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The Association Between Radiocontrast Media and Acute Kidney Injury: A Review of the Evidence on Contrast-Induced Nephropathy

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ABSTRACT

Introduction: Iodinated radiocontrast media are indispensable for many modern diagnostic and interventional procedures. However, their use is associated with a significant risk of iatrogenic acute kidney injury (AKI), known as contrast-induced nephropathy (CIN), which is a leading cause of hospital-acquired renal failure.

Literature Review: A review of the pivotal literature establishes CIN as a major clinical concern, particularly in patients with pre-existing chronic kidney disease (CKD), the single most important risk factor. The pathogenesis is understood to be multifactorial, involving direct tubular epithelial cell toxicity and profound intrarenal vasoconstriction leading to medullary ischemia. A large body of evidence confirmed that the most effective and foundational strategy for prevention is periprocedural intravenous volume expansion with isotonic saline. The role of adjunctive pharmacological therapies was a subject of intense investigation and controversy. An influential randomized trial suggested a powerful protective effect of sodium bicarbonate infusions over saline, sparking widespread debate. Similarly, the antioxidant N-acetylcysteine

was widely used based on initial promising results, but subsequent, larger trials yielded conflicting and often negative findings, leaving its role uncertain.

Conclusion: The body of evidence reviewed cemented risk stratification and adequate intravenous hydration as the undisputed cornerstones of CIN prevention. While the potential benefits of adjunctive agents like sodium bicarbonate and N-acetylcysteine were vigorously debated, their efficacy remained controversial and unproven, highlighting the complexity of this iatrogenic condition and shaping the standard of care around risk factor modification and prevention.

Keywords: Contrast-Induced Nephropathy (CIN), Acute Kidney Injury (AKI), Radiocontrast Media, Chronic Kidney Disease (CKD), Hydration.

INTRODUCTION

The use of iodinated radiocontrast media is an essential component of modern medical practice, enabling a vast array of critical diagnostic and interventional procedures, including computed tomography (CT), coronary angiography, and peripheral vascular interventions. While these agents are generally safe, they carry a significant risk of causing a decline in renal function, a condition termed contrast-induced nephropathy (CIN). CIN is one of the most common causes of hospital-acquired acute kidney injury (AKI) and is associated with prolonged hospital stays, an increased risk of long-term renal impairment, and higher mortality.

The rising volume of contrast-enhanced procedures has made the prevention of CIN a major focus of clinical research and patient safety initiatives. The primary challenge has been to identify patients at the highest risk and to validate effective prophylactic strategies to mitigate this common and serious iatrogenic complication. This literature review will synthesise the pivotal scientific and clinical evidence that has defined the risk factors for CIN and evaluated the various strategies aimed at its prevention.

LITERATURE REVIEW

The scientific investigation into CIN has focused on understanding its pathophysiology, identifying high-risk patients, and testing preventative interventions.

The pathogenesis of CIN is understood to be a result of a dual insult to the kidney. First, contrast agents exert a direct cytotoxic effect on the renal tubular epithelial cells, inducing oxidative

stress and apoptosis. Second, and perhaps more importantly, they cause profound alterations in renal hemodynamics. Contrast administration leads to intense and sustained vasoconstriction of the renal medullary blood vessels, which reduces blood flow to a region of the kidney that is already operating at the brink of hypoxia, leading to significant ischemic injury (McCullough, 2008).

A large body of epidemiological research has been dedicated to identifying patients most vulnerable to this injury. The single most powerful and consistent predictor of CIN is pre-existing chronic kidney disease (CKD), as indicated by a reduced estimated glomerular filtration rate (eGFR). The risk increases exponentially as baseline renal function declines. Other major, independent risk factors that were consistently identified include diabetes mellitus (particularly in the presence of CKD), congestive heart failure, volume depletion, and factors related to the procedure itself, such as the use of large volumes or high-osmolar types of contrast media. This knowledge led to the development of clinical risk scores to help clinicians quantify an individual patient's risk prior to a procedure (Mehran et al., 2004). Landmark trials also demonstrated that using iso-osmolar or low-osmolar contrast agents was associated with a lower risk of CIN compared to older, high-osmolar agents in high-risk patients (Aspelin et al., 2003).

The cornerstone of prevention, supported by a broad consensus of evidence, is periprocedural volume expansion with intravenous fluids. Hydration with isotonic sodium chloride, typically started several hours before and continued for several hours after contrast exposure, has been shown to be effective in reducing the risk of CIN. The proposed mechanisms include the dilution of the contrast agent within the renal tubules and the mitigation of the vasoconstrictive effects, thereby preserving renal blood flow.

The search for additional, more potent pharmacological interventions yielded significant controversy. The antioxidant N-acetylcysteine (NAC) was widely adopted into practice based on early, small, promising trials. However, a subsequent wave of larger, more methodologically rigorous randomized controlled trials produced highly conflicting results, with many showing no benefit, leaving its role in perpetual debate (Briguori et al., 2007). A similar controversy was ignited by an influential single-center randomized trial that reported a dramatic reduction in CIN with an intravenous sodium bicarbonate infusion compared to standard saline hydration. The hypothesis was that alkalinizing the tubular fluid would reduce the formation of pH-

dependent free radicals. This striking finding led to widespread interest and further trials, but its superiority over saline remained a topic of intense discussion throughout the period (Merten et al., 2004).

CONCLUSION

The pivotal literature on contrast-induced nephropathy successfully characterized it as a common, predictable, and potentially serious complication of contrast-enhanced imaging. The research definitively identified patients with pre-existing chronic kidney disease and diabetes as being at the highest risk.

The body of evidence established a clear standard of care for prevention, centered on robust risk stratification and the universal application of periprocedural intravenous hydration with isotonic saline. In contrast, the role of adjunctive pharmacological agents became a defining controversy of the era. Despite initial enthusiasm, the evidence for agents like N-acetylcysteine and sodium bicarbonate remained conflicting and inconclusive. This work was crucial for embedding the principles of risk assessment and prevention into routine clinical practice, even as it highlighted the need for more research to identify more effective targeted therapies.

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