Updated Risk Score for Contrast-Associated Acute Kidney Injury: An Opportunity for Action Instead of Renalism

By Daniel Edmonston and Neha Pagidipati

The nomenclature shift from contrast-induced to contrast-associated acute kidney injury (CA-AKI) reflects a waning confidence in the nephrotoxicity of iodinated contrast. Despite early animal and observational data supporting this nephrotoxicity (1, 2), more appropriately controlled and matched studies have failed to demonstrate this link (3–6). In 2004, Mehran and colleagues (7) developed a risk score to predict CA-AKI in people undergoing percutaneous coronary intervention (PCI). In a recent study published in *The Lancet* (8), the investigators aimed to update this risk score to reflect more contemporary clinical practices.

This single-center, US-based, retrospective observational study included >14,000 patients undergoing PCI from 2012 to 2020, excluding patients requiring maintenance dialysis. Each patient received a standard clinical protocol that included saline infusion ≤12 hours before and 6–24 hours after PCI. With the use of stage 1 AKI criteria, as defined by the Acute Kidney Injury Network (creatinine increase ≥0.3 mg/dL or ≥1.5 × baseline) (9), within 48 hours, the investigators derived a model of pre-PCI clinical parameters that aligned with CA-AKI for patients between 2012 and 2017 and validated this model in patients between 2018 and 2020.

The overall incidence of stage 1 AKI was 4.3%. Notable predictors included age, baseline kidney function, clinical presentation (ranging from asymptomatic to ST-elevation myocardial infarction), left ventricular ejection fraction, history of diabetes or heart failure, hemoglobin, and glucose. Unlike the previous model, the primary model in this study excluded pre-procedural variables (Table 1). This model predicted CA-AKI very well (C-statistic = 0.84) and did not significantly improve when procedural parameters (e.g., contrast volume) were included; however, the investigators did not evaluate predictive performance for more severe AKI. Although the occurrence of CA-AKI aligned with a higher risk of 1-year mortality (hazard ratio 1.76, 95% confidence interval 1.31–2.36), this risk was mostly driven by 30-day mortality.

The study includes some important limitations. Although the association with mortality implies some clinical relevance to the prediction of stage 1 AKI, the association only with 30-day mortality suggests that the risk score likely captures sicker patients at higher risk for cardiovascular and/or peri-procedural complications. Additionally, this risk score was derived for administration of arterial contrast for PCI and should not be extrapolated to the use of intravenous contrast or other studies.

Sidestepping the concern for whether contrast truly *induced* AKI in these patients, the results of this well-designed study suggest that pre-procedural clinical parameters can predict CA-AKI with decent accuracy and that this CA-AKI coincides with poor 30-day outcomes. However, the potential harm from misuse of such risk-stratification tools cannot be understated. As coined by Dr. Glenn Chertow et al. (10), the term "renalism" encompasses the tendency to irreparably increase therapeutic inertia for otherwise life-prolonging therapies in people with kidney disease through excessive and often unnecessary risk avoidance. Rather than reinforcing aversion, high-risk scores should prompt action. Such scores should trigger efforts to address modifiable risk factors for AKI and balance these efforts with the urgency for PCI.

Additionally, such risk stratification may have better use in clinical research to identify enriched cohorts for inclusion in clinical trials to investigate peri-procedural interventions targeted to lower the risk of AKI and perhaps finally determine whether contrast is sufficiently nephrotoxic to defer clinically indicated studies and procedures. Although real-world use of these risk scores in clinical practice by cardiologists remains variable, providers should use these scores as a tool to modify peri-procedural AKI risk rather than a tool for renalism.

Table 1. Comparison of 2004 with 2021 CA-AKI risk scores

2004 Score[a]	Points	2021 Score[b]	Points
Hypotension	5	Clinical Presentation	
Intra-aortic balloon pump	5	Asymptomatic	0
Heart failure	5	Stable angina	0
Age, >75 years	4	Unstable angina	2
Diabetes	3	NSTEMI	4
Anemia[c]	3	STEMI	8
Contrast volume, per 100 cc	1	eGFR, mL/min/1.73 m^2	
eGFR, mL/min/1.73 m^2		≥60	0
>60	0	30–59	1
40–60	2	<30	4
20–39	4	Diabetes status	
<20	6	No diabetes	0
		Diabetes, no insulin	1
		Diabetes, insulin treated	2
		LVEF, <40%	2
		Hemoglobin, <11 g/dL	1
		Basal glucose, ≥150 mg/dL	1
		Heart failure	1
		Age, >75 years	1

eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST-elevation myocardial infarction. [a]Risk strata: low risk (≤5), moderate risk (6–10), high risk (11–15), very high risk (≥16). [b]Risk strata: low risk (≤2), moderate risk (3–7), high risk (8–11), very high risk (≥12). [c]Defined as hematocrit <39% for men and <36% for women.

Daniel Edmonston, MD, MHS, is with the Division of Nephrology, Duke University, and Duke Clinical Research Institute, Durham, NC. Neha Pagidipati, MD, MPH, is with the Division of Cardiology, Duke University, and Duke Clinical Research Institute, Durham, NC.

Dr. Edmonston serves on a consultation/advisory panel for Akebia Therapeutics. Dr. Pagidipati declares research support from Amgen, AstraZeneca, Boehringer Ingelheim, Eggland's Best, Eli Lilly, Novartis, Novo Nordisk, Regeneron, Sanofi, and Verily Life Sciences; serves on consultation/advisory panels for Boehringer Ingelheim, Eli Lilly, AstraZeneca, and Novo Nordisk; and is an executive committee member for trials sponsored by Novo Nordisk and Amgen.

References

1. Parfrey PS, et al. Contrast material-induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. A prospective controlled study. *N Engl J Med* 1989; 320:143–149. doi: 10.1056/NEJM198901193200303
2. Katzberg RW, et al. Acute systemic and renal hemodynamic effects of meglumine/sodium diatrizoate 76% and iopamidol in euvolemic and dehydrated dogs. *Invest Radiol* 1986; 21:793–797. doi: 10.1097/00004424-198610000-00005
3. Newhouse JH, et al. Frequency of serum creatinine changes in the absence of iodinated contrast material: Implications for studies of contrast nephrotoxicity. *Am J Roentgenol* 2008; 191:376–382. doi: 10.2214/AJR.07.3280
4. Bruce RJ, et al. Background fluctuation of kidney function versus contrast-induced nephrotoxicity. *Am J Roentgenol* 2009; 192:711–718. doi: 10.2214/AJR.08.1413
5. Wilhelm-Leen E, et al. Estimating the risk of radiocontrast-associated nephropathy. *J Am Soc Nephrol* 2017; 28:653–659. doi: 10.1681/ASN.2016010021
6. Davenport MS, et al. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: Risk stratification by using estimated glomerular filtration rate. *Radiology* 2013; 268:719–728. doi: 10.1148/radiol.13122276
7. Mehran R, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: Development and initial validation. *J Am Coll Cardiol* 2004; 44:1393–1399. doi: 10.1016/j.jacc.2004.06.068
8. Mehran R, et al. A contemporary simple risk score for prediction of contrast-associated acute kidney injury after percutaneous coronary intervention: Derivation and validation from an observational registry. *Lancet* 2021; 398:1974–1983. doi: 10.1016/S0140-6736(21)02326-6
9. Mehta RL, et al. Acute Kidney Injury Network: Report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007; 11:R31. doi: 10.1186/cc5713
10. Chertow GM, et al. "Renalism": Inappropriately low rates of coronary angiography in elderly individuals with renal insufficiency. *J Am Soc Nephrol* 2004; 15:2462–2468. doi: 10.1097/01.ASN.0000135969.33773.0B