CIN in the Cath Lab: Understanding the Problem and Improving Patient Outcomes

Based on an interview with Dr. Richard Solomon of the University of Vermont College of Medicine and Fletcher Allen Health Care (Burlington, Vermont)

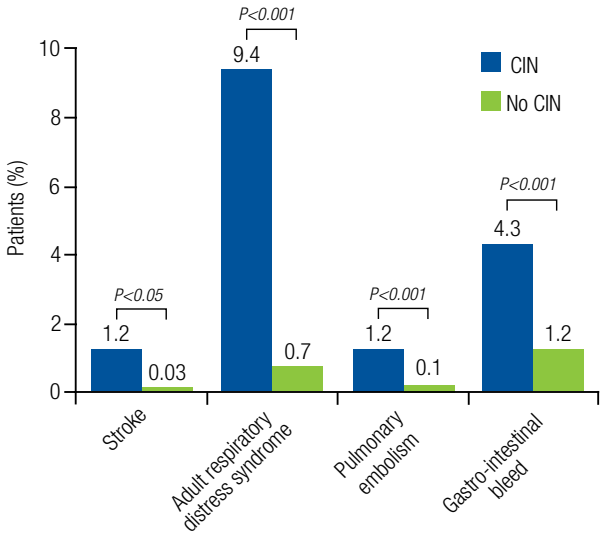
Richard Solomon, MD

Dr. Solomon is Chief of the Nephrology Unit in the Department of Medicine at the University of Vermont College of Medicine and Fletcher Allen Health Care. He gained his medical degree at Yale University School of Medicine and completed his nephrology specialization at Harvard Medical School and the Beth Israel Hospital (Boston, MA) in 1975. Dr. Solomon became involved with contrast-induced nephropathy (CIN) from a research perspective in the early 1990s, when he designed and conducted the first prospective randomized trial evaluating different therapies for prevention of CIN.

The increasing risk of CIN

Along with advances in catheterization techniques, the complexity of interventional procedures is increasing significantly. In parallel, the complexity of the conditions being treated is also rising as they often present in older patients and those with comorbidities and chronic illnesses. While interventions have the potential to bring significant health benefits to these patients, they are not without risk: in particular, the risk of contrast-induced nephropathy (CIN). CIN has been estimated to occur in 3–31% of patients undergoing coronary intervention, depending on the type of procedure, patient risk factors and duration of follow-up.[1]

Simply put, CIN is an acute form of kidney injury occurring as a result of exposure to a radiocontrast agent during a diagnostic or interventional catheterization procedure. But why focus on CIN now? As we employ newer and more complex interventional procedures such as transcatheter aortic valve replacement, which require extensive imaging in preparation for the procedure, patients are subject to greater contrast exposure. And as the need for increased use of contrast agents rises, so does the risk of CIN.



Systemic complications after PCI in patients with and without CIN from an analysis of data from 7,586 patients in the Mayo Clinic PCI Registry. Reprinted with permission from Rudnick M, Feldman H. *Clin J Am Soc Nephrol.* 2008;3(1):263-272.

All quotes are taken from the interview with Dr. Solomon.

The clinical significance of CIN

The pathophysiology of CIN is complex. Essentially, iodinated contrast agents cause kidney damage via two mechanisms: direct nephrotoxicity to cells of the proximal tubule and vasoconstriction of the arterioles in the renal medulla leading to ischemic injury.

> CIN is defined as an elevation in serum creatinine within 48–72 hours of the intervention—either an absolute increase of ≥0.5 mg/dL or a relative increase of ≥25%.

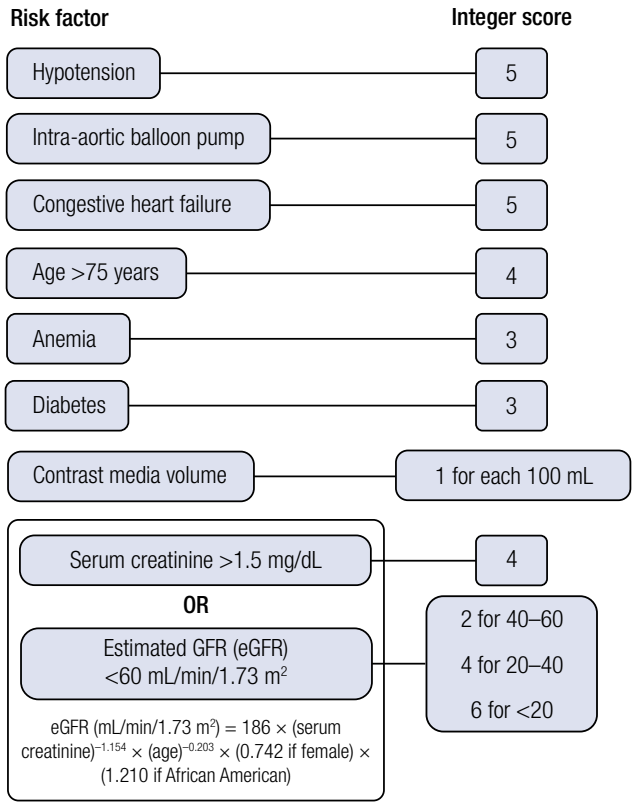
Importantly, it is not just kidney health that is affected by CIN. It is increasingly recognized that CIN is not only an acute renal condition but also a significant long-term risk factor for systemic adverse events. Dr. Solomon reveals that patients who develop CIN following exposure to contrast are **"more likely to develop chronic kidney disease… more likely to have future cardiovascular events, and they are more likely to die within the next year than patients who do not develop this injury."** As well as causing greater short- and long-term morbidity and mortality, CIN also has a substantial economic impact, both in the form of higher immediate costs due to longer hospital stays and more demanding patient care, and an increased long-term financial burden in managing future adverse events.

Risk stratification and management

By identifying patients at increased risk of CIN before a procedure, the cath lab team will be able to employ appropriate preventative strategies. A major factor is the amount of contrast delivered to the patient. The longer and more complex the procedure, and the more images needed, the more contrast required and the higher the risk of CIN. There are also patient-specific risk factors, which can be categorized into three main groups: inadequate kidney function, often due to chronic kidney disease, defined as a glomerular filtration rate (GFR) of <60 mL/min/1.73 m^2; diminished renal blood flow (hypotension, congestive heart failure or anemia); and impaired renal vasodilatory vascular responses (older age or diabetes).

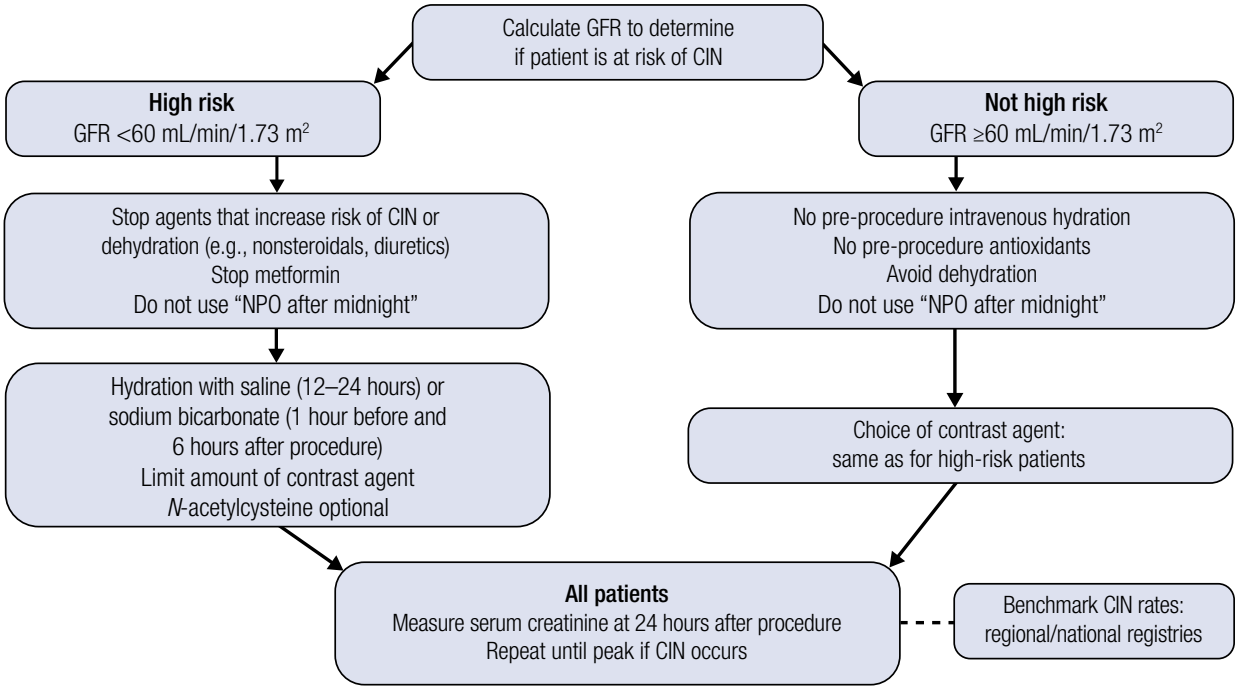
> **Prevention of CIN requires:**
> 1. Identification of patients at risk
> 2. Elimination of factors that may increase risk
> 3. Use of appropriate prophylactic measures
> 4. Application of an intervention to minimize risk
> 5. Appropriate follow-up to determine whether CIN occurred and, if so, to address the long-term adverse outcomes

The Mehran risk score model.



Risk score	Risk of CIN	Risk of dialysis
≤5	7.5%	0.04%
6–10	14.0%	0.12%
11–16	26.1%	1.09%
≥16	57.3%	12.6%

Example of a set protocol for CIN risk reduction. NPO: nil per os (no food or drink orally).



In addition to using a GFR measurement for all patients undergoing a diagnostic or interventional procedure, Dr. Solomon recommends using the Mehran risk score.[2] This takes into account eight variables—hypotension, use of an intra-aortic balloon pump, heart failure, age, anemia, diabetes, contrast media volume and baseline kidney function—and produces a predicted risk score for CIN. It also predicts whether the patient is likely to need dialysis and provides a 1-year mortality rate.

Dr. Solomon is keen to point out that teamwork is vital when it comes to protecting patients. Fletcher Allen Health Care uses a set protocol developed by a multidisciplinary team of cardiologists and nephrologists to ensure consistent assessment and management of patients regardless of operator. Dr. Solomon explains that **"if you have a protocol where every provider is operating under the same rules, your incidence of CIN goes down. Where you don't have a protocol and everybody does what they think is the right thing, you have a higher incidence."** Guidance on prophylactic strategies and controlling CIN risk in the cath lab has been published in Europe[3] and the USA.[4] In addition, Dr. Solomon advocates developing best practice guidance at each institution that takes into account the types of procedures and equipment used, along with any treatment algorithms or needs of particular patient populations.

Strategies for preventing CIN

Maintaining balanced hydration is a well-known and clinically proven method of reducing the risk of CIN. However, increasing urine output by administering high doses of diuretics results in blood volume depletion, which actually contributes to CIN. Therefore, optimal approaches involve increasing urine flow without causing volume depletion. Dr. Solomon gives the example of a device available in Europe that facilitates volume replacement: **"The two European trials that have been published show that this was beneficial in terms of protection against contrast-induced nephropathy."**[5,6]

What about the choice of contrast agent? Although experimental evidence suggests that viscosity and osmolality can influence renal toxicity, the incidence does not seem to differ between iso- and low-osmolar, low-viscosity agents.[7,8] Therefore, non-ionic, iso-osmolar (e.g., iodixanol) and non-ionic, low-osmolar, low-viscosity (e.g., iopamidol) contrast agents are recommended.

Antioxidants, such as *N*-acetylcysteine, sodium bicarbonate or ascorbic acid, have been suggested for reducing the risk of CIN. However, prospective, randomized clinical trials evaluating such agents have not produced convincing data, so this approach remains discretionary.

Reducing contrast dose to reduce the risk of CIN

As contrast volume is a key risk factor for CIN, the aim should be for all cath lab staff to work toward using the minimum amount of contrast possible. One approach to reduce contrast dose is to "stage" a procedure by splitting it into separate sessions. Also, the use of an automated contrast delivery system, compared with manual hand injection, is an established strategy to reduce the amount of contrast delivered. Manual hand injections tend to offer limited control over contrast volume delivery. And with repeated manual injections, particularly in complex anatomies or procedures, operators can become fatigued and the accuracy of injection volume can be reduced. Automated contrast delivery systems that also have a user-responsive, variable-flow rate function, such as the ACIST | CVi® Contrast Delivery System, allow precise control of contrast volume and flow rate, and potentially decrease procedure times.

Shorter procedures may play a role in reducing the amount of contrast delivered and potentially allow post-procedural hydration sooner. Studies have shown that an automated system can reduce contrast volume used in percutaneous coronary intervention and diagnostic procedures by 30%, and that the use of such a system, in conjunction with contemporary hydration and pharmacological strategies, is associated with a significant reduction in the incidence of CIN.[9-11]

The AngioTouch® Hand Controller in the ACIST CVi system allows precise control of contrast volume and flow rate.

Experimental and future approaches to CIN reduction and prevention

In the future we may have more options for reducing CIN risk. There are currently a number of pharmacological agents in clinical trials that work by various mechanisms associated with protection against CIN, including compounds with anti-inflammatory or vasodilatory characteristics, and those involved in prevention of reactive oxygen species generation.[12,13] A clinical trial is ongoing with a suction catheter device that is placed in the coronary sinus. Following coronary injection, the suction function is activated to remove the contrast medium, thereby significantly reducing the amount that enters the circulation.

Furthermore, Dr. Solomon predicts CIN will come to be defined by a direct marker of kidney injury—a "kidney troponin"—rather than by increased serum creatinine levels caused by impaired kidney function. As a result, more cases of CIN will be identified, and at an earlier stage. This will increase the impetus for developing effective strategies to minimize the injury. In addition, as we better understand the long-term consequences of CIN, new endpoints for evaluating preventative strategies will be defined, further improving patient care and outcomes.

References

1. McCullough PA, Wolyn R, Rocher LL, et al. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *Am J Med*. 1997;103(5):368-375.
2. Mehran R, Aymong ED, Nikolsky E, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. *J Am Coll Cardiol*. 2004;44(7):1393-1399.
3. Stacul F, van der Molen AJ, Reimer P, et al. Contrast induced nephropathy: updated ESUR Contrast Media Safety Committee guidelines. *Eur Radiol*. 2011; 21(12):2527-2541.
4. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *J Am Coll Cardiol*. 2011;58(24):e44-e122.
5. Briguori C, Visconti G, Focaccio A, et al. Renal insufficiency after contrast media administration trial II (REMEDIAL II): RenalGuard System in high-risk patients for contrast-induced acute kidney injury. *Circulation*. 2011;124(11):1260-1269.
6. Marenzi G, Ferrari C, Marana I, et al. Prevention of contrast nephropathy by furosemide with matched hydration: the MYTHOS (Induced Diuresis With Matched Hydration Compared to Standard Hydration for Contrast Induced Nephropathy Prevention) trial. *JACC Cardiovasc Interv*. 2012;5(1):90-97.
7. Heinrich M, Haberle L, Muller V, et al. Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low-osmolar contrast media: meta-analysis of randomized controlled trials. *Radiology*. 2009;250(1):68-86.
8. Reed M, Meier P, Tamhane UU, et al. The relative renal safety of iodixanol compared with low-osmolar contrast media. *JACC Cardiovasc Interv*. 2009;2(7):645-654.
9. Anne G, Gruberg L, Huber A, et al. Traditional versus automated injection contrast system in diagnostic and percutaneous coronary interventional procedures: comparison of the contrast volume delivered. *J Invasive Cardiol*. 2004;16(7):360-362.
10. Brosh D, Assali A, Vaknin-Assa H, et al. The ACIST power injection system reduces the amount of contrast media delivered to the patient, as well as fluoroscopy time, during diagnostic and interventional cardiac procedures. *Int J Cardiovasc Intervent*. 2005;7(4):183-187.
11. Call J, Sacrinty M, Applegate R, et al. Automated contrast injection in contemporary practice during cardiac catheterization and PCI: effects on contrast-induced nephropathy. *J Invasive Cardiol*. 2006;18(10):469-474.
12. Lameire NH. Contrast-induced nephropathy—prevention and risk reduction. *Nephrol Dial Transplant*. 2006;21(suppl 1):i11-i23.
13. Cronin RE. Contrast-induced nephropathy: pathogenesis and prevention. *Pediatr Nephrol*. 2010;25(2):191-204.

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