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Review Article

Acute Kidney Injury After Exposure to Iodized Contrast Medium

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Abstract

Acute Kidney Injury can be caused by a series of conditions. In this paper, the focus is the use of iodinated contrast and the conditions that may even diminish this risk. Precautions are indicated in admitted patients: isotonic saline solution seems to be better than more hypotonic fluids. It is proposed that the saline be used instead of bicarbonate, because it has no greater benefits than the saline and is more expensive. Generally, contrast nephropathy is defined as an increase of at least 0.5 mg/dL or 25% of baseline creatinine within 2 to 5 days of contrast exposure. A study group of Kidney Disease Improving Global Outcomes (KDIGO) suggested a definition of an increase of 1.5 times or more in basal creatinine within 7 days of contrast use, an increase of at least 0.3 mg per deciliter above baseline within 48 hours after exposure to contrast or a urinary volume of less than 0.5 ml/kg of body weight per hour persisting per hour, at least 6 hours after exposure. Risk factors for contrast-associated nephropathy: preexisting chronic kidney disease; use of high osmolarity contrast; high volume of contrast (>350 mL or >4 ml/kg); repeat contrast in less than 72 hours. Contrast-associated nephropathy impacts in clinical practice: many studies have shown that contrast-associated renal injury is related to increased mortality, in addition to being related to the progression of underlying chronic kidney disease.

Keywords: acute kidney injury; iodized contrast; kidney protection; creatinine

Abbreviations

AKI: Acute Kidney Injury

CIN: Contrast-Induced Nephropathy

ICM: Iodinated Contrast Medium

PC-AKI: Post-Contrast Acute Kidney Injury

Scr: Serum Creatinine

Introduction

Acute kidney injury (AKI) after exposure to iodinated contrast medium (ICM), or simply post-contrast AKI (PC-AKI) is one of the forms of AKI, where ICM plays a prominent role in pathophysiology and represents a marker of poor prognosis, being associated with serious adverse events such as death, infarction, dialysis as well as longer hospital stay and cost. Because it is a form of renal deterioration with well-known and predictable risk factors, its prevention plays a prominent role. Thus, full knowledge of the disease, risk factors and evolution are fundamental elements for prevention, early diagnosis, reduction of incidence and optimization of treatment [1-5].

Terminology

Contrast-Induced Nephropathy (CIN) is the most widely used terminology. However, evidence shows that many individuals who develop PC-AKI also exhibit other factors potentially capable of facilitating or inducing kidney injury. Thus, the contrast medium would not be the only causal agent as the term CIN may erroneously suggest.

Based on this evidence, the 2011 Guideline of the Contrast Media Safety Committee of the European Society of Urogenital Radiology (ESUR) proposed that the term PC-AKI should be preferred over the term CIN, thus placing the ICM as a potential causal agent and not the main responsible for renal injury [6].

Epidemiology and definition

PC-AKI is a constant concern for interventionists and radiologists, with an occurrence ranging from 3% to 19% of contrasted procedures. This

wide variability in incidence is a reflection of differences in the study designs regarding the route of administration of the ICM, the type of population, the type of procedure and, finally and more importantly, the criteria that define PC-AKI. The criteria most frequently used to characterize PC-AKI are based on absolute elevation of basal serum creatinine (SCr) >0.5 mg/dL or relative increase >25% within 48h-72h after exposure [7-8]. However, there has never been a consensus on these values.

In order to standardize the nomenclature and refine diagnostic and prognostic sensitivities, two criteria of wide acceptance were developed. The first of these, the RIFLE criterion (Risk, Injury and Failure, Loss of kidney function, and End-stage kidney disease of 2004 prioritized the definition in three stages of renal damage (risk, injury and failure) and two stages of evolution (loss of function and end-stage) based on changes in SCr and urinary output in a time interval of seven days. Later in 2007, the Acute Kidney Injury (AKIN) criterion, based on the premise that even small changes in SCr can significantly impact mortality, sought to make the RIFLE criterion more rigorous and thus achieve better levels of sensitivity and reproducibility.

In the new proposal, the AKIN criterion proposed that minimum SCr changes, such as an increase ≥0.3 mg/dl within 48 hours or a relative increase ≥ 50% of baseline value within seven days already configure AKI [9]. Despite good sensitivity and reproducibility, the RIFLE and AKIN criteria reflect the reality of patients hospitalized in intensive care settings who accumulate multiple health problems, which makes it difficult to separate cases actually related to ICM from those in which AKI originates from other causes.

In 2012, the KDIGO (Kidney Disease Improving Global Outcome) working group sought to broaden the scope of the RIFLE and AKIN criteria to encompass both adults and children at risk of AKI, including for the first time in a kidney injury criterion, PC-AKI. The KDIGO criterion classifies AKI into stages 1, 2 and 3 (Table 1) by defining it as an elevation of SCr ≥0.3 mg/dl within 48 hours, or elevation of serum levels in at least 50% of the reference value in seven days, or urinary volume less than 0.5 mL/Kg/h for six consecutive hours [10].

INTERNSHIP	SERUM CREATININE	URINARY OUTPUT
1	1.5-1.9 times baseline Or Increase ≥0.3 mg/dL (≥26.5 umol/L)	1.5-1.9 times baseline Or Increase ≥0.3 mg/dL (≥26.5 umol/L)
2	2.0-2.9 times baseline 3.0 times baseline Or ≥4.0 mg/dL (≥353.6 umol/L) Or Initiation of renal replacement therapy	<0.5 mL/Kg/h for more than 12 hours <0.3 mL/Kg/h for ≥ 24 hours
3	Or In patients < 18 years, drop in glomerular filtration rhythm estimated to < 35 mL/min by 1.73 m2	Or Anuria for ≥12 hours

Table 1: *Kidney Disease Improving Global Outcome (KDIGO) criteria for acute kidney injury.*

Pathophysiology and evolution

AKI exhibits complex pathophysiology, with several pathways of aggression to the endothelium and tubular cell. The main risk factor is previous renal dysfunction accompanied by others such as diabetes, anemia, hyperglycemia, heart failure, volume depletion and hemodynamic instability [6]. Clinically, she is studying SCr elevation starting between the second and third days, peaking between the seventh and tenth days, and complete or almost complete resolution between the second and third weeks after exposure to ICM. However, in some cases (0.06% to 0.3%) it may progress to chronic kidney disease requiring dialysis [11].

Prevention

Risk Prediction

Risk assessment has been a key element in the effort to define which factors impact the chance of developing a given outcome and thus identify new markers, identify and access potential targets and optimize the cost effectiveness of a given therapy or the implementation of interventions. These models gain greater relevance in contemporary medical practice, where the vision of a more cost-effective and patient-centered medicine requires an even greater concern for institutions and health professionals with the quality of care and patient safety [12-14].

The currently available research data is insufficient to state that contrast agents are not nephrotoxic. Then, a prudent approach to the care of patients undergoing contrast procedures involves the careful implementation of evidence-based preventive care for patients identified as being at higher risk of AKI.

Research on the prevention of contrast-associated AKI has focused mainly on the use of renal replacement therapies, pharmaceutical agents and intravenous crystalloids. The benefits of prophylactic renal replacement therapy and most pharmaceutical agents have not been proven, making the supply of epiprocedural intravenous crystalloids the main intervention to reduce risks.

There is still no defined protocol for the prevention of contrast-associated nephropathy with saline use. The uptodate suggests the following scheme:

Outpatients: administer 3 mL/kg in one hour before the procedure and 1 to 1.5 mL/kg/hour for four to six hours after the procedure, with administration of at least 6 mL/kg after the procedure.

Hospitalized patients: administer 1 mL/kg/hour for 6 to 12 hours pre-procedure, intraprocedure and for 6 to 12 hours after the procedure.

It is recognized that, collectively, these studies [15-34] and others similarly, increased awareness of AKI associated with contrast and stimulated research to identify preventive strategies. However, it points out that it is possible that AKI associated with contrast injury is actually a marker of increased risk of adverse outcomes rather than a mediator of such results.

Although small postoperative elevations in plasma creatinine levels are associated with increased mortality at 30 days, small decreases in creatinine plasma (≤ 0.5 mg per deciliter) were also associated with increased mortality. In addition, a meta-analysis by Coca et al [35]. showed that interventions that reduced the incidence of AKI by almost 50% failed to reduce the risk of long-term death or the development of chronic kidney disease. These observations raise doubts about the causal relationship between small increments in plasma creatinine levels after contrast administration and adverse side events.

Another important problem is that creatinine is not specific to contrast kidney injury, so using it as a definition parameter can lead to misinterpretations. To date, there have been no adequate clinical trials showing that prevention of AKI results associated with contrast in a survival benefit.

Conclusion

There are a number of precautions to be taken when there is use of iodinized contrast as to the risk of AKI, such as preexistence of kidney disease, contrast osmolarity, contrast volume, among many others that the clinician will point out depending on the peculiarities of each patient.

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None.

Conflicts of Interest

No conflict of interest.

References

1. van der Molen AJ, Reimer P, Dekkers IA, Bongartz G, Bellin MF, et al. (2018). Post contrast acute kidney injury - Part 1: Definition, clinical features, incidence, role of contrast medium and risk factors: Recommendations for updated ESUR Contrast Medium Safety Committee guidelines. *Eur Radiol* 28(7): 2845-2855.
2. Goldenberg I, Chonchol M, Guetta V. (2009). Reversible acute kidney injury following contrast exposure and the risk of long-term mortality. Am J Nephrol 29(2): 136-144.
3. Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, et al. (2002) Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation 105(19): 2259-2264.
4. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. (2005). Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol 16(11): 3365-3370.
5. Forman DE, Butler J, Wang Y, Abraham WT, O'Connor CM, et al. (2004). Incidence, predictors at admission, and impact of worsening renal function among patients hospitalized with heart failure. J Am Coll Cardiol 43(1): 61-67.
6. Stacul F, van der Molen AJ, Reimer P, Webb JA, Thomsen HS, et al. (2011). Contrast induced nephropathy: updated ESUR Contrast Media Safety Committee guidelines. Eur Radiol 21(12): 2527-2541.
7. Ronco C, Stacul F, McCullough PA. (2013). Subclinical acute kidney injury (AKI) due to iodine-based contrast media. Eur Radiol 23(2): 319-323.
8. McCullough PA, Sandberg KR. (2003). Epidemiology of contrast-induced nephropathy. Rev Cardiovasc Med 4(Suppl 5): S3-S9.
9. Levi TM, Souza SP, Magalhães JG, Carvalho MS, Cunha AL, et al. (2013). Comparison of the RIFLE, AKIN and KDIGO criteria to predict mortality in critically ill patients. Rev Bras Ter Intensiva 25(4): 290-296.
10. International Society of Nephrology (2012). KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl 2(1): 1-138.
11. Morcos SK, Thomsen HS, Webb JA. (1999). Contrast-media-induced nephrotoxicity: a consensus report. Contrast Media Safety Committee, European Society of Urogenital Radiology (ESUR). Eur Radiol 9(8): 1602-1613.
12. Lloyd-Jones DM. (2010). Cardiovascular risk prediction: basic concepts, current status, and future directions. Circulation 121(15): 1768-1777.
13. Kooiman J, Gurm HS. (2014). Predicting contrast-induced renal complications in the catheterization laboratory. Interv Cardiol Clin 3(3): 369-377.
14. Bertakis KD, Azari R. (2011). Patient-centered care is associated with decreased health care utilization. J Am Board Fam Med 24(3): 229-239.
15. Mehran R, Dangas GD, Weisbord SD. (2019). Contrast-associated acute kidney injury. N Engl J Med 380(22): 2146-2155.
16. Isaka Y, Hayashi H, Aonuma K, Horio M, Terada Y, et al. (2020). Guideline on the use of iodinated contrast media in patients with kidney disease 2018. Clin Exp Nephrol 24(1): 1-44.
17. Davenport MS, Perazella MA, Yee J, Dillman JR, Fine D, et al. (2020). Use of intravenous iodinated contrast media in patients with kidney disease: Consensus Statements from the American College of Radiology and the National Kidney Foundation. Kidney Med 2(1): 85-93.
18. Zhang P, Ma X, Guo R, Ye Z, Fu H, et al. (2021). Organic nanoplatforms for iodinated contrast media in CT imaging. Molecules 26(23): 7063.
19. Maeda T, Oda M, Kito S, Tanaka T, Wakasugi-Sato N, et al. (2020). Can the lower rate of CT- or MRI-related adverse drug reactions to contrast media due to stricter limitations on patients undergoing contrast-enhanced CT or MRI? Dentomaxillofac Radiol 49(2): 20190214.
20. Sudarski D, Naami R, Shehadeh F, Elias A, Kerner A, et al. (2021). Risk of worsening renal function following repeated exposures to contrast media during percutaneous coronary interventions. *J Am Heart Assoc* 10(18): e021473.
21. Stacul F, Bertolotto M, Thomsen HS, Pozzato G, Ugolini D, et al. (2018). Iodine-based contrast media, multiple myeloma and monoclonal gammopathies: literature review and ESUR Contrast Media Safety Committee guidelines. *Eur Radiol* 28(2): 683-691.
22. Kurihara O, Takano M, Uchiyama S, Fukuizumi I, Shimura T, et al. (2015). Microvascular resistance in response to iodinated contrast media in normal and functionally impaired kidneys. Clin Exp Pharmacol Physiol 42(12): 1245-1250.
23. Lamby P, Jung F, Graf S, Schellenberg L, Falter J, et al. (2017). Effect of iodinated contrast media on renal perfusion: a randomized comparison study in pigs using quantitative contrast-enhanced ultrasound (CEUS). Sci Rep 7: 13125.
24. Zhang M, Hao P, Jiang C, Hao G, Li B, et al. (2020). Personalized application of three different concentrations of iodinated contrast media in coronary computed tomography angiography. J Cell Mol Med 24(10).
25. Lakhal K, Ehrmann S, Robert-Edan V. (2020). Iodinated contrast medium: is there a re(n)al problem? A clinical vignette-based review. Crit Care 24: 641.

26. Lee SY, Rhee CM, Leung AM, Braverman LE, Brent GA, et al. (2015). A review: radiographic iodinated contrast media-induced thyroid dysfunction. J Clin Endocrinol Metab 100(2): 376-383.
27. Chomicka I, Kwiatkowska M, Lesniak A, Malyszko J. (2021). Post-contrast acute kidney injury in patients with various stages of chronic kidney disease-is fear justified? Toxins (Basel) 13(6): 395.
28. Hur KY, Kim MK, Ko SH, Han M, Lee DW, et al. (2020). Metformin treatment for patients with diabetes and chronic kidney disease: a Korean Diabetes Association and Korean Society of Nephrology Consensus Statement. Diabetes Metab J 44(1): 3-10.
29. Butt T, Lehti L, Apelqvist J, Gottsäter A, Acosta S. (2022). Contrast-associated acute kidney injury in patients with and without diabetes mellitus undergoing computed tomography angiography and local thrombolysis for acute lower limb ischemia. Vasc Endovascular Surg 56(2): 151-157.
30. Li X, Liu H, Zhao L, Liu J, Cai L, et al. (2017). Clinical observation of adverse drug reactions to non-ionic iodinated contrast media in population with underlying diseases and risk factors. Br J Radiol 90(1070).
31. Yanfei Li, Ren K. (2020). The mechanism of contrast-induced acute kidney injury and its association with diabetes mellitus. Contrast Media Mol Imaging ID 3295176.
32. Kusirisin P, Chattipakorn SC, Chattipakorn N. (2020). Contrast-induced nephropathy and oxidative stress: mechanistic insights for better interventional approaches. J Transl Med 18(1): 400.
33. Kiss N, Hamar P. (2016). Histopathological evaluation of contrast-induced acute kidney injury rodent models. Biomed Res Int:3763250.
34. Fujiwara N, Tateishi R, Akahane M, Taguri M, Minami T, et al. (2013). Changes in risk of immediate adverse reactions to iodinated contrast media by repeated administrations in patients with hepatocellular carcinoma. PLoS One 8(10): e76018.
35. Coca SG, Singanamala S, Parikh CR. (2012). Chronickidney disease after acute kidney injury: a systematic review and meta-analysis. Kidney Int 81(5): 442-448.

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