



## SGLT2 Inhibitors: A Game-Changer for Patients with Atrial Fibrillation?

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### Dear Editor,

We read with great interest the recently published article by Haloot et al.<sup>1</sup> assessing the effect of sodium-glucose co-transporter 2 (SGLT2) inhibitors on the risk of adverse cardiovascular events in patients with atrial fibrillation (AF). This interesting observational study used data from a large multi-center dataset of electronic health records to provide valuable insight into the cardiovascular benefits of SGLT2 inhibitors in an AF population. Their findings suggest that AF patients treated with an SGLT2 inhibitor, compared to an untreated propensity-matched control group, live longer, are less likely to require cardioversion, and are at increased risk of ischemic stroke.

Despite these important findings, the authors could not investigate cardiovascular deaths due to the lack of cause-specific mortality data. However, we wonder about the effect of SGLT2 inhibitors on hospitalization for heart failure (HF). HF is the leading cause of death in patients with AF and accounts for the majority of cardiovascular mortality<sup>2</sup>. Our recent systematic review and meta-analysis showed that SGLT2 inhibitors maintain their efficacy in reducing cardiovascular death or HF hospitalization in patients with AF (hazard ratio 0.70, 95% confidence interval 0.57 – 0.85, p-for-interaction=1.00), similar to those in sinus rhythm<sup>3</sup>. However, these data were derived from the subgroup analysis of phase 3 SGLT2 inhibitor randomized controlled trials, and a consistent signal in a large observational series would strengthen this finding. Furthermore, we recently showed that a large proportion of AF patients are not eligible to receive an SGLT2 inhibitor based on the current approved indications, and these ineligible patients still have a substantial rate of cardiovascular death (approximately 1.5

events/100 person-years) and hospitalization for HF (approximately 1.9 events/100 person-years)<sup>4</sup>. An analysis testing the effect of SGLT2 inhibitors on HF hospitalization in those without a prior HF diagnosis would provide further insight into the effect of SGLT2 inhibitors in primary prevention of HF and HF-related outcomes in patients with AF.

Overall, SGLT2 inhibitors are a promising therapeutic agent for patients with AF both in those with eligibility indications like diabetes mellitus or HF, but also potentially in those without these comorbidities as well. Information from well-conducted observational studies can help guide future randomized studies testing the efficacy of SGLT2 inhibitors in patients with AF.

Sincerely,  
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### Disclosures

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### Key Words

Atrial fibrillation; Heart Failure; Sodium-Glucose Transporter 2 Inhibitors.

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