Preventing Contrast-Induced Acute Kidney Injury

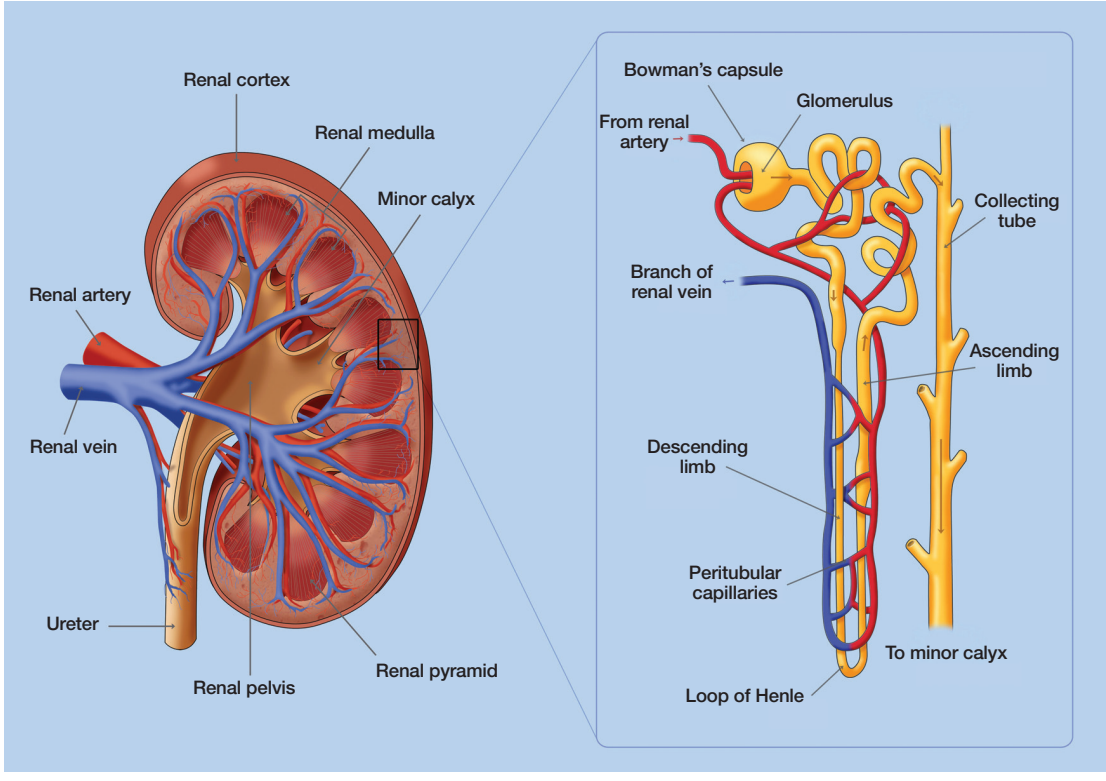
An evidence-based review of screening, risk assessment, and hydration protocols.

ABSTRACT: Diagnostic radiographic imaging scans using intravascular iodinated contrast media can lead to various complications. The most salient of these is contrast-induced acute kidney injury (CI-AKI) or contrast-induced nephropathy, a potentially costly and serious patient safety concern. Prevention strategies are the cornerstone of evidence-based clinical management for patients receiving contrast agents. These include preprocedure screening, stratification of patients based on risk factors, and protective interventions, the most important of which is hydration both before and after the radiographic imaging scan. There is a gap, however, between best evidence and clinical practice in terms of exact hydration protocols. Nurses play an important role in nephropathy prevention and need to be familiar with CI-AKI as a potential complication of radiographic imaging scans. In order to ensure safe, high-quality care, nurses must be involved in efforts to prevent CI-AKI as well as interventions that minimize patients' risk of kidney injury.

Keywords: acute kidney injury, contrast agents, contrast-induced acute kidney injury, contrast-induced nephropathy, radiographic imaging scans

Intravascular iodinated contrast agents used in radiographic imaging studies are an essential part of the clinical management of many patient conditions, and millions of contrast doses are administered safely in North America each year.[1,2] Yet contrast agents can cause adverse effects in some patients, including acute kidney injury (AKI).[1,2] The terms *contrast-induced AKI* (CI-AKI) and *contrast-induced nephropathy* are used interchangeably; both refer to the adverse effects that can occur as the result of administering contrast agents. CI-AKI increases health care costs and adversely affects patient morbidities and quality of life. The National Kidney Foundation estimates that, depending on the definition used

Figure 1. The Kidney and the Nephron



A cross-section of the kidney is shown, with a more detailed view of the nephron, the kidney's basic structural and functional unit. Contrast agents can cause tubular cell necrosis. They also increase blood viscosity, stiffen red blood cells, and cause prolonged vasoconstriction in the kidney; all of these injure the kidney by reducing blood flow and oxygen delivery. Image by Photo Researchers, Inc / Alamy Stock Photo.

and the population studied, between 5% and 40% of patients who receive contrast agents develop CI-AKI.[3]

CI-AKI is usually a transient and reversible form of acute renal failure; in most cases, symptoms such as oliguria are not present, and kidney function normalizes within one to three weeks. However, there is currently no available treatment to reverse structural damage when a severe reaction occurs; patients with risk factors such as diabetes may sustain permanent damage. In those cases, supportive treatment, including careful fluid and electrolyte management, renal replacement or hemofiltration therapy, and renal dialysis, may be needed to restore kidney function.[3-5] The cumulative effect of multiple contrast agent administrations is also a concern. Normal kidneys take approximately 20 hours to clear the contrast agent; therefore guidelines recommend avoiding dosing intervals of less than 24 hours to reduce the incidence of CI-AKI.[2]

Prophylactic strategies need to be considered in order to protect the kidneys and prevent injury. The aims of this article are to discuss the epidemiology, complications, and clinical effects of CI-AKI; screening methods to identify at-risk patients; early diagnosis of CI-AKI complications; and nursing implications related to prevention and patient education.

CI-AKI

Epidemiology. CI-AKI, the third most common hospital-acquired AKI, occurs after the administration of an intravascular iodinated contrast agent and is not attributable to other causes.[3] The clinical practice guidelines issued in 2012 by Kidney Disease: Improving Global Outcomes (KDIGO) defines AKI as any of the following[6]:

- an increase in serum creatinine greater than or equal to 0.3 mg/dL within 48 hours, or

- an increase in serum creatinine to 1.5 times the baseline that is known or presumed to have occurred in the past seven days, or
- a urine volume of less than 0.5 mL/kg/hr for six hours

Serum creatinine typically starts to rise in the first 24 to 72 hours after exposure to the contrast agent, peaks in two to five days, and returns to baseline in seven to 14 days.[3] CI-AKI manifests most commonly as an asymptomatic, nonoliguric acute kidney failure.[7] Although rare, some patients may progress to serious kidney impairment with oliguria (a 24-hour urine volume of less than 400 mL in adults), requiring hospitalization and supportive treatment. A European Renal Best Practice position statement on the 2012 KDIGO clinical practice guidelines noted that "even mild, reversible AKI conveys the risk of persistent tissue damage, and severe AKI can be accompanied by an irreversible decline of kidney function and progression to end-stage kidney failure."[8]

literature, coronary angiography and percutaneous coronary interventions were the procedures most often associated with CI-AKI.[6,17] Coronary angiography differs from more routine procedures using a contrast agent in three ways: the contrast is administered by the intraarterial route; the injection requires a catheter procedure that can dislodge atheroemboli; and the contrast dose is highly concentrated and delivered more abruptly.[2] The route of administration is a key risk factor, as contrast agents tend to be more toxic when administered intraarterially. In the 1960s and 1970s, reports of CI-AKI resulting from angiography and other procedures involving intraarterial administration contributed to an overestimation of the risk of CI-AKI when the contrast agent is administered intravenously.[9,18] All of these factors contribute to the lack of a standard definition and universally accepted prevention guidelines for CI-AKI.[9]

Pathophysiology. Researchers have identified a variety of mechanisms underlying CI-AKI.[7] At the

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In the general population of patients with normal kidney function who receive IV contrast-enhanced radiographic imaging scans, the risk of developing CI-AKI is low.[9] According to a 2013 meta-analysis by Moos and colleagues, the overall incidence of CI-AKI is 5%, and it's associated with preexisting kidney impairment, diabetes, presence of malignancy, advanced age, and chronic use of nonsteroidal antiinflammatory drugs (NSAIDs).[10] However, when focused specifically on high-risk patients, including those with preexisting kidney impairment and diabetes, the incidence of CI-AKI can be as high as 40%.[10-13] CI-AKI is responsible for one out of six critical care patients experiencing decreased kidney function, prolonged hospital length of stay, or need for dialysis due to iodinated contrast exposure.[14] CI-AKI can occur in as many as 10% of ambulatory patients who receive a contrast agent.[15] Dangas and colleagues reported an increase of hospital-related costs as a result of CI-AKI–related admission, increased length of stay, and mortality.[16]

Intravascular iodinated contrast agents can be administered by IV and intraarterial routes. In the moment of contact, contrast agents cause initial vasodilation followed by prolonged vasoconstriction in the kidney.[19] Vasoconstriction injures the kidney by reducing blood flow and oxygen delivery, resulting in both stasis of the contrast agent in the renal vasculature and medullary ischemia.[20] Contrast agents cause direct tubular toxicity and cell necrosis[21]; they also increase blood viscosity and decrease red cell deformability, further reducing blood flow.[22] The frequency of administration and length of exposure of the contrast agent in the kidney vasculature is thought to have a direct influence on the development of CI-AKI.[23]

PATIENT- AND PROCEDURE-RELATED RISK

For any given patient, the likelihood of developing CI-AKI depends on the severity of preexisting kidney impairment and is mediated by procedure-related factors and the characteristics of the contrast agents themselves.[19] Not all patients have the same vulnerability for developing AKI after receiving a contrast agent.[10] According to Dangas and colleagues, the most important patient-related risk factor is preexisting

kidney disease.[16] According to Moos and colleagues, the most important risk factors are renal insufficiency, diabetes, age greater than 65 years, and use of NSAIDs.[10]

Factors that can increase procedure-related risks include the use of high-osmolality contrast agents, larger doses of contrast agents, and repeated doses of contrast agents given within a short time.[2, 24] (Osmolality refers to the concentration of a solution, such as a contrast agent, expressed as the total number of solute particles [osmoles] per kilogram of solution.[25]) High-osmolality intravascular contrast agents contain a greater proportion of iodine, an element that enhances the radiopaqueness of vascular structures, organs, and other soft tissue.[25, 26] Contrast agents that have a higher osmolality than that of blood are known as *hyperosmolar*; they can cause shifts of both solute and water in organs, especially the kidneys, which can lead to greater nephrotoxic reactions and risk of CI-AKI.[14] Contrast agents can also be classified as ionic (containing charged molecules) or nonionic; ionic contrast agents, available since the 1950s, usually have a higher osmolality and are associated with more frequent and severe adverse reactions.[14, 27, 28] Nonionic agents, introduced in the 1980s, are of lower osmolality, greatly reducing the risk of CI-AKI.[14, 21] Contrast agents that are nonionic and iso-osmolar (having approximately the same osmolality as human blood) have been developed; while they cause less fluid shifting in the kidneys, they are expensive, so they're not used universally.[14, 29] Currently, most institutions use the nonionic, low-osmolality iodinated contrast agents; however, the risk of CI-AKI remains, because all contrast agents have higher osmolality than plasma.[14]

Kidney impairment can be expressed using several indices of kidney function. Despite widespread use, a patient's serum creatinine level is a poor indicator of CI-AKI occurrence, because it isn't a real-time biomarker and is influenced by sex, muscle mass, nutritional status, and age.[17] Measures of serum creatinine level reflect filtration in the renal tubules and glomeruli and rise only after significant loss of functioning nephrons. According to the American College of Radiology, renal function can be impaired despite normal serum creatinine values, which may be maintained until filtration function loss is reduced by nearly 50%.[2]

Glomerular filtration rate (GFR), the amount of blood that passes through the glomeruli per minute, provides a more accurate assessment of nephron function. An estimated GFR (eGFR) can be derived from the serum creatinine level, adjusted for variables such as age, sex, weight, nutritional status, and race.[30] (There is evidence supporting the use of formulas that include cystatin C, a protein filtered by the glomeruli and a more accurate marker for GFR and a better predictor of clinical outcomes.[22, 31]) In most healthy young adults, the normal eGFR is 90 mL/min/1.73 m² or higher.[30] Patients who have an eGFR less than 60 mL/min/1.73 m² are at risk for further renal injury, such as that caused by contrast agents.[30] For unknown reasons, as people grow older, GFR declines gradually, even in persons without kidney disease, but there is substantial variation among individuals.[30]

PREVENTION GUIDELINES

Many organizational and collaborative consensus statements currently address CI-AKI prevention.[2, 6, 17, 24, 32] As part of a quality improvement initiative led by one of us (YG), we reviewed the available guidelines and observed that all agreed on three critical areas in which nurses can help prevent CI-AKI: baseline screening, risk assessment and stratification, and treating those at risk for developing kidney injury with hydration for blood volume expansion.

Screening and risk assessment. Baseline screening of all patients, including outpatients, should be completed before administering IV contrast media. This can be accomplished by reviewing medical records, checking to make sure the laboratory tests of serum creatinine and eGFR have been completed and results are available, having patients respond to questionnaires, and evaluating patients according to a scoring system such as the RIFLE (risk, injury, failure, loss, end-stage renal disease) criteria (see Table 1). There is no consensus on the acceptable maximum time period between baseline renal function screening and contrast administration, but according to the American College of Radiology, screening may occur immediately before the procedure and up to 30 days prior.[2]

CI-AKI can occur in as many as 10% of ambulatory patients who receive a contrast agent.

All guidelines include the recommendation that the risk of CI-AKI be compared with the benefit of administering a contrast agent and suggest, for high-risk patients, considering the use of alternative imaging technology that doesn't require exposure to these substances. Further, all guidelines recommend minimizing patient exposure to contrast agents by using the lowest possible dose and volume necessary to obtain diagnostic accuracy.

Table 1. The RIFLE Classification of Acute Kidney Injury

RIFLE Category	GFR Criteria		Urine Output Criteria
Risk	Serum creatinine increased 1.5 times or GFR decreased > 25%	AND/OR	< 0.5 mL/kg/hr for 6 hours
Injury	Serum creatinine increased 2 times or GFR decreased > 50%	AND/OR	< 0.5 mL/kg/hr for 12 hours
Failure	Serum creatinine increased 3 times or GFR decreased > 75%	AND/OR	< 0.3 mL/kg/hr for 24 hours
	OR		OR
	Serum creatinine ≥ 4 mg/dL (with an acute increase ≥ 0.5 mg/dL)		Anuria for 12 hours
Loss	Persistent acute renal failure: complete loss of kidney function for > 4 weeks		
ESRD	ESRD > 3 months (3+ months of dialysis)		

ESRD = end-stage renal disease; GFR = glomerular filtration rate.

Source: Bellomo R, et al. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 2004;8(4):R204-R212.

Hydration. Hydration using both IV and oral administration of fluids is a universally accepted preventive measure.[33]

It's preferable to begin hydration before administering the contrast agent; this sequence results in more effective volume expansion.

Protocol for administration of IV fluids. North American and European guidelines recommend standard IV fluid therapy with isotonic IV solution (normal saline or lactated Ringer's solution) both before and after administration of contrast agents when eGFR is less than 60 mL/min/1.73 m² or the patient has diabetes or both.[17] While hydration is a relatively inexpensive and low-risk intervention when done properly, it isn't used as often as it should be. For example, in a Dutch CI-AKI prevention initiative that included approximately 4,300 patients and was conducted in 38 hospitals, only about two-thirds of high-risk patients received hydration before contrast administration despite hydration being specified in their prevention guideline.[34]

Guideline recommendations vary on timing, rate, duration, and volume of IV fluids both before and after administration of contrast agents. Isotonic fluids appear to better expand intravascular volume than sodium bicarbonate and half-isotonic saline.[35] It's preferable to begin hydration before administering the contrast agent; this sequence results in more effective volume expansion and inhibits the renin–angiotensin vasoactive response.[36] Postprocedure hydration increases blood flow, enhances urinary excretion of the contrast agent, and dilutes the contrast agent remaining in the renal tubules.[24]

The 2012 KDIGO guidelines suggest the use of oral N-acetylcysteine (a potent antioxidant with vasodilatory properties) with isotonic IV fluids in patients at high risk for CI-AKI; however, this is based on low-quality, inconsistent evidence, so it isn't considered a formal recommendation.[6] In their 2016 executive summary on the effectiveness of preventive measures for CI-AKI, the Agency for Healthcare Research and Quality noted that oral N-acetylcysteine with IV saline appeared to confer only a small benefit in reducing the risk of CI-AKI as compared with IV saline alone.[37]

Protocol for oral administration of fluids. Guidelines favor volume expansion with IV fluids over oral hydration,[2, 24] especially in patients who have any kidney dysfunction.[6] However, in two recent meta-analyses of oral hydration protocols, the authors concluded that the use of oral hydration may be more acceptable in some clinical settings—with outpatients, for example—because of its ease of use and lower cost.[1, 38] Further, evidence shows that for CI-AKI prevention, oral fluids were no more risky and may be as effective as IV hydration in outpatient settings. However, the oral route can be unreliable in some patients and adequately powered trials have not been conducted.[1] Guidelines don't give specific preprocedural oral hydration protocols; the general advice is to avoid fluid restriction and, when practical, encourage patients to drink fluids containing salt (such as salty soup) for volume expansion before and after contrast studies.[1, 17]

was integrated with a Korean hospital's computerized provider order entry system, Cho and colleagues found that the use of standardized prophylaxis increased, while the risk of CI-AKI decreased by more than 50%.[41] In the Dutch study mentioned previously, computerized alerts correctly identified 96% of high-risk patients.[34] Nevertheless, the researchers found large differences in rates of hydration across hospitals, leading them to conclude that hospital-related factors accounted for most of the variance.

The factors that interfere with CI-AKI prevention will vary by institution. In one recent study, nurses described overcoming multiple barriers in a large hospital as one radiology staff nurse initiated an evidence-based CI-AKI protocol that included oral hydration for patients at moderate risk.[39] Sharing evidence about the recommended practices with department leaders proved to be the most important strategy in implementing the new practice protocol.

Evidence shows that for CI-AKI prevention, oral fluids are no more risky and may be as effective as IV hydration in outpatient settings.

Issues in clinical practice. Despite the many different clinical practice guidelines available, not all clinicians consistently assess for CI-AKI risk factors or incorporate prevention strategies into their protocols.[39] As noted above, current guidelines are somewhat inconsistent, making it more difficult for nurses and other providers to develop institutionally appropriate protocols or checklists to enable clear, well-informed clinical decision making. Current CI-AKI prevention guidelines also lack detail and do not cover all aspects of patient management, such as who is or should be responsible for guideline adherence, screening, hydration, and patient follow-up (the radiologist, a hospital or clinic specialist, a nephrologist, the referring provider, or the nurse, for example).[40] Many health care settings lack appropriate management protocols for patients who are at risk for CI-AKI. Recommended preventive measures may not be followed because a facility may have organizational issues or a lack of necessary resources.[40] Many facilities also lack appropriate follow-up protocols for patients at risk for CI-AKI.

Computerized tools and aids such as standardized order sets and electronic alert systems that identify high-risk patients can improve patient management. In an evaluation of an electronic alert program that

Successful implementation led to substantial cost savings as a result of fewer IV bicarbonate infusions for the highest-risk patients and less time spent at the ambulatory facility after the procedure, decreasing length of stay and increasing patient satisfaction.[39]

In our own clinical experience, the barriers to implementing an updated, evidence-based protocol included a lack of communication across departments, the need for ongoing multidisciplinary education, and resistance among some staff members, for reasons that included fear of adopting a new practice (such as lifting the rule on preprocedural fasting to encourage hydration) and "turf protection."

NURSING IMPLICATIONS

Nurses play important roles both before and after imaging studies and need to be proactive in screening, risk assessment, patient education, and pre- and postprocedure hydration. As a growing number of patients undergo procedures that require contrast administration on an outpatient basis, the nurse's role in ensuring patient safety becomes increasingly important.

When a contrast-based imaging procedure is planned, patient assessment includes a determination of risk level and careful documentation of current

medications. The nurse should assess for preexisting kidney disease and ensure that laboratory tests of serum creatinine and eGFR are completed and that the ordering clinician is aware of the results. Ask the patient about any previous testing that included contrast material. If the patient is already taking potentially nephrotoxic drugs such as metformin (Glucophage and others), angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or NSAIDs, confer with the prescriber to confirm whether any should be discontinued prior to the procedure. Metformin and metformin-containing medications are often discontinued (even though metformin, itself, confers no additional risk of CI-AKI) because they're thought to cause severe and even fatal lactic acidosis in the presence of contrast-induced acute kidney failure.[2, 17, 24] Current metformin prescribing information recommends discontinuation before and after contrast administration.[42] Diuretics are sometimes withheld before a procedure in order to prevent dehydration. The nurse should be sure the patient understands why some medications may be temporarily discontinued and exactly when the medications can be restarted after the procedure.

When an oral hydration strategy is planned, assess if the patient is at risk for fluid overload (because of a history of congestive heart failure, for example). This assessment is particularly important in outpatients. If there is no medical reason to restrict fluids, educate the patient on the critical importance of fluid intake both before and after the procedure, and offer guidance about the amount and type of fluids to drink (salty ones, for example).

On the day of the procedure, nurses will implement, evaluate, and document the hydration protocol (oral or IV fluids). They will also monitor patients for fluid overload, as many patients who require hydration are older and have preexisting comorbidities, such as reduced left ventricular function, making them vulnerable to pulmonary edema.

Nurses should educate patients on possible postprocedure symptoms of CI-AKI, including fatigue, anorexia, conditions related to fluid retention (such as swelling of feet and ankles, puffiness around the eyes, and dry and itchy skin).[43]

Nurses should ensure that outpatients, in particular, understand the importance of postprocedure hydration, and should also instruct them to monitor the color and amount of urine output, as a decrease in volume and darkening color may be indications of worsening renal function. Patients need to know the specific provider to call if they develop symptoms; they also need to understand the importance of following up on laboratory tests and return appointments, as instructed.

If there is no medical reason to restrict fluids, educate the patient on the critical importance of fluid intake both before and after the procedure.

In view of the increasing number of patients who receive and benefit from IV contrast agents for computed tomography and angiography studies, nurses need to be familiar with CI-AKI as a potential complication and understand evidence-based strategies for prevention. Continuing efforts to prevent CI-AKI and interventions that attempt to reduce the risks of CI-AKI are the main nursing challenges in delivering safe, efficient, high-quality care to patients who receive contrast agents. ▼

For two additional continuing nursing education activities on acute kidney injury, go to www.nursingcenter.com/ce.

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