Defining AKD: The Spectrum of AKI, AKD, and CKD

Andrew S. Levey
Division of Nephrology, Tufts Medical Center, Boston, MA, USA

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Abstract
Kidney Disease Improving Global Outcomes (KDIGO) guidelines address the definition, classification, and management of acute kidney injury (AKI) and chronic kidney disease (CKD). In practice, some clinical presentations of acute kidney diseases and disorders (AKD) do not meet the criteria for AKI or CKD. In principle, these presentations may be caused by the same diseases that cause AKI or CKD, which could be detected, evaluated, and treated before they evolve to AKI or CKD. In 2020, KDIGO convened a consensus conference to review recent evidence on the epidemiology of AKD and harmonize the definition and classification of AKD to be consistent with KDIGO definitions and classifications of AKI and CKD.

Kidney Disease Improving Global Outcomes (KDIGO) guidelines address the definition, classification, and management of acute kidney injury (AKI) and chronic kidney disease (CKD) [1, 2]. AKI and CKD represent common presentations for heterogeneous disorders. In practice, some clinical presentations of acute kidney diseases and disorder (AKD) do not meet the criteria for AKI or CKD. The absence of an accepted definition and nomenclature for these presentations represents a logical gap in the classification of kidney disease and disorder (KD) and leaves patients and clinicians without management recommendations that could potentially improve care and outcomes.

The KDIGO AKI guideline of 2011 suggested an operational definition of AKD designed to address this gap and to harmonize the criteria for the spectrum of clinical presentations of AKI, AKD, and CKD, and also the absence of these presentations as no known kidney diseases or disorder (NKD) [1]. The guideline conceived of AKD as a more heterogeneous group of disorders than AKI, and considered AKI as a subset of AKD. Because of the absence of a substantial evidence base on the epidemiology of AKD, the KDIGO guideline did not propose recommendations for classification or management. In 2017, the Acute Dialysis Quality Initiative (ADQI) 16 report proposed an alterna-
tive definition and a classification of AKD, as well as a revised definition of AKI [3]. The report conceived of AKI as preceding AKD in most cases; proposed a limitation for the duration of AKI as 7 days, with persistence beyond this time as AKD; and suggested a classification of AKD according to the preceding AKI stage. In 2020, KDIGO convened a consensus conference to review recent evidence on the epidemiology of AKD and more fully discuss these topics. The consensus of the conference attendees was to retain the KDIGO definition of AKD, recommend a classification of KD consistent with the KDIGO AKI and CKD definitions, provide general recommendations on evaluation and management, and outline a research agenda [4]. In this brief review, I will summarize the evidence review presented at the consensus conference, the proposed KDIGO definition and classification of AKD, and the spectrum of AKI, AKD, and CKD.

Review of data from James et al. [5], using an integrated approach to laboratory measurements in a Canadian provincial universal health-care system, showed that AKD without AKI (using the KDIGO definitions) was observed in approximately 3.8% of the people with laboratory measurements, corresponding to approximately 1.5% of the provincial population, which was approximately 1/3 as common as CKD and 3 times more common than AKI. Compared to people with NKD, AKD without AKI were associated with an increased risk for mortality and kidney failure requiring replacement therapy. Among people without preexisting CKD, people with AKD without AKI had an increased risk of new onset of CKD compared to people without AKD. Among people with preexisting CKD, AKD without AKI were associated with an increased risk of CKD progression compared to people without AKD. In general, risks for adverse outcomes for people with AKD without AKI were lower than or similar to risks in people with AKI.

Review of data from Sawhney et al. [6, 7] demonstrated that many existing studies of AKI included people with serum creatinine (S_c) changes within 7 days (AKI according to the KDIGO guidelines) and people with S_c changes between 8 and 90 days (AKD without AKI according to the KDIGO guidelines). Additional data presented at the conference (Sawhney, personal communication), using similar methods to those of James et al. [5], compared the outcomes of AKI and AKD without AKI (using the KDIGO definitions) in the UK, Denmark, and Canada. People with AKD without AKI had similar short- and intermediate-term mortality as people with AKI, consistent with the results from James et al. [5]. Altogether, the data of James et al. [5] and Sawhney et al. [6, 7] provide a substantial evidence base that AKD without AKI, as defined by KDIGO, is common and harmful, and provide the rationale for accepting the existing KDIGO definition for AKD.

Figure 1 provides a conceptual framework for the time course of the spectrum of KD, defined as abnormalities in
AKD and CKD differ from each other by the duration of disease, either <3 or ≥3 months, respectively. By definition, AKD precedes CKD, but AKD may also be superimposed on preexisting CKD, either due to another disease or due to an exacerbation of the same disease. AKI is a subgroup of AKD, defined by abnormalities in kidney function over 6 h–1 week. AKI may occur either at the onset of AKD or after the onset of AKD. AKD without AKI is a subgroup of AKD, in which there are either abnormalities in kidney structure or abnormalities in kidney function that are less severe than in AKI or that do not develop as rapidly as in AKI. NKD represents no known KD, defined as either no abnormalities in kidney structure or function or abnormalities without implications for health. People without AKI, AKD, or CKD are classified as NKD.

Figure 2 details the conceptual overlap and diagnostic criteria for each disorder, according to duration and measures of function and structure. The criteria for AKI and CKD are as defined by the existing KDIGO guidelines. The criteria for CKD are intended to address most presentations of chronic diseases and disorders, but the criteria for AKI are intended to be more restrictive and not to address all presentations of acute diseases and disorders. The functional criteria for AKI include a rise in $S_{cr}$ within 2–7 days or oliguria for ≥4 h, with duration <3 months. The structural criteria for AKI and CKI are intended to be more restrictive and not to address all presentations of acute diseases and disorders. The functional criteria for AKI include a rise in $S_{cr}$ within 2–7 days or oliguria for ≥4 h, with duration <3 months. The structural criteria for AKI and CKI are intended to be more restrictive and not to address all presentations of acute diseases and disorders.
The absence of criteria for AKI, AKD, and CKD signifies NKD. Of note, assignment of NKD requires ascertainment of markers of kidney damage and GFR. The extent of ascertainment depends on the clinical circumstance, research question, or public health purpose.

Classification of AKD, like AKI and CKD, includes cause of disease, which directs cause-specific treatment. Causes of AKD are generally the same as for AKI, but without or before sufficient GFR decline to fulfill the criteria for AKI (GFR decline is too small or too slow), or the same as for CKD, but without sufficient duration to fulfill the criteria for CKD (<3 months). Examples include decreased kidney perfusion (volume depletion, heart failure, cirrhosis, segmental arterial, or venous infarction), parenchymal diseases (acute glomerulonephritis, new-onset nephrotic syndrome, pyelonephritis, interstitial nephritis, papillary necrosis, thrombotic microangiopathy, mild acute tubular necrosis, and mild transplant rejection), and obstruction of the urinary tract (stone or tumor, especially if unilateral). Irrespective of cause, further classification of AKD is based on the severity (staging), which directs stage-specific treatment. AKD with AKI would be classified according to the AKI stage (stages 1, 2, and 3, defined by the severity of oliguria or SCr increase), whereas AKD without AKI would be classified according to the level of GFR and albuminuria (corresponding to G and A categories for CKD). Following resolution of AKI, persistence of AKD would represent AKD after AKI. Classification of AKD after AKI may be difficult because it is challenging to estimate the GFR when SCr or the extracellular fluid volume is not in the steady state. It would be reasonable to classify AKD after AKI according to AKI stages when in the steady state, and according to G and A categories when in the steady state. Alternatively, a “kinetic eGFR” equation could be used in the nonsteady state [8, 9].

In conclusion, the KDIGO conference report proposes a definition and classification of AKD that enables a comprehensive approach to the interpretation of abnormalities of kidney function and structure across the spectrum of AKD and CKD, including an operational definition for NKD. Linkage to recommendations for evaluation and management for AKD may improve clinical practice and patient outcomes, and suggestions for a research agenda should strengthen the evidence base for future recommendations.

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Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

References