Diagnostic Criteria for Acute Kidney Injury

Present and Future

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KEYWORDS

• Acute kidney injury • Renal-replacement therapy • Dialysis • Clinical trials
• Biomarkers • Renal recovery • Mortality

KEY POINTS

- The criteria for acute kidney are based on changes in serum creatinine and urine output. Standardized criteria, such as KDIGO criteria, allow for uniform implementation of guidelines and reliable estimates of incidence and outcomes.
- However, acute kidney injury (AKI) remains a clinical diagnosis and clinical judgment is necessary to apply diagnostic criteria and to evaluate the changing clinical status of the patient.
- Baseline renal function is also based on clinical judgment and is best determined by prior serum creatinine measurements; when none are available estimating equations can be used with caution.
- Both serum creatinine and urine output provide independent and complementary information on renal function. Novel biomarkers can provide information on kidney damage and the latest markers can assess kidney stress.
- In the near future, function, damage, and stress may all be used to define AKI.

INTRODUCTION

Acute kidney injury (AKI) is a clinical diagnosis. Already in ancient times it was noted that the failure to pass urine was lethal if untreated and might be caused by either "an

Disclosure: This work was supported in part by R01DK070910 and R01DK083961 from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of NIDDK or National Institutes of Health.
Competing Financial Interest: J.A. Kellum has received grant support and consulting fees from Alere, Astute Medical, Bard and numerous companies developing treatments for Acute Kidney Injury.
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Crit Care Clin 31 (2015) 621–632
http://dx.doi.org/10.1016/j.ccc.2015.06.001 **criticalcare.theclinics.com**
0749-0704/15/$ – see front matter

empty bladder" or an obstruction. Indeed, urinary catheters were used as early as 3000 BC. It was Galen who first established the kidneys as the source of urine and as organs that "filtered the blood."[1] Before this, it was generally believed that urine was made in the bladder from food and drink. Progress in the clinical assessment of renal function was quite limited from the time of Galen until the eighteenth century when urea was discovered. However, it would be more than a century later before increases in blood urea and serum creatinine would be used to quantify azotemia ("azote" is a very old name for nitrogen). Azotemia results from reductions in glomerular filtration rate (GFR) and together with oliguria ("small" urine) or anuria (no urine) form the cardinal features of kidney failure.

However, azotemia and oliguria represent not only disease but a normal response of the kidney to extracellular volume depletion or a decreased renal blood flow. Conversely, a "normal" urine output and GFR in the face of volume depletion could only be viewed as renal dysfunction. Thus, changes in urine output and GFR are neither necessary nor sufficient for the diagnosis of renal pathology.[2] Still, they serve as the backbone for the existing diagnostic criteria.[3]

CRITERIA FOR ACUTE KIDNEY INJURY

Little progress was made in the understanding of AKI throughout the first two millennia AD. Although the term nephritis dates back to the sixteenth century it was not really until the late nineteenth century that Bright described renal failure (Bright disease) and included acute and chronic forms.[4] A century later Bywaters and Beall described "acute renal failure" following crush injury.[5] Throughout the remainder of the twentieth century, however, acute renal failure had no widely accepted biochemical definition. As many as 60 different definitions littered the field. In 2004 the RIFLE criteria (Risk Injury Failure Loss End-stage renal disease) were put forth by the Acute Dialysis Quality Initiative.[6] RIFLE included either change in serum creatinine or urine output as criteria recognizing that AKI could be nonoliguric but at the same time creatinine may not increase as rapidly as urine output falls and it is therefore better to have both criteria available. It was not understood at the time, the degree to which urine output and creatinine criteria interact (discussed later in the section on creatinine and urine output). One shortcoming of the RIFLE criteria was its application in patients with preexisting chronic kidney disease (CKD). In patients with elevated baseline creatinines, the proportional changes required by RIFLE seemed excessive. For example, although a patient with a baseline creatinine of 1.0 mg/dL would fulfill criteria for AKI with an increase to 1.5, a patient with a baseline of 2.0 mg/dL would need to reach 3.0. Furthermore, the higher the baseline creatinine the longer the time required to reach a 50% increase. In essence it does not seem credible that a patient with a baseline of 2.6 mg/dL would need to increase to 3.9 and take 3 days to do it just to get to RIFLE-R. For this reason the AKI Network proposed a modification to RIFLE that would also classify AKI when only a small increase in creatinine (0.3 mg/dL or greater) is observed in a short period of time (48 hours or less).[7] Finally, to harmonize RIFLE, AKI Network, and pRIFLE (a modification for pediatrics), the Kidney Disease Improving Global Outcomes (KDIGO) proposed a unified version of these rules (**Table 1**).[3]

THE PURPOSE OF STANDARDIZED CRITERIA FOR ACUTE KIDNEY INJURY

If AKI is clinical diagnosis, why are standard criteria desirable? The answer to this question comes in two parts. First, even though clinical judgment is required, a framework for the clinical diagnosis is needed. In general diagnoses are not based on pure