

# N-acetylcysteine prevented contrast-medium–induced nephropathy in primary angioplasty

Marenzi G, Assanelli E, Marana I, et al. N-acetylcysteine and contrast-induced nephropathy in primary angioplasty. *N Engl J Med*. 2006;354:2773-82.

**Clinical impact ratings:** Hospitalists ★★★★★☆ Cardiology ★★★★★☆ Nephrology ★★★★★★

## QUESTION

In patients having primary angioplasty, how effective is N-acetylcysteine (NAC) for preventing contrast-medium–induced nephropathy?

## METHODS

**Design:** Randomized placebo-controlled trial.

**Allocation:** Unclear allocation concealment.\*  
**Blinding:** Blinded (study investigators involved in the procedures).\*

**Follow-up period:** Up to hospital discharge.

**Setting:** A coronary care unit in Centro Cardiologico Monzino, Milan, Italy.

**Patients:** 354 patients (mean age 62 y, 81% men) who received primary angioplasty for ST-elevation myocardial infarction within 12 hours (18 h for cardiogenic shock) after onset of symptoms. Exclusion criteria were long-term dialysis and allergy to NAC.

**Intervention:** Standard dose NAC ( $n = 116$ ), high-dose NAC ( $n = 119$ ), or placebo ( $n = 119$ ). The standard-dose group received an intravenous (IV) bolus of NAC, 600 mg, before angioplasty plus a 600-mg tablet, orally twice daily for 48 hours after angioplasty. The high-dose group received a 1200-mg IV bolus and 1200 mg orally twice daily for 48 hours. All patients received IV isotonic saline, 0.9% at 1 mL/kg

of body weight per hour (0.5 mL/kg per h for heart failure) for 12 hours.

**Outcomes:** Contrast-medium–induced nephropathy ( $\geq 25\%$  increase from baseline in serum creatinine level within 72 h after angioplasty). Secondary outcomes included in-hospital mortality and the composite endpoint of death, acute renal failure requiring renal-replacement therapy, or need for mechanical ventilation.

**Patient follow-up:** 99.4%.

## MAIN RESULTS

The standard- and high-dose NAC groups had lower incidences of contrast-medium–induced nephropathy and the composite endpoint than did the placebo group; the high-

dose NAC group had a lower incidence of in-hospital mortality than did the placebo group (Table). Standard-dose NAC and placebo groups did not differ for in-hospital mortality (Table).

## CONCLUSION

In patients having primary angioplasty, N-acetylcysteine reduced the incidence of contrast-medium–induced nephropathy.

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\*See Glossary.

## Standard-dose N-acetylcysteine (NAC) or high-dose NAC vs placebo in patients having primary angioplasty at 48 hours†

Outcomes	Standard NAC	High NAC	Placebo	RRR (95% CI)	NNT (CI)
Contrast-medium–induced nephropathy‡	15% —	— 8.5%	33% 33%	55% (26 to 73) 74% (52 to 86)	6 (4 to 14) 5 (3 to 7)
In-hospital death	4.3% —	— 2.5%	11% 11%	60% (–3.3% to 85) 77% (26 to 93)	Not significant 12 (7 to 46)
Composite endpoint§	7.0% (8/115) —	— 5.1% (6/118)	18% (21/119) 18% (21/119)	61% (17 to 82) 71% (34 to 88)	10 (6 to 43) 8 (5 to 22)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

‡Defined as  $\geq 25\%$  increase from baseline in serum creatinine level.

§Death (standard NAC vs high NAC vs placebo = 4.3% vs 2.5% vs 11%), acute renal failure requiring renal-replacement therapy (1.7% vs 0.9% vs 5.0%), or need for mechanical ventilation (0.9% vs 1.7% vs 1.7%).

## COMMENTARY

The study by Marenzi and colleagues examined the effects of NAC specifically in patients receiving primary angioplasty for acute myocardial infarction and compared efficacies of low- and high-dose NAC with a control group. Patients in the study received a higher dose of contrast medium than did those in previous studies (about 260 mL), and NAC reduced the incidence of contrast nephropathy regardless of baseline renal or left-ventricular function.

Despite results from  $\geq 22$  randomized trials and 12 meta-analyses, the effectiveness of NAC has remained controversial. Previous studies were limited because they relied on a surrogate endpoint (i.e., change in serum creatinine level). While this surrogate endpoint is associated with greater patient morbidity and mortality, a beneficial effect of NAC on clinical endpoints has never been shown. The observations of Marenzi and colleagues showing lower mortality and a lower composite endpoint of death, dialysis, or mechanical ventilation in NAC-treated patients are of great interest. However, these findings should be interpreted with caution. The placebo group had more frequent events than expected, and such dramatic clinical benefit has not been previously observed in high-risk patients (1). Differences might be attrib-

uted to chance alone. The lack of blinding of patients, clinicians, and outcome assessors, and the fact that these clinical events were not pre-specified, may introduce bias.

Nevertheless, in light of its potential clinical benefit, safety, and low cost, prophylactic NAC should be considered for high-risk patients receiving intraarterial contrast in addition to appropriate hydration and judicious use of a low or isoosmolar contrast agent (1). High-dose NAC (IV or oral) may be more effective in preventing contrast nephropathy when the administration of large doses of contrast medium ( $> 140$  mL) is anticipated (2). A larger multicenter clinical trial is needed to confirm whether high- or low-dose NAC reduces the incidence of clinical endpoints.

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## References

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2. Briguori C, Colombo A, Violante A, et al. *Eur Heart J*. 2004;25:206-11.