

Radiocontrast Nephropathy: Managing the High-Risk Patient

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It is with great pleasure that we bring you the following educational initiative: ***Radiocontrast Nephropathy: Managing the High-Risk Patient***. A world-class faculty of thought leaders has been assembled to produce a comprehensive review of this very important subject. The goals of this endeavor include the following: 1. Increase awareness of radiocontrast nephropathy (RCN) as a relatively common, under-appreciated, and very serious adverse event associated with contrast requiring diagnostic and interventional procedures; 2. Gain an understanding that the pathophysiology of RCN is directly related to contrast-induced hypoperfusion of the renal tubules; 3. Demonstrate that despite the variety of measures that in the past have been ineffective in preventing RCN, we now have evidence supporting the use of fenoldopam, a novel selective dopamine receptor agonist, for this purpose; 4. Announce the initiation of the CONTRAST trial, a large ongoing, multi-center, prospective, randomized trial comparing fenoldopam to saline hydration for the prevention of RCN.

As a relatively common complication of contrast-requiring procedures, RCN is a concern to interventional cardiologists, radiologists, and consulting nephrologists. There are a variety of definitions of RCN ranging from absolute increases of serum creatinine of 0.50 to 1.0 mg/dL from baseline or a relative increase of 25% to 50% from baseline. The incidence of RCN varies from 3.7% to 70%.¹⁻⁴ Patients having baseline renal insufficiency (serum creatinine > 1.5 mg/dL) and diabetes are at particular risk. The implications of developing RCN are far more complicated than the associated 10% to 25% risk for dialysis and 30% chance that renal function will not return to baseline. The odds ratio for in-hospital mortality is 5.5 even after corrections for co-morbid conditions.⁵ Causes of mortality include, for the most part, non-renal etiologies, such as respiratory failure/pneumonia,

stroke, and bleeding. Medical resource utilization is also much higher, as hospital stays are longer in those patients who develop RCN.

The impact of RCN seems to be under-appreciated in part because a connection is not intuitively made between acute renal insufficiency and the associated non-renal causes of mortality. It has become increasingly clear that renal insufficiency of any cause is associated with poor outcomes in a variety of settings. In a recent report by Batchelor et al, octogenarians had a three times greater likelihood for developing RCN than younger patients.⁶ Renal insufficiency was associated with a mortality rate ten times that of patients with normal renal function, as potent a risk factor as those patients with left ventricular ejection fractions of less than 35%. This was confirmed in an article by Rihal et al, from the Mayo Clinic database, reviewing predictors of death after percutaneous coronary interventions (PCI).⁷ McCullough et al found renal dysfunction to be a significant, independent risk factor for acute arrhythmias and hemodynamic complications during coronary care

unit stays, with risk increasing in direct proportion to magnitude of renal dysfunction.⁸ It seems that there are some unknown factors related to renal insufficiency that mediate the associated increased mortality. Whether it is diastolic dysfunction, electrolyte abnormalities, volume overload, left ventricular hypertrophy, or adverse interactions with drugs remains to be proven.

It was not long ago that attempts at preventing RCN involved the use of combination hydration, diuresis, and mannitol. Clinical trials showed not only a lack of benefit but also a worsening of renal function with these interventions.⁹ A variety of other interventions, including low-dose (renal dose) dopamine have also not proven effective.¹⁰ N-acetyl cysteine was shown in a single center trial involving non-catheterization laboratory patients given a relatively small volume of contrast to prevent RCN.¹¹ A landmark pilot trial by Tumlin and associates in patients undergoing cardiac catheterization procedures showed an impressive benefit of fenoldopam in preventing RCN.¹² This study confirms the prospective findings of Sharma,

Madyoon,¹³ and Lepor based on historic controls that fenoldopam is effective in preventing the renal complications of contrast. In addition to its effectiveness, these trials have confirmed not only the safety of fenoldopam when used in the catheterization laboratory setting, but its ease of use and its "nurse friendliness."

At the present time, the **CON-TRAST Trial** will test the effectiveness of fenoldopam in a large, randomized, double-blind, multi-center clinical trial. This trial will evaluate the effectiveness of fenoldopam in patients undergoing coronary angiography and percutaneous interventions. Patients will be included if they have a baseline creatinine clearance between 20 cc/minute and 60 cc/minute. Patients will be randomized to intravenous fenoldopam plus hydration or hydration only. The primary end-point will be serum creatinine between 48 hours and 96 hours following contrast infusion. Additional secondary endpoints, such as hospital length of stays, will also be studied.

The faculty participating in this educational endeavor has been

Main Points

- Radiocontrast nephropathy (RCN) is a significant source of morbidity and in-hospital mortality related to interventions in the cardiac catheterization laboratory.
- Patients at risk for RCN include those with baseline renal insufficiency, especially in association with diabetes.
- The pathophysiology of RCN seems to be related to both the renal vasoconstrictive effects and the shunting of blood from the medullary segments to the cortical segments, resulting in medullary ischemia and tubular injury; if this injury is severe, permanent loss of tubular function can result.
- There is no evidence that the use of mannitol, furosemide, aminophylline, natriuretic peptide, or low-dose dopamine provides any significant prophylactic benefit.
- The use of aggressive hydration strategies before contrast infusion has been shown to be important in preventing RCN.
- Using low-osmolar nonionic contrast agents seems to benefit patients with pre-existing renal insufficiency.
- Evidence is accumulating showing a potential benefit of fenoldopam, a selective DA₁, in preventing RCN; the CONTRAST Trial, a multicenter, randomized, blinded clinical trial, is now assessing this hypothesis.

selected because of their leadership roles in the management of patients with coronary artery disease or renal preservation. **Dr. Vandana Mathur**, UCSF School of Medicine, our nephrologist contributor, will present the pathophysiology of RCN and the importance of the selective dopamine receptors (DA₁ and DA₂) in this process. **Dr. Roxana Mehran**, Lenox Hill Heart and Vascular Institute, will present the implications of contrast-induced renal insufficiency in terms of procedural success in the cath lab and medical resource allocation. **Dr. Stephen R. Bailey**, University of Texas, will provide important historical perspective as he details the results of previous attempts to prevent RCN. **Dr. Samin Sharma**, Mount Sinai School of Medicine, and **Dr. Hooman Madyoon**, St. Joseph's Medical Center, will discuss new advances in preventing RCN. Dr. Sharma will share his experience, having the largest single prospective experience with fenoldopam for preventing RCN in patients undergoing PCI. Dr. Madyoon will share his extensive experience with

fenoldopam in patients undergoing both coronary artery and peripheral vascular interventions. **Dr. Gregg Stone**, Lenox Hill Heart and Vascular Institute, will provide the insights for the design of the CONTRAST Trial as well as its primary and secondary goals. The entire text of this program will be available on the Internet at **www.medreviews.com**.

Our most important goal is to provide you, the reader, with the practical and theoretical information allowing you to have a positive impact in the care of your patients. We feel that by gaining a greater appreciation for radiocontrast nephropathy as a relatively common and serious complication of cardiac catheterization and PCI, reviewing relevant basic renal pathophysiology, and presenting the latest encouraging results of a new and potentially effective treatments we have been able to reach this milestone. ■

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