



Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care

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Kidney and Cardiovascular Outcomes of SGLT2 Inhibitors as Add-On Therapy to Metformin in Frail Patients with Type 2 Diabetes

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Objectives : Sodium-glucose cotransporter-2 inhibitors (SGLT-2is) offer cardiorenal protection in type 2 diabetes (T2D) but raise concerns regarding adverse events like dehydration and muscle mass loss, particularly in frail elderly patients. Since randomized trials often exclude individuals with severe frailty, real-world evidence is essential to validate safety and efficacy in this vulnerable subgroup. This study compared long-term kidney and cardiovascular outcomes of SGLT-2is versus other second-line glucose-lowering drugs (oGLDs) in elderly T2D patients, stratified by frailty status.

Methods : We utilized the Korean National Health Insurance Service-Senior cohort to conduct a retrospective study applying a target trial emulation framework to minimize biases. Eligible participants were aged ≥ 60 years, on first-line metformin, and initiated SGLT-2is or oGLDs. Frailty was assessed using five validated claims-based indices. Propensity score matching was performed to adjust for confounders, and both intention-to-treat and per-protocol analyses were conducted. The primary outcome was a composite of kidney events; the secondary outcome was major adverse cardiovascular events (MACE).

Results : The study included 151,134 patients, with 14.0% classified as frail. Among frail individuals, SGLT-2i use was associated with a significant 30% risk reduction in composite kidney outcomes and a 19% reduction in MACE compared to oGLDs. Comparable benefits were observed in non-frail patients. While findings were generally robust, the kidney benefit in frail patients lost statistical significance when frailty was defined specifically by the electronic or global frailty scores, indicating potential heterogeneity.

Conclusions : SGLT-2i therapy demonstrated consistent cardiovascular and kidney benefits in elderly T2D patients regardless of frailty status, supporting its utility as a second-line option. However, the potential attenuation of kidney benefits observed with certain frailty definitions warrants careful patient monitoring and individualized treatment planning in this high-risk population.

Figure1.png



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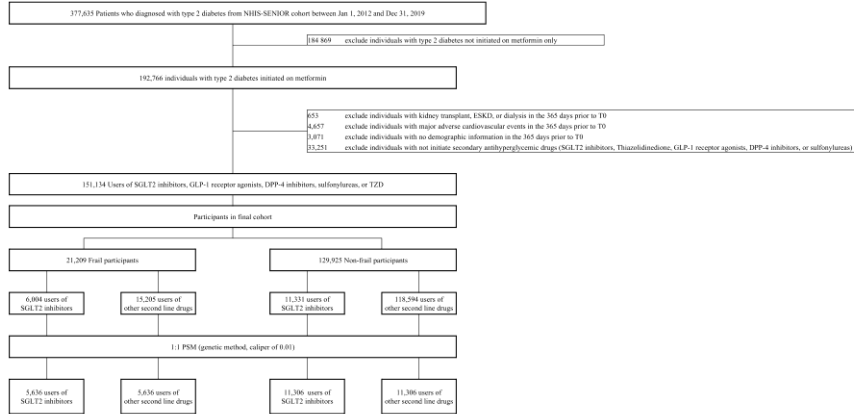


Figure1.png

