



Sodium Glucose Co-transporter-2 Inhibitors in Heart Failure: Why the Elderly are Missing Out

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INTRODUCTION

Heart failure (HF) constitutes a significant disease burden in the USA. Its prevalence has doubled between 1990–2020, showing an increase in the age-standardised prevalence rate of 3.08%, largely due to improved life expectancy.¹ It is a leading cause of morbidity and mortality among the elderly population (>65 years).² Unlike other medications constituting goal-directed medical therapy (GDMT), sodium-glucose co-transporter-2 inhibitors (SGLT2i) are strongly recommended for patients with HF, regardless of HF phenotypes.³

Among patients with HF who have reduced ejection fraction, SGLT2i reduce cardiovascular (CV) mortality (hazard ratio [HR]: 0.82; 95% CI: 0.69–0.98), all-cause mortality (HR: 0.83; 95% CI: 0.71–0.97), and HF admissions (HR: 0.70; 95% CI: 0.59–0.83).⁴ Similar benefits have been observed in patients with HF who have preserved ejection fraction, where SGLT2i

reduced HF admissions (odds ratio: 0.71; 95% CI: 0.61–0.83) and the composite outcome of HF hospitalisation or CV mortality (HR: 0.78; 95% CI: 0.70–0.87).⁵ Notably, these favourable outcomes extend to elderly patients (age ≥75 years), among whom SGLT2i reduced the composite of HF hospitalisations or CV mortality (HR: 0.61; 95% CI: 0.41–0.91), as well as HF readmissions (HR: 0.61; 95% CI: 0.31–0.95).⁶

However, the utilisation of SGLT2i has remained suboptimal, especially in elderly patients, despite a Class IA recommendation.^{3,7} Although there was an increase in the utilisation of SGLT2i among Medicare beneficiaries between 2016–2019, from 0.34–0.58 per 100 person-months, its prescriptions have largely remained low,⁷ with only 0.13 initiations per 100 person-months among patients with chronic HF.⁸

Available data suggest many barriers to the use of SGLT2i in elderly patients with HF in the USA. However, this population

may benefit the most from this medication due to its favourable effects on many comorbidities commonly seen in the elderly, such as chronic kidney disease, aortic stenosis, hypertension, and diabetes.⁸⁻¹⁰ Moreover, it may mitigate the healthcare costs associated with high mortality and morbidity rates among elderly patients with HF, which are mainly driven by recurrent HF admissions, the associated progressive frailty, and declining quality of life.¹¹

BARRIERS TO SODIUM-GLUCOSE CO-TRANSPORTER-2 INHIBITOR PRESCRIPTION

A common reason for avoiding prescriptions is the fear of increasing urinary tract and genital mycotic infections in elderly patients.^{12,13} SGLT2i promote the excretion of glucose and sodium in urine, which encourages the growth of bacterial and fungal infections.^{6,12,13} Moreover, natriuresis and glycosuria may lead to dehydration, which can be detrimental, especially in elderly patients.¹⁴ However, multiple studies have shown no significant difference in therapy discontinuation due to adverse effects, including urinary tract infection-related adverse events, between those above and below 75 years, nor between the SGLT2i and placebo groups.^{14,15} Interestingly, recent evidence suggests that SGLT2i has reno-protective effects among elderly patients.⁶ It significantly reduces the worsening of kidney function in the long term. It also mitigates the deleterious effects of loop diuretics on kidney function by increasing the tubuloglomerular feedback and maintaining fluid homeostasis.⁶ Zhuo et al.¹⁶ also reported a significantly lower risk of acute kidney injury with SGLT2i among the elderly (HR: 0.71 and 0.81) compared to other commonly used medications, such as glucagon-like peptide-1 agonists.¹⁶ Moreover, SGLT2i use was not associated with a significantly increased risk of the composite safety outcome (dehydration, urinary tract infection, or ischaemic stroke) compared to non-SGLT2i therapy (adjusted HR: 0.80; 95% CI: 0.49–1.29). Additionally, SGLT2i consistently demonstrated significant reductions in all-cause mortality and HF

readmissions, even after adjusting for BMI, frailty, and nutritional status, factors that often deter prescribing in elderly patients.¹¹

Second, physician inertia plays an important role in suboptimal prescription rates.¹⁷ Many patients with HF are managed by primary care physicians (PCP) who may be more reluctant to try new medications. PCPs practising outside of metropolitan centres or away from the main academic centres may be more prone to physician inertia due to a lack of support from HF specialists. Moreover, a lack of infrastructure to keep abreast with the latest developments in pharmacopoeia, HF management, and a dearth of experience in dealing with elderly patients may contribute to the suboptimal prescription rates among elderly patients with HF.¹⁸

Third, sex disparities in the prescription of SGLT2i also lead to overall reduced utilisation of this drug.⁷ Elderly females have a higher prevalence of HF compared to men.¹⁹ Factors such as a lack of healthcare access, awareness of disease process, and a lack of evidence, due to under-representation of females in HF trials, may contribute to reduced prescription rates among women.²⁰ In addition, women often present with atypical symptoms that may delay diagnosis and, consequently, management. Furthermore, disparities in the utilisation of HF management among Black people also manifest as decreased utilisation of HF pharmacotherapies among elderly patients. Despite a higher prevalence of HF among elderly Black people, the utilisation of HF pharmacotherapies has remained suboptimal, raising concerns for healthcare equity.²¹ Moreover, the Black population has a significantly higher burden of risk factors and comorbidities such as hypertension, diabetes, and chronic kidney disease that may benefit more from SGLT2i utilisation. It may also help in reducing the cost of HF management among Black patients with a significantly higher burden of comorbidities. However, several factors, such as healthcare access, suboptimal insurance coverage, low health literacy, under-representation of Black people in HF trials, and mistrust in the healthcare system,

may play a role in the underutilisation of GDMT, including SGLT2i in Black people.²²

Lastly, the financial toxicity associated with HF management may jeopardise the optimisation of HF management, especially the initiation and maintenance of relatively expensive drugs like SGLT2i. Many elderly patients are on different Medicare plans with different copays and co-insurances that add to the growing financial burden of healthcare costs. The total cost of HF management, which was estimated to be 30.7 billion USD in 2012, is expected to increase to 69.8 billion USD by 2030, with significant contributions by GDMT, especially novel pharmacotherapies.^{23,24} The out-of-pocket costs for Medicare beneficiaries have ranged as high as 2,849 USD annually, with a significant cost reduction to 1,319 USD by excluding SGLT2i.²⁵ The inability to afford SGLT2i or to continue the therapy would ultimately add to increasing healthcare costs in the form of hospital readmissions, increased use of healthcare services, and increased morbidity and mortality. Therefore, avoiding the utilisation of SGLT2i among elderly patients because of the cost of the medication would ultimately add to the growing healthcare costs and compromise optimal healthcare delivery for elderly patients.

FUTURE DIRECTIONS

Given their favourable profile, efforts should be made to increase the use of SGLT2i in the elderly, disregarding age as a barrier. Physician education and promotion of the benefits of these medicines among the elderly are needed. Focused seminars to educate PCPs and incorporate biannual continued medical education may give more comfort to PCPs and general cardiologists in prescribing and monitoring SGLT2i, as they stay abreast of the latest developments in HF management pharmacopoeia.^{17,26} Moreover, advocating for multidisciplinary team management, whether in person or via telehealth, may also optimise the utilisation of SGLT2i therapy. In addition, creating awareness among elderly patients with HF via different types of media such as social media, as well as conducting

periodic regional HF management seminars and HF awareness camps, may equip elderly patients with more information to make an informed decision after discussing with their providers. These strategies can also be adopted to achieve healthcare equity among races/ethnicities and sexes through patient and physician education. Furthermore, leveraging technologies such as telehealth may enhance access to care and facilitate the timely delivery of health services. Finally, reducing the shared costs of medications with patients may be a stepping stone to the increased adoption of HF medications. The amount of cost sharing should be determined based on the appropriate clinical and financial outcomes. One way could be to inversely link the value and benefit of the medication to the shared cost for patients. Benefit-based copayment is one such model of value-based insurance design that shares the cost of medications based on the clinical benefit they provide.²⁷ High-value medications providing morbidity and mortality benefits, such as SGLT2i (as determined by ongoing research), are provided at lower and more affordable out-of-pocket costs to patients.²⁸ This may address one of the barriers to increased utilisation of these novel drugs, providing better clinical outcomes and improving equity. This contrasts with the current model of cost sharing with patients, which is based on the absolute price of the medications.²⁹

CONCLUSION

Despite robust evidence of the clinical benefits of SGLT2i, their utilisation among elderly patients with HF has remained suboptimal. Future studies are needed to develop a comprehensive framework to increase the utilisation of these life-saving drugs among this population. Such a framework should address critical barriers, including financial burdens, physician inertia, and healthcare disparities, to ensure optimal HF care delivery for older adults, who represent one of the most vulnerable segments of society.

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