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EDITORIAL COMMENTARY

Improving outcomes from acute kidney injury: report of an initiative

Arvind Bagga · Aysin Bakkaloglu · Prasad Devarajan · Ravindra L. Mehta · John A. Kellum · Sudhir V. Shah · Bruce A. Molitoris · Claudio Ronco · David G. Warnock · Michael Joannidis · Adeera Levin · Acute Kidney Injury Network

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Abstract Acute kidney injury (AKI) is a clinical condition characterized by acute decline in renal function, with manifestations ranging from minimal elevation of serum creatinine concentration to anuric renal failure. Keeping in view that acquisition of knowledge and research in this important area requires multi-disciplinary collaboration, a group representing members of the Acute Dialysis Quality Initiative and nephrology and critical care societies has established the Acute Kidney Injury Network (AKIN). The First Consensus Conference of this network focused on defining diagnostic and staging criteria for AKI. Changes in serum creatinine levels and urine output were used to define and stage three levels of renal dysfunction. These criteria require evaluation and validation in prospective clinical studies and, perhaps, modifications as more sensitive markers of kidney injury are identified. Other issues that need to be examined include global epidemiology and outcome of AKI and development of strategies to improve outcomes. The vital role of multi-disciplinary conferences for disseminating knowledge and clarifying issues in clinical practice was recognized.

A. Bagga (✉)
Division of Pediatric Nephrology,
All India Institute of Medical Sciences,
New Delhi 110029, India
e-mail: arvindbagga@hotmail.com

A. Bakkaloglu
Department of Pediatric Nephrology and Rheumatology,
Hacettepe University, Sihhiye,
Ankara, Turkey

P. Devarajan
Department of Nephrology and Hypertension,
Cincinnati Children's Hospital,
Cincinnati, OH, USA

R. L. Mehta
Department of Medicine,
University of California San Diego Medical Center,
San Diego, CA, USA

J. A. Kellum
Department of Critical Care Medicine, University of Pittsburgh,
Pittsburgh, PA, USA

S. V. Shah
Division of Nephrology, UAMS College of Medicine,
Little Rock, AR, USA

B. A. Molitoris
Department of Medicine, Indiana University,
Indianapolis, IN, USA

C. Ronco
Department of Nephrology Dialysis & Transplantation,
San Bortolo Hospital,
Vicenza, Italy

D. G. Warnock
Department of Medicine, University of Alabama,
Birmingham, AL, USA

M. Joannidis
Department of Medicine, University of Innsbruck,
Innsbruck, Austria

A. Levin
Department of Medicine, University of British Columbia,
St Pauls Hospital,
Vancouver, BC, Canada

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Acute kidney injury (AKI) is a common clinical problem defined by an abrupt (<48 h) increase in serum creatinine resulting from an injury or insult that causes a functional or structural change in the kidney. Recent epidemiological studies have demonstrated wide variation in etiologies and risk factors associated with AKI [1–4] and increased hospital mortality following AKI that further worsens if dialysis is required [1–4]. There is emerging recognition that even minor short-term changes in serum creatinine concentrations are associated with increased mortality [5–9]; other important consequences of AKI are progression of pre-existing chronic kidney disease (CKD) and even development of end-stage renal disease (ESRD) [10–12].

A major limitation in improving outcomes from AKI has been the lack of common standards for diagnosis and classification. Recognizing that future clinical and translational research in AKI will require the development of multi-disciplinary collaborative networks of investigators, a group representing members from the Acute Dialysis Quality Initiative (ADQI) [13] and nephrology and critical care societies recently established the Acute Kidney Injury Network (AKIN) [14] to facilitate international, inter-disciplinary and inter-society collaboration that will ensure progress in this field. The fundamental goal is to ensure the best outcomes for patients with and at risk of AKI. The first AKIN conference, held in Amsterdam in September 2005, focused on the development of uniform standards for definition and classification of AKI. While the complete report is published elsewhere [14], key elements are summarized below.

Recommendations

Proposal for uniform standards for definition and classification of AKI

Previous studies have used assorted definitions for AKI, including serum creatinine changes, absolute levels of serum creatinine, changes in urine output or blood urea nitrogen or the need for dialysis.

The wide variation in definitions has made it difficult for information to be compared across studies and populations [15]. The proposed diagnostic criteria for AKI are shown in Table 1 and are based on the following considerations:

(a) The definition should be based on readily obtained criteria that are available worldwide, and it needs to be broad enough to accommodate variations in clinical presentation over age groups, locations and clinical situations.
(b) Serum creatinine levels and urine output are two common measures reflecting renal function; however, they are each influenced by factors other than the glomerular filtration rate and do not provide information on the nature and site of kidney injury.
(c) Currently, there is a lack of sensitive and specific markers for kidney injury available in clinical practice, although several kidney-specific biomarkers are under development [16].

Table 1 Diagnostic criteria for acute kidney injury. From Mehta et al. [14], with permission

Characteristics
An abrupt (within 48 h) reduction in kidney function currently defined as an absolute increase in serum creatinine concentration by either >0.3 mg/dl (>26.4 μmol/l) or an increase of ≥50% (1.5-fold from baseline) or reduction in urine output (documented oliguria of <0.5 ml/kg per hour for >6 h)[a]

[a] The above criteria should be used in the context of clinical presentation and following adequate resuscitation with fluid, when applicable

The absolute criteria for diagnosing AKI were based on evidence that small changes in serum creatinine levels are associated with adverse outcomes in a variety of settings [17, 18]. These changes are manifested both with short-term increase in morbidity and mortality and with

Table 2 Classification and staging system for AKI. Modified from RIFLE criteria [13] and Mehta et al. [14], with permission

Stage	Creatinine criteria	Urine output criteria
1	Rise of serum creatinine by >0.3 mg/dl (>26.4 μmol/l) or increase to ≥150–200% (1.5-fold to twofold) from baseline	<0.5 ml/kg per hour for >6 h
2	Increase of serum creatinine to >200–300% (twofold to threefold) from baseline	<0.5 ml/kg per hour for >12 h
3	Increase of serum creatinine to >300% (>threefold) from baseline (or serum creatinine ≥ 4.0 mg/dl (≥354 μmol/l with an acute rise of at least 0.5 mg/dl (44 μmol/l)	<0.3 ml/kg per hour for 24 h, or anuria for 12 h

Given the wide variation in indications and timing of initiation of renal replacement therapy (RRT), individuals who receive RRT are considered to have met the criteria for stage 3, irrespective of the stage they are in at the time of RRT

longer term outcomes including 1-year mortality. The coefficient of variation of serum creatinine levels with modern analyzers is relatively small; therefore, changes of >0.3 mg/dl are unlikely to be due to assay variation [19]. Urine output was included as a diagnostic criterion, as, in patients in intensive care units (ICUs), it often portends renal dysfunction prior to changes in serum creatinine level, although hydration state, use of diuretics and presence of obstruction can influence the urine volume. A time constraint of 48 h for diagnosis was proposed to ensure that the process was acute and representative of events within a clinically relevant period.

Table 2 shows the proposed staging system for AKI that is intended to define the level of renal dysfunction at the time of diagnosis and to track the course of the disease over time. The RIFLE criteria [risk, injury, failure, loss and ESRD] [13] utilize changes in serum creatinine concentration and urine output to characterize three levels of renal dysfunction. The proposed staging system retains the emphasis on changes in serum creatinine levels and urine output and corresponds to the risk, injury and failure categories of the RIFLE classification, with the stage 1 criteria representing the new diagnostic criteria for AKI. The loss and ESRD categories of the RIFLE system were removed from the staging system, as they are outcomes of AKI itself. The proposed diagnostic and staging criteria for AKI are designed to facilitate acquisition of new knowledge in this field and validate the emerging concept that small alterations in kidney function may contribute to adverse outcomes. The Network recognizes that these criteria may be overly sensitive; accordingly, there may be an increase in false positives, such that some patients labeled with AKI will not have the disease. Further, it is evident that these criteria will require evaluation and validation and, eventually, amendment as new biomarkers emerge that may better identify AKI [16].

International collaborative network

Establishment of an international collaborative research network could facilitate acquisition of evidence through well-designed and well-conducted clinical trials, dissemination of information via multi-disciplinary joint conferences and publications, and translation of knowledge from pre-clinical research. The group proposed to develop the AKIN collaborative effort further, based on four major principles:

(a) identifying the key roles of each of the existing societies/groups to allow retention of their identities and strengths while levering the opportunity for collaboration
(b) defining the scope of collaboration
(c) ascertaining and developing the infrastructure needed for a collaborative network, and
(d) identifying unifying principles and initial projects that would form the basis of ongoing collaboration [14].

Future directions

The AKIN conference recognized that collaborative and integrated joint conferences are essential to facilitate the dissemination of knowledge, clarify clinical practice and enhance research. The group described the five key elements that should be addressed by the professional communities involved in the care of patients with AKI [14]. These key elements included evaluation of the global epidemiology of AKI; delineation of clinically meaningful outcomes; development and implementation of strategies to improve outcomes; promotion of research studies to enhance knowledge; and assessment of the effectiveness of these collaborative approaches. A follow-up conference was held in Vancouver in 2006, and the results will be published soon.

Conclusions

AKI is a complex disorder comprising several etiological factors and occurring in multiple settings with varied clinical manifestations that may range from minimal elevation of serum creatinine concentration to anuric renal failure. We have described the formation of a multi-disciplinary collaborative network focused on AKI, and within this network, have proposed uniform standards for diagnosing and classifying AKI. While these proposed standards will need to be validated in future studies, the Acute Kidney Injury Network offers a forum to encourage knowledge acquisition to improve patients' outcomes.

Acknowledgment The AKIN working group consists of multiple representatives from pediatric and adult nephrology and critical care medicine from around the world. The names of individuals are listed in the reference article published in Critical Care 2007 [14].

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