Section 1. DEFINITION AND CLASSIFICATION OF ACUTE KIDNEY INJURY

Authors: Zoltan Endre, Robyn Langham

GUIDELINES

a. We recommend using the KDIGO definition to define and to stage functional change in AKI (Table 2). (refer to KDIGO guideline)

b. We recommend that all causes of AKI including contrast-induced-AKI be defined using the same criteria as other causes of AKI. (1D)

c. We recommend that the cause of AKI be defined as soon as possible after diagnosis of AKI (1D)

UNGRADED SUGGESTIONS FOR CLINICAL CARE

- Biomarkers of kidney cellular damage should be incorporated into the AKI definition when sufficient cut-offs are available for each biomarker in the context of renal injury. (Ungraded)

- Functional parameters in addition to structural parameters (determined by elevated biomarkers of structural damage) should be considered in determining the diagnosis, prognosis and outcome of AKI. (Ungraded)

IMPLEMENTATION AND AUDIT

Individual Units should consider an audit of definitions used to diagnose acute kidney injury (AKI) in separate clinical contexts and review against patient outcomes in those contexts.
The following background is based on that provided in the KDIGO guideline and edited to reflect the review conducted for the adaptation.

Functional AKI is defined as any of the following:

2.1.1: AKI is defined as any of the following *(Not Graded)*:
- Increase in SCr by ≥0.3 mg/dl (≥26.5 µmol/l) within 48 hours; or
- Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume <0.5 ml/kg/h for 6 hours.

*Kidney International Supplements (2012) 2, 19–36*

**Table 2 | Staging of AKI**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5–1.9 times baseline OR ≥0.3 mg/dl (≥26.5 µmol/l) increase</td>
<td>&lt;0.5 ml/kg/h for 6–12 hours</td>
</tr>
<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
<td>&lt;0.5 ml/kg/h for ≥12 hours</td>
</tr>
<tr>
<td>3</td>
<td>3.0 times baseline OR Increase in serum creatinine to ≥4.0 mg/dl (≥353.6 µmol/l) OR Initiation of renal replacement therapy OR, In patients &lt;18 years, decrease in eGFR to &lt;35 ml/min per 1.73 m²</td>
<td>&lt;0.3 ml/kg/h for ≥24 hours OR Anuria for ≥12 hours</td>
</tr>
</tbody>
</table>

*Fig 2. KDIGO staging of AKI. (Kidney International Supplements (2012) 2; 19)*
Acute kidney injury (AKI), formerly known as acute renal failure (ARF), is common, especially in hospitalised patients and is independently and strongly associated with morbidity and mortality. AKI is not a single disease, but a complex clinical syndrome that may arise in response to many etiologies, such as circulatory shock, sepsis and nephrotoxins [1]. The underlying pathophysiology of AKI is incompletely understood [2]. Early detection and treatment of AKI may improve outcomes. The KDIGO consensus definition of AKI combines two similar definitions based on SCr and urine output [3,4].

AKI is a subset of acute kidney disease (AKD) and can occur in the presence or absence of other acute or chronic kidney disease (Figure 4 and Table 3).
Fig 4. Overview of AKI, CKD and AKD. (Kidney International Supplements (2012) 2; 20

Table 11 | Definitions of AKI, CKD, and AKD

<table>
<thead>
<tr>
<th>Functional criteria</th>
<th>Structural criteria</th>
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<tbody>
<tr>
<td><strong>AKI</strong></td>
<td>Increase in SCr by 50% within 7 days, OR Increase in SCr by 0.3 mg/dl (26.5 μmol/l) within 2 days, OR Oliguria</td>
</tr>
<tr>
<td><strong>CKD</strong></td>
<td>GFR &lt; 60 ml/min per 1.73 m² for &gt; 3 months</td>
</tr>
<tr>
<td><strong>AKD</strong></td>
<td>AKI, OR GFR &lt; 60 ml/min per 1.73 m² for &lt; 3 months, OR Decrease in GFR by ≥ 35% or increase in Scr by &gt; 50% for &lt; 3 months</td>
</tr>
<tr>
<td><strong>NKD</strong></td>
<td>GFR ≥ 60 ml/min per 1.73 m² Stable Scr</td>
</tr>
</tbody>
</table>

GFR assessed from measured or estimated GFR. Estimated GFR does not reflect measured GFR in AKI as accurately as in CKD. Kidney damage assessed by pathology, urine or blood markers, imaging, and—for CKD—presence of a kidney transplant. NKD indicates no functional or structural criteria according to the definitions for AKI, AKD, or CKD. Clinical judgment is required for individual patient decision-making regarding the extent of evaluation that is necessary to assess kidney function and structure. AKD, acute kidney diseases and disorders; AKI, acute kidney injury; CKD, chronic kidney disease; GFR, glomerular filtration rate; NKD, no known kidney disease; Scr, serum creatinine.

Fig 5. Table of definitions of AKI, CKD and AKD (Kidney International Supplements (2012); 2:33)

**SEARCH STRATEGY**

The search strategy was an update of that used by KDIGO (refer to Table 21 in the Appendix of the KDIGO guideline) (Kidney International Supplements 2 (2012); 2: 102-113). Additional key papers have been identified by the authors that were published after the KHA-CARI update search.
Databases searched: Medline, Central, Cochrane database of systematic reviews

Date of searches: June 2012

ADEQUACY OF KDIGO SEARCH STRATEGY

The search strategy and evidence provided by KDIGO was comprehensive and included some important randomised controlled trials (RCTs). A number of systematic reviews and RCTs have subsequently been identified in the updated search by KHA-CARI and included in this update.

APPLICABILITY OF KDIGO RECOMMENDATIONS AND SUGGESTIONS

The KDIGO recommendations are applicable to the Australian and New Zealand settings.

OVERVIEW OF THE EVIDENCE

The following provides an overview of the evidence as identified in the KDIGO guidelines and the update searches conducted by KHA-CARI as part of the adaptation process.

Definition

The conceptual model of AKI (Figure 6) is analogous to the conceptual model of CKD and is also applicable to AKD [1,4]. The criteria for the diagnosis of AKI and stage of severity are currently based on changes in kidney function. It is widely recognized that GFR is the most useful overall index of kidney function in health and disease, and changes in SCr and/or urine output are surrogates for change in GFR. In clinical practice, an abrupt decline in GFR is assessed from an increase in SCr or oliguria. Changes in SCr are inevitably delayed after any step change in GFR and this will delay detection of AKI [4, 5]. Nevertheless, the current international and interdisciplinary consensus is based on two successive consensus definitions. The modified RIFLE criteria proposed by ADQI [6] and the AKIN [7] which better account for small absolute changes in SCr not captured by RIFLE, comparison of both criteria demonstrate only small differences [3]. Epidemiological studies in over 500,000 subjects collectively support the validity of both criteria to identify groups of hospitalized patients with increased risk of death and/or need for RRT. However application of both RIFLE and AKIN criteria to a single large multicentre cohort of 14,536 patients with sepsis in the SAPS 3 database highlighted differences in the patients captured by the two criteria [8]. In particular AKIN captured mostly (90.7%) Stage 1 AKI missed by RIFLE and, in cases missed by AKIN and identified by RIFLE, 30% were RIFLE-I and 18% RIFLE-F. These AKIN-missed cases had a hospital mortality that was similar.
to cases identified by both criteria (37% for I and 41% for F). Similarly, the RIFLE missed cases that were identified as stage 1 AKI by AKIN, had double the hospital mortality rate (25%) of patients with no evidence of AKI by either criteria (13%). A further large retrospective single centre observational study of 4,836 consecutive patients undergoing cardiac surgery with cardiopulmonary bypass similarly demonstrated excellent association to outcome variables with worse outcome by increased severity of AKI regardless of whether AKIN or RIFLE classification was used [9]. However, potential misclassification of AKI was higher in AKIN (in stage 1/RIFLE class R, because of the larger number of patients who developed a greater than 0.3 mg/dl increase within a 48-hour diagnostic window after cardiopulmonary bypass surgery. Such patients were not misclassified by RIFLE since the increases in creatinine are referred to the baseline (pre-bypass) value. The authors noted that application of AKIN criteria in patients undergoing cardiac surgery without correction of serum creatinine for fluid balance may lead to over-diagnosis of AKI. These data provide a strong rationale for use of both criteria to identify patients with functional AKI but also the caveat discussed below that serum creatinine values should be corrected for fluid balance.

![Conceptual Model](image)

**Fig 6.** Conceptual Model, figure modified after reference 4.

SCr and urine output can only indirectly reflect that kidney damage has occurred.

The availability of new biomarkers of “kidney damage” provides a new opportunity to identify patients with AKI in addition to SCr and urine output criteria. A large number of renal cellular damage markers have been identified over the last decade, many using genomic or proteomic strategies. The urinary biomarkers can be categorized [5] as filtered proteins increased due to
glomerular injury, such as albumin and protein, pre-formed markers released from damaged cells, such as the tubular enzymes gamma glutamyl transpeptidase and alpha- and pi-glutathione S-transferase, and biomarkers induced or up-regulated in response to cellular or tissue injury, including urinary neutrophil gelatinase-associated lipocalin NGAL, kidney injury molecule 1 (KIM-1), interleukin 18 (IL-18), cystatin C and liver-type fatty acid binding protein (L-FABP). Some have been commercialized and two, cystatin C and NGAL, are now available in many routine hospital laboratory biochemistry platforms.

At present all damage biomarkers remain research tools. In homogeneous populations, such as after cardiopulmonary bypass surgery, damage biomarkers have usually been found to be more sensitive, and detect AKI earlier than change in renal function based on SCr \[10-15\]. In heterogeneous populations, such as the critically ill and in the emergency department, individual biomarker performance is reduced unless there is awareness of baseline renal function, duration and cause of renal injury \[14\].

Some biomarkers can be used as markers of change in GFR, such as serum cystatin C, while others reflect tubular injury, such as urinary NGAL, KIM-1, IL-18 and L-FABP. Many urinary markers have been validated by the Food and Drug Administration and European Medicines Agency as damage markers for preclinical drug development and for use in phase 1 or 2 clinical trials \[16, 17\] but none have been validated for routine clinical use. Some change with recovery or treatment \[18, 19\], which suggests utility in monitoring outcome after intervention. Since some of the biomarkers are site and mechanism specific, they will increase our understanding of AKI pathogenesis and may even facilitate specific intervention. Most importantly, patients with increased damage biomarkers but no increase in creatinine may have an increased risk of dialysis or death similar to patients with an increase in creatinine without an increase in damage biomarkers. This points to the existence of new category of AKI, namely patients who are biomarker-positive, and creatinine-negative.

Two large studies demonstrated that biomarker detection of renal injury in patients prior to a rise in creatinine can predict the same or worse outcomes in terms of need for dialysis and of mortality. A review of 10 large observational studies amalgamated to 2322 critically ill patients with predominantly cardiorenal syndrome monitored prospectively using plasma or urinary NGAL observed that the cohort of biomarker-positive, creatinine-negative patients were at a similar increased risk of dialysis and death to the creatinine-positive, biomarker negative group \[20\]. Similarly, a multicentre prospective cohort study of 1,635 unselected emergency department patients revealed that, a substantial subpopulation with increased urinary biomarkers (NGAL or KIM-1) but low SCr at hospital admission were at increased risk of dialysis or death in hospital. In the latter study, of the 5 urinary biomarkers assessed at the time of admission (NGAL, KIM-1, L-FABP, IL-18 and cystatin C), NGAL was most useful (81% specificity, 68% sensitivity at a 104-ng/ml cutoff) in diagnosis and prediction of the severity and duration of AKI \[21\]. In related observations, two studies of critically ill patients with apparent pre-renal AKI, defined as transient AKI (less than 48 hours) with preserved tubular function, detected urinary
biomarkers at concentrations intermediate between patients without AKI and those where AKI became established for more than 48 hours [22, 23]. These latter observations suggested that what has been described as "pre-renal AKI" is simply the mild end of a continuum of renal injury, rather than a reversible functional form of AKI without cellular damage.

As a consequence of these observations, the ADQI group at a meeting in Dublin in September 2011, recommended the addition of biomarker estimation to the definition, staging and differential diagnosis of AKI to complement the KDIGO (RIFLE/AKIN) criteria [24]. The group also recommended that the pathophysiological terms "functional change" and "kidney damage" be used in preference to the anatomical classification using the terms pre-renal, renal and post-renal AKI. Future revisions of the definition of AKI will need to include both biomarkers of function and damage, leading to three categories of AKI, namely functional, damage and combined functional and damage AKI. There are currently insufficient quantitative biomarkers data for AKI staging and biomarker guided interventions have not yet been shown to be of benefit [25].

However functional and damage markers will be combined in the future. Such combinations are likely to enhance diagnosis [26]. For example, a number of studies have highlighted that "old" biomarkers detected by urine microscopy are of significant value in the early differential diagnosis of AKI [26-28]. Combining the high specificity of epithelial cell casts with the high sensitivity of urinary NGAL led to improved predictive performance in AKI diagnosis [29, 30]. Further large scale studies are required to determine context specific biomarker thresholds in AKI of different aetiologies.

While serum creatinine and urinary volume currently remain the clinical pointers to AKI diagnosis, we consider that using the term “functional AKI” to distinguish AKI defined only by change in creatinine or urine volume, from “structural AKI” defined, in the future, by the presence of elevated biomarkers of structural damage.

A number of additional concerns remain concerning definitions of functional AKI, with respect to baseline function and the effect of fluid loading. Firstly, creatinine-based definitions rely on knowing the baseline creatinine and approximately 50% of admissions do not have one [25]. Consequently a number of strategies have been proposed including back calculation of SCr using the MDRD formula and assuming a 75% GFR [31]. This performs well when near-normal baseline kidney function is present [32], but leads to consistent errors [32, 33] especially in patients with pre-existing CKD [33]. These errors are best overcome by using a hierarchical approach favouring a measured creatinine in the 3 months prior to admission, the lowest observed creatinine at or after discharge and creatinine on-admission (in that order)[34]. While this is fine for post-hoc analysis, it is of no benefit in patient management, where either the back-calculation method or on admission values must be used despite the inherent problems. While this will be solved to some extent by use of the damage biomarkers, some of these are increased in CKD (e.g. KIM-1, NGAL) and some conditions may differentially increase others (e.g. NGAL in sepsis) leading to higher baseline and
diagnostic threshold biomarker values. An analysis of nadir-to-peak creatinine increments stratified by baseline eGFR in 29,645 adults in a single centre found that a greater absolute increase in creatinine was required to have an equivalent risk of in-hospital mortality as eGFR decreased [35]. The validation of novel direct methods of measuring true GFR in close to real-time fashion [22] will likely supersede calculation of eGFR and provide additional ways of identifying or excluding AKI in the future. However, even future definitions of functional AKI will still need to consider the patient’s baseline GFR.

Secondly, large volume resuscitation is common in critically ill patients. While many negative consequences of fluid overload are well known [36], the significant dilution of serum creatinine can delay or obscure diagnosis of AKI. In a study of 253 patients recruited from a prospective observational study of critically-ill patients with AKI, 64 (25%) were recognized late (by more than 24 hours) when the serum creatinine value was not adjusted for fluid loading [37]. In contrast, as discussed earlier, dilution of serum creatinine after cardiopulmonary bypass can lead to misclassification of patients as having AKI when the AKIN criteria are used [9]. It is therefore important that serum creatinine values, and by inference the concentrations of other biomarkers, are corrected for fluid balance when patients receive large volumes of intravenous fluid after resuscitation, cardiopulmonary bypass and other relevant clinical scenarios.

**Staging**

For staging purposes, patients should be staged according to the criteria that give them the highest stage. Thus when creatinine and urine output map to different stages, the patient is staged according to the highest (worst) stage. The changes in GFR that were published with the original RIFLE criteria do not correspond precisely to changes in SCr [38]. As SCr is measured and GFR can only be estimated, creatinine criteria should be used along with urine output for the diagnosis (and staging) of functional AKI. One additional change in the criteria was made for simplicity. For patients automatically qualifying as Stage 3 by an increase in SCr to 354 \( \mu \text{mol}/l \) (4.0mg/dl), these patients must first satisfy the creatinine-based change specified in the definition of functional AKI (either an increase of at least 26.5 \( \mu \text{mol}/l \) [0.3mg/dl] within a 48-hour time window or an increase of 1.5 times baseline).

We note and support the KDIGO recommendation to modify these criteria for paediatric patients. The pediatric-modified RIFLE (pRIFLE) AKI criteria [6] were developed using a change in estimated creatinine clearance (eCrCl) based on the Schwartz formula. In pRIFLE, patients automatically reach Stage 3 if they develop an eCrCl <35 ml/min per 1.73 m\(^2\). However, with this automatic pRIFLE threshold, the SCr change-based AKI definition (recommendation 2.1.1) is applicable to pediatric patients, including an increase of 26.5 \( \mu \text{mol}/l \) (0.3 mg/dl) in SCr.

The use of urine output criteria for diagnosis and staging is less well validated and in individual patients the need for clinical judgment regarding the effects of
drugs (e.g. angiotensin-converting enzyme inhibitors), fluid balance, and other factors must be included. For very obese patients, urine output criteria for AKI may include some patients with normal urine output. However, these recommendations serve as the starting point for further evaluation for a group of patients recognized to be at increased risk.

Importantly, it is axiomatic that patients always be managed according to the cause of their disease. Thus it is important to determine the cause as soon as possible whenever AKI is diagnosed. In particular, patients with decreased kidney perfusion, rapidly progressive glomerulonephritis, vasculitis, interstitial nephritis, thrombotic microangiopathy, and urinary tract obstruction require immediate diagnosis and specific therapeutic intervention, in addition to the general recommendations for AKI management (Figure 1 and in the remainder of this guideline). It is therefore always necessary to search for the underlying cause of AKI.

Finally, we recognize that the definition of AKI will continue to evolve. The use of functional and damage biomarkers will facilitate identification of functional and/or structural AKI. The validation of novel measurements of GFR in near real-time will provide additional ways of identifying or excluding functional AKI and allowance for fluid balance will reduce misclassification by these groups of biomarkers. These refinements will need to be incorporated progressively into the definition of AKI.

Risk factors for AKI

Numerous risk factors for AKI have been identified, including dehydration or volume depletion, advanced age, female gender, black race, CKD, other chronic diseases (heart, lung, liver), diabetes mellitus, cancer and anaemia. In the KDIGO guidelines these are summarised in Table 6 as exposures and susceptibilities [39]. A more thorough understanding of risk factors will help to achieve better prevention and prognosis. Newly identified risk factors for AKI are hypoalbuminaemia, burns and inflammation as measured by C-reactive protein in the setting of coronary artery stenting:

- A meta-analysis of observational studies of hypoalbuminaemia has identified this as an independent risk factor for AKI and post-AKI death [40]. Although the link has not been shown to be causal, further controlled-clinical trials are required to clarify the risk.
- A meta-analysis examining AKI in severe burn patients found a 25% incidence of AKI and associated it with increased mortality [41].
- Two retrospective studies have found that elevated preprocedural levels of C-reactive protein (CRP) before percutaneous coronary intervention is associated with an increased risk of CI-AKI [42, 43].
WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative (2013): [44]

2.1.1- AKI is defined as any of the following (Not Graded):
- Increase in SCr by $\geq 0.3$ mg/dL ($\geq 26.5$ μmol/L) within 48 hours; or
- Increase in SCr to $\geq 1.5$ times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume $< 0.5$ mL/kg/h for 6 hours.

2.1.2- AKI is staged for severity according to the following criteria. (Not Graded)
Stage 1: Increase in SCr by 1.5-1.9 times baseline; OR
Increase in sSCr by ($\geq 0.3$ mg/dL ($\geq 26.5$ μmol/L); OR
Urine output $< 0.5$ mL/kg/h for 6-12 hours

Stage 2: Increase in SCr by 2.0-2.9 times baseline; OR Urine output $< 0.5$ mL/kg/h for 12 hours

Stage 3: Increase in SCr by 3.0 times baseline; OR
Increase in SCr to 4.0 mg/dL (353.6 μmol/L); OR
Initiation of renal replacement therapy; OR
In patients $< 18$ years, decrease in eGFR to 35 mL/min/1.73 m2; OR
Urine output $< 0.3$ mL/kg/h for $\geq 24$ hours; OR Anuria for $\geq 12$ hours

2.1.3: The cause of AKI should be determined whenever possible. (Not Graded)

2.2.1: We recommend that patients be stratified for risk of AKI according to their susceptibilities and exposures. (1B)

2.2.2: Manage patients according to their susceptibilities and exposures to reduce the risk of AKI (see relevant guideline sections). (Not Graded)

2.2.3: Test patients at increased risk for AKI with measurements of SCr and urine output to detect AKI. (Not Graded). Individualize frequency and duration of monitoring based on patient risk and clinical course. (Not Graded)

2.3.1: Evaluate patients with AKI promptly to determine the cause, with special attention to reversible causes. (Not Graded)

2.3.2: Monitor patients with AKI with measurements of SCr and urine output to stage the severity, according to Recommendation

2.1.2. (Not Graded)
2.3.3: Manage patients with AKI according to the stage (Fig 2) and cause. (Not Graded)

2.3.4: Evaluate patients 3 months after AKI for resolution, new onset, or worsening of pre-existing CKD. (Not Graded)
- If patients have CKD, manage these patients as detailed in the KDOQI CKD Guideline (Guidelines 7-15). (Not Graded)
- If patients do not have CKD, consider them to be at increased risk for CKD and care for them as detailed in the KDOQI CKD Guideline 3 for patients at increased risk for CKD. (Not Graded)

UK Renal Association (2011): [45]
1.1- We recommend that the international Kidney Disease: Improving Global Outcomes (KDIGO) definition of acute kidney injury (AKI) should be adopted. (Not Graded)
1.2- We recommend that the international Kidney Disease: Improving Global Outcomes (KDIGO) Staging classification* of acute kidney injury (AKI) should be adopted. (Not Graded)
1.3- We recommend that serum creatinine and urine output remain the best biomarkers for AKI. Serum creatinine should be measured using the enzymatic technique. (1B)

Canadian Society of Nephrology (2013): [46]
The Canadian Society of Nephrology (CSN) commentary on KDIGO Clinical Practice Guideline for Acute Kidney Injury, states that the KDIGO definition of AKI should be limited to research purposes of this time. CSN states

‘When diagnosing and managing AKI, clinicians should consider other factors in addition to SCr level and urine output, such as trends in renal function, cause of AKI, concurrent diseases and comorbid conditions, as well as fluid balance and acid-base and/or electrolyte complications’.

European Renal Best Practice Guidelines (2012): [47]
1.1.1 We recommend using a uniform definition of AKI, based on urinary output and on changes in serum creatinine (SCr) level. It is important that both criteria are taken into account. (1C)
1.1.2 We recommend diagnosing and indicating the severity of AKI according to the criteria in the table below: (ungraded statement)
Table 1. European Renal Best Practice Guidelines: Acute Kidney Injury Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
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| 1     | Serum creatinine increased 1.5–1.9 times baseline  
• Serum creatinine increase >0.3mg/dl (26.5 μmol/l)  
• Urinary output < 0.5ml/kg/h during a 6 hour block |
| 2     | Serum creatinine increase 2.0–2.9 times baseline  
• Urinary output <0.5ml/kg/h during two 6 hour blocks |
| 3     | Serum creatinine increase >3 times baseline  
• Serum creatinine increases to >4.0mg/dl (353 μmol/l)  
• Initiation of renal replacement therapy  
• Urinary output <0.3ml/kg/h during |

1.1.2a We recommend using the first documented serum creatinine value of the episode as ‘baseline’, rather than historical creatinines or a calculated value based on a presumed glomerular filtration rate (GFR) of 75 mL/min. (1C)

1.1.2b We suggest using ‘shift-based’ calculation of the urinary output criteria, especially in patients without a bladder catheter (1C). We recommend to use the ideal weight rather than the true weight in calculating the diuresis in mL/min/kg. (Ungraded statement)

1.1.3 The cause of AKI should be determined whenever possible. As a minimal work-up, the presence of hypovolaemia, post-renal causes, low cardiac output, use of nephrotoxic agents, acute glomerulonephritis and renal micro-angiopathy as underlying contributors to AKI should be evaluated. (Ungraded statement)

SUGGESTIONS FOR FUTURE RESEARCH

The role of biomarkers other than SCr in the early diagnosis, differential diagnosis, and prognosis of AKI patients should be explored in all contexts of risk. Some important areas in which to focus include:

- Early detection where the gold standard is AKI by clinical diagnosis after the fact and the biomarker is compared to existing markers (SCr and urine output) at the time of presentation.
• Prognosis where a biomarker is used to predict risk for AKI or risk for progression of AKI.
• Prognosis where a biomarker is used to predict recovery after AKI vs. death or need for acute or long-term RRT.
• The influence of urinary output criteria on AKI staging needs to be further investigated, including how urine volume criteria should be applied (e.g., average vs. persistent reduction for the period specified).
• The influence of fluid balance, percent volume overload, diuretic use, and differing weights (actual, ideal body weight, lean body mass) on all functional and structural biomarkers should be considered.
• The influence of SCr or eGFR criteria on AKI staging needs to be further investigated. The use of different relative and absolute SCr increments or eGFR decrements at different time points and with differently ascertained baseline values requires further exploration and validation in various populations.
• The development of real-time measures of GFR and the potential for using biomarkers to assess outcome should be explored.

CONFLICT OF INTEREST

Z Endre has received an Honorarium from Novartis Transplant Advisory Board (2012, 2013), financial support for travel from Alere (2010) and Novartis (2011) and Accommodation Amgen (2013). Research funding has been provided by Alere, Argutis, Abbot (2007-2010) for provision of assay kits.

R.G. Langham has received honorarium and travel support from Amgen (2010-2013), consulting fees from Astra Zeneca (2013), travel support to travel to a European nephrology meeting from Novartis (2012) and honorarium for Advisory Board role from MSD (2011).
REFERENCES


