A Practical Approach to Preventing Renal Complications in the Catheterization Laboratory

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KEYWORDS

• Radiocontrast • Nephropathy • Kidney • Hydration • Catheterization

KEY POINTS

- Kidney injury associated with cardiac catheterization occurs infrequently but may have serious and prolonged complications.
- Patients at risk for renal complications may be identified by risk factors and risk-prediction models.
- Institutions should follow a standardized approach to minimize the risk of contrast injury in all patients.
- The 3 key elements of this approach are:
  - Ensuring appropriate hydration before, during, and after the procedure
  - Preprocedural assessment of glomerular filtration rate and appropriate dosing of contrast media
  - Preferentially using iso-osmolar contrast or low-osmolar contrast media that have been associated with lower risk of renal complications
- High-dose statin preloading may be potentially beneficial in reducing the risk of contrast injury, and should be considered in all patients undergoing percutaneous coronary intervention given the other benefits of statin therapy in this patient population.

BACKGROUND

Kidney injury following cardiac catheterization may occur for several reasons, including radiocontrast exposure, atheroembolism, or hypotension and renal hypoperfusion. The rates of acute kidney injury (AKI) following cardiac catheterization are variably reported in the literature depending on the definition used, type of contrast media, and patient subset, typically ranging from as low as 1% to as high as 20% of cases.[1–3] When it does occur, AKI can lead to accumulation of metabolic byproducts, fluid retention, electrolyte and acid-base abnormalities, and a high correlation with death both in the hospital and following discharge.[4–6] In a cohort analysis of more than 16,000 patients undergoing radiocontrast procedures, the risk of developing postprocedure AKI was less than 2%; those who did develop AKI, however, were more than 5 times more likely to die in the hospital.[7]

AKI, as defined by the international Kidney Disease: Improving Global Outcomes (KDIGO) initiative, is either an increase in serum creatinine by 0.3 mg/dL or more ($\geq$26.5 μmol/L) within 48 hours,

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an increase in serum creatinine to greater than 1.5 times baseline within 7 days, or urine volume of less than 0.5 mL/kg/h for 6 hours.[8] Of note, the studies that have established the poor outcome in association with AKI among patients undergoing cardiac procedures have generally used an absolute increase in serum creatinine of 0.5 mg/dL or greater to define AKI. There has been considerable investigation into strategies to mitigate the development of AKI following cardiac catheterization, with the majority focused on the prevention of contrast-induced nephropathy (CIN).

MECHANISM AND CLINICAL MANIFESTATIONS

The details of the mechanism and pathophysiology of CIN are discussed at greater length elsewhere in this issue by Geenen and colleagues. In brief, CIN, despite its association with increased mortality, is generally a reversible process. Serum creatinine levels typically increase 24 to 48 hours after radiocontrast exposure, with a peak at 4 to 5 days before return to baseline levels at 7 to 10 days.[9] The need for dialysis following CIN appears to be low, and varies depending on underlying risk factors. When the need for dialysis does occur, however, it portends a grim prognosis. A single-center study found an in-hospital mortality of more than 35% for patients who developed AKI requiring dialysis following coronary intervention, with a 2-year survival rate of 19%.[4] The extrarenal manifestations and symptoms of CIN are relatively few, and the renal failure is typically nonoliguric.[10] Laboratory abnormalities including electrolyte and acid-base disturbances are reflective of decreased renal clearance, and urinalysis may show nonspecific casts suggestive of tubular injury.[11]

CIN may occur through both renal vasoconstriction and direct tubular injury, although the exact mechanism remains unclear. Studies in both animal and human models have suggested a complex interplay between vasodilator and vasoconstrictor influences including nitric oxide, prostaglandin, and endothelin systems, in addition to generated reactive oxygen species and direct cytotoxic properties of contrast medium itself.[10,12] Investigation into these mechanisms has suggested several possible targets for prevention or mitigation of CIN, although clinical adaptation has been limited.

RISK FACTORS AND PREDICTION MODELS

Kidney injury following cardiac catheterization has been clearly associated with multiple patient-related and procedure-related risk factors, with the risk increasing additively along with the number of risk factors.[13] Preexisting renal insufficiency, defined as a serum creatinine greater than 1.5 mg/dL or estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2 is the strongest baseline predictor of CIN following percutaneous coronary intervention (PCI) according to a large data set reported by Mehran and colleagues,[14] with higher risk associated with more severe baseline renal dysfunction.[3] Other prominent risk factors for the development of CIN include New York Heart Association (NYHA) class III to IV congestive heart failure, advanced age, and history of diabetes mellitus with associated renal insufficiency.[12] In elderly cohorts older than 65 years, women appear to be at increased risk for development of CIN following cardiac catheterization in comparison with men.[2]

These risk factors have been assimilated into several different risk-prediction models that have sought to identify patients at risk for developing CIN. In 2004, Mehran and colleagues[14] published a risk score based on 8 different patient-related and procedure-related risk factors. In this model, risk factors of hypotension, necessity of intra-aortic balloon pump (IABP), NYHA class III to IV congestive heart failure, age older than 75 years, anemia, diabetes, contrast volume, and preprocedure renal function were weighted into 4 quartiles of increasing risk of developing CIN or requiring dialysis with a *c*-statistic of 0.67. However, the poor discrimination of this model and the inclusion of procedural variables limit the utility of this risk score for preprocedural risk stratification.

A more contemporary risk model for the development of renal complications in patients undergoing PCI was proposed in 2013; developed from 15 different influential variables associated with the patient's history, presentation, and preprocedure laboratory assessments. The patient characteristics shown in **Box 1** are factored into a weighted algorithm that stratifies patients into low (<1%), intermediate (1%–7%), and high (>7%) risk groups based on the risk of CIN.[15] This model was validated in a cohort of patients undergoing PCI and requires a computer for calculation (https://bmc2.org/calculators/cin); however, it appears to be statistically superior, with an area under the curve of 0.839, and has the added the benefit of being composed solely of preprocedural variables.

At present, however, neither the 2012 American College of Cardiology Foundation/Society for Cardiovascular Angiography and Interventions (ACCF/SCAI) nor the KDIGO guidelines have made formal recommendations for preprocedure risk-algorithm utilization other than establishing those at risk via eGFR.[8,16] The suggested protocol