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SPECIAL ANNOUNCEMENT

Improving Outcomes From Acute Kidney Injury: Report of an Initiative

Acute kidney injury (AKI) is a common clinical problem defined by an abrupt (within 48 hours) 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 are associated with increased mortality[5-9]; other important consequences of AKI are progression of pre-existing chronic kidney disease and even development of end-stage renal disease.[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 multidisciplinary collaborative networks of investigators, a group representing members of the Acute Dialysis Quality Initiative (ADQI)[13] and nephrology and critical care societies recently established the Acute Kidney Injury Network (AKIN)[14] in order to facilitate international, interdisciplinary, and intersociety collaboration that will ensure progress in the field of AKI. The fundamental goal is to ensure the best outcomes for patients with and at risk for 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 here.

RECOMMENDATION 1: 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 to compare information across studies and populations.[15] The proposed diagnostic criteria for AKI are shown in Table 1 and are based on the following considerations:

1. The definition should be based on readily obtained criteria that are available worldwide and should be broad enough to accommodate variations in clinical presentation over age groups, locations, and clinical situations.
2. Serum creatinine and urine output are 2 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.

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Table 1. Diagnostic Criteria for Acute Kidney Injury (AKI)

Diagnostic criteria for AKI: An abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of either ≥0.3 mg/dL (≥26.4 μmol/L) or a percentage increase of ≥50% (1.5-fold from baseline) or a reduction in urine output (documented oliguria of <0.5 mL/kg/h for >6 hours).

Note: The above criteria should be used in context of the clinical presentation and following adequate fluid resuscitation when applicable. From Mehta et al[14]; used with permission.

3. 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]

The absolute criteria for diagnosing AKI were based on evidence that small changes in serum creatinine are associated with adverse outcomes in a variety of settings. These changes manifest both with short-term increases in morbidity and mortality and with longer term outcomes including 1 year mortality.[17,18] The coefficient of variation of serum creatinine with modern analyzers is relatively small; therefore, changes of 0.3 mg/dL or more are unlikely to be due to assay variation.[19] Urine output was included as a diagnostic criterion because in patients in intensive care units it often portends renal dysfunction prior to changes in serum creatinine, although hydration state, use of diuretics, and presence of obstruction can all influence the urine volume. A time constraint of 48 hours for diagnosis was proposed to ensure that the process was acute and representative of events within a clinically relevant time period.

Table 2 shows the proposed staging system for AKI, which 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 Risk, Injury, Failure, Loss, and End-stage kidney disease (RIFLE) criteria[13] utilize changes in serum creatinine and urine output to characterize 3 levels of renal dysfunction. The proposed staging system retains the 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 criteria representing the new diagnostic criteria for AKI. The Loss and End-stage kidney disease 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 maybe overly sensitive; accordingly, there may be an increase in false positives, such that some 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]

RECOMMENDATION 2: INTERNATIONAL COLLABORATIVE NETWORK

Establishment of an international collaborative research network could facilitate acquisition of evidence through well-designed and conducted clinical trials, dissemination of information via multidisciplinary joint conferences and publications, and translation of

Table 2. Classification/Staging System for Acute Kidney Injury

Stage	Creatinine Criteria	Urine Output Criteria
1	Increase in serum creatinine of ≥0.3 mg/dL (≥26.4 μmol/L) or increase of ≥150%-200% (1.5-fold to 2-fold) above baseline	<0.5 mL/kg/h for >6 h
2	Increase in serum creatinine of >200%-300% (>2-fold to 3-fold) above baseline	<0.5 mL/kg/h for >12 h
3	Increase in serum creatinine of >300% (>3-fold) above baseline, or serum creatinine ≥4.0 mg/dL (≥354 μmol/L) with an acute rise of ≥0.5 mg/dL (≥44 μmol/L)	<0.3 mL/kg/h x 24 h or anuria x 12 h

Note: Modified from RIFLE criteria, in Mehta et al[14]; used with permission.

knowledge from preclinical research. The group proposed to further develop the AKIN collaborative effort based on 4 major principles: (1) identifying the key roles of each of the existing societies/groups to allow retention of their individual identities and strengths while leveraging the opportunity for collaboration, (2) defining the scope of collaboration, (3) ascertaining and developing the infrastructure needed for the collaborative network, and (4) identifying unifying principles and initial projects that would form the basis of ongoing collaboration.[14]

RECOMMENDATION 3: 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 5 key elements that should be addressed by the professional communities involved in the care of patients with AKI.[14] These include 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 in serum creatinine to anuric renal failure. We have described the formation of a multidisciplinary 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, AKIN offers a forum to encourage knowledge acquisition to improve patient outcomes.

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