CE 2.0 CONTACT HOURS

Acute kidney injury after cardiovascular surgery

Abstract: Acute kidney injury (AKI) is a complication experienced by many patients undergoing cardiovascular surgery. Postoperative deterioration in renal function is associated with an increased risk of in-hospital mortality and affects long-term survival. Developing strategies to identify and treat AKI is important to reduce incidence and optimize outcomes.

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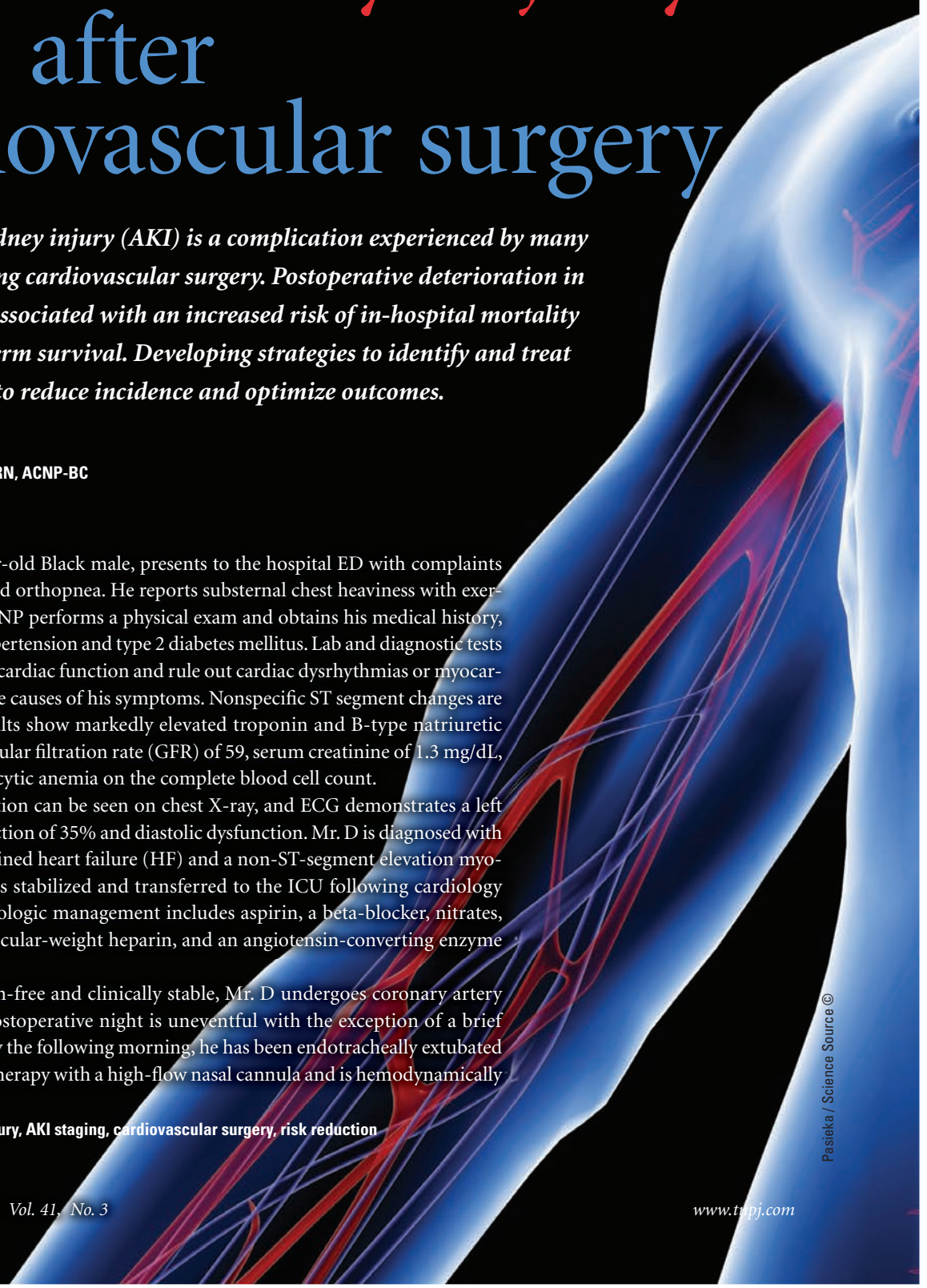
Mr. D, a 64-year-old Black male, presents to the hospital ED with complaints of dyspnea and orthopnea. He reports substernal chest heaviness with exertion. The ED NP performs a physical exam and obtains his medical history, which is notable for hypertension and type 2 diabetes mellitus. Lab and diagnostic tests are ordered to evaluate cardiac function and rule out cardiac dysrhythmias or myocardial ischemia as possible causes of his symptoms. Nonspecific ST segment changes are seen on ECG. Lab results show markedly elevated troponin and B-type natriuretic peptide levels, a glomerular filtration rate (GFR) of 59, serum creatinine of 1.3 mg/dL, and findings of normocytic anemia on the complete blood cell count.

Pulmonary congestion can be seen on chest X-ray, and ECG demonstrates a left ventricular ejection fraction of 35% and diastolic dysfunction. Mr. D is diagnosed with acute on chronic combined heart failure (HF) and a non-ST-segment elevation myocardial infarction. He is stabilized and transferred to the ICU following cardiology consultation. Pharmacologic management includes aspirin, a beta-blocker, nitrates, I.V. diuretics, low-molecular-weight heparin, and an angiotensin-converting enzyme (ACE) inhibitor.

Two days later, pain-free and clinically stable, Mr. D undergoes coronary artery bypass grafting. His postoperative night is uneventful with the exception of a brief hypotensive episode. By the following morning, he has been endotracheally extubated and placed on oxygen therapy with a high-flow nasal cannula and is hemodynamically

Keywords: acute kidney injury, AKI staging, cardiovascular surgery, risk reduction



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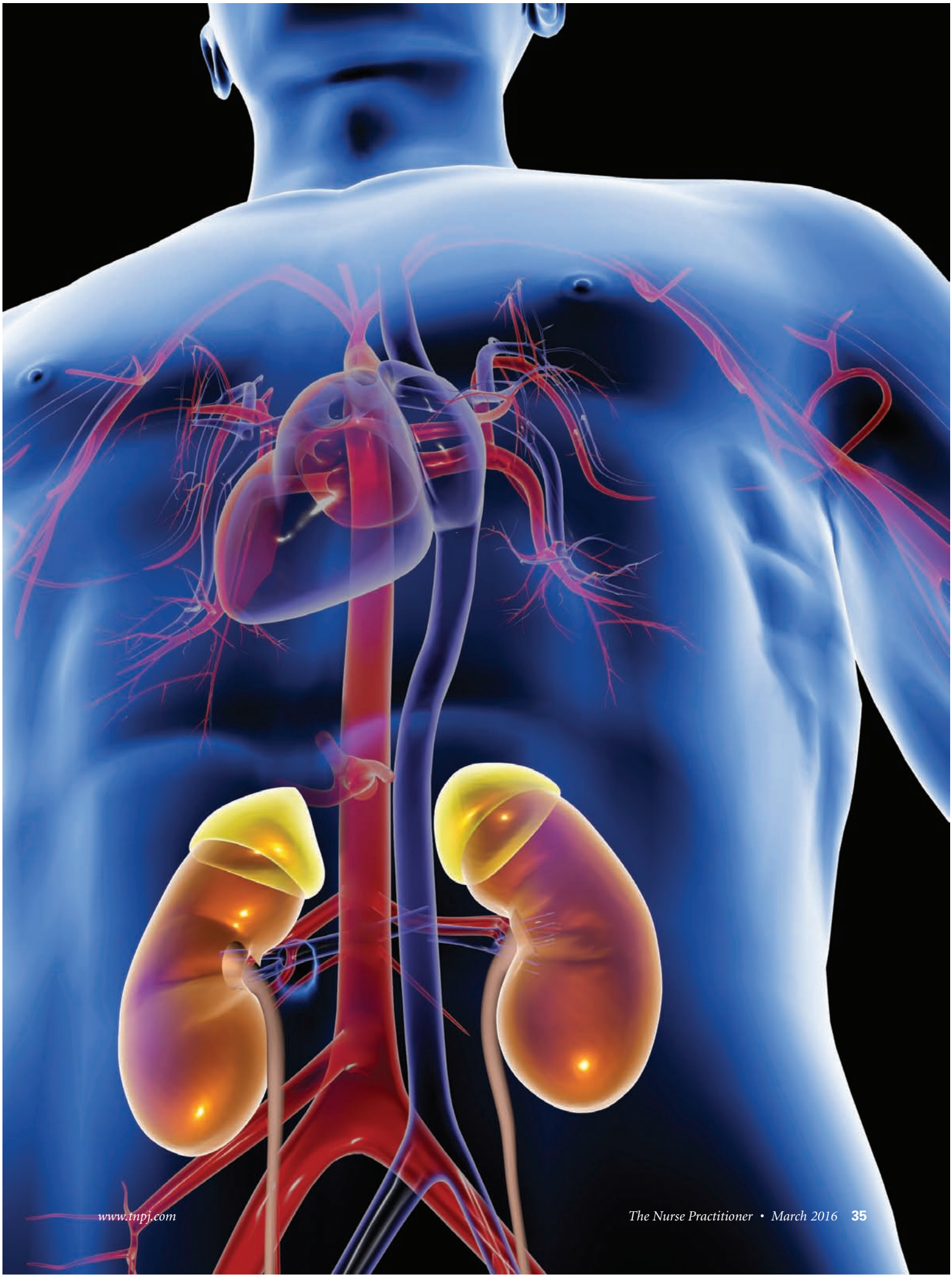


stable. Pulmonary congestion previously noted on X-ray persists, and mild oliguria has developed with a urine output (UO) of 0.3 mL/kg/hr for the last 6 hours. His creatinine is close to his admission baseline at 1.3 mg/dL, so diuretics are resumed.

UO improves, and Mr. D is subsequently transferred to the cardiac stepdown unit. Within 48 hours, he is hyperkalemic, uremic, and his volume overload is now refractory to diuretics. The nephologist is consulted and diagnoses Mr. D with acute kidney injury (AKI). Concerned for progressive respiratory insufficiency and/or dysrhythmias secondary to hypervolemia and electrolyte abnormalities, Mr. D is returned to ICU for continuous renal replacement therapy as recommended.

Overview of acute kidney injury

AKI following cardiovascular surgery carries a poor prognosis. Despite improvements in management strategies, studies have shown that in-hospital mortality and long-term survival are adversely affected when kidney function deteriorates postoperatively.[1-5] Early detection and aggressive early intervention are critical to optimizing outcomes for those at risk for kidney injury.

AKI, previously referred to as acute renal failure (ARF), is defined as an abrupt change in kidney function.[6] The change in terminology is based on the understanding that kidney injury is a broad spectrum of acute disease with different levels of severity.[7] Ambiguous diagnostic criteria have historically contributed to the underrecognition, management, and reporting of kidney injury. Different definitions of AKI have also made the body of research on treatment and outcomes difficult to compare.[7-9] Efforts by workgroups such as Kidney Disease Improving Global Outcomes (KDIGO) and Acute Dialysis Quality Initiative (ADQI) have improved the early detection and treatment of AKI by developing standardized measures for defining injury and staging severity.[7,8,10] Three classification systems are commonly used to qualify AKI. Risk, Injury,-Failure, Loss of kidney function, and End-stage renal disease (RIFLE), proposed by ADQI in 2004, defines AKI in stages of increasing severity. Three years later, the Acute Kidney Injury Network (AKIN) modified the RIFLE criteria based on evidence that even incremental changes in kidney function were clinically significant and should be acknowledged and treated as early as possible. The revised classification system increased the sensitivity and specificity of the measures used to identify AKI.[6,8]

Both RIFLE and AKIN demonstrated predictive validity and both were used in practice; however, concerns regarding the continued use of different definitions for AKI led to further refinement. After reviewing the evidence on RIFLE and AKIN, the KDIGO workgroup proposed a third classification system for AKI, creating one definition for use in research and practice (see *KDIGO criteria*).[7,11]

Despite this important consensus, criticism has been raised in regards to the KDIGO staging convention, as AKI may be diagnosed based solely on UO. This approach is not without limitations; changes in UO do not always indicate changes in the GFR. Urine volumes can vary in response to a variety of clinical situations; fever, hyperthyroidism, increased fluid intake, or diuretic use can cause UO to increase or decrease. A corresponding change in serum creatinine (SCr) is not always seen when UO decreases, particularly when low UO is caused by inadequate fluid volume resuscitation.

Diagnosing AKI based on SCr changes can be problematic as well. Creatinine levels can vary in response to nonrenal causes. Medications, muscle injuries, or increased muscle mass can cause creatinine elevations; a decreased SCr may result from low muscle mass. Determining the change in creatinine is difficult when patients present with AKI who have no prior baseline for comparison.

There has also been concern that determining AKI based on a single biomarker (such as SCr or an isolated variable such as UO) may lead to inappropriate treatment and unnecessary specialty consultations. While changes in UO and SCr are perhaps the easiest way to identify kidney injury, it is important to consider whether these changes are affecting glomerular filtration. The RIFLE classification system is used most often for these reasons.[12]

KDIGO criteria[7,11]

AKI stage	SCr change from baseline	SCr acute change	UO
Stage 1	1.5–1.9 x	≥0.3 mg/dL in 48 h	<0.5 mL/kg/hr x 6–12 h
Stage 2	2.0–2.9 x	No data	<0.5 mL/kg/hr x ≥12 h
Stage 3	≥3 x	≥4.0 mg/dL	<0.3 mL/kg/hr x ≥24 or anuria ≥ 12 h or renal replacement therapy initiated

Evaluating kidney function

Once AKI has been recognized and the degree of kidney dysfunction staged, etiology should be determined. Differentiating between prerenal, intrinsic-renal, and postrenal causes is a useful approach. Obtaining a careful medication and medical history provides useful information that aids classification (for example, recent vomiting, diarrhea, nephrotoxin exposure, or aggressive diuresis).

Clinical signs and symptoms found on the physical exam may also provide clues as to the cause of AKI (features of volume depletion, HF, hypotension, or bladder distension). Diagnostic testing and urine studies can help clarify the mechanism of kidney injury if the history and physical exam are inconclusive. Urinalysis, urine osmolality, fractional excretion (FE) of electrolytes, FE of uric acid, and quantification of urine protein should be included in the initial testing (see *Urinary findings in AKI*).

Urinary findings in AKI[16]

	Prerenal	Intrinsic renal	Postrenal
Urinalysis	Normal	Proteinuria/ casts	WBCs/RBCs
Fractional excretion of sodium (FENa)	<1%	>1%	Acute <1%; chronic >1%
Fractional excretion of uric acid (FEUric acid)	<10%	>10%	Variable
Fractional excretion of urea (FEUrea)	<35%	>35%	Variable
Urine osmolality	>600 mOsm/kg	300 mOsm/kg ~	Variable

A complete urinalysis (which includes gross exam, dipstick analysis, and microscopic exam of urine sediment) is one of the most useful and cost-effective diagnostic tools for evaluating acute and chronic kidney function; however, it is important to remember that it has limitations. For instance, urine dipstick for protein can be unreliable. Dipstick testing is not sensitive enough to detect moderately increased proteinuria; even severe proteinuria may not be identified if urine is very dilute.[13] This is particularly important when evaluating patients with diabetes mellitus, who are at high risk for chronic kidney disease (CKD). Initiating ACE inhibitor or angiotensin II receptor blocker (ARB) therapy would be considered for these patients when clinically appropriate when proteinuria is present.[13]

Spot testing urine protein-to-creatinine ratio provides better proteinuria quantification. Finally, AKI is often present despite a normal urinalysis. Prerenal kidney injury, acute tubular necrosis, urinary tract obstruction, tumor lysis syndrome, and hypertensive emergencies are just a few of the clinical conditions that cause kidney injury without changes in the urinalysis. Clinicians should be mindful that urinary testing must be appropriately timed and interpreted in relation to a patient's history and clinical presentation. Urine studies should be done prior to giving diuretics, as they can falsely affect study results.[12]

Creatinine is the most common biomarker used to evaluate kidney function. In healthy individuals, SCr levels remain in a steady state because it is neither reabsorbed nor secreted by the kidneys. This makes creatinine an ideal agent for calculating the GFR and evaluating kidney injury or recovery. Creatinine use is not without limitations, however. In early injury, there has not been sufficient time for creatinine to accumulate in the blood. This means that kidney injury, as defined by changes in creatinine levels, may not be apparent for hours to days. It follows that the use of creatinine to estimate GFR will not always reflect actual filtration. Rising creatinine levels can overestimate GFR; creatinine removal during dialysis makes assessing kidney recovery difficult. Finally, creatinine has little efficacy in forecasting the duration and clinical course of AKI.[13]

Urea, a byproduct of protein metabolism, is commonly used in managing AKI to monitor levels of nitrogenous waste and uremic solutes; however, levels can be affected by several extrarenal factors, such as diet, hypercatabolism, tissue necrosis, volume depletion, and steroids.[13] Ultimately, once blood urea nitrogen (BUN) and SCr levels rise, kidney injury has already occurred. Because of these factors, even minor elevations in BUN and SCr must be evaluated using a staging model, such as AKIN for clinical significance. Information technology can be a helpful tool in systematic monitoring of high-risk individuals; built-in triggers can alert providers when lab changes consistent with AKI develop.

Technologic advances have led to the development of new biomarkers that may predict risk for developing AKI; lab and point-of-care tests are being designed that aid early identification of AKI and predict its clinical course.[14-16] Neutrophil gelatinase-associated lipocalin (NGAL), normally present at low levels in human tissue, becomes markedly elevated following prerenal or intrinsic renal injury. Because it can be easily detected in serum and urine, it has been studied for its ability to predict the severity, duration, and mortality associated with AKI.[17-19]

The kidney injury molecule dipstick is a rapid urine test shown in clinical trials to have specificity for detecting preclinical nephrotoxicity and renal recovery.[20] Urinary interleukin-18 (IL-18), a cytokine that plays a role in inflammatory disorders, is being evaluated for its ability to predict AKI.[20] The combination of urinary IL-18, urine NGAL, and plasma NGAL was shown to significantly improve risk prediction and poor outcomes among patients undergoing cardiac surgery.[16]

While sophisticated biomarkers of AKI have great potential to improve care management and patient outcomes, there is still much to be understood about their value. Until these advanced technologies become better understood and more cost effective, simple, evidence-based strategies such as AKIN criteria to aid early recognition

and evaluating urinary tests remain among the most helpful management tools available.

AKI following cardiovascular surgery

AKI following cardiovascular surgery (CVS) can have a complex and multifactorial etiology. The most common mechanisms of injury include decreased kidney perfusion (prerenal), direct tissue injury, and hypersensitivity reactions that cause renal inflammation (intrinsic-renal). Obstruction (postrenal) can also contribute to AKI but is rarely the etiology after CVS.[3,5,21-25]

Numerous preexisting and acute medical conditions are associated with AKI development. Women appear to be at increased risk for AKI. There also appears to be an association between lower serum ferritin levels and AKI risk. Other risk factors include advanced age; race; diabetes; HF; the use of ACE inhibitors, ARBs, or nonsteroidal anti-inflammatory drugs (NSAIDs); exposure to contrast media prior to surgery; cardiopulmonary bypass; vasopressors; cardiovascular collapse; and preoperative proteinuria.[26-29] Prediction scorecards, such as the one developed by the Cleveland Clinic, are now being used and validated to help predict AKI after CVS.[30-32]

Preexisting CKD appears to be the most predictable risk factor for AKI following CVS.[26-31] Most treatment is supportive once injury develops. Renal protective strategies have not been found that prevent AKI development. Providers caring for the CVS patient population must be vigilant in screening for kidney disease and modifying risk in the absence of treatment options.[33]

They must also become as skilled in preventive care as they are in acute care, using interventions that minimize risk throughout the perioperative period. A useful approach might be to develop a comprehensive, intercollaborative strategy to promote kidney care best practice. Early consultation with a nephrologist for high-risk individuals should be part of this strategy. General recommendations include:

Preoperative

- Using preoperative checklists to screen for baseline kidney function, anemia, glycemic control, recent contrast media and diuretic use; standardizing preoperative lab surveillance
- Using an evidence-based scorecard to identify at-risk individuals
- Providing a 48-hour drug holiday (if possible) from contrast media, diuretics, and ACE inhibitors or ARBs
- Avoiding nephrotoxic agents, including NSAIDs, aminoglycosides, and mesalamine
- Providing a preoperative nephrology consult for patients with CKD stage 2+ (see *CKD stages*)
- Evaluating/optimizing glycemic control
- Conducting an anemia workup if hemoglobin (Hgb) is less than 11 g/dL
  - Consider treatment with I.V. iron
  - Consider treatment with erythropoiesis-stimulating agents

Intraoperative

- Reviewing the risk assessment scorecard (Cleveland Clinic or facility-specific scorecard)
- Optimizing volume status and BP
- Avoiding anemia

Postoperative

- Recognizing AKI
- Optimizing volume status and BP
- Avoiding volume depletion
- Early endotracheal extubation
- Providing nutritional support
- Maintaining immunocompetence
- Avoiding or reducing diuretic therapy.[26,28,29-31]

Recommendations can be incorporated into a treatment algorithm that can be referenced by all providers (see *AKI algorithm: Treatment considerations*).

CKD stages[6]

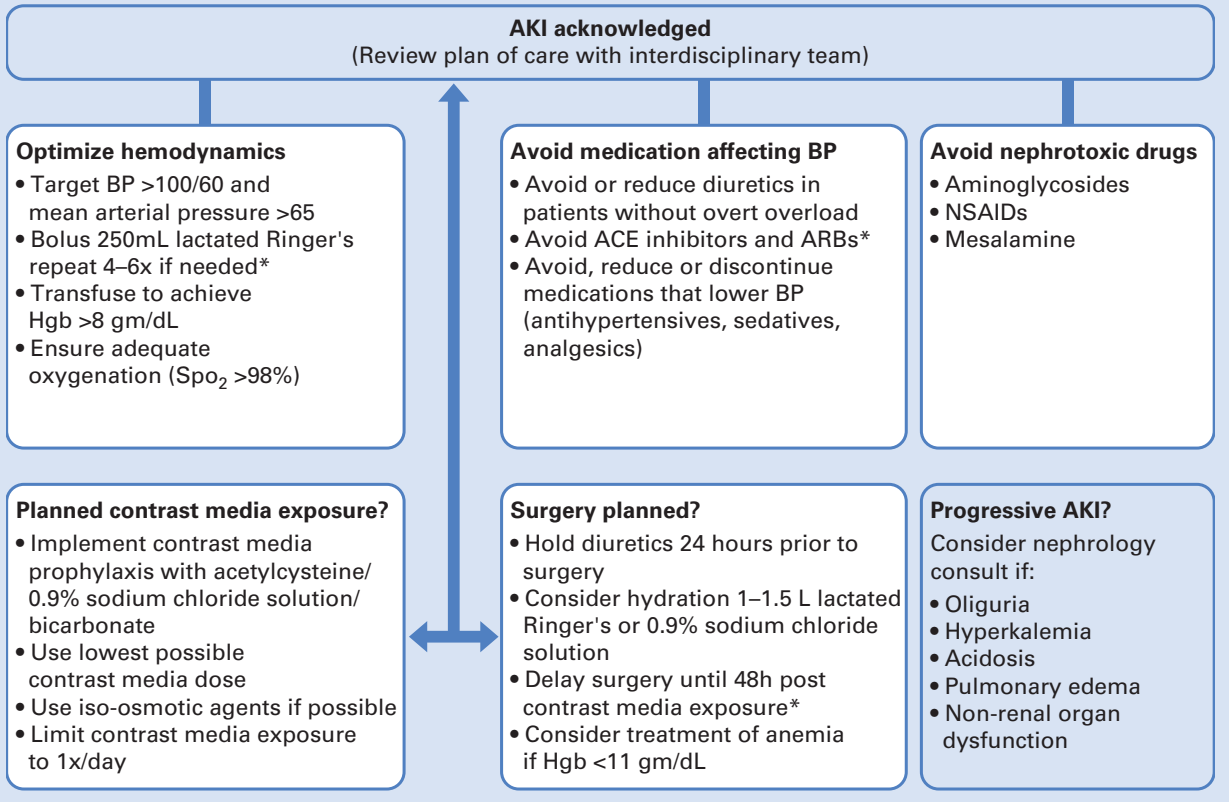
Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
GFR ≥90	60–89	30–59	15–29	<15

Case study follow-up

Mr. D presented with numerous risk factors for AKI: CKD stage 3, a Cleveland Clinic Risk score of 6, diabetes mellitus, and HF. He received contrast medium less than 48 hours prior to surgery and was medically managed preoperatively on an ACE inhibitor and diuretics. Postoperative hypertension and the resumption of diuretics likely added to the severity of kidney injury. Postoperative hypertension and the resumption of diuretic therapy likely added to him developing RIFLE Risk/AKIN Stage I AKI, that untreated, progressed to RIFLE Failure/AKIN Stage 3 AKI. There were opportunities to identify AKI and modify risk factors, but these clues were unrecognized, resulting in dialysis dependence.

Healthcare professionals managing the CVS patient population must be able to deliver evidence-based care and medical management that identifies at-risk individuals and initiate preventive acute and supportive care. All members

AKI algorithm: Treatment considerations[26,28, 29-31]



*If clinically appropriate

of the healthcare team must increase their awareness for AKI development and take advantage of opportunities for risk reduction throughout the perioperative course.

Moving forward

AKI is a complex process, and its development after CVS has a poor prognosis. Individuals who develop AKI as classified by the RIFLE criteria or AKIN stage III have an almost twofold increase in mortality.[32-35] Older adult patients with CKD are particularly vulnerable; many who develop AKI may need lifelong renal replacement therapy. Even a mild deterioration in kidney function can lead to adverse outcomes. Therefore, prevention is the most important treatment approach.

In the absence of definitive treatment options, general interventions should be designed to optimize the patient's overall condition: proper nutrition; daily modification of medication dosing; avoiding potentially nephrotoxic medications; restoring hemodynamics; and cautious volume management with fluid administration or diuresis (depending on the clinical situation). NP

REFERENCES

1. Bove T, Monaco F, Covello RD, Zangrillo A. Acute renal failure and cardiac surgery. *HSR Proc Intensive Care Cardiovasc Anesth*. 2009;1(3):13-21.
2. Engoren M, Habib RH, Arslanian-Engoren C, Kheterpal S, Schwann TA. The effect of acute kidney injury and discharge creatinine level on mortality following cardiac surgery. *Crit Care Med*. 2014;42(9):2069-2074.
3. Gude D, Jha R. Acute kidney injury following cardiac surgery. *Ann Card Anaesth*. 2012;15(4):279-286.
4. Prowle JR, Kirwan CJ. Acute kidney injury after cardiac surgery: the injury that keeps on hurting? *Crit Care Med*. 2014;42(9):2142-2143.
5. Thiele RH, Isbell JM, Rosner MH. AKI associated with cardiac surgery. *Clin J Am Soc Nephrol*. 2015;10(3):500-514.
6. Ricci Z, Cruz DN, Ronco C. Classification and staging of acute kidney injury: beyond the RIFLE and AKIN criteria. *Nat Rev Nephrol*. 2011;7(4):201-208.
7. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl (2011)*. 2012;2(1):6.
8. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative workgroup. 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.
9. Cruz DN, Ricci Z, Ronco C. Clinical review: RIFLE and AKIN—time for reappraisal. *Crit Care*. 2009;13(3):211.
10. Mehta RL, Chertow GM. Acute renal failure definitions and classification: time for change? *J Am Soc Nephrol*. 2003;14(8):2178-2187.
11. Pickering JW, Endre ZH. GFR shot by RIFLE: errors in staging acute kidney injury. *Lancet*. 2009;373(9672):1318-1319.

12. Jha V, Kumar V. Acute kidney injury: validating the KDIGO definition and staging—one step at a time. *Nat Rev Nephrol*. 2014; 10(10):550-551.
13. Perazella MA, Coca SG. Traditional urinary biomarkers in the assessment of hospital-acquired AKI. *Clin J Am Soc Nephrol*. 2012;7(1):167-174.
14. Lassnigg A, Schmidlin D, Mouhieddine M, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. *J Am Soc Nephrol*. 2004;15(6):1597-1605.
15. Han WK, Wagener G, Zhu Y, Wang S, Lee HT. Urinary biomarkers in the early detection of acute kidney injury after cardiac surgery. *Clin J Am Soc Nephrol*. 2009;4(5):873-882.
16. Koyner JL, Garg AX, Coca SG, et al. Biomarkers predict progression of acute kidney injury after cardiac surgery. *J Am Soc Nephrol*. 2012;23(5):905-914.
17. Parikh CR, Devarajan P, Zappitelli M, et al. Postoperative biomarkers predict acute kidney injury and poor outcomes after pediatric cardiac surgery. *J Am Soc Nephrol*. 2011;22(9):1737-1747.
18. McIlroy DR, Wagener G, Lee HT. Neutrophil gelatinase-associated lipocalin and acute kidney injury after cardiac surgery: the effect of baseline renal function on diagnostic performance. *Clin J Am Soc Nephrol*. 2010;5(2):211-219.
19. Bennett M, Dent CL, Ma Q, et al. Urine NGAL predicts severity of acute kidney injury after cardiac surgery: a prospective study. *Clin J Am Soc Nephrol*. 2008;3(3):665-673.
20. Wagener G, Gubitosa G, Wang S, Borregaard N, Kim M, Lee HT. Urinary neutrophil gelatinase-associated lipocalin and acute kidney injury after cardiac surgery. *Am J Kidney Dis*. 2008;52(3):425-433.
21. Bonventre JV, Vaidya VS, Schmouder R, Feig P, Dieterle F. Next-generation biomarkers for detecting kidney toxicity. *Nat Biotechnol*. 2010;28(5): 436-440.
22. Morgan CJ, Gill PJ, Lam S, Joffe AR. Peri-operative interventions, but not inflammatory mediators, increase risk of acute kidney injury after cardiac surgery: a prospective cohort study. *Intensive Care Med*. 2013;39(5):934-941.
23. Sadeghi MM, Gharipour M, Nilforoush P, et al. Influence of the timing of cardiac catheterization and amount of contrast media on acute renal failure after cardiac surgery. *J Res Med Sci*. 2011;16(4):502-508.
24. Nigwekar SU, Kandula P, Hix JK, Thakar CV. Off-pump coronary artery bypass surgery and acute kidney injury: a meta-analysis of randomized and observational studies. *Am J Kidney Dis*. 2009;54(3):413-423.
25. Seabra VF, Alobaidi S, Balk EM, Poon AH, Jaber BL. Off-pump coronary artery bypass surgery and acute kidney injury: a meta-analysis of randomized controlled trials. *Clin J Am Soc Nephrol*. 2010;5(10):1734-1744.
26. Huen SC, Parikh CR. Predicting acute kidney injury after cardiac surgery: a systematic review. *Ann Thorac Surg*. 2012:93(1):337-347.
27. Sirvinskas E, Andrejaitiene J, Raliene L, et al. Cardiopulmonary bypass management and acute renal failure: risk factors and prognosis. *Perfusion*. 2008;23(6):323-327.
28. Karkouti K, Wijeysundera DN, Yau TM, et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. *Circulation*. 2009;119(4): 495-502.
29. Huang TM, Wu VC, Young GH, et al. Preoperative proteinuria predicts adverse renal outcomes after coronary artery bypass grafting. *J Am Soc Nephrol*. 2011;22(1):156-163.
30. Coleman MD, Shaefi S, Sladen RN. Preventing acute kidney injury after cardiac surgery. *Curr Opin Anaesthesiol*. 2011;24(1):70-76.
31. Demirjian S, Schold JD, Navia J, et al. Predictive models for acute kidney injury following cardiac surgery. *Am J Kidney Dis*. 2012;59(3):382-389.
32. Thakar CV, Arrigain S, Worley S, Yared JP, Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. *J Am Soc Nephrol*. 2005;16(1):162-168.
33. Thakar CV. Predicting acute kidney injury after cardiac surgery: how to use the "crystal ball". *Am J Kidney Dis*. 2010;56(4):605-608.
34. Malov AA, Borisov AS, Lomivorotov VV, et al. Mortality prediction in patients with dialysis-dependent acute kidney injury after cardiac surgery with cardiopulmonary bypass. *Heart Lung Circ*. 2014;23(4):325-331.
35. Coca SG, Yusuf B, Shlipak MG, Garg AX, Parikh CR. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis*. 2009;53(6):961-973.

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