

Major Adverse Events One Year After Acute Kidney Injury After Contrast-Enhanced Computed Tomography

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Study objective: Recent studies have demonstrated that a single episode of acute kidney injury from a number of causes can increase the risk of severe long-term outcomes, including major cardiovascular events and death. We tested the hypothesis that patients who develop acute kidney injury consistent with contrast-induced nephropathy after contrast-enhanced computed tomography (CT) imaging are at increased risk of major adverse events at 1 year.

Methods: We followed a prospective, heterogeneous cohort of consecutive emergency department patients undergoing contrast-enhanced CT for the outcomes of acute kidney injury consistent with contrast-induced nephropathy and major adverse events, defined as the combined outcome of death (all cause), renal failure, myocardial infarction, and stroke or other arterial vascular events, in any anatomic territory, requiring intervention within 1 year. The primary outcome, major adverse events, was determined by the consensus of 2 of 3 blinded adjudicators.

Results: We followed 633 patients undergoing contrast-enhanced CT, of whom 11% developed acute kidney injury consistent with contrast-induced nephropathy and 15% (95/633; 95% confidence interval [CI] 12% to 18%) experienced at least 1 major adverse event within 1 year, including 7% (46/633; 95% CI 5% to 9%) who died. The development of acute kidney injury after contrast-enhanced CT was associated with an increased risk of 1-year major adverse event: the incident risk ratio was 4.01 (95% CI 2.61 to 6.05) and was 2.36 (95% CI 1.49 to 3.75) after adjusting for age, existing coronary artery disease, active malignancy, and 1 or more additional exposures to intravascular iodinated contrast media.

Conclusion: The development of acute kidney injury after contrast-enhanced CT was associated with a 2-fold increase in 1-year major adverse events. Further research is needed to validate this observation. [*Ann Emerg Med.* 2015;66:267–274.]

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INTRODUCTION

Contrast-induced nephropathy has long been recognized as an important source of acute kidney injury in the inpatient setting, studied primarily in patients exposed to iodinated contrast media with percutaneous coronary intervention.¹⁻⁴ Previous research demonstrates that contrast-induced nephropathy in the context of percutaneous coronary intervention in the inpatient setting is associated with an increased risk of subsequent, long-term, major adverse events, including renal failure and cardiovascular events such as acute myocardial infarction and stroke.^{2,5} In fact, an increase in major adverse events risk has also been observed after acute kidney injury from several causes.⁵⁻⁷ However, percutaneous coronary intervention is not the most common source of patient exposure to intravascular

iodinated contrast media; currently, greater than 70 million computed tomography (CT) imaging studies are performed in the United States annually compared with approximately 2 million coronary catheterization procedures.⁸ The rate of CT imaging in the emergency department (ED) has increased exponentially.⁹ Up to 25% of serum creatinine measurements performed in the ED setting are specifically intended to identify patients at increased risk of contrast-induced nephropathy with contrast-enhanced CT,¹⁰ contributing to increased costs and lengths of stay.¹⁰⁻¹²

The clinical significance of contrast-induced nephropathy after contrast-enhanced CT remains controversial. Several recent retrospective studies demonstrate that patients undergoing contrast-enhanced CT and either no imaging or unenhanced CT imaging studies may develop interval increases in serum creatinine at similar rates.^{13,14} However, these studies have 2 major weaknesses. First, contrast-induced

Editor's Capsule Summary*What is already known on this topic*

Contrast administered for computed tomography (CT) can cause nephropathy.

What question this study addressed

This prospective, observational trial followed for 1 year 633 patients who received contrast CT to compare the incidence of major adverse events in those who did and did not have contrast-induced nephropathy.

What this study adds to our knowledge

Major adverse events occurred in 36% of the 70 patients who developed contrast-induced nephropathy and 12% of the 561 patients who did not.

How this is relevant to clinical practice

Even after risk adjustment, major adverse events were more common in patients who had contrast-induced nephropathy. Further research will be required to determine whether this association is causal or a reflection of increased susceptibility for both major adverse events and contrast-induced nephropathy among some patients.

nephropathy is defined by a small interval increase in creatinine level occurring up to a week after exposure to iodinated contrast media. Because this increase is not expected to accompany clinically apparent symptoms and patients are not routinely screened for contrast-induced nephropathy,¹⁵ it is highly likely that contrast-induced nephropathy often remains undetected, especially with retrospective data. Second, because contrast-enhanced CT is performed for specific clinical indications, there are inherent and important population differences, defined at exposure, limiting the comparison of the contrast-enhanced CT population with either those undergoing unenhanced CT or who do not receive imaging. Physicians themselves limit contrast-enhanced CT in patients they perceive as having an increased risk of acute kidney injury, further limiting the comparability of these groups. None of these limitations are easily overcome, even with large populations.

Of course, the ideal study design to evaluate both causation and clinical significance would be a prospective randomized controlled trial of contrast media exposure with long-term outcomes. However, such a study is simply not feasible. Even

with advances in unenhanced imaging techniques, such a trial cannot be justified unless there are prospective data demonstrating that patients who undergo contrast-enhanced CT and develop a small interval increase in serum creatinine level, consistent with contrast-induced nephropathy, are at increased risk of severe, long-term, major adverse events compared with those who do not develop acute kidney injury after contrast-enhanced CT. Moreover, given the importance of iodinated contrast media to clinical practice, a randomized trial of contrast media exposure would not be justified unless the association of contrast-induced nephropathy and long-term major adverse events were both strong and consistent for contrast media exposures from percutaneous coronary intervention and contrast-enhanced CT. The absence of a strong association would argue against contrast-induced nephropathy as a mechanism of acute kidney injury that is of clinical importance, and efforts are better spent investigating other mechanisms of acute kidney injury. With either outcome, continued efforts to reduce acute kidney injury in the ED setting, from either contrast-induced nephropathy or other causes, may improve patient outcomes.

In the present study, we tested the hypothesis that, compared with those who did not develop acute kidney injury, patients who did develop it after contrast-enhanced CT are at increased risk of 1-year major adverse events, defined as death, renal failure, myocardial infarction, stroke, or other severe arterial vascular complication requiring surgical or medical therapy. As secondary outcomes, we also tested the association of acute kidney injury after contrast-enhanced CT and 1-year mortality alone, and the rate of major adverse events with increasing acute kidney injury severity.

MATERIALS AND METHODS**Study Design and Setting**

This was a planned long-term analysis of a single-center prospective observational study of 633 patients who underwent contrast-enhanced CT in the emergency care setting between June 2007 and November 2008. Patients were enrolled when the contrast-enhanced CT order was placed and followed prospectively for the development of contrast-induced nephropathy and major adverse events within 1 year. This study was approved by the institutional review board, and written informed consent was obtained from all study participants.

Patients were enrolled in the ED of Carolinas Medical Center in Charlotte, NC. This medical center is an urban, academic center with more than 900 beds, and the ED is continuously staffed by board-certified emergency physicians. More than 110,000 patients are treated in this ED annually. Contrast-enhanced CT imaging studies are

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