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How can we be sure that renal dysfunction after coronary angiography is just explained by contrast nephropathy?

To the Editor: A review has been performed on the very hot topic of the role of N-acetylcysteine (NAC) on contrast nephropathy (CN) [1], of great clinical impact as a result of the CN-linked role in worsening prognosis and increasing costs. The authors wrote that they "assess the efficacy of NAC for preventing CN after . . . *intravenous* contrast media," and concluded that "NAC may reduce the incidence of increased creatinine after administration of *intravenous* contrast, but this was of borderline statistical significance." However, both sentences are wrong and misleading, as are similar conclusions reached by another meta-analysis [2], because all 15 [1] or 16 [2] reviewed papers regarded coronary angiography (CA), except one [3]. First of all, to perform CA, contrast media are introduced into the arterial vascular bed, and not intravenously, as when performing computed tomography (CT). Second, mechanisms of renal dysfunction after CA are not only caused by CN, but also by other causes such as, for instance, cholesterol crystal embolization.

We suggest that: (*1*) further studies be analyzed by separating prevention strategies for CT from those for CA; (*2*) for CA, attempts will be made to dissect other causes of renal damage by looking for the blue toes syndrome or eosinophilia, in order to exclude cholesterol embolization; (*3*) even urea increase was considered as end point, to avoid the possibility that creatinine changes might be resulting simply from a direct effect of NAC [4].

The only quoted paper regarding the use of NAC before performing CT did demonstrate a protection, by also using urea values as end point [3].

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Reply from the Authors

We thank Dr. Canavese et al for their letter. We agree that the term "intravenous contrast administration" may have been misleading. Perhaps the term "parenteral contrast administration" would have been preferable.

As we mentioned in our article, atheroemboli might explain why NAC seemed to be less efficacious than computed tomography in the context of coronary angiography. For this reason we performed subgroup analysis including only trials of patients undergoing coronary angiography. Although "looking for blue toes or eosinophilia" has theoretical appeal, we are uncertain how helpful this would be, because such findings may take weeks to appear [1], and clinically silent cholesterol embolization after invasive procedures appears to be common [2].

The suggestion to use serum urea rather than creatinine as an outcome measure seems to miss one of the main points of our article—that data on costs or clinically relevant outcomes such as death or hospitalization (and not surrogates such as estimated kidney function) are needed.

After reading their letter carefully, we are uncertain whether Dr. Canavese et al feel that our conclusions are