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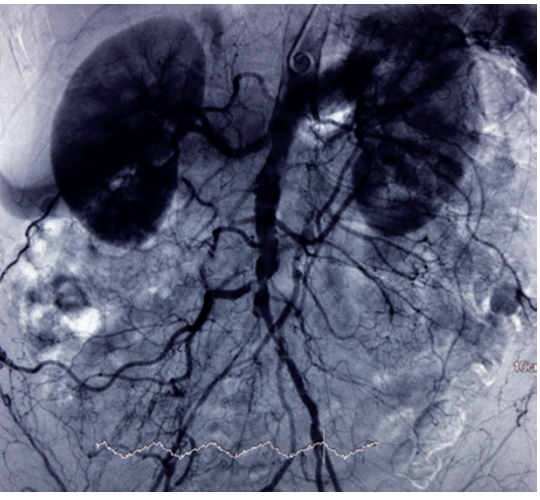
ACUTE KIDNEY INJURY

Acetylcysteine does not prevent contrast-induced acute kidney injury

A large, randomized, placebo-controlled trial has found that acetylcysteine does not reduce the risk of contrast-induced acute kidney injury (AKI) in high-risk patients undergoing angiography.

Acetylcysteine has been assessed for the prevention of contrast-induced AKI in a number of trials as this drug is thought to reduce direct oxidative stress and improve renal hemodynamics following the use of contrast medium. However, current guidelines disagree on whether this intervention should be recommended for patients at high risk and clinicians remain unsure about the effectiveness of acetylcysteine. "Over 40 acetylcysteine studies have been completed in the past 10 years and reached inconsistent results," says Otavio Berwanger on behalf of the Acetylcysteine for Contrast-Induced Nephropathy Trial (ACT) Investigators. "These studies were limited by low statistical power and most failed to meet quality standards." The conflicting results highlighted the need for a large-scale trial.

In the largest trial conducted in this field, the ACT Investigators enrolled 2,308 patients from 46 centers in Brazil who were undergoing coronary or peripheral arterial diagnostic intravascular angiography or percutaneous intervention. Patients were eligible if they had at least one risk factor for contrast-induced AKI. Risk factors included age >70 years, chronic renal failure, diabetes mellitus, congestive heart failure, left ventricular ejection fraction <0.45 or hypotension. The patients were randomly assigned to acetylcysteine ($n = 1,172$) or placebo ($n = 1,136$). Participants, health-care staff, data collectors and outcome assessors were blinded to allocation.



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Two doses of 1,200 mg acetylcysteine or placebo were administered orally both before and after the procedure. A hydration scheme was also strongly recommended. Data were collected at baseline (immediately after randomization), on the day of angiography, 48–96 h after the procedure and 30 days after angiography.

The primary end point of contrast-induced AKI (defined as a 25% increase in serum creatinine level above baseline between 48 h and 96 h after angiography) occurred in 12.7% of patients in the acetylcysteine group and 12.7% of patients in the placebo group. The incidence of secondary outcomes, which included mortality, need for dialysis, elevation in serum creatinine and cardiovascular death, did not significantly differ in the two groups. "These results were consistent among all subgroups evaluated, including patients at increased risk, such as those with renal failure, diabetes mellitus, and patients who received the largest amounts of contrast," adds Berwanger. The incidence of other adverse events was also similar in the two groups, although vomiting was significantly more common in the placebo group.

A prespecified random-effects meta-analysis was carried out to evaluate the results of the ACT in the context of previous trials comparing acetylcysteine with placebo (or no acetylcysteine). The heterogeneity between the studies meant that the results could not be combined, so the analyses were stratified according to the methodological characteristics of the trials. From this meta-analysis, the authors concluded that trials with inadequate methodology (for example, unclear or inadequate allocation concealment) tended to overestimate the treatment effects, whereas high-quality studies (that used allocation concealment, double-blinding and intention-to-treat analysis) supported the findings of the ACT, suggesting a lack of effect of acetylcysteine for the prevention of contrast-induced AKI.

The ACT had a number of limitations: the low number of events meant that the investigators could not assess the effects of acetylcysteine on end points such as mortality and need for dialysis; cystatin C might be a more reliable marker than creatinine for detecting contrast-induced AKI (as the authors acknowledge); the median volume of contrast medium used was low and the risk of contrast-induced AKI is likely to be dose-dependent; the investigators' definition of contrast-induced AKI may have high sensitivity but lack specificity; and the duration of therapy might not have been sufficient. Despite these limitations, the results of the ACT reinforce the findings of previous studies. "On the basis of our results, we do not recommend routine use of acetylcysteine for patients undergoing angiography," says Berwanger. "These findings have important implications for clinical practice, and may prevent unnecessary procedure delays and health expenditures associated with the administration of acetylcysteine."

Helene Myrvang

Original article ACT Investigators. Acetylcysteine for prevention of renal outcomes in patients undergoing coronary and peripheral vascular angiography: main results from the randomized Acetylcysteine for Contrast-Induced Nephropathy Trial. *Circulation* **124**, 1250–1259 (2011)