CONTACT HOUR: 2.0 HRS

Preventative care to reduce the risks of acute kidney injury in people with chronic kidney disease undergoing cardiac catheterization

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OBJECTIVES

By the end of this module, readers will be able to:

1. Define the purpose, benefits, and risks of coronary angiography and angioplasty procedures
2. Describe the pathophysiology manifestation of contrast-induced acute kidney injury (CI-AKI) in patients who have undergone cardiac catheterization procedures
3. Evaluate a patient's risk for developing CI-AKI based on patient-associated and procedure-associated risk factors
4. Define various strategies to lower the patient's risk for developing CI-AKI
5. Describe the nursing interventions for high-risk patients with an estimated glomerular filtration rate (GFR) of 30mL/min/1.73m^2

BACKGROUND

Cardiovascular disease (CVD) is the most prevalent cause of mortality globally with 17.3 million deaths per year; unfortunately, the prevalence continues to grow as the population ages (Husein et al., 2021). People with chronic kidney disease (CKD) are at a higher risk of manifesting coronary artery disease (CAD), and the incidence of cardiovascular events is much higher in people within estimated GFR categories 3a (45–59 mL/min/1.73 m^2), 3b (30–44 mL/min/1.73 m^2), 4 (15–29 mL/min/1.73 m^2), and 5 (<15 mL/min/1.73 m^2) (Akbari et al., 2015) compared to the general population (Jankowski et al., 2021). CVD is the major cause of mortality in this patient population (as well as in hemodialysis) (Jankowski et al.) and is 20 times higher than in the general population (Cozzolino et al., 2018). People with CKD undergo frequent cardiac diagnostic and interventional procedures for transplant purposes and to monitor cardiac-related symptoms.

Coronary angiography is the gold standard diagnostic procedure to identify the presence and extent of stenosis due to plaque build-up in the coronary arteries using contrast enhanced imaging through iodinated contrast medium (ICM). However, ICM is hard for the kidneys to clean and filter out of the blood and can lead to a serious complication called contrast-induced acute kidney injury (CI-AKI) (Macdonald et al., 2022). People with CKD who are planning for transplant or experiencing cardiac symptoms will undergo diagnostic coronary angiography. Unfortunately, one of the common causes of hospital-acquired AKI is believed to be from intravascular contrast media exposure (Weferling et al., 2021). The incidence of CI-AKI is associated with the severity and the number of risk factors such as CKD. People with eGFR ⩽ 30mL/min/1.73 m^2 have been shown to be at a higher risk of developing CI-AKI (Macdonald et al., 2022). There is no current therapy for CI-AKI; therefore, effective risk management and prevention are critical.

This article describes the current understanding about the pathogenesis of CI-AKI, benefits and risks of cardiac catheterization in people with CKD, ongoing research about possible therapeutic options, and recent guidelines on how to mitigate these risks in people with CKD undergoing this procedure.

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CORONARY ANGIOGRAPHY

Coronary angiography is a procedure that uses X-ray guided imaging to diagnose and treat narrowing or blockages of the coronary arteries. The procedure is performed percutaneously by accessing the radial, ulnar, or femoral arteries. The puncture site is injected with local anaesthetic such as lidocaine, then a needle guidewire is used to secure the artery, and a 6-French sheath is inserted to allow the guidewire and the cardiac catheter to be advanced to visualize the left ventricle and coronary arteries through the ascending aorta by injecting ICM (Watson & Gorski, 2011).

Coronary angiography allows for the assessment and quantification of stenoses and calcification of coronary arteries (Schmermund et al., 2018). Percutaneous coronary interventions (PCI) such as balloon angioplasties with or without stent placements have been shown to preserve ventricular function and increase survival in acute myocardial infarction (MI) by quickly re-establishing coronary artery patency, which benefits patients who suffer from angina and atherosclerosis, and lowers the risk of having an acute MI and other cardiac-related problems (Keeley et al., 2003).

Like any invasive procedure, coronary angiography poses risks such as bleeding, hematoma formation, infection at the incision site, and arrhythmias, and can cause dissection of the coronary vessels. Certain medical comorbidities increase the chances of complications occurring after an angiogram, which include older age, kidney insufficiency, diabetes mellitus, obesity, congestive heart failure (CHF) with low ejection fraction, recent MI, or stroke (Tavakol et al., 2012). A potential serious complication is CI-AKI regardless of baseline kidney function. Although the chance of kidney impairment is low (about 2% for the general population), the risk increases to 20% depending on the risks and characteristics of the individual, especially those with CKD and/or CVD (Zhou et al., 2022; Firouzi et al., 2020).

CONTRAST-INDUCED AKI

CI-AKI is defined as acute kidney impairment presenting with 44 mol/L or 25% increase in serum creatinine (SCr) levels after 48–72 hours following contrast exposure compared to baseline SCr, despite other potential causes of kidney impairment ruled out (Mehran & Nikolsky, 2006; Zhang et al., 2020). Patients with a past medical history of AKI and other comorbidities such as diabetes may make them vulnerable to CI-AKI (Zhang et al.).

CI-AKI Pathophysiology

The exact pathophysiology by which CI-AKI occurs is not clearly understood. It has been attributed to the toxic effects of the contrast agent, which induces hemodynamic changes in the kidney and oxidative stress on renal tubular epithelial and vascular cells (Zhou et al., 2022), swelling, inflammation, and epigenetic regulation (Zhang et al., 2020). McCullough et al. (2016) state that the contrast produces a high osmotic environment in the kidneys, which plays a role in cell apoptosis (cell death) and necrosis.

The kidneys undergo numerous hemodynamic changes following contrast exposure. First, there is momentary vasodilation, followed by persistent vasoconstriction with increased vascular resistance and reduced blood flow and oxygen supply in the kidneys (Zhang et al., 2020). Endothelin and adenosine are released because of the contrast's toxic effects which reduces prostaglandin and nitric oxide (NO) concentration; prostaglandin and NO are secreted to increase oxygen supply and local blood flow while down-regulating ion-exchange (Dugbartey & Redington, 2018). The GFR is reduced as outer medullary ischemia is elicited because of vasoconstriction induced by the contrast (Zhang et al.).

Hypoxia causes increased free radical and reactive oxygen species (ROS) production in the mitochondria and a lack of oxidative phosphorylation, which is a vital step in adenosine triphosphate (ATP) production. The ICM speeds up the breakdown of ATP into adenosine diphosphate (ADP) and adenosine monophosphate (AMP), and limits the mitochondrial enzyme actions (Zhang et al., 2020). Since the plasma membrane is not intact, excessive ROS can harm renal tubular epithelial cells and surrounding cells by inducing apoptosis via intrinsic pathway and stress kinase activation, such as p38 mitogen-activated protein kinase (MAPK) stress kinases (Mamoulakis et al., 2017). The combination of several stress stimuli such as those mentioned above cause a significant amount of apoptosis, which may lead to kidney damage (Zhang et al.).

Individuals who are coming in for cardiac catheterization procedures with past inflammatory states who had no known risks for CI-AKI, had a greater chance of developing CI-AKI, as their C-reactive protein levels are increased (Kwasa et al., 2014). In experimental animal models, contrast exposure caused renal failure and tubular damage, along with a substantial rise in inflammatory cytokines such as interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-) (Zhang et al., 2020). Recent studies propose a range of stressors such as ROS and osmotic stress caused by contrast activate NOD-like receptor pyrin domain containing 3 (NLRP3) and nuclear factor kappa B (NF-B), likely triggering an inflammatory response (Zhang et al.).

Risk Factor Development of CI-AKI

The risk factors for CI-AKI can be separated into two categories – patient-associated and procedure-associated risk factors. Patient-associated risks include kidney insufficiency with a GFR 60 mL/min, diabetic nephropathy, age > 70 years, hypertension, CHF, anemia, hyperuricemia, and taking nephrotoxic drugs such as NSAIDs (Zhang et al., 2020). Procedure-associated factors include excess ICM, use of high-osmolality contrast media, repeated contrast exposure (Zhang et al.; Zhou et al., 2022), and transfemoral access (TFA) compared to transradial access (TRA) (Firouzi et al., 2020). The risk of CI-AKI increases with TFA compared to TRA when undergoing angiography or PCI procedures (Firouzi et al.). As can be noted, procedure-associated risks can be mitigated to reduce the chances of patients experiencing CI-AKI.

PREVENTATIVE MEASURES AND CARE

Previous studies have shown that CI-AKI is associated with severe clinical outcomes, including risk of hospitalization, end-stage kidney failure, and death (Zhou et al., 2022), heavily emphasizing the importance of preventative protocols as at the present time there are no treatments available. Many catheterization labs will develop their own risk prediction models, as there is no universal risk prediction model presently available. Intervention is based on the results of the scoring. Mehran et al. developed a risk score that is the most widely studied CI-AKI risk model for patients undergoing cardiac catheterization (Mehran et al., 2004; Zhang et al., 2020). The risk model includes eight identified variables such as hypotension, intra-aortic balloon pump, CHF, CKD, diabetes, age > 75 years, anemia, and contrast volume. Patients are also categorized by their risk of developing CI-AKI into four levels from low to very high risk. This risk model was created in 2004 and it has been reviewed and used in many research studies with good clinical results. However, this model does not include some procedure-related factors, and comparable risk models had the same limitations (Zhang et al., 2020), warranting the need for further developments of risk models.

Screening patients prior to the procedure is an important step as it allows for examining kidney function, comorbidities and to identify risks for CI-AKI. This will determine what kind of preventative measures will be used by the interventional cardiologist (Macdonald et al., 2022), which will be discussed later in this article.

Measuring Biomarkers

Since one of the main risk factors for CI-AKI occurring is pre-existing kidney insufficiency, it is important to screen for kidney function prior to contrast exposure. SCr is frequently utilized as a marker to measure how well the kidneys are filtering waste from the blood. When the kidneys are functioning normally, creatinine is filtered out from the blood and excreted out of the body as a waste product in urine. Another way to test for kidney function is measuring the GFR, which indicates how much blood passes through the glomeruli each minute. An eGFR of 60 mL/min/1.73 m^2 is considered within normal limits. Normally in clinical practice, SCr levels are monitored and GFR is calculated prior to the patient being exposed to contrast to assess the risk of CI-AKI (Zhang et al., 2020).

Unfortunately, SCr levels may not quickly detect declining renal function as it can be within normal limits even if there is a degree of impaired kidney function (Wang et al., 2016). SCr levels are affected by other factors not related to CI-AKI such as age, gender, diet, muscle mass, arteriosclerosis, and renal tubular secretion (Bellomo et al., 2004). Multiple studies have made advancements to find novel biomarkers that are more sensitive and for earlier detection of kidney functioning (e.g., IL-8, KIM-1, Cys-C; Zhang et al., 2020). These biomarkers present many advantages such as stability and sensitivity for kidney function (Wang et al., 2016). However, given that these novel biomarkers can easily be influenced by other variables, such as thyroid dysfunction, age, and systemic inflammation, more controlled prospective research is required to determine the viability of these biomarkers for CI-AKI prediction (Zhang et al., 2020).

Appropriate Use of Contrast

Fortunately, effective preventative approaches and care are presently available, and more research is ongoing to find therapies to lower the incidence of CI-AKI for patients. Clinicians should choose contrast agents and monitor the volume used cautiously as direct contrast toxicity is largely reliant on the composition of the contrast medium. CI-AKI can be brought on by using any ICM. High-osmolality contrast medium has been progressively phased out of usage due to its increased nephrotoxicity opposed to other ICM (Zhang et al., 2020). Presently, low-osmolality contrast medium and isotonic osmolality contrast medium have been frequently utilized for cardiac catheterization procedures. Iohexol (Omnipaque) is the standard contrast used in procedures and iodixanol (Visipaque) is used for patients with impaired kidney function with an eGFR 30 mL/min/1.73 m^2 as it is less viscous (Eivindvik & Sjøgren, 1995) and has the lowest osmolality of all available contrast media (From et al., 2010).

Using less contrast volume is another way to mitigate the risks of CI-AKI. It was found that there was a positive correlation among contrast volume and the extent of kidney injury (Mehran et al., 2019). There was a lower occurrence of CI-AKI when less contrast volume was used in people with impaired kidney function (Chaabouni et al., 2021). Currently, carbon dioxide (CO_2) angiography has been characterized as a non-nephrotoxic and non-anaphylactic option to ICM for those allergic to iodinated medium and high-risk patients (Zhang et al., 2020). CO_2 displaces the blood and generates a negative contrast for digital subtraction imaging. Although CO_2 angiography presents potential benefits, the use of CO_2 as a visualizing medium is not suggested for use in the coronary arteries. (Cho, 2015). Stegemann et al. (2016) proposed a hybrid angiography approach utilizing CO_2 and a lower dose of ICM, which considerably reduced CI-AKI occurrence in peripheral vascular interventions. Last, if possible, avoiding angiography for high-risk patients is the last resort. Other imaging options include intravascular ultrasound and magnetic resonance angiography (Zhang et al., 2020).

Other Therapy Options

Zhang et al. (2020) proposed hydration therapy to be an effective therapy, as the contrast's excretion is rapid when the patient is hydrated compared to greater absorption when in a volume-depleted state. Although, hydration has been used frequently and seen to be helpful, it is not a definitive cure for CI-AKI, hence, emphasizing the importance of preventative measures (Zhan et al., 2019).

It has been postulated that certain pharmacological agents such as statins and antioxidants could provide

protective role in high-risk patients of CI-AKI (Zhang et al., 2020). High dose rosuvastatin (Leoncini et al., 2014) and atorvastatin (Quintavalle et al., 2012) have been shown to have potential in preventing the incidence of CI-AKI. This protective effect mainly relies on the statin's anti-inflammatory characteristics. One of the recognized pathogeneses of CI-AKI is oxidative stress. Intracellular ROS created from contrast exposure causes an oxidative-antioxidant imbalance (Zhang et al., 2020). N-acetylcysteine (NAC) (Trivedi et al., 2009) and sodium bicarbonate (Calvin et al., 2010) are two antioxidants frequently used to prevent CI-AKI. Nonetheless, further research is needed to support the evidence and efficacy of the above pharmacological agents (Zhang et al., 2020).

Several trials have explored the effects of remote ischemic condition (RIC) in the prevention of CI-AKI, suggesting a protective effect against renal ischemia (Zhan et al., 2019; Zhang et al., 2020). In RIC, brief episodes of reversible ischemia produced by alternating cycles of inflation and deflation of a blood pressure cuff in a limb will induce a protective effect to remote tissues and organs with an increase of blood supply to the kidneys (Er et al., 2012). RIC is incorporated prior to and after coronary angiography. Interestingly, a meta-analysis of 1,167 patients showed a reduced incidence of CI-AKI in patients who had undergone RIC prior to the procedure (13.5% vs 6.5%, $p < 0.001$) (Hu et al., 2016). Unfortunately, CI-AKI was not preventable in people with diabetes (Moretti et al., 2018).

INTERVENTIONS FOR PATIENTS WITH GFR 30 ML/MIN

In May 2022, the Canadian Association of Radiologists published the consensus guidelines for prevention of CI-AKI (Macdonald et al., 2022). Pre-procedure risk analysis and intervention should be done on a case-by-case basis. The benefits and risks need to be assessed for people with kidney insufficiency, as the procedure would be saving the heart but killing the kidneys. In the event an individual with kidney impairment presented with a life-threatening event, such as an MI, the benefits of the procedure would outweigh the risks. The procedure should not be delayed for emergent life-threatening illnesses even if bloodwork results may not be available (Macdonald et al.). The following include some guidelines healthcare professionals (HCPs) can implement.

Blood work and laboratory tests should be obtained within six weeks prior to the procedure and should include hemoglobin/hematocrit, white blood cell count, platelet count, sodium, potassium, blood urea nitrogen, creatinine, international normalized ratio (INR) for patients on warfarin, and current eGFR. Any test results that are outside normal limits and ranges should be evaluated by the physician prior to the procedure in order to determine if additional interventions such as intravenous (IV) hydration should be implemented to prevent CI-AKI. In patients with severe CKD (eGFR is 30 mL/min/1.73 m^2) and patients with pre-existing AKI, it is suggested to consider if contrast exposure is required (Macdonald et al., 2022).

In patients with known AKI or severe CKD, metformin should be stopped prior to and during the time of contrast exposure, and it should not be restarted for at least 48 hours and only if kidney function remains stable (Macdonald et al., 2022). This is done because metformin is heavily excreted by the kidneys and contrast slows down kidney function, causing a build-up of metformin in the body leading to lactic acidosis.

Although there is a lack of evidence on the benefits of IV hydration as a cure, patients with reduced kidney function may receive IV hydration using normal saline, 0.9% saline, or 1.26% sodium bicarbonate, or oral salt and water prior to the procedure (Macdonald et al., 2022).

Visipaque, a contrast agent with lower osmolality, compared to Omnipaque, can be administered by hand injection instead of auto-injection, allowing the physician to reduce the volume of contrast to 50% benefitting high-risk patients (Watson & Gorski, 2011). Patients with end-stage kidney disease (ESKD) receiving hemodialysis or peritoneal dialysis will need dialysis post-procedure. This allows for effective removal of the contrast from the blood (Lee et al., 2007).

After the procedure, patients are instructed to seek medical attention if they develop shortness of breath, peripheral edema, or decreased urine output (Macdonald et al., 2022). Discharge instructions include increasing hydration to help excrete the contrast through urination. It is also recommended to do follow-up bloodwork to measure SCr levels 48 hours up to one week after contrast injections, to identify if there is development of AKI and provide immediate treatment in a timely manner.

SUMMARY

Cardiac catheterization presents many benefits for the patient and their well-being. The use of ICM allows for visualization of the coronary arteries and left ventricle, but poses the risk of CI-AKI and AKI. Preventative measures to prevent CI-AKI must be implemented in the care of people with CKD with eGFR < 30 mL/min/1.73m^2. Healthcare providers (HCPs) can mitigate the risk of CI-AKI development from ICM exposure by implementing care for patients in many ways, such as assessing the patient's kidney function from blood work and laboratory testing. IV hydration and holding certain medications such as metformin are additional ways to reduce this risk in clinical practice. There are other less harmful contrast agents that can be used in the catheterization lab to reduce CI-AKI development further. Following the procedure, HCPs can continue supporting people with ESKD through dialysis and follow-up care one week after ICM exposure.

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CONTINUING EDUCATION STUDY QUESTIONS **CONTACT HOUR: 2.0 HRS**

Preventative care to reduce the risks of acute kidney injury in people with chronic kidney disease undergoing cardiac catheterization

By Gayathirie Packiyanathan, Joy A. Gatmaitan, Simerdeep Chouhan, Shy Amlani, and Rosa M. Marticorena

1. Angiography allows for the:
   a) Assessment of stenoses
   b) Quantification of calcification
   c) Quantification of stenoses
   d) All the above
2. CI-AKI is the ___ increase in serum creatinine (SCr) levels after 48–72 hours following contrast exposure compared to baseline SCr.
   a) 15%
   b) 25%
   c) 35%
   d) 45%
3. An eGFR of ___mL/min is considered high-risk for CI-AKI.
   a) 30
   b) 60
   c) 45
   d) None of the above
4. RIC incorporates the application of intermittent inflation and deflation of a BP cuff to a limb prior to the procedure to cause a protective effect in the kidneys.
   a) True
   b) False
5. Procedure-based factors can be mitigated to reduce the incidence of CI-AKI. Which of the following does not reduce the incidence of CI-AKI?
   a) Use of high-osmolality contrast
   b) Less volume of contrast
   c) Other imaging options like magnetic resonance angiography
   d) CO_2 angiography
6. Which biomarkers can be used to monitor kidney function?
   a) Ca^{2+} and K+
   b) Na+
   c) SCr and eGFR
   d) All the above
7. Angiography and PCI preserve ventricular function and increase survival of MI patients by:
   a) Improving blood flow in the heart
   b) Preventing further damage to heart muscles
   c) Re-establishing coronary artery patency
   d) All the above
8. Patients with an eGFR of 30mL/min should stop metformin use prior and during contrast injections. When can metformin be restarted?
   a) After the procedure
   b) 48 hours after with stable kidney function
   c) 24 hours after with unstable kidney function
   d) None of the above
9. Patients should be instructed to seek medical attention if they develop SOB, peripheral edema, or decreased urine output following the days after contrast imagining.
   a) True
   b) False
10. Some studies have found high dose rosuvastatin and atorvastatin showed potentiation in preventing the incidence of CI-AKI due to _____ characteristics.
    a) Anti-inflammatory
    b) Antioxidant
    c) Anticoagulant
    d) Antihistamine

CONTINUING EDUCATION STUDY ANSWER FORM

CE: 2.0 HRS CONTINUING EDUCATION

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8.	a	b	c	d
9.	a	b		
10.	a	b	c	d

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