Contrast-induced nephropathy in acute coronary syndromes: Causal or casual?

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Related article
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Contrast-induced nephropathy (CIN), also known as contrast-induced acute kidney injury or contrast-associated acute kidney injury, is a well-known complication of intravascular contrast media (CM) administration. CIN peaks three to five days after CM exposure, and its reported incidence is highly variable depending on the subset of patients analyzed and the CIN definition [1]. Importantly, the true incidence could be underestimated because CIN also occurs after discharge (i.e., within the first seven to ten days from the index procedure) and, therefore, could be undetected when asymptomatic. Observational studies have shown a significant association between CIN and adverse cardiovascular outcomes including death in both the short and long term [2]. However, it remains uncertain if this association is causative or if CIN should be just considered a marker of adverse clinical outcomes. The evidence supporting CIN prevention strategies to reduce the risk of subsequent events is scant at best [3–5]. While some strategies have effectively shown to reduce CIN, the impact on harder endpoint is weak. Although the true clinical significance of CIN is not well established, there is a sizeable proportion of patients with acute coronary syndromes (ACS) who are denied procedures that require CM administration due to safety concerns [6, 7]. Notably, the incidence of CIN is higher in patients with ACS than in those without, but few studies looked specifically at this topic [8, 9].

In this issue of the *Kardiologia Polska* (*Kardiol Pol*, *Polish Heart Journal*), Rakowski et al. [10] report on the incidence and predictors of CIN in a prospective institutional registry of 2368 consecutive ACS patients undergoing invasive coronary angiography [10]. The most common clinical presentation was non-ST-segment elevation myocardial infarction, which was reported in about half of the patients. The definition of CIN used by the authors (i.e., a ≥25% relative increase in serum creatinine from baseline or a ≥0.5 mg/dl absolute increase) is sensitive and reflects a wide approach adopted in the literature. Most patients (79%) had normal renal function (i.e., defined as an estimated glomerular filtration rate ≥60 ml/min/1.73 m^2) at baseline. At discharge, CIN was reported in ~11% of patients, which is consistent with prior studies on ACS that used the same definition. Risk factors that were significantly associated with CIN at discharge were older age, *ad hoc* percutaneous coronary intervention (PCI) immediately after angiography, presentation with ST-segment elevation myocardial infarction (STEMI), and anemia.

The authors should be congratulated for adding another piece to the puzzle of CIN, and for their endeavor in providing real-world and contemporary data from a substantial number of ACS patients. The incidence of CIN at discharge was relatively high, occurring in one patient out of ten despite the use of hydration protocols. The predictors that the investigators were able to identify have a sound biological plausibility. Older age is a well-described risk factor for any kind of acute kidney injury, as it may lead to progressive renal dysfunction caused by morphological and functional changes [11]. *Ad hoc* PCI typically implies the use of higher amounts of intravascular CM, and primary PCI for STEMI is not

only a good example of *ad hoc* PCI but also a setting where hemodynamic instability may contribute to acute kidney injury in susceptible patients. Interestingly, anemia was the strongest risk factor (odds ratio [OR], 2.14; 95% confidence interval [CI], 1.43–3.21), regardless of whether considered as a categorical variable (i.e., anemia status) or as a continuous variable (i.e., by hemoglobin levels expressed in g/dl). This finding has a logical explanation if we consider the multifactorial and inter-dependent pathophysiology of anemia, which may indicate impaired renal function at baseline, a propensity for bleeding and hemodynamic instability, and low levels of oxygen in tissue (e.g., hypoxia at the level of renal tubules and medulla) combined with local abnormalities in renal vascular resistance induced by CM.

Some limitations of this study should be acknowledged, including its single-center design, which makes the results less generalizable, and the lack of follow-up data. Although the systematic collection of creatinine values at discharge has contributed to detecting more cases of CIN, this registry could also have reported an underestimation because discharge after ACS occurred at different time intervals and because no collection of creatinine values occurred thereafter (e.g., at 7 to 10 days).

CIN remains a concern among patients who receive intravascular iodinated CM, especially in the acute setting, with consequences that are poorly understood. However, subsets of patients at risk can be identified that are well characterized and may benefit from more targeted preventive strategies and closer monitoring. Importantly, no CIN-specific therapies are available, therefore, the focus remains on prevention. A contemporary approach that clinicians may consider to hinder the onset of CIN includes three steps: (1) identifying patients at risk of developing CIN, considering risk factors, and/or using one of the many available risk stratification tools [10, 12]; (2) administering prevention regimens with the best supportive (yet nonunivocal) clinical evidence, such as hydration and high-intensity statins, whenever feasible and compatible with the timing of the procedure [1]; (3) utilizing CM with iso-osmolarity or low-osmolarity, minimizing the volume administered and following simple precautions (i.e., discontinuing concurrent nephrotoxic drugs) [1]. It should be emphasized that after administration of intravascular CM, not all the episodes of acute kidney injury are necessarily attributable to CIN, and efforts should be directed towards a comprehensive and case-by-case evaluation of other causes of acute renal failure. Finally, more research is required to better elucidate the link between CIN and cardiovascular outcomes and to define if CIN after an invasively managed ACS is just a complication or a coincident epiphenomenon.

Article information

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