A Contrast in Risk: Radiographic Imaging in the Renally Compromised Patient

Peter A. McCullough, MD, MPH, FACC, FACP, FCCP, FAHA

Department of Medicine, Divisions of Cardiology, Nutrition and Preventive Medicine, William Beaumont Hospital, Royal Oak, MI

[Rev Cardiovasc Med. *2003;4(suppl 5):S1-S2*]

Recently, considerable advances have been made in the field of interventional cardiology, including the employment of safe and effective methods of vascular access, percutaneous coronary intervention (PCI), and the use of adjunctive antithrombotic and antiplatelet agents. Drug-coated stents represent a major advance in terms of absolute treatment benefit for patients undergoing PCI. In young, otherwise healthy patients, we can expect outstanding short- and long-term outcomes after PCI in the present day. Unfortunately, with the obesity pandemic fueling a secondary epidemic of diabetes and chronic kidney disease, the interventionalist is faced with large proportions of patients undergoing PCI concomitant with diabetes and/or renal insufficiency.

Angiography and PCI require the use of iodinated, intravascular contrast. While contrast facilitates rapid, high-quality images on cineangiographic systems, its use represents some degree of risk to every patient who undergoes a procedure. Most adverse events attributable to contrast, including nausea, hypotension, pain, and allergic reactions, are transient and easily managed. However, when a patient exhibits identifiable evidence of contrast-induced nephropathy (CIN), one can expect, based on the published literature, that catastrophic short- and long-term outcomes are possible. It is now known that a transient rise in serum creatine after a cardiovascular procedure confirms a higher rate of in-hospital and long-term cardiovascular mortality. The mechanism by which CIN confirms poor long-term outcomes is not well understood. Clearly, affected patients are older, sicker, and are more likely to have chronic kidney disease at baseline.

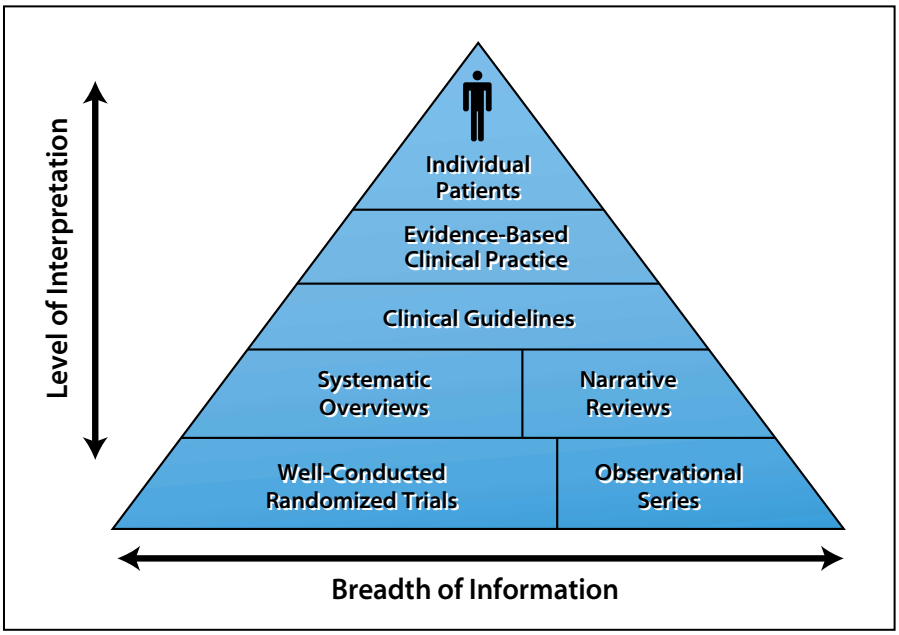

Figure. *Evidence pyramid for biomedical studies.*

However, when controlling for all other factors, CIN remains a strong, independent predictor of adjusted mortality for years following the procedure. Although acute renal failure requiring dialysis is rare (< 1% occurrence), when it happens, it is associated with > 30% short-term, and > 80% long-term (2-year) mortality. Approximately half of these patients remain on dialysis for the rest of their lives; half require dialysis only transiently. Recognition of these outcomes has led to active efforts to reduce rates of CIN, and hence, improve outcomes after angiography and PCI.

This supplement issue to *Reviews in Cardiovascular Medicine* will discuss what every cardiologist needs to know about contrast and how it causes renal damage. It is important to remember that when the kidneys have a reduced filtration function (estimated glomerular filtration rate < 60 mL/min/1.73 m^2) the remaining, or "remnant," nephrons have an increased load in terms of oxygen demand and are thereby much more susceptible to ischemic and direct cellular injury. The reader will also learn that not all contrast agents are the same, having important differences with respect to their structure and osmotic properties. Over the years, there have been advances in the design of these agents, largely aimed at mimicking the osmolality of blood, thus minimizing the possibility of adverse events, including CIN.

This supplement will also provide a comprehensive, evidence-based review of the clinical trials that have been carried out to prevent CIN. There have been more than 30 trials of various types of contrast, with a clear outcome favoring the isotonic, iso-osmolar agent iodixanol. However, there are now over 40 trials completed examining a variety of adjunctive measures, including intravenous and oral hydration, dopamine receptor agonists, diuretics, methylxanthines, prostaglandins, and endothelin receptor antagonists. These trials have all been small, but importantly, have not shown consistent reductions in the rate of CIN. There has been recent enthusiasm for the oral antioxidant N-acetylcysteine (NAC) with over 12 trials completed. Half of these trials have been neutral, and half have been positive. Two separate meta-analyses have found significant treatment effects from NAC, but with wide confidence intervals, indicating considerable variance in the studies and uncertain levels of efficacy, as of this writing. The investigation of CIN requires a clinical trials network and a multicenter approach to reduce or eliminate the issue of multiple, small, inconclusive trials.

Currently there are no approved strategies or guidelines for the prevention of CIN. We believe this supplement to *Reviews in Cardiovascular Medicine* goes a long way in summarizing the evidence in this field and filling in the missing blocks of knowledge in the pyramid shown in Figure 1. Ultimately, the interventional community needs a clear and concise approach for patients at risk for CIN. As part of that approach, the understanding that there is a "contrast in risk" among the choices for iodinated contrast is fundamental. ■