF ACUTE KIDNEY INJURY – DOES IT MATTER? A SINGLE CENTRE EXPERIENCE

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Aim: Acute kidney injury (AKI) is a common complication of hospital admission. Identification of post-admission AKI is poor. This study identifies

differences in outcomes between patients admitted with AKI, and those who develop AKI during their admission.

Methods: Single centre retrospective analysis of 306 patients with AKI who received intermittent haemodialysis. Data were collected for a period of three years. Patients were divided into two groups: 'early' and 'late'. The early group were admitted with AKI, or developed it within 48 hours of admission. The late group developed AKI after 48 hours. Primary outcomes measured were: renal and patient survival. Secondary outcomes include length of stay and admission to critical care

Results: The most common cause of AKI was pre-renal. Patients in the early group had a lower mortality rate (24.5%), compared to the late group (50.5%). The length of their hospital stay was shorter. However, a higher percentage of patients (27.1%) in this group were dependent on renal replacement therapy at discharge. The timing of the AKI did not have an impact on the rate of admission to a critical care unit.

Conclusions: Early recognition and intervention reduces patient mortality in AKI. Patients who receive early intervention have higher survival rates and shorter hospital stays. However, there is no improvement in renal survival, with a higher proportion of the early AKI group remaining dialysis-dependent on discharge.

PB22 **RENAL OUTCOMES IN CRITICALLY ILL PATIENTS REQUIRING SUSTAINED LOW EFFICIENCY DIALYSIS (SLED) IN THE INTENSIVE CARE UNIT**

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Ninewells Hospital was one of the first UK intensive care units (ICU) to adopt sustained low efficiency dialysis (SLED) as its primary mode of renal replacement therapy (RRT) in the critically ill. We present the renal outcomes of patients admitted to ICU with multi-organ failure, who required SLED for the management of acute kidney injury (AKI) between 1 January 2011 and 31 December 2011.

During 2011 there were 349 patients admitted to Ninewells ICU. A total of 43/349 (12.3%) required RRT. The mean age of the RRT group was higher at 61.5±18.1 versus 54.5±20.0, $p=0.03$ in the non-RRT group. Length of ICU stay was longer with a median of 6.9 days (IQR 2.7 to 14.2) versus 2.1 days (IQR 0.9 to 4.4) $p<0.001$. Apache II score was also higher at 29.0±8.6 versus 19.1±7.3, $p=0.001$.

Mortality was higher in the RRT group with 21/43 (49%) dying during their ICU stay. This compares with a mortality of 67/305 (22%) in the non-RRT group.

A total of 18 of the 22 patients discharged alive from ICU, survived to hospital discharge. Three patients have required ongoing renal follow up at six months post-discharge. One patient has defaulted from follow up. Of particular note, no patients remained dialysis-dependent at six months post-discharge.

Renal replacement therapy in the critically ill population is often reflective of illness severity as is evidenced by this cohort. This group of patients were older, sicker, had a longer ICU stay and a greater ICU mortality. Despite this, of those that survived only a minority have required long term renal follow up.

PB23 **IMPROVING OUTCOMES OF ACUTE KIDNEY INJURY THROUGH EDUCATION**

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The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report *Improving Outcomes in Acute Kidney Injury* identified deficiencies in acute kidney injury (AKI) education and training. We designed and piloted a multifaceted educational intervention and assessed its effectiveness in improving confidence and knowledge of AKI in medical staff.

Method: Knowledge and confidence of AKI was assessed using a multiple choice question (MCQ) survey of 342 doctors (63% Foundation year doctors) before the educational tool kit was introduced in October/November 2011. The education package comprised a new AKI eLearning package, face-to-face ward teaching sessions and formal AKI teaching sessions. A follow-up survey was carried out in June/July 2012.

Results: In the initial survey, Foundation year doctors scored 40% on MCQs designed to test knowledge. After completion of the educational intervention in the follow-up survey the average score for Foundation year doctors increased by 6%.

A total of 215 people used the eLearning tool within the first three months. The completion rate was 61%; 87% of those who completed the eLearning felt more confident about managing AKI, 97% would recommend the tool to others. Foundation year doctors who had completed the AKI eLearning tool showed the largest increase in confidence on managing AKI and were more likely to initiate investigations and management plans.

Poster abstracts

Conclusion: A blended educational package on AKI can have a positive effect on confidence and knowledge of non-specialist clinicians.

PB24 DOES SILDENAFIL PREVENT POST-CARDIOPULMONARY BYPASS ACUTE KIDNEY INJURY VIA NON-ENDOTHELIAL DEPENDENT MECHANISMS?

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Aim: Sildenafil citrate, a PDE-5 inhibitor, promotes endothelial homeostasis. The aim of this study was to evaluate the effects of sildenafil on post-cardiopulmonary bypass (CPB) acute kidney injury (AKI) and determine whether the effects were exerted by preservation of endothelial and glycocalyx integrity.

Methods: Adult pigs (n=8 per group) were randomised to undergo sham procedure, CPB, or CPB plus administration of sildenafil, with recovery and kidney harvesting at 24 hours. The primary outcome was measurement of creatinine clearance as an index of GFR. Secondary outcomes were assessment of endothelial function and markers of endothelial and glycocalyx integrity using immunofluorescence and western blotting. Groups were analysed using ANOVA with Bonferroni adjustment for multiple comparisons. The effect sizes are reported as CPB vs sham mean difference; (95% confidence intervals [CI]).

Results: CPB resulted in reduction of creatinine clearance (MD: -47.9 mL/min [-93.7 to -2.2], p=0.039). CPB also resulted in loss of the glycosaminoglycan component of endothelial glycocalyx as demonstrated by reduction in DBA lectin (MD: -0.27 [CI .79-.94], p=.019), SBA lectin, WGA lectin binding and glycocalyx core protein syndecan-4. In addition CPB resulted in loss of VE-cadherin (MD: -0.14 [CI .69-.78], p<.001) and thrombomodulin (MD -0.13 [CI .29-.39], p=.01) signifying endothelial loss. Sildenafil prevented reduction in creatinine clearance but did not reverse endothelial or glycocalyx loss.

Conclusions: Sildenafil citrate reversed the loss in GFR and renal endothelial dysfunction attributable to CPB. However these effects are not exercised via preservation of structural integrity of the vascular endothelium.

PB25 ACUTE KIDNEY INJURY IN STROKE PATIENTS

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Introduction: Acute kidney injury (AKI) is associated with increased mortality and length of stay (LOS) across a broad spectrum of conditions. Moreover, outcomes are related directly to the severity of AKI, whether characterised by nominal or percentage changes in serum creatinine. There is little data in patients with acute stroke; we aimed to investigate this further.

Methods: We retrospectively analysed our stroke database to obtain data for 2,151 patients admitted to the Acute Stroke Unit (ASU) from August 2009 to July 2011 with diagnosis of ischaemic or haemorrhagic stroke. The cohort was followed up for one year after discharge.

Results: A total of 58 patients had AKI according to Acute Kidney Injury Network definition. The mean length of stay was 15.38 days for overall admissions versus 27.15 days for AKI patients and mortality 15.21% versus 24.13% respectively. Five patients had AKI with creatinine in the normal range and none of them were recognised. The mean baseline creatinine was 114.64 with eGFR of 57.19 and 132.56 and 52.96 on discharge. Renal input was not sought as inpatient in any of the patients. Two out of 58 discharge summaries mention the diagnosis of AKI during admission.

Conclusion: Patients with AKI showed longer LOS in hospital, poorer functional outcome and increased mortality following stroke, similar to other conditions. AKI may not be recognised; eGFR does not return to baseline on discharge and it is not being communicated to primary care for follow up. Nephrologists are not being involved in management; joint stroke/renal management of these patients may improve their outcome. We recommend further studies with regards to this.

PB26 MULTIMODAL APPROACH TO THE REDUCTION OF ACUTE KIDNEY INJURY IN ORTHOPAEDIC PATIENTS

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Acute kidney injury (AKI) occurs in hospitalised patients with an incidence of 7.5% of individuals admitted with normal renal function. It is associated with an increased

morbidity, mortality and decreased long-term survival following surgery. In many cases the incidences of AKI is preventable.

In August 2011 all orthopaedics admissions during a 14-day period were audited. Ninety-seven elective and emergency orthopaedic patients were admitted. Of those patients 14 (14.4%) were found to have an AKI with nine (9.3%) of these patients developing AKI during their admission.

The incidence of patients developing AKI was greater than those figures quoted in the literature and as a result three interventions were put into practice; an AKI guideline accessible on the intranet, education of junior medical staff on the subject of fluid management and later, a change in prophylactic antibiotic practice with the avoidance of aminoglycosides. Our intervention had the aim of reducing the incidence of developing AKI during admission.

A re-audit was carried out in August 2012 using similar methodology. Eighty-four patients were admitted and five (6%) were diagnosed with AKI, of those two (2.4%) developed AKI during admission. Therefore there was an absolute risk reduction of 6.9%; however using Fisher's exact test the results were not statistically significant with $p=0.06$. The numbers were small and higher patient numbers may produce more statistically significant results as a result of the interventions.

PB27 **OUTCOMES FOLLOWING ITU ADMISSION WITH AKI: A FIVE-YEAR SINGLE CENTRE EXPERIENCE**

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Aim: To assess outcomes in patients requiring renal replacement therapy (RRT) following admission to the Intensive Therapy Unit (ITU).

Methods: We identified all patients requiring ITU care at Monklands Hospital between 2007–2011 and assessed variables such as age, sex, and severity of illness and whether patients required RRT. We used the electronic patient record to extract subsequent mortality as well as renal outcomes. Statistical analysis was done using SAS v 9.2. For this analysis we excluded patients who were on chronic RRT (dialysis or transplant) prior to admission.

Results: Of the 1,183 patients, 203 required RRT and ventilation and 980 required ventilation alone. The RRT and ventilation group had a higher mean stay in ITU (13.33 v 4.04 $p<0.0001$) compared to the ventilation-only group, as well as higher in-ITU mortality (45.3% v

19.9% $p<0.0001$). One hundred of the RRT patients were discharged home (49.3%) and excluding the 21 who were lost to follow-up, 90 were alive at six months; 22% had ongoing nephrology input.

In the RRT group there was a higher proportion of chronic renal failure/chronic kidney disease (CRF/CKD) (p value=0.0084), diabetes (p value=0.006), hypertension (p value=0.005), and liver disease/alcohol dependence (p value=0.0045) but there was no difference between the groups with regards to heart disease (p value=0.34) and chronic lung disease (p value=0.86). In patients who had CRF/CKD and required RRT there was no statistically significant difference with regards to in-hospital death (p value=0.5335).

Conclusion: Patients who require RRT have a higher in-hospital length of stay and mortality. Not surprisingly, this group also has a higher degree of co-morbidity.

PB28 **USING A MULTIMEDIA APPROACH TO IMPROVE MANAGEMENT OF ACUTE KIDNEY INJURY IN A BUSY DISTRICT HOSPITAL**

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While acute kidney injury (AKI) accounts for 20% of hospital admissions, the 2009 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report identified multifaceted deficiencies in the management of AKI across the NHS.

Our aim was to investigate and optimise the recognition and management of AKI at a busy district general hospital. We began by auditing current practice against local guidelines provided by the London Kidney Network. Our first audit cycle revealed that only 25% of patients with AKI had a blood gas performed on presentation, were catheterised, and had hourly urine output measured. One-third had no fluid balance recorded. Only 37% of patients had a urine dip, and 15% were investigated with renal ultrasound.

To address this, we began a comprehensive group of interventions to raise awareness and educate on recommended clinical practice. This included informal and departmental teaching, presentations, and grand rounds. Posters of local guidelines were strategically placed in the Emergency Department and Acute Admissions Unit. Implementation of media included an e-learning module, ease of access intranet links, and the London Kidney Network phone app.

Poster abstracts

Post-intervention audit revealed a significant improvement in the management of AKI; the number of patients receiving blood gases, urine dips, catheters, and hourly urine measurements doubled. Renal ultrasound increased three-fold. Fluid balance was measured in 90% of patients.

Our audit shows evidence of improved clinical practice. We conclude that the findings from the NCEPOD report are reflected on a local level, but that targeted intervention improves standards. This can easily be adapted by the wider medical community.