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PATIENT SAFETY NETWORK

The Perils of Contrast Media

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Case Objectives

- Recognize that contrast media are potentially nephrotoxic.
- Identify key risk factors for the development of contrast-induced kidney injury.
- Describe reliable evidence-based strategies to prevent contrast-induced kidney injury.
- Realize that contrast-enhanced imaging for identification of a potentially life-threatening condition must always take precedence over the risk of development of contrast-induced kidney injury.

Case & Commentary—Part 1

A 66-year-old man with a past medical history of atrial fibrillation (not on anticoagulation) presented with abdominal pain and hematochezia (bloody stool). He was found to be febrile with abdominal pain on examination. Laboratory test results were notable for leukocytosis (29,100 ?L), lactic acidosis (9.9 mmol/L), and new acute kidney injury (creatinine 1.8 mg/dL, up from a baseline of 0.6 mg/dL).

Given the clinical presentation, there was concern for mesenteric ischemia (impaired blood flow to the intestines), possibly secondary to emboli from his atrial fibrillation. The emergency department provider believed a computed tomography (CT) study with contrast was the best diagnostic test to evaluate for possible mesenteric ischemia or other cause for the symptoms. However, out of concern for worsening the renal failure with contrast (i.e., contrast-induced nephropathy) in the setting of acute kidney injury, the physician instead ordered a noncontrast abdominal CT scan. This scan showed thickening of the jejunal loop but was not diagnostic for mesenteric ischemia, nor other cause for the symptoms. The patient was evaluated by vascular surgery who recommended conservative management with intravenous fluids and supportive care.

Even though the provider in this case believed that a CT scan with contrast was indicated, he ordered a noncontrast CT out of concern for the patient's kidney function. Contrast-induced acute kidney injury (CIAKI) is one of the most widely discussed and debated topics in cardiovascular medicine. Iodinated contrast media can cause kidney injury through direct cytotoxic effects on renal tissue.(1) An increasing number of individuals are exposed to iodinated contrast media during imaging-based investigations for

either diagnostic or interventional purposes. Moreover, increasing life expectancy has resulted in a growing elderly population with comorbidities such as hypertension, diabetes mellitus, renal disease, and cardiovascular disease, all of which predispose to renal impairment. Thus, providers should understand the etiology of and risk factors for CIAKI and harness evidence-based prophylactic and therapeutic regimens to reduce its incidence.

Many different organizations, including the American College of Radiology have proposed definitions for CIAKI.(2) Some examples include the RIFLE criteria (Risk, Injury, Failure, Loss, End-stage renal disease) and the Kidney Disease Improving Global Outcomes classification.(1) A systematic review found that these definitions do not differ significantly in their ability to diagnose and stage AKI or to predict future adverse outcomes.(1) With regard to CIAKI, the most common and accepted definition is a rise in serum creatinine of at least 0.5 mg/dL or a 25% increase from the baseline value, assessed 48 hours following contrast media administration.(3) Evidence suggests that CIAKI is associated with multiple adverse events including progressive loss of kidney function, major cardiac complications, and prolonged length of hospitalization.(3)

Using the common definition of CIAKI, the general incidence of CIAKI in hospitalized patients exposed to contrast is approximately 7%.(4) However, the incidence reported varies depending on the definition used, ranging in one study from 7% to more than 18%.(5) The most common risk factors for the development of CIAKI are hypotension, congestive heart failure, chronic kidney disease, diabetes, age older than 75 years, anemia, and volume/type of contrast media.(6) The risk in the setting of chronic kidney disease depends on the degree of baseline renal dysfunction. In one set of patients, the incidence of CIAKI following contrast-enhanced CT was 0.0%, 2.9%, and 12.1% in patients with an estimated glomerular filtration rate (eGFR) of 45–59, 30–44, and less than 30 mL/min/1.73 m^2, respectively.(7) In that study, only 1 patient out of the 520 studied (0.2%) had severe CIAKI that required urgent hemodialysis. This finding is consistent with other studies (8,9) that have shown that while AKI in the setting of contrast is relatively common, CIAKI requiring urgent hemodialysis is rare.

Recent information suggests that the literature has overestimated the risk of developing CIAKI after contrast-enhanced imaging, and that the risk may be comparable for CT studies with and without contrast enhancement.(10) According to the most recent consensus guidelines published by the Contrast Media Safety Committee of the European Society of Urogenital Radiology (11), patients referred for contrast-enhanced CT are genuinely at risk of CIAKI if they have an eGFR less than 45 mL/min/1.73 m2 (i.e., chronic kidney disease stage 3b, 4, or 5 or new acute kidney injury). It follows that the decision to offer contrast-enhanced CT imaging in patients with reduced eGFR (i.e., < 60 mL/min/1.73 m^2) should be based on the clinical need for the contrast-enhanced diagnostic imaging and whether its benefits outweigh the risk of CIAKI. Case-by-case assessment is therefore recommended.

In the case under discussion, in the presence of a past medical history of atrial fibrillation (without anticoagulation), the clinical presentation of the patient and laboratory investigations strongly favor the diagnosis of acute mesenteric ischemia. Despite the presence of new onset AKI and some increased risk for CIAKI, a contrast-enhanced CT was essential to confirm the clinical diagnosis. The study likely would have shown a thrombus/embolus within the mesenteric arteries and/or lack of enhancement of bowel wall (due to ischemia). Without urgent intervention, mesenteric ischemia carries 100% mortality. Unless there is significant patient frailty and/or comorbidities that precluded surgical intervention, conservative

management for mesenteric ischemia would not be advisable.

Case & Commentary—Part 2

Later that evening, the patient developed acute paralysis and loss of sensation of the bilateral lower extremities. An urgent CT scan with contrast was performed, which revealed complete occlusion of the abdominal aorta with blood clot from the superior mesenteric artery to the bilateral common iliac arteries. The patient was taken emergently to the operating room and underwent aortic thrombectomy (removal of the blood clot). Unfortunately, the extent of ischemia to multiple organs was so profound that he developed progressive multi-organ failure and died a few days later.

In a root cause analysis (RCA), providers who reviewed the case believed a contrast CT scan should have been ordered in the emergency department, and that diagnosing the blood clot earlier might have prevented the adverse event. During the RCA, the emergency medicine physician reflected that she had contacted the on-call radiologist about the CT scan and the radiologist had strongly recommended that a noncontrast study be ordered. The RCA also revealed that there were no standard protocols in place at this hospital for deciding when contrast studies should be ordered or describing the evidence-based best practices for prevention of contrast nephropathy when contrast studies were used.

Comprehensive specialty-specific protocols have been proposed to prevent CIAKI for eGFR-based, risk-stratified patient groups.(12) These guidelines more or less form the basis of various institution-built nephroprotective protocols. Such measures should include halting nephrotoxic medications (such as metformin, etc.), minimizing contrast media volumes, and using low- or iso-osmolality contrast media.(3,12) High osmolality contrast media have been completely replaced by low osmolality contrast media and increasing use of iso-osmolality contrast media in western countries due to lower incidence of adverse effects (including CIAKI) from the latter two with no difference in image quality. High osmolality agents are no longer used in routine clinical practice.

Hydration has been shown to decrease the rates of CIAKI as it reduces the contrast media concentration in the kidneys, limiting the cytotoxic effects. All three of the specialty-specific protocols recommend hydration through intravenous volume expansion using an isotonic electrolyte solution before and after contrast media administration.(12) The recommendations vary as to the type of hydration recommended. Evidence has shown that isotonic solutions, such as isotonic sodium chloride (0.9 %), are more protective than hypotonic solutions (e.g., hypotonic saline [0.45%]).(13,14) Many different regimens have been investigated, and there is conflicting evidence regarding the optimal isotonic fluid and optimal rate. This has led to variability in the specialty-specific guidelines. Providers should explore the guidelines relevant to the test being ordered (e.g., CT scanning, interventional cardiology) and develop local protocols, all of which should involve pre- and postcontrast intravenous infusions with isotonic fluids.

Various pharmacological agents such as N-acetylcysteine, statins, ascorbic acid, and theophylline have also been investigated as nephroprotective agents. Based on its ability to ameliorate contrast media–induced vasoconstriction and limit free radical injury, N-acetylcysteine has been the most widely studied agent. A recent meta-analysis suggested that N-acetylcysteine plus normal saline may be associated with greater reduction in CIAKI.(15) However, the use of the above agents lacks level 1

evidence to date, and it is difficult to make firm recommendations.(3)

Given the uncertainty in the literature, institutions should consider developing standardized protocols for the prevention of CIAKI. A large prospective multicenter study explored the impact of a quality improvement intervention on rates of CIAKI in the setting of cardiac catheterization.(16) The intervention included (i) development of a multidisciplinary team; (ii) participation in conference calls; (iii) review of the literature; (iv) participation in focus groups to discuss barriers and successes; and (v) biannual review of CIAKI rates. Adjusted rates of CIAKI were reduced by 21% in intervention hospitals. In reviewing the program, the key factors associated with improvement were building multidisciplinary teams, limiting contrast media volume, standardizing fluid orders, using an intravenous fluid bolus, and educating patients about oral hydration.(16)

In this case, the delay in diagnosis of a potentially life-threatening condition led to profound worsening of the patient's condition and, ultimately, his death. It remains widely accepted among surgical specialists that making a prompt diagnosis of a potential life-threatening condition (in this case, ischemic bowel) should trump a comparatively small risk of likely reversible CIAKI. In emergency situations, prolonged debates are inappropriate; prompt action and definitive treatment must be foremost. The recognized nephroprotective measures can all be administered after the appropriate diagnostic and therapeutic actions.

Take-Home Points

- Contrast-induced acute kidney injury is defined as a rise in serum creatinine of 0.5 mg/dL or a 25% increase from the baseline value, assessed 48 hours following contrast media administration, and has been associated with multiple adverse events.
- Although CIAKI is common, permanent kidney damage is fairly rare.
- Providers should screen patients for key risk factors for CIAKI including hypotension, congestive heart failure, chronic kidney disease, diabetes, age older than 75 years, anemia, and volume/type of contrast media.
- Introducing qualitative system factors such as building multidisciplinary teams, standardizing fluid orders, using an intravenous fluid bolus, and educating patients about oral hydration can reduce the risk of developing CIAKI.
- In case of a potentially life-threatening condition, contrast-enhanced imaging should be used without concern for the development of CIAKI.

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