CORRESPONDENCE

Hemofiltration and the Prevention of Radiocontrast-Agent–Induced Nephropathy

TO THE EDITOR: Marenzi et al. (Oct. 2 issue)[1] offer a provocative article on the role of hemofiltration in preventing radiocontrast-agent–induced nephropathy. We disagree with the assumption that a lower creatinine concentration in the hemofiltration group, relative to the control group, implies less renal dysfunction, since hemofiltration itself lowers the creatinine concentration. We wonder why hemofiltration, with its low clearance of radiocontrast material, should have prevented nephropathy, since many believe that renal injury occurs on initial exposure to radiocontrast material,[2] and particularly since hemofiltration was stopped during the procedure and restarted after contrast injection. In theory the timing of hemofiltration should also affect the degree of renal injury.[3,4] The volume status of the patients before the procedure is unclear. Before hemofiltration, which is a complex and costly treatment, can be recommended as a way of preventing contrast-agent–induced nephropathy, more comprehensive studies should be performed.

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TO THE EDITOR: Marenzi et al. do not provide information about the number of patients in whom atheroembolism developed after cardiac catheterization. Contrast-agent–induced nephrotoxicity can be confused with the syndrome of atheroembolism that develops after such procedures and that results from trauma to atherosclerotic blood vessels, precipitating cholesterol microemboli.[1] The patients in this study were at high risk for atheroembolism to the renal arteries after interventions involving the use of a percutaneous catheter.

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THIS WEEK'S LETTERS

TO THE EDITOR: Various pathogenic factors may contribute to contrast-agent–induced nephropathy, including medullary ischemia and damage caused by oxygen radicals.[1] Marenzi et al. attribute most of the benefit observed in the hemofiltration group to high-volume hydration and the removal of the contrast agent from the circulation by hemofiltration, even though removal by hemodialysis has not been shown to have a benefit in other trials. However, experimental and clinical data show that heparin inhibits acute inflammation,[2] attenuates ischemia–reperfusion injury,[3] and may have a suppressant action on oxidative stress.[4] Heparin infusion in the hemofiltration group may have protected the patients from contrast-agent–induced ischemia–reperfusion injury and accounted, to a greater extent than noted by the authors, for the differences between the two groups.

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TO THE EDITOR: Several key points cast doubt on the conclusions drawn by Marenzi and colleagues. First, relying on an increase in the serum creatinine concentration to define acute renal failure creates bias toward the finding of less acute renal failure in the hemofiltration group, which had creatinine concentrations below base line at day 1, than in the control group.

Second, the benefits of randomization were attenuated when confounding by indication was built into the treatment protocols. Patients who underwent hemofiltration also received anticoagulant therapy and intensive care. It thus becomes difficult to argue that hemofiltration, rather than anticoagulation or intensive care, accounted for the improved mortality rate in the hemofiltration group. Because six of eight in-hospital deaths in the control group were attributable to cardiovascular disease, these built-in confounders are highly important.

Finally, information about the timing and distribution of deaths in the control group is needed. If the six deaths attributable to cardiovascular disease occurred on the first day after angiography, it would be difficult to regard acute renal failure as being of paramount importance. In addition, on the basis of the literature, one would expect approximately seven of the eight deaths in the control group to occur in patients with acute renal failure.

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TO THE EDITOR: The article by Marenzi et al. raises some questions. We have reported that prophylactic hemodialysis had no benefit in preventing radiocontrast-agent–induced nephropathy and associated morbidity.[1] We analyzed, a posteriori, renal and other outcomes in 39 of our subjects with stable renal failure who underwent coronary investigations (Table 1). Our patients were at higher risk than those of Marenzi et al. but had lower rates of renal

Table 1. Base-Line Characteristics and Postprocedural Complications in 39 Patients with Stable Renal Failure.*

Characteristic	Hemodialysis Group (N=26)	Control Group (N=13)	P Value
Age — yr	68±9	65±9	0.27
Diabetes — no. (%)	9 (35)	11 (85)	0.81
Use of ACE inhibitors — no. (%)	10 (38)	5 (38)	1.00
Creatinine at base line — mg/dl	3.5±1.0	3.7±1.3	0.62
Urea at base line — mg/dl	66±17	66±24	0.97
Volume of contrast agent — ml	295±157	261±170	0.53
Change in creatinine — no. (%)			
>25%	11 (42)	4 (31)	0.48
>50%	6 (23)	1 (8)	0.24
Dialysis required — no. (%)	4 (15)	0	0.13
Myocardial infarction — no. (%)	1 (4)	1 (8)	0.61
Stroke — no. (%)	2 (8)	0	0.31
In-hospital death — no. (%)	0	0	1.00

* Data are from Vogt et al.[1] Plus–minus values are means ±SD. ACE denotes angiotensin-converting enzyme.

and nonrenal morbidity, and none of them died in the hospital.[1] In the study by Marenzi et al., the patients' renal-function status before angiography — a factor that could affect the course of radiocontrast-agent–induced nephropathy — is unknown. The high mortality rate is probably not the sole consequence of radiocontrast-agent–induced nephropathy. Thus, we would question whether preventive hemofiltration is justified and cost effective. As many as 90 percent of intensive care units are unable to provide an appropriate bed when needed.[2] If every patient with chronic renal failure needed hemofiltration before undergoing coronary studies, life-saving coronary interventions might be delayed.

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1. Vogt B, Ferrari P, Schonholzer C, et al. Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. Am J Med 2001;111:692-8.
2. Green LV. How many hospital beds? Inquiry 2002;39:400-12.

THE AUTHORS REPLY: We agree with Dr. Kancha and colleagues. Indeed, reduction of creatinine values during hemofiltration may be seen as a cosmetic effect resulting from creatinine removal and blood dilution. In our study, a renoprotective role of hemofiltration can be inferred only from the differences between the hemofiltration group and the control group in daily urine output and creatinine and blood urea values at the time of hospital discharge. We would like to point out that in our study, creatinine returned within 24 hours to the values observed before percutaneous coronary intervention, confirming the fact that the cosmetic effect of hemofiltration terminates at the end of treatment. If we consider the fact that radiocontrast-agent–induced nephropathy is usually observed 48 to 72 hours after percutaneous coronary intervention, it is unlikely that its development was masked by hemofiltration.

Dr. Forman asks about the timing and distribution of deaths in the control group. In our study, six of the eight in-hospital deaths in that group occurred among patients in whom acute renal failure developed, and no deaths occurred the first day after coronary intervention; they occurred 3 to 14 days afterward.

The precise mechanisms of the observed clinical benefit of hemofiltration remain unclear. Its benefit may stem from the removal of radiocontrast material from the circulation or from other factors, such as hemodynamic stability, high-volume controlled hydration, the intensity of the care provided in an intensive care unit, or, as Dr. Jacobs suggests, the positive action of concomitant heparin infusion on oxidative stress and contrast-agent–induced ischemia–reperfusion injury. On the other hand, acute renal dysfunction occurring after percutaneous coronary intervention cannot be ascribed only to the toxicity of the contrast agent. Although all our patients were exposed to contrast agents, other factors, such as hemodynamic instability, concomitant pharmacologic therapy, and atheroembolism, may have contributed to renal impairment and influenced the clinical outcome. Thus, the combined positive properties of hemofiltration may confer a broad-spectrum renoprotective effect, instead of acting through a single mechanism, such as removal of the contrast agent. Indeed, as Drs. Ferrari and Vogt point out, hemodialysis — the most efficient method of removing a solute (contrast agent) — showed no benefit in preventing radiocontrast-induced nephropathy and associated morbidity.[1]

A preventive strategy based on hemofiltration cannot be directly applicable to all patients at risk, given the relatively high cost of this procedure and the limited availability of beds in intensive care units. Further studies are certainly needed for a better delineation of the risk profile of patients exposed to contrast agents and for the selection of those in whom a preventive strategy with hemofiltration is justified and cost effective.

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1. Vogt B, Ferrari P, Schonholzer C, et al. Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. Am J Med 2001;111:692-8.