Contrast-Induced Acute Kidney Injury: Is There a Risk after Intravenous Contrast?

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Contrast-induced nephropathy (CIN) is a form of acute kidney injury (AKI) that follows exposure to intravascular contrast media. Its pathogenesis involves renal ischemia, particularly in the outer medulla, where oxygen delivery is already at critical levels, and direct epithelial cell toxicity. There is no consensus regarding the definition of CIN. Changes in serum creatinine (a marker of glomerular filtration rather than injury) are the most widely used, but different definitions (e.g., ≥0.5 mg/dl or ≥25% increase) are often used in clinical trials. These definitions have been validated as surrogate markers because those who experience changes of this magnitude have a significant increase in short- and long-term morbidity and mortality. This association between CIN and long-term adverse outcomes has been best demonstrated by retrospective analyses of cardiac angiography cohorts (1–3); however, 90% of contrast media are used for computed tomography (CT) imaging, and patients who undergo contrast-enhanced CT may differ significantly from those who undergo angiography.

First, less contrast medium is given during a contrast-enhanced CT scan than is usually used in cardiac angiography, particularly when an intervention is performed. Second, more advanced vascular disease (e.g., diabetes, hypertension) and hemodynamic instability are usually present in the cardiac angiography cohort than in a CT population. Finally, the administration of contrast media intra-arterially may be associated with atheromatous emboli. For these reasons, the incidence of CIN is often considered to be higher in the cardiac population.

Using a prospective design, routine repeat serum creatinine determinations 48 to 72 h after contrast, six definitions of contrast-induced AKI (CI-AKI), and the electronic medical record of the VA health care system, Weisbord et al. (4) were able to determine the incidence of CIN and its long-term consequences in a group of patients who received intravenous contrast media for CT imaging. The minority of patients received any prophylaxis, in the form of intravenous saline before and/or after contrast exposure, use of N-acetylcysteine, or advice regarding discontinuation of nephrotoxins. What does their observational study tell us?

First, they restrict their analyses to individuals with an estimated GFR (by Modification of Diet in Renal Disease [MDRD]) of <60 ml/min per 1.73 m². As expected, the incidence of CI-AKI varied with the definition used, from 0 to 11%. Furthermore, the incidence of CI-AKI (defined as an increase in creatinine of ≥0.5 mg/dl or ≥25%) increased two- to four-fold, respectively, as kidney function decreased from 45 to 60 to <45 ml/min per 1.73 m². A novel finding was that the incidence was much higher in inpatients compared with outpatients, although this effect was mitigated at the lower GFR range. Use of prophylaxis was not associated with a lower incidence of CI-AKI.

What do these observations mean for the treatment of patients who have kidney disease and undergo contrast-enhanced CT procedures? For outpatients, the risk for CI-AKI, particularly in patients with estimated GFR (eGFR) >45 ml/min per 1.73 m², is extremely low (approximately 2%). These patients do well even in the absence of prophylaxis. Conclusions that are consistent with this were reached in a systematic review of intravenous contrast by Katzberg and Barrett (5). In addition, three recent prospective, randomized trials involving contrast-enhanced CT in patients with eGFR <60 ml/min per 1.73 m²—IMPACT (Isovue-370 and Visipaque-320 in renally impaired patients undergoing computed tomography) (6), ACTIVe (Abdominal computed tomography: Iomeron-400 versus Visipaque-320 enhancement study) (7), and PREDICT (Patients with renal impairment and diabetes undergoing computed tomography) (8)—found an overall incidence of CI-AKI (defined as a ≥25% increase in creatinine) of approximately 5%. The majority of the patients did not receive any intravenous fluid administration or pharmacologic prophylaxis. For hospitalized patients and/or those with eGFR ≤45 ml/min per 1.73 m², the incidence of CI-AKI was significantly higher in the cohort described by Weisbord et al. Whether prophylaxis is efficacious in these patients is not addressed in the article. It would nevertheless seem that prophylaxis is unnecessary for outpatients with eGFR >45 ml/min per 1.73 m² and should be considered for inpatients and for outpatients with an eGFR <45 ml/min per 1.73 m².

What about the relationship of CI-AKI to long-term adverse outcomes? Are the worse outcomes that are seen with coronary administration of contrast also seen with intravenous contrast...
administration? A clear trend toward worse outcomes was seen by Weisbord et al., although this did not reach statistical significance. It is likely that too few adverse events occurred in this population, reducing the statistical power; however, a retrospective review by Levy et al. (9) involving more than 16,000 contrast administrations of which 48% involved contrast-enhanced CT did find an association with hospital mortality.

Although the incidence of CI-AKI may be less with intravenous contrast administration, the widespread and increasing use of contrast-enhanced CT examinations still leaves a sizable population vulnerable to this event. The threshold for high risk for CI-AKI is shifted toward a lower eGFR because of the smaller dosage of contrast administered. It is the amount of contrast agent per nephron that is the best metric for contrast dosage, and this is approximated by mgI/eGFR (10). Further clinical trials are necessary to determine whether prophylaxis in this high-risk group is efficacious.

Disclosures

None.

References


See related article, “Incidence and Outcomes of Contrast-Induced AKI Following Computed Tomography,” on pages 1274–1281.