Renal Risk of Contrast-Enhanced Imaging – Is It a Myth? The Latest Opinions of the Guidelines

Daniela RADULESCU¹,², Cristiana DAVID¹,², Ileana Adela VACAROIU¹,²

Abstract

Over the last decade, several divergent views have been expressed regarding the effect that iodinated contrast agents may have on renal function. Evidence-based medicine often requires the recommendation of high-performance contrast-enhanced imaging exams for precise positive diagnosis. The fear of intravenous contrast use in patients with elevated serum creatinine seems to become an old dogma, outdated by the benefits of the procedures. Patients with glomerular filtration rate below 30 mL/min/1.73 m² can be protected by peri-procedural hydration and withdrawal of other nephrotoxics. Whatever the degree of risk, current guidelines recommend contrast-enhanced investigations in any situations where the advantages for the diagnosis are certain.

Keywords: contrast agent, nephrotoxic, contrast-induced AKI, risk, prophylaxis, hydration.

REVIEW

Over the last decade, several divergent views have been expressed regarding the effect that iodinated contrast agents may have on renal function. From the classic contraindication of intravenous contrast use in patients with elevated serum creatinine, to the more nuanced indication of proper hydration and after-investigation monitoring of the renal patient to whom we decide to administer a contrast media, in the recent years it has been reached to the denial of the nephrotoxic risk of these investigations.

A precise positive diagnosis is crucial in our days, and this often requires the prescription of high-performance imaging. On the other hand, the modern evidence-based medicine penalizes us when it detects iatrogenic adverse events, complications which could have been avoided by better medical decisions. There-
fore, is it the risk of acute kidney injury enough to justify the fear for prescribing imaging investigations, or is time to reconsider the old dogma? In order to decide where we stand at the moment and what attitude to follow in our current practice, it is imperative to study the most recent opinions of the guidelines and the results of the latest studies on the subject of renal injuries due to contrast media.

It has been documented that iodinated contrast agents administered intravenously can act in the renal tubules by direct cell toxicity and by the release of vasoactive mediators, inducing medullary vasoconstriction that causes hypoxia in tubular cells. Several studies conclude that they are also involved in cytotoxicity with the consequences of an imbalance in the local level of vasodilators, activation of oxidative stress, increased viscosity in the peritubular capillaries and functional deficit of mitochondria in the tubular cells.

Due to these tubular processes, contrast-induced acute kidney injury (AKI) develops, diagnosed as an increase in serum creatinine of more than 0.5 mg/dl or more than 25% of baseline within 2–5 days after administration of the contrast media.

There are specialists that consider the contrast-induced AKI (CI-AKI) as a serious condition, one of the most common cause of AKI and an important cause of in-hospital morbidity and mortality, underlying its potential to develop nonreversible renal damage and chronic kidney disease. In consensus with these opinions, the KDIGO (Kidney Disease Improving Global Outcomes) 2012 guidelines rely on studies performed in that period and concludes that contrast-induced AKI incidence is extremely variable but it can reach 25% of the investigated patients in some facilities; therefore, for safety, it recommends prophylactic actions in all patients with glomerular filtration rate (GFR) below 60 mL/min/1.73 m² to whom we intend to administer intravascular contrast (intravenous or intra-arterial).

The European Society of Urogenital Radiology, based on studies by Choyke and colleagues, indicates to assess the risk of CI-AKI by determining the presence of proteinuria, an investigation that is easier to perform than creatinine and GFR calculation, requiring only urinary strips screening; the guide indicates pre- and post- contrast hydration prophylaxis and serum creatinine monitoring at 2–5 days after contrast only in patients with detected proteinuria, considered to have pre-existing renal impairment.

Classic cardiology guidelines contain warnings of the risk that coronary angiography poses to the patient with any kind of renal function impairment, even though that modification is not clinically manifest; a percentage of 5-10% is stated for patients who may develop CI-AKI after intravascular injected contrast during the procedure. Prophylaxis actions are indicated in all patients with GFR below 60 mL/min/1.73 m², namely the use of low contrast doses, low-osmolarity agents, the avoidance of other nephrotoxic drugs and ensuring an appropriate hydration during the procedure.

The last five years bring a change of opinion. Unlike the recommendations of classical guidelines, the latest statement from the American Society of Radiology is based on the results of recent clinical trials and considers that the effect of iodinated contrast media on renal tubules has been overestimated. In support of this assertion, the experts point out the differences stated by KDIGO between ‘contrast-associated AKI’ (CA-AKI) and ‘contrast-induced AKI’ (CI-AKI), meaning that different kind of subsequent causes of AKI were blamed on the contrast media. We should diagnose CI-AKI only when a direct causality relation can be established between the contrast administration and the renal damage. This separates the situations in which AKI develops in patients with multiple renal risk factors and who have undergone an imaging investigation in the last week, versus patients who develop AKI immediately after performing the contrast imaging and in whom the causal relationship between the two is certain. According to this guideline, CI-AKI is a rare entity, being highlighted in very few cases of renal insufficiency developed after an imaging investigation/procedure. The combination of other nephrotoxic drugs and dehydration are factors that far exceed the risk potential of iodinated contrast media. For these reasons, pre-contrast hydration and withdrawal of nephrotoxic medication would almost completely cover the risk of contrast media nephrotoxicity. Therefore, the guideline imposes these two precise actions only for patients with GFR value situated below 30 mL/min/1.73 m², considering that above this rate of glomerular filtration there is no risk for the performance of contrast imaging.

Consistent with this new perspective, the Medscape platform states in February 2020 that pre-contrast hydration would no longer be considered necessary before contrast enhanced computed tomography examination in renal patients with GFR over 30 mL/min/1.73 m². This time, the claim is based on the results of a recent Dutch study, Kompas, which demonstrated the same creatinine values 2-5 days after iv contrast administration in patients with chronic kidney disease (CKD) stage 3 (GFR 30–60 mL/min/1.73 m²) included in the
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CONCLUSIONS

Acute renal injury is a severe condition with significant lethal potential, but its occurrence due to the administration of iodinated contrast agents is an exception in patients without renal impairment and is minimal in early chronic kidney disease. Patients with glomerular filtration rate below 30 mL/min/1.73 m² can be protected by pre-contrast hydration and withdrawal of other nephrotoxics. Whatever the degree of risk, current guidelines recommend the administration of contrast in any situations where the benefits for the diagnosis or for the treatment are certain.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

Table 1. CI-AKI prophylaxis methods and pros / cons studies11

| Prophylaxis strategies                           | „Pros“ studies                                                                 | „Cons“ studies                                                                 |
|-------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| Hydration with 0.9% saline 1 ml/kg/h, 4-6 h pre and post | Mueller 200227, Trivedi200328, Brar 201429, Luo 201430                        | Timal 202031, Nijssen 201932                                                 |
| Sodium Bicarbonate alone or added in 0.9 % saline solution | Van der Molen 201841, Merten 200433, Hoste 201042                            | Brar 200835, Solomon 201544                                                   |
| N-acetylcytostine 600 mg bid                      | KDOG0 2012, Lameire 200636                                                   | ACT investigators 201137, Zagler 200638                                      |
| Prophylactic hemodialysis                         |                                                                                | Ozkok 201737, Cruz 201238                                                    |
| Stop nephrotoxic medication ACEI/ARB, metformin   | Rim 201239, Thomsen 199940                                                   | Rosenstock 200839, Owen 201440                                               |

The prognosis is good in the majority of cases, with renal function normalizing in 1-3 weeks17,26,43. Prophylactic hemodialysis has no benefits in CI-AKI; in confirmed AKI, initiating of dialysis follows the same indications as in other types of AKI, with the peculiarity of substantial benefit in early initiation in patients with clinically manifest hyperhydration8,25,44.

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