PRIMER

Defining acute renal failure

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The initial management of episodes of acute renal failure is often done by clinicians who are not specialists in nephrology. Their efforts may be hampered by several factors, such as deficiencies in our understanding of acute renal failure, and consensus and anecdote forming the basis of much of our practice rather than high-quality evidence. This situation has been partly engendered by the lack of a uniform definition of acute renal failure. The aims of this article are to highlight recent attempts to develop a standard definition for diagnosing and classifying acute renal failure and to explain how these attempts may help clinicians in everyday practice.

The traditional definition

Acute renal failure is traditionally defined as a rapid fall in the rate of glomerular filtration, which manifests clinically as an abrupt and sustained increase in the serum levels of urea and creatinine with an associated disruption of salt and water homeostasis.[1]

This definition has several important limitations that have implications for clinical practice. The terms "rapid," "abrupt" and "sustained" are not defined. Acute renal failure can evolve over hours or days, depending on the cause. The rapidity of onset may correlate with the severity of the episode, but this is not implicit within the definition.

There is no precise biochemical definition for acute renal failure. Different studies use different quantitative definitions: some are based on absolute or percentage increases in creatinine, whereas others are based on the need for dialysis.[2] The use of different definitions has led to widely differing reports of incidence and outcome, confounded comparisons between studies and undermined the evaluation of preventive strategies.

The serum concentration of urea is a poor estimate of the rate of glomerular filtration, as it can be modified by factors such as protein intake, critical illness, gastrointestinal hemorrhage or drug therapy.[3] Relying on changes in the concentration of urea to indicate alteration in the rate of glomerular filtration can therefore lead to potential delays in the detection of acute renal failure.

The rate of production of creatinine is dependent on muscle mass. Hence the rate at which creatinine concentration increases in acute renal failure depends on both muscle mass and the rate of glomerular filtration. Definitions based on absolute changes in creatinine levels disregard the major modifying effects of age, sex and ethnicity on muscle mass and the generation of creatinine.[4] In addition, serum level of creatinine does not accurately reflect the rate of glomerular filtration unless the patient is in a steady state. Changes in creatinine level generally lag behind changes in the rate of glomerular filtration, which is why calculations that use serum levels of creatinine to estimate glomerular filtration are unreliable unless the creatinine level is stable over several days. Also, because creatinine is removed by dialysis, it is not possible to assess kidney function using serum levels of creatinine once dialysis has started.

The RIFLE classification

In 2000, expert intensivists and nephrologists came together as the Acute Dialysis Quality Initiative (ADQI) to develop guidelines for the treatment and prevention of acute renal failure. The consensus process relied on published evidence where available and, in the absence of evidence, on consensus expert opinion. From that work, a consensus definition, the RIFLE (Risk, Injury, Failure, Loss, and End-stage kidney disease) classification, was developed.[5]

KEY POINTS

- Traditional definitions of acute renal failure lack precision, leading to confusion and lack of consensus.
- Graded definitions of acute renal failure have been proposed to enable the standardization of clinical and epidemiologic studies.
- The term "acute kidney injury" encompasses the entire spectrum of acute kidney dysfunction, from mild to severe.
- Using these revised definitions will enable earlier recognition and treatment of this potentially devastating condition.

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The RIFLE classification (Figure 1)[5] comprises three grades of injury (risk, injury and failure) and two outcomes (loss and end-stage kidney disease). The assessment of grade of injury is based on the presence of one of the following parameters: an increase in the serum level of creatinine, a decrease in the rate of glomerular filtration or a change in the volume of urine output. The scheme has been widely validated[6] and shown to predict outcomes.

There are several shortcomings to using the RIFLE criteria to define acute renal failure. The assignment of corresponding changes in serum level of creatinine and volume of urine output to the same RIFLE level is arbitrary, as serum level of creatinine predicts mortality more accurately than the volume of urine output.[7] It is therefore important that the parameters resulting in the least favourable RIFLE level be applied. A rapid change in the serum level of creatinine is also problematic, as it does not directly correlate with an actual change in the rate of glomerular filtration. Furthermore, many patients may present with acute renal dysfunction without any baseline measurement of renal function. This presents a problem for a classification system that considers the change from baseline as a diagnostic parameter.

Acute kidney injury

In 2005, the Acute Kidney Injury Network (AKIN), comprising the ADQI group and others,[8] proposed changes to the RIFLE criteria. As before, the process relied on review of the published evidence and consensus expert opinion. The term "acute kidney injury" was proposed to encompass the entire spectrum of renal dysfunction, from minor changes in kidney function to dependency on dialysis.

The proposed definition of acute kidney injury is an abrupt (within 48 h) reduction in kidney function defined as at least one of the following: (*i*) an absolute increase in the serum level of creatinine of 26.4 μmol/L (0.3 mg/dL) or more; (*ii*) a percentage increase in the serum level of creatinine of more than 50% (a 1.5-fold increase from baseline); or (*iii*) a reduction in the volume of urine output (oliguria < 0.5 mL/kg hourly for > 6 h). AKIN also proposed a staging system for acute kidney injury (Figure 2)[8] that was intended to define the degree of renal dysfunction at diagnosis and to facilitate tracking of the clinical course.

As with the RIFLE criteria, the inclusion of a percentage change in the serum level of creatinine accommodates variations related to age, sex and ethnicity and reduces the need for a baseline measurement of creatinine level. However, at least two measurements of creatinine level within 48 hours are required. The volume of urine output remains one of the criteria, but with the assumption that an obstruction of the urinary tract has been excluded and that the patient's volume status has been optimized.

One can see that the RIFLE categories of risk, injury and failure correspond to stages 1, 2 and 3 of the AKIN system. The RIFLE categories of

	Change in serum level of creatinine	Change in GFR	Urine output
Risk of kidney dysfunction	Increase > 50%	Decrease > 25%	< 0.5 mL/kg hourly for > 6 h
Injury to the kidney	Twofold increase	Decrease > 50%	< 0.5 mL/kg hourly for > 12 h
Failure of kidney function	Threefold increase or ≥ 350 μmol/L with an acute rise of ≥ 44 μmol/L	Decrease > 75%	< 0.5 mL/kg hourly for > 24 h or anuria for > 12 h
Loss of kidney function	Loss of kidney function, which requires dialysis, lasting longer than 4 w		
End-stage kidney disease	Loss of kidney function, which requires dialysis, lasting longer than 3 mo		

Figure 1: The RIFLE classification for acute renal failure.[5] The grade of injury or outcome is determined by either the serum level of creatinine or the rate of glomerular filtration (GFR), whichever indicates the more severe grade of renal failure.

	Change in serum level of creatinine	Urine output
Stage 1	Increase of ≥ 26.4 μmol/L or 150%–200% from baseline	< 0.5 mL/kg hourly for > 6 h
Stage 2	Increase > 200%–300% from baseline	< 0.5 mL/kg hourly for > 12 h
Stage 3	Increase > 300% from baseline or ≥ 354 μmol/L with an acute increase of ≥ 44 μmol/L	< 0.3 mL/kg hourly for > 24 h or anuria for > 12 h

Figure 2: The staging scheme for acute kidney injury.[8] The stage of injury is determined by either the serum level of creatinine or volume of urine output, whichever indicates the more severe stage of renal injury.

loss and end-stage kidney disease have been removed from the staging system, but they remain outcomes of kidney injury.

Implications for clinicians

These new definitions are crucial for epidemiologic and clinical studies so that we can finally compare "apples with apples."[9] Their bedside utility is less immediately apparent, as neither definition provides any insight into the pathophysiological cause of increased creatinine levels or oliguria. However, these new definitions are still an important first step in developing a uniform definition for acute kidney injury.

First, we must remember that the traditional definition of acute renal failure was vague, and we now have a clear definition of "abrupt," as well as clear parameters for changes in serum level of creatinine and volume of urine output. Second, the change in terminology from "failure" to "injury" reminds us that kidney damage is most commonly due to extrinsic insults such as sepsis, hypotension and the use of nephrotoxic drugs, and much of this damage is either preventable or reversible.

The revised terminology highlights the existence of acute kidney injury along a continuum and that, regardless of the cause, more severe injuries are likely to have more unfavourable outcomes. Not only will applying these definitions aid in the earlier recognition of patients with acute kidney injury, it will prompt clinicians to monitor and adjust fluid balance in their patients, give antibiotics where indicated and stop medications that may be having nephrotoxic effects.

Using the revised definitions, studies now show that even modest changes in kidney function indicated by relatively small changes in the serum level of creatinine are associated with substantial adverse clinical consequences, such as increased hospital mortality, decreased renal recovery, increased risk of requiring renal replacement therapy and increased length of stay in hospital.[10] Given that acute renal failure remains a devastating illness with high mortality despite advances in supportive care, it is important to recognize, prevent or treat even the mildest forms of acute kidney injury.

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