Acute Medicine

Guest Editorial

Altered kidney function on the Acute Medical Unit

Reduced kidney function, whether acute or chronic, is a highly significant biomarker of in most clinical settings. This is particularly true on the acute medical take where altered renal function is associated with a worse prognosis, and may also impact on immediate management strategies such as drug choice, dosing and suspension, and the use of contrast agents for imaging. In this edition of the Acute Medical Journal, Yang *et al* present the results of their study describing the renal function and associated characteristics in 2,070 consecutive patients presenting on the unselected medical take at their hospital over a 40 day period.[1] In this study, the authors provide a wealth of information on the general characteristics of acute medical patients admitted with altered kidney function, be it CKD or AKI. Importantly, both chronic kidney disease (CKD) and acute kidney injury (AKI) are very highly prevalent. Indeed, in this study more than 5% of all medical admissions actually demonstrated evidence of both.

Whilst we are familiar with this narrative of altered kidney function, as acute physicians the downstream impact may be less obvious to us. For example, the risk of a patient with CKD progressing to dialysis is nearly 30 fold if they have suffered 2 or more previous AKI compared to those who have not suffered any.[2] Statistics such as this remind us why strategies to prevent the occurrence and progression of AKI must be at the forefront of our minds on the Acute Medical Unit.[3]

A number of figures from the study by Yang *et al* deserve to be highlighted and discussed as further reminders to us of the importance of this clinical scenario. Of the patients they assessed with an admission eGFR <60mL/min/1.73m^2, half were taking a diuretic and half were on a renin-angiotensin-aldosterone (RAAS) blocking agent, most commonly an ACE inhibitor. For these patients, volume depletion and overload were the most common presenting diagnoses and 38% of patient had had a recent change in their medication.

The role of medication in contributing to changes in renal function is evident in the wider literature, but the necessary response to this is not. Prominent examples of this conundrum lay in the field of heart failure. This is due to the high prevalence of CKD and AKI in this population (21% for AKI in a recent study of the prevalence and impact of AKI in selected acute medical diagnoses),[4] and that the staple of therapy for heart failure includes a number of drugs classed as nephrotoxic. The presence of an AKI will most often lead to the suspension of drugs such as ACE inhibitors and mineralocorticoid receptor antagonists, despite recommendations to the contrary in all but the most extreme cases. This recommendation is borne of evidence that the continued use of RAAS blockade post-discharge after AKI is actually associated with better prognosis.[5]

More fundamentally, the presumption that AKI is drug related in patients on these agents may well be misplaced more often than not. For

Acute Medicine is indexed in PubMed and EMBASE and cited in Medline

Published by
Rila Publications Ltd.
73, Newman Street,
London W1T 3EJ, UK
Tel: +44(0)20 7631 1299
Fax: +44(0)20 7580 7166
Website: www.acutemedjournal.co.uk

Design & Production
Georgina DaCambra

Enquiries
Circulation and Foreign Distribution rights contact
Rila Publications Limited

Advertising
Tel: +44 (0)20 7631 1299
Fax: +44 (0)20 7580 7166

Subscription Rates:
Personal

Print & Online:	*UK £100*	*Overseas £140*
Online Only:	*Personal:£60*	*Students: £45*

Institutional/Library

Print Only:	*UK £140*	*Overseas £180*
Online Only:	*£500*	

ISSN: 1747-4884

example, in the SOLVD trial (Enalapril versus placebo for heart failure), 12% of patients in the placebo arm experienced a significant rise in serum creatinine during follow up (defined as ≥44mcmol/L), compared with 16% in the treatment arm *i.e.* change in renal function was just 4% more common in patients on an ACE inhibitor compared to placebo.[6]

The high baseline risk of change in eGFR, independent of medication, reflects the age and multi-morbidity of the study patients. This is similarly highlighted in the study by Yang *et al* presented in this edition, wherein the patients with reduced eGFR selected for the "deep dive" phenotype analysis were older with greater morbidity than the overall study population. This likely reflects that altered renal function in the shape of CKD is very often a signal of multi-morbidity and, with that, frailty.

With multi-morbidity and frailty comes polypharmacy. Yang *et al* provide details of the medication burden in patients presenting on the acute medical take with CKD and AKI. Four in every 5 patients evaluated in detail were taking 5 or more medications, and 1 in 3 were prescribed 10 or more. Of patients admitted with altered renal function and evidence of intravascular volume depletion, only one was on neither a diuretic nor RAAS blockade. The figure was similar for those admitted with falls.

These prescriptions will all have been provided to serve a purpose, and the challenge for us is to determine the relative risks and benefits in the acute setting. Generally, if a drug is a potential culprit in an acute clinical abnormality then it will be suspended. As detailed above from the SOLVD trial, these drugs may be less frequently implicated in AKI than we instinctively believe. However, we cannot always easily know which patients are suffering drug complications and which are not. The default position is most often to err on the side of caution and discontinue a drug until renal recovery is noted. If this practice is to continue as the norm then an important point of learning is to recognise that communicating such prescription changes to the primary care team and relevant specialities at the point of discharge is an absolute necessity.

However, should we always suspend potentially nephrotoxic agents when AKI occurs? For ACE inhibitors the answer is evidently no. Of course, if there is evidence of harm to which the drug is contributing such as hyperkalaemia then it is reasonable for the drug to be suspended. On the other hand, if a patient presents with a stage 1 AKI caused by obstruction and the patient is known to have an improvement in heart failure symptoms as a result of its use there is generally no need to discontinue the drug.

Diuretics are the other class of drugs frequently discontinued at the point of admission in the presence of AKI. Using heart failure as an example again, an improvement in eGFR at 72 hours after admission with decompensation of heart failure is actually associated with a worse prognosis in terms of death and re-admission.[7] This is probably a function of improved eGFR reflecting inadequate fluid management. Current guidance is that heart patients with fluid overload requiring hospitalisation should have their diuretics increased regardless of kidney function.[8]

I have used the word "nephrotoxic" on three occasions up to this point. This is a highly emotive word amongst those with an academic and clinical interest in AKI. Anecdotally, simply labelling a drug as nephrotoxic may increase the likelihood that it will be inappropriately suspended. That a drug has the potential to cause harm does not mean that it will, and also means that the drug's benefits will be lost. As an example, calcineurin inhibitors (CNI) such as tacrolimus are a staple of immunosuppression treatment for kidney transplants but are a common cause of AKI in this population and up to 21% of transplant recipients on a CNI will develop CKD because of the drug. However, assessing risk versus benefit, most patients will stay on this treatment.

So how do we make decisions of balancing the risk versus benefit in the acute medical setting? Although I have described some basic principles here, the answer remains rather vague and clichéd in that we must approach this on a case by case basis. What is therefore vital is we are aware of the evidence base behind the use of these drugs in the acute setting to help us make these challenging decisions.

Beyond this, if our understanding of appropriate management of altered renal function in the acute setting is limited, how else can we use these biochemical data in a useful way? The above commentary highlights the need for robust safety netting and communication between primary and secondary care, and between clinicians and patients, their families, and carers around follow up.

For the Acute Physician, a greater use may come from communicating the immediate prognostic impact of an acute kidney injury. In one study the in-patient mortality for community acquired pneumonia was 8%, but for those with a concurrent AKI was 38% and for concurrent stage 3 AKI was 53%. For COPD the respective values were 2%, 24% and 50%, and for decompensated liver disease was 10%, 26%, and 53%.[4] Thereby, and in conclusion, regardless of how we manage the change in renal function itself, recognising its huge prognostic burden can help us shape the overall care for all acute medical patients presenting with altered renal function.

Darren Green
MRCP PhD
Acute Medicine, Salford Royal NHS Foundation Trust
Division of Cardiovascular Sciences, University of Manchester

Guest Editorial

References

1. E Yang, A Chalisey, ME Reschen, B Shine, DS Lasserson, CA O'Callaghan. Reduced kidney function at presentation in unselected acute emergency medical admissions: incidence, outcome and associated factors. *Acute Medicine*. 2019. **18(3)**: 158-164.
2. Sykes L, Asar O, Ritchie J, Raman M, Vassallo D, Alderson HV, O'Donoghue DJ, Green D, Diggle PJ, Kalra PA. The influence of multiple episodes of acute kidney injury on survival and progression to end stage kidney disease in patients with chronic kidney disease. *PLoS One.* 2019 Jul 18;**14(7)**:e0219828. doi: 10.1371/journal.pone.0219828.
3. Sykes L, Sinha S, Hegarty J, Flanagan E, Doyle L, Hoolickin C, Edwards L, Ferris P, Lamerton E, Poulikakos D, Green D, Nipah R. Reducing acute kidney injury incidence and progression in a large teaching hospital. *BMJ Open Qual*. 2018 Nov 26;**7(4)**:e000308. doi: 10.1136/bmjoq-2017-000308.
4. Sykes L, Kalra PA, Green D. Comparison of impact on death and critical care admission of acute kidney injury between common medical and surgical diagnoses. *PLoS One.* 2019 Apr 11;**14(4)**:e0215105. doi: 10.1371/journal.pone.0215105.
5. Brar S, Ye F, James MT, Hemmelgarn B, Klarenbach S, Pannu N; Interdisciplinary Chronic Disease Collaboration. Association of Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker Use With Outcomes After Acute Kidney Injury. *JAMA Intern Med.* 2018 Dec 1;**178(12)**:1681-1690. doi: 10.1001/jamainternmed.2018.4749.
6. SOLVD Investigators, Yusuf S, Pitt B, Davis CE, Hood WB, Cohn JN. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med.* 1991 Aug 1;**325(5)**:293-302. doi: 10.1056/NEJM199108013250501
7. Testani JM, McCauley BD, Chen J, Coca SG, Cappola TP, Kimmel SE. Clinical characteristics and outcomes of patients with improvement in renal function during the treatment of decompensated heart failure. *J Card Fail.* 2011 Dec;**17(12)**:993-1000. doi: 10.1016/j.cardfail.2011.08.009.
8. Clark AL, Kalra PR, Petrie MC, Mark PB, Tomlinson LA, Tomson CR. Change in renal function associated with drug treatment in heart failure: national guidance. *Heart.* 2019 Jun;**105(12)**:904-910. doi: 10.1136/heartjnl-2018-314158.