Contrast-Induced Nephropathy
Definitions, Epidemiology, and Implications

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KEYWORDS

• Contrast-induced acute kidney injury • Serum creatinine • Chronic kidney disease • Biomarkers

KEY POINTS

- Contrast-induced acute kidney injury (CI-AKI) is defined by the Kidney Disease Global Outcomes (KDIGO) guidelines as an increase in serum creatinine of 0.3 mg/dL or greater within 48 hours of contrast use or a 50% or greater increase from baseline serum creatinine within 7 days.
- CI-AKI has been consistently associated with risk for the development of end-stage renal disease, rehospitalization for cardiac renal and other causes, and all-cause mortality.
- Reduced glomerular filtration at baseline (eGFR <60 mL/min) is the single most important risk predictor for CI-AKI, and should be a trigger for preventive measures.
- Avoidance of dehydration by using preprocedure intravenous volume expansion, particularly when the left ventricular end-diastolic pressure is low, and holding nephrotoxic drugs (nonsteroidal anti-inflammatory agents, aminoglycosides, vancomycin, calcineurin inhibitors) are the most important interventions to prevent CI-AKI.

INTRODUCTION

Contrast-induced nephropathy is now termed contrast-induced acute kidney injury (CI-AKI) to align with the Kidney Disease International Global Outcomes Guidelines (KDIGO) published in 2012.[1] Before these guidelines were created there were various terms and definitions for acute renal injury or failure, without agreement on a uniform standard. Hence the literature on the epidemiology, outcomes, and even randomized clinical trials has a plethora of inconsistent and arbitrary definitions of CI-AKI.[2] Some common definitions have included an increase level of serum creatinine (Cr) greater than 25%, 25% to 50%, greater than 50%, 50% to 100%, greater than 100%, and/or 0.5 mg/dL or higher.[3] This review summarizes the KDIGO definition as the only guidelines-proposed definition that has gone through a full consensus, open comment period, and endorsement process. Moreover, this set of guidelines puts CI-AKI in context of other causes of AKI, including sepsis and cardiac surgery.[1]

The KDIGO definition of AKI is given in **Box 1**; **Table 1** shows the criteria for staging AKI. An increase in serum Cr of at least 0.3 mg/dL is the minimal detectable change considered above the baseline variation or noise level of this assay.[1] It is now a desired standard that all clinical laboratories use isotope dilution mass spectrophotometry (IDMS) or IDMS-traceable methods, as this is the only way of confirming Cr results between different laboratories. If there is a known time of injury, one would expect an increase of 0.3 mg/dL or more in Cr within 48 hours of the insult.[4] However, many times it is not clear when the injury occurred, and therefore, if a 1.5-fold or greater increase in Cr is seen within 7 days, this

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Box 1
Definition of acute kidney injury (AKI)

AKI is defined as any of the following

- Increase in serum creatinine by at least 0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
- Increase in serum creatinine to at least 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days
- Urine volume less than 0.5 mL/kg/h for 6 hours

AKI is staged according to the criteria in Table 1.

From Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int 2012;Suppl 2:1–138; with permission.

will also meet a definition of AKI. In addition to the Cr criteria, KDIGO has also endorsed a sustained reduction in urine output of less than 0.5 mL/kg/h for at least 6 hours as another criterion to meet a definition of AKI.[1] So, for example, if a 100-kg patient had accurately measured urine output of less than 50 mL/h for 6 hours after contrast, this could meet a definition of CI-AKI. As of this writing, there are several clinical trials under way to ascertain CI-AKI using changes in both serum Cr and measured urine output, and the KDIGO definition. Thus the descriptive epidemiology described in this article relies on the older literature, which has been purely based on changes in serum Cr after exposure to iodinated contrast.

EPIDEMIOLOGY AND RISK PREDICTION

The distribution of CI-AKI and its determinants is well known. A normal human kidney has between 800,000 and 1.3 million functional nephron units. One of the most important determinants of the number of nephrons is birth weight. Lower birth weight infants start life with fewer nephrons, and thus are at greater risk of chronic kidney disease (CKD) from a variety of diseases over time.[5] With 1.6 to 2.6 million functional nephrons in a young individual, there would need to be approximately 50% loss of function before there would be a detectable change in serum Cr. Thus, in young individuals with normal renal function there is very little chance that a significant change in serum Cr would be seen after contrast exposure. Even if contrast caused some permanent loss of renal filtration function, without a reduced mass of nephrons, CI-AKI based on a change in serum Cr would not be detectable. For this reason there are novel markers now commercially available to detect AKI without any increase in serum Cr (see later discussion).

The epidemiology and risk factors for CI-AKI thus far have been based on changes in serum Cr after contrast exposure. As a general heuristic, there needs to be an estimated glomerular filtration rate (eGFR) less than half of normal (ie, <60 mL/min/m^2, normal being 130 mL/min/m^2) before CI-AKI is observed in populations. Thus when eGFR is less than 60 mL/min/m^2 there is probably half the normal numbers of functioning nephrons, so when injury occurs there is an insufficient renal reserve to maintain filtration of creatinine at the normal rate, and one would see an increase in serum Cr of greater than 0.3 mg/dL within 48 hours. However, with the same degree of injury, if the remaining nephrons can adapt and increase their contribution to filtration, no significant change in serum Cr will be observed. Residual renal filtration function and the reserve capacity of the kidneys to respond to injury therefore account for what has been seen in the epidemiology of CI-AKI. As eGFR becomes lower in populations, there is greater certainty that Cr will increase after contrast exposure, and rates of CI-AKI will progressively increase as eGFR declines. In addition to a reduced eGFR, albuminuria, proteinuria, diabetes, heart failure, age older than 75 years, female gender, anemia, and

Table 1
Staging of acute kidney injury

Stage	Serum Creatinine	Urine Output
1	1.5–1.9 times baseline, or ≥0.3 mg/dL (≥26.5 μmol/L) increase	<0.5 mL/kg/h for 6–12 h
2	2.0–2.9 times baseline	<0.5 mL/kg/h for ≥12 h
3	3.0 times baseline, or increase in serum creatinine to ≥4.0 mg/dL (≥353.6 μmol/L), or initiation of renal replacement therapy, or, in patients <18 y, decrease in estimated glomerular filtration rate to <35 mL/min/1.73 m^2	<0.3 mL/kg/h for ≥24 h, or anuria for ≥12 h

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