SGLT2 inhibitors and the risk of contrast-induced acute kidney injury: Time for a PCI Trial?

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Related article
by Kültürsay et al.

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Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are effective in reducing major adverse cardiovascular events in patients with type 2 diabetes who have established atherosclerotic cardiovascular disease or are at high risk of this condition [1, 2]. Additionally, in SGLT2i users, a reduction in cardiovascular death and hospitalization for heart failure has been shown, irrespective of diabetes or left ventricular ejection fraction [3, 4]. In patients with chronic kidney disease, SGLT2i reduce the risk of disease progression or cardiovascular death [5]. Yet, the potential protective effect against contrast-induced acute kidney injury (CI-AKI) in patients who are on SGLT2i at the time of primary percutaneous coronary intervention (PCI) has not been assessed. ST-segment elevation myocardial infarction is associated with various complications, among which CI-AKI significantly impacts patient mortality [6].

In this issue of the Journal, Kültürsay et al. [7] shed some light on this topic with a report on their retrospective study of 295 diabetic patients with ST-segment elevation myocardial infarction undergoing primary PCI. The authors compared the risk of CI-AKI in patients with or without background therapy with SGLT2i (including empagliflozin and dapagliflozin). In the treatment group, the exposure time to the medication was at least 6 months before to PCI, ensuring sufficient time for the drug to exert its pleiotropic effects and impact the cardiorenal system. The authors employed a CI-AKI definition aligned with Kidney Disease: Improving Global Outcomes guidelines, characterized by a rise in creatinine level of ≥0.3 mg/dl above the baseline value within 48 hours of contrast media exposure or an increase of at least 1.5 times compared to the baseline value within 7 days. This definition is sensitive and commonly used in various studies, providing a comprehensive approach to identifying CI-AKI.

Interestingly, the incidence of CI-AKI after PCI was lower in the group using SGLT2i compared to the non-user group. This difference remained after statistical adjustment (adjusted odds ratio: 0.86 [0.76–0.98]; 95% confidence interval; $P = 0.028$). This effect size is consistent with previous research demonstrating the cardiovascular and renal benefits of SGLT2i in individuals with diabetes and cardiovascular disease [4]. However, some limitations of this study should be acknowledged. First and perhaps foremost, the study was nonrandomized. The effect of potential confounders was mitigated by the use of robust adjustment methods, but there is no statistical method that may account for unidentified confounders [8]. Second, the retrospective nature and single-center design may limit the generalizability of the findings. Third, the relatively small sample size and heterogeneity in the specific SGLT2i agents and dosages used by patients could also impact the results. Fourth, the average hospitalization time of four days in this study is considerably lower than the 7 days in the CI-AKI definition, which could have lead to the detection of only acute events and underdiagnosing late CI-AKI.

Despite these limitations, the finding of a potential renoprotective role of SGLT2i in patients undergoing PCI and exposed to contrast media is biologically plausible and

clinically intriguing. The glycosuric effect of SGLT2i, known for promoting active diuresis, may help maintain renal function during the critical period of contrast administration [9]. Additionally, the anti-inflammatory and anti-oxidative properties of SGLT2i could counteract hypoxic pathways involved in CI-AKI development [10]. This complements their metabolic role in reducing harmful uremic toxin buildup and enhancing renal protection with lower proximal tubule glucotoxicity [11].

Recently, the DAPA-MI study suggested that non-diabetic patients using SGLT2 inhibitors after a myocardial infarction experience metabolic improvements without impacting the composite of cardiovascular death or hospitalization for heart failure compared with placebo [12]. The study by Kultursay et al. [7] now suggests that diabetic patients already on SGLT2i before myocardial infarction might experience synergistic benefits due to the combined metabolic effect on diabetes and the renal system, potentially leading to better long-term cardiovascular outcomes after myocardial infarction.

The reported potential protective effect against CI-AKI in this investigation opens avenues for future research exploring the application of SGLT2i beyond current indications, possibly in PCI, to improve not only cardiac but also renal outcomes. As the field evolves, the potential of SGLT2i as a safeguard against renal complications in high-risk cardiac patients is promising. Future randomized studies with larger cohorts and comparative analyses of different SGLT2i may further validate and refine this hypothesis.

Article information

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