THE CCU CORNER

Preventing Contrast-Induced Nephropathy

BY GEORGE PHILIPPIDES, M.D., AND ERIC AWTRY, M.D.

The Patient

A 65-year-old woman with a history of hypertension and cigarette smoking presents with stuttering chest pain, mild heart failure, elevated serum troponin, and a serum creatinine level of 1.0 mg/dL. She is admitted to the CCU, stabilized medically, diuresed, and sent for cardiac catheterization and percutaneous coronary revascularization of a severely stenotic left circumflex coronary artery. She receives postprocedural hydration; however, the day after catheterization her creatinine rises to 1.8 mg/dL. One week later her creatinine is greater than 7 mg/dL and she requires hemodialysis.

The Problem

Contrast-induced nephropathy (CIN), defined as a rise in serum creatinine of 0.5 mg/dL or 25% above baseline, occurs in 8%-15% of patients undergoing coronary angiography. Although the majority of cases of CIN are transient, about 0.5% of patients undergoing percutaneous coronary intervention will develop CIN that requires dialysis. In addition, CIN is associated with increased length of hospitalization, increased medical costs, and increased mortality.

The Theory

CIN is thought to result from a combination of direct toxic effects of contrast on the renal tubules, renal ischemia mediated in part via reactive oxygen species, and decreased renal blood flow exacerbated by volume depletion. The incidence of CIN may be reduced by periprocedural hydration, administration of *N*-acetylcysteine as an antioxidant, and through the use of low-osmolar contrast.

The Evidence

Early studies evaluating the use of intravenous fluids, diuretics, and mannitol for the prevention of CIN revealed no benefit of diuretics or mannitol beyond that of volume expansion with fluids. The optimal fluid regimen, however, is not clear. In one study comparing isotonic saline (0.9%) with half-normal saline (0.45%), administered at 1 mL/kg per hour for 24 hours, a rise in serum creatinine of more than 0.5 mg/dL occurred in 2% of patients given half-normal saline versus 0.7% of patients given isotonic saline. The benefit was greatest in women, diabetics, and patients receiving more than 250 cc of contrast. Hydration with sodium bicarbonate as opposed to saline in patients with renal insufficiency was recently investigated in a single-center trial in which the incidence of CIN was markedly reduced by the use of sodium bicarbonate (1.7% vs. 13.6%). However, because of methodologic concerns with this study, the routine use of sodium bicarbonate awaits further study.

Multiple studies have investigated the utility of the antioxidant *N*-acetylcysteine (NAC) for the prevention of CIN, and have revealed conflicting results. Similarly, several recent meta-analyses have failed to show a consistent benefit of NAC, likely in part because of inconsistent study design between individual trials. Nonetheless, in small trials of patients with renal insufficiency, and especially in those with concomitant diabetes, NAC appears to have a more reproducible beneficial effect.

The effects of contrast osmolality have been studied in several trials. A study comparing the use of the high-osmolar contrast agent diatrizoate with the low-osmolar agent iohexol showed a significantly lower rate of CIN when the low-osmolar agent was used (12% vs 27%). Additionally, a recent study comparing iohexol with the iso-osmolar agent iodixanol in patients with diabetes and pre-existing renal insufficiency demonstrated improved rates of CIN with the iso-osmolar agent (3% vs 26%).

Discussion

The risk of CIN is not the same for all patients. Factors that substantially increase the risk of CIN after angiography include renal insufficiency, diabetes, volume depletion, age greater than 75 years, hypertension, heart failure, and proteinuria. In addition, the higher the volume of contrast used, the higher is the risk of CIN. In patients undergoing coronary angiography, a thorough history should be taken to identify these factors, and the serum creatinine should be assessed. Furthermore, the creatinine clearance or glomerular filtration rate (GFR) should be estimated based on the serum creatinine [(140 – age) × weight in kg/(72 × serum creatinine)].

In our institution, all patients undergoing coronary angiography (with or without PCI) undergo periprocedural hydration when clinically feasible. Isotonic saline is preferred; however, half-normal saline may be warranted in patients with a history of congestive heart failure. Patients with baseline creatinine greater than 2.5 mg/dL should start to receive intravenous hydration at least 12 hours prior to the procedure. Aggressive diuresis and potentially nephrotoxic agents such as ACE inhibitors, angiotensin receptor antagonists, and nonsteroidal agents should be used judiciously, especially in patients whose serum creatinines have been rising. We have not routinely used sodium bicarbonate, owing to the conflicting data and lack of consensus regarding its utility. *N*-acetylcysteine (600 mg b.i.d. for the 24 hours before and after the procedure) is routinely prescribed to diabetics and patients with decreased creatinine clearance (less than 60 mL/min). Low-osmolar contrast is used in the majority of patients, with iso-osmolar contrast reserved for patients with both diabetes and chronic renal insufficiency.

The patient described above required diuresis to manage her heart failure prior to the catheterization. Unfortunately, this may have predisposed her to CIN, despite treating her with intravenous fluids post procedure. Fortunately, 1 week following the catheterization her renal function improved and she did not require further dialysis.

Summary

CIN remains a significant complication of coronary angiography. All patients undergoing contrast-based procedures should be carefully screened for risk factors known to be associated with CIN. All patients should receive periprocedural hydration, and consideration should be given to the use of NAC and iso-osmolar contrast in high-risk patients.

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Follow Published Criteria to Eliminate Unnecessary Imaging

BY DOUG BRUNK
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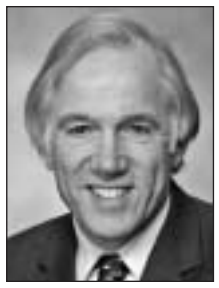
SAN DIEGO — The way Dr. Raymond J. Gibbons sees it, the best way to practice appropriate single-photon emission computed tomography myocardial perfusion imaging is to apply the appropriateness criteria established by the American College of Cardiology Foundation and the American Society of Nuclear Cardiology.

These criteria grade clinical scenarios with respect to whether they are appropriate or inappropriate uses of SPECT myocardial perfusion imaging (J. Am. Coll. Cardiol. 2005;46:1587-605). When Dr. Gibbons and his associates at the Mayo Clinic Nuclear Cardiology Laboratory in Rochester, Minn., applied the criteria to several hundred patients in their nuclear cardiology laboratory, they discovered that 64% of the SPECT myocardial perfusion imaging studies they did were appropriate, 11% could not be classified, 11% were of uncertain appropriateness, and about 14% were inappropriate.

"We need to reduce this number of inappropriate tests," Dr. Gibbons said at the annual meeting of the American Society of Nuclear Cardiology. "I would urge all of you to do this same study in your own laboratory. The goal should be to educate ordering physicians to reduce this segment of the pie."

In Dr. Gibbon's study, four inappropriate indications for SPECT myocardial perfusion imaging accounted for almost all of the inappropriate studies. These included studies in asymptomatic low-risk patients; preoperative studies in patients who were undergoing intermediate-risk surgery and had good exercise capacity; studies in symptomatic patients with a low pretest likelihood of coronary artery disease, an interpretable ECG; and who are able to exercise, and studies conducted as preoperative testing in patients undergoing low-risk surgery.



'We have initiated a program to try to educate our physicians and nurses to reduce these inappropriate studies.'

DR. GIBBONS

"Together, these four indications accounted for 88% of the inappropriate studies," said Dr. Gibbons, who is a codirector of Mayo's Nuclear Cardiology Laboratory. "We have initiated a program to try to educate our physicians and nurses to reduce these inappropriate studies."

Dr. Gibbons, a former president of the American Heart Association, expressed concern about the future of health care and imaging in the United States. In the summer of 2007 the House of Representatives passed State Children's Health Insurance Program and Medicare reform legislation that eliminated a 9.9% decrease in physician payment in 2008 and a 5% decrease in 2009. That's the good news. The bad news is that in 2010 the sustainable growth rate formula will be replaced with a new system with six separate targets, one of which is imaging.

"Growth in those targets will be limited to the growth in gross domestic product," Dr. Gibbons said. "Given the interest in CT and MR, and the dramatic growth in cardiac imaging, this will have a draconian effect if it goes into law." ■