
See the related article, “Regression of Nephropathy Developed in Diabetes by (Pro)renin Receptor Blockade,” on pages 2054–2061.

Improving Outcomes from Acute Kidney Injury

Bruce A. Molitoris,* Adeera Levin,‡ David G. Warnock,§ Michael Joannidis,§ Ravindra L. Mehta,∥ John A. Kellum,¶ Claudio Ronco,** and Sudhir Shah;†† on behalf of the Acute Kidney Injury Network

*Division of Nephrology, Indiana University School of Medicine, Indianapolis, Indiana; ‡Division of Nephrology, University of British Columbia, Vancouver, British Columbia, Canada; §Division of Nephrology, University of Alabama School of Medicine, Birmingham, Alabama; ¶Medical Intensive Care Research Unit, Department of Internal Medicine, Innsbruck Medical School, Innsbruck, Austria; **Division of Nephrology, University of California, San Diego, California; ††Departments of Critical Care Medicine and Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; **Department of Nephrology, San Bortolo Hospital, Vicenza, Italy; and ¶¶Division of Nephrology, University of Arkansas, Little Rock, Arkansas

Acute kidney injury is a common clinical problem that is defined by an abrupt increase in serum creatinine over 48 h resulting from injury or insult that causes a functional or structural change in the kidney. Recent epidemiologic studies demonstrate wide variation in causes and risk factors associated with acute kidney injury and increased hospital mortality that worsens when dialysis is required. Even minor short-term changes in serum creatinine are associated with increased mortality. Other important consequences of acute kidney injury are progression of preexisting chronic kidney disease and development of end-stage renal disease.

A major limitation in improving outcomes from acute kidney injury has been the lack of common standards for diagnosis and classification. Recognizing that future clinical research in acute kidney injury requires a multidisciplinary collaborative network of investigators, a group representing members from the Acute Dialysis Quality Initiative, nephrology, and critical care societies recently established the Acute Kidney Injury Network (AKIN). The purpose of this network is to facilitate international, interdisciplinary, and intersociety collaborations to ensure progress in the field of acute kidney injury. The fundamental goal is to improve best outcomes for patients who are at risk. The first AKIN conference, held in Amsterdam in September 2005, focused on the development of uniform standards for definition and classification of acute kidney injury. Although the complete report is published elsewhere, key elements are summarized here as recommendations.

First, there need to be uniform standards for definition and classification of acute kidney injury. Previous studies have used a variety of definitions, including change in serum creatinine, absolute levels of serum creatinine, changes in urine output or blood urea nitrogen, or need for dialysis.

The wide variation in definitions has made it difficult to compare information across studies and populations. AKIN’s diagnostic criteria for acute kidney injury include an abrupt (within 48 h) reduction in kidney function currently defined as an absolute increase in serum creatinine of ≥0.3 mg/dl (≥26.4 μmol/L), a percentage increase of ≥50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of <0.5 ml/kg per h for >6 h). These diagnostic criteria are based on the following considerations: The definition should depend on

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Bruce A. Molitoris, Department of Medicine, Indiana University School of Medicine, R2, Room 202, 950 W. Walnut Street, Indianapolis, IN 46202 Phone: 317-274-5287; Fax: 317-274-8575; E-mail: bmolitoris@iupui.edu

Copyright © 2007 by the American Society of Nephrology
readily obtained measurements that are available worldwide, and it needs to be broad enough to accommodate variations in age groups, locations, and clinical presentation. Although serum creatinine and urine output are two common measures reflecting renal function, they each are influenced by factors other than the GFR and do not provide information on the nature and site of kidney injury. Finally, there is a lack of sensitive and specific markers for kidney injury in clinical practice, although several kidney-specific biomarkers are under development.

The absolute criteria for diagnosing acute kidney injury is based on evidence that small changes in serum creatinine are often associated with adverse outcomes in a variety of settings. These changes manifest as short-term increases in morbidity and mortality and as longer term outcomes, including 1-yr mortality. The coefficient of variation of serum creatinine with modern analyzers is relatively small; therefore, changes of ≥0.3 mg/dl are unlikely to be due to assay variation.12 Urine output is often included as a diagnostic criterion because it often portends renal dysfunction in critical care patients before changes in serum creatinine, although state of extracellular blood volume, use of diuretics, and presence of obstruction all can influence urine volume. A time constraint of 48 h for diagnosis is proposed to ensure the process is acute and representative of events within a clinically relevant time period.

Second, AKIN proposes a staging system for acute kidney injury that defines the level of renal dysfunction at the time of diagnosis and tracks the course of the disease over time: Stage 1, serum creatinine of ≥0.3 mg/dl (≥26.4 μmol/L) or an increase to ≥150 to 200% (1.5- to two-fold) from baseline with a urine output of <0.5 ml/kg per h for >6 h; stage 2, serum creatinine of >200 to 300% (more than two- to three-fold) from baseline with a urine output of <0.5 ml/kg per h for >12 h; and stage 3, serum creatinine of >300% (more than three-fold) 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) with a urine output of <0.3 ml/kg per h for 24 h or anuria for 12 h. These RIFLE (risk, injury, failure, loss, end-stage renal disease) criteria13 use changes in serum creatinine and urine output to characterize three levels of renal dysfunction. The proposed staging system retains emphasis on changes in serum creatinine and urine output and corresponds to the risk, injury, and failure categories of the RIFLE classification, with the stage 1 definition representing new diagnostic criteria for acute kidney injury. The loss and end-stage renal disease categories of the RIFLE system were removed from the staging system, because they are outcomes of acute kidney injury itself. The proposed diagnostic and staging criteria for acute kidney injury are designed to facilitate acquisition of new knowledge in this field and validate the emerging concept that small alterations in kidney function contribute to adverse outcomes. AKIN recognizes these criteria may be overly sensitive; accordingly, there may be an increase in false positive rates, such that some patients who are labeled with acute kidney injury will not have the disease. Furthermore, these criteria will require evaluation and validation and eventually amendment as new biomarkers that may better identify acute kidney injury emerge.13

Third, the establishment of an international collaborative research network could facilitate acquisition of evidence through well-designed clinical trials, dissemination of information through multidisciplinary joint conferences and publications, and translation of knowledge from preclinical research. The group intends to develop further the AKIN collaborative effort on the basis of four major principles: Identifying the key roles of each of the existing societies and practice groups to allow retention of their individual identities and strengths while leveraging the opportunity for collaboration, defining the scope of collaboration, ascertaining and developing the infrastructure needed for a collaborative network, and identifying unifying principles and initial projects that would form the basis of ongoing work.9

Fourth, our 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 that are involved in the care of patients with acute kidney injury.9 These include evaluation of the global epidemiology of acute kidney injury, delineation of clinically meaningful outcomes, development and implementation of strategies to improve outcomes, promotion of research 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. It is our belief that AKIN offers a unique forum to focus on improvements in patient outcome.

DISCLOSURES
None.

REFERENCES
6. Liano F, Junco E, Pascual J, Madero R, Verde E: The spectrum of acute renal failure in the intensive care unit compared with that seen in other