

LETTERS TO THE EDITOR

More Positive Fluid Balance Could Explain Lower Risk of Contrast Nephropathy

The paper by Marenzi et al. (1) in *JACC: Cardiovascular Interventions* on prevention of contrast-induced nephropathy (CIN) using furosemide with matched hydration deals with a pertinent and pervasive problem. In this randomized trial of 170 patients who received contrast media during coronary procedures, the investigators compared standard-of-care hydration using intravenous (IV) isotonic saline with furosemide-forced diuresis and IV isotonic saline infusion matched to the urine output. This intervention arm was associated with a lower incidence of CIN (4.6% vs. 18% in control subjects, $p = 0.005$). However, a crucial piece of data missing in the study, which might confound the results, is the patients' net fluid balance at the end of their respective protocols. Adequate hydration before contrast administration is considered the cornerstone of CIN prevention, although no randomized controlled trial has studied the benefit of hydration alone. It would have added to the validity of the study had the patients' weights been mentioned before and after the protocol because that could be a good surrogate of the patients' net hydration status. Estimation of the net fluid balance based just on the difference between the cumulative IV hydration and the urine outputs shows that patients in the furosemide-matched hydration group were perhaps much better volume repleted than the control subjects were. Patients in the intervention arm received cumulative IV saline volume of $3,995 \pm 1,401$ ml, with infusion rates matched to the urine output (minus the initial 250-ml IV saline bolus). This indicates an even-to-slightly-positive net fluid balance over the duration of the protocol. The control group, however, received a cumulative IV saline volume of $1,742 \pm 290$ ml while putting out a urine volume of $3,117 \pm 876$ ml. This clearly suggests a net negative fluid balance of about 1.3 l. Hence, how much of the final efficacy of furosemide-matched hydration protocol over standard saline hydration in preventing CIN could be attributed to the use of furosemide, versus to the fact that patients in the intervention arm just happened to be much better hydrated, remains debatable. Some of the classic studies that studied volume repletion as a measure to prevent CIN have shown that patients who did better tended to be in an even-to-positive fluid balance, although the results were not always statistically significant (2,3)

The study, however, definitely forces us to question our purported definition of "adequate" isotonic saline hydration in preparation for contrast administration (1.0 to 1.5 ml/kg/h for 3 to 12 h before the procedure and continuing for 6 to 24 h after the procedure, per current guidelines) (4). The control group clearly received hydration that was commensurate with guidelines, yet did significantly worse than the intervention "superhydrated" arm. This could be a novel proof of concept, worth validating by future trials, wherein an isotonic saline hydration rate of as much as 600

ml/h for a shorter duration of about 6 h (as was used in the study) might be a better prophylactic regimen against CIN compared with what current guidelines recommend. A shorter hydration regimen might also be logistically easier to implement and have implications for cost savings.

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Hydration Is Critical for Prevention of Contrast-Induced Nephropathy

Marenzi et al. (1) recently reported the results on a single-center, prospective, randomized, nonblinded trial to investigate the role of combined furosemide-induced high-volume diuresis and automated matched hydration (intervention group), combined with standard saline hydration (control group), for the prevention of contrast-induced nephropathy (CIN) in chronic kidney disease patients undergoing coronary procedures.

However, it is worth noting that the 2 study groups were different with respect to the fluids infused. In the intervention group during the 6 ± 1 h of treatment, the volume of saline hydration was $3,995 \pm 1,401$ ml. Urine output was matched to the infusion rate (minus the 250-ml fluid bolus received as specified in the protocol). The intervention group thus had a net positive fluid