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## LETTERS

*The Reply:*

We wish to address the apparent limitations of our report pointed out by Coca and Perazella. Bicarbonate was not used because the Merten study was published after we designed our trial. The same is true for the contrast agent, given that the Nephrotoxic Effects in High-Risk Patients Undergoing Angiography (NEPRHIC) study with iodixanol was published in 2003, and for N-acetylcysteine, whose first meta-analyses were published in 2003 and 2004. However, neither of our study groups received these prophylactic measures, and, therefore, both shared the lack of any potential benefit.

Moreover, further studies are needed to confirm the iodixanol and bicarbonate potential benefits. Although iodixanol was associated with a lower incidence (3%) of contrast-induced nephropathy (CIN) as compared with iohexol (26%),[1] doubt still exists regarding the superiority of iso-osmolar versus low-osmolar contrast agents, as a class. Indeed, other studies with iodixanol showed that CIN incidence was significantly higher (12% and 21%) than that observed in the NEPHRIC trial.[2] This also was demonstrated by other investigators using different iso-osmolar contrast media. Moreover, no significant difference between iodixanol and low-osmolar agents was observed by other studies, particularly when combined prophylaxis with hydration and N-acetylcysteine was used.[2,3] Therefore, to the exclusion of iohexol, the available evidence does not support the superiority of iodixanol over low-osmolar contrast media.

CIN prophylaxis with bicarbonate shares similar limitations. Indeed, the Merten study control group had the same "handicaps" as those evidenced in our control group. N-acetylcisteine and iso-osmolar agents were not used, and hydration was started only 1 hour before contrast exposure. Moreover, their patients had less severe renal dysfunction and no data on the impact of bicarbonate on hard clinical end points were obtained. Thus, the present efficacy proofs of iso-osmolar contrast media and bicarbonate in severe renal insufficiency cannot be defined as "robust."

Finally, we agree that the hemofiltration mechanisms are still not completely understood. However, it is noteworthy that even during intravenous hydration, the patient does not necessarily reach a positive fluid balance because urine output is usually increased by fluid administration, so that intravenous hydration may be isovolemic in most cases. We did not measure daily urine output, intravascular volume, and glomerular filtration rate changes, but intravascular volume stability can be inferred from our first hemofiltration trial, showing that in the hemofiltration-treated group, urine output was unchanged, whereas it was significantly reduced in the control group.[4]

Currently, hemofiltration represents the only strategy that has shown itself effective for CIN prevention and for the improvement of clinical outcome in severe renal insufficiency. Further studies, however, are needed to elucidate its mechanisms, as they remain elusive.

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