Burden of Cardio-Kidney and Metabolic Disease and Use of SGLT2 Inhibitors in Patients with Heart Failure. A Real-World Population-based Study

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Background

Heart failure (HF) is a global health concern, affecting approximately 1–2% of the general population. It is often linked with cardiovascular and metabolic comorbidities like type 2 diabetes (T2DM), chronic kidney disease (CKD), and obesity. These interconnected conditions compound the risk of cardiovascular morbidity and mortality, collectively termed as cardio-kidney-metabolic (CKM) disease. Despite clear evidence supporting the reduction of cardiovascular risk, the utilization of Guideline-directed medical therapy (GDMT), particularly sodium-glucose cotransporter 2 inhibitors (SGLT2i), remains notably low in routine medical practice for patients with multiple comorbidities.

Objective

Assess the burden of kidney and metabolic comorbidities in patients with HF, use of SGLT2i and determine all-cause mortality events in a HF population.

Methods

Using the TriNetX database from 77 healthcare organizations across multiple countries, we included patients aged 18 and older diagnosed with HF between January 1st, 2018, and August 3rd, 2023, using International Classification of Disease-10 codes (ICD-10). We accounted for instances of SGLT2i to assess medication use rates in each cohort. Propensity score matching (1:1) was performed accounting for age, gender, race, and other comorbidities at baseline. The primary outcome was all-cause mortality events at one and five-year post-admission.

Table 1. Baseline characteristics and SGLT2 inhibitors use of patients with heart failure and patients with heart failure + comorbidities.

Variables	HF patients* n=734,206	HF+CKD n=340,292 (46.3%)	HF+DM type 2 n=346,685 (47.2%)	HF+ obesity n=284,262 (38.7%)	HF + CKD + DM type 2 n=206,323 (28.1%)	HF + Obesity + DM type 2 n=167,128 (22.7%)	HF + Obesity + CKD n=150,051 (20.4%)	HF + CKD + DM type 2 + Obesity n=111,664 (15.2%)
Age – median	69.3 ± 14.5	71±13.6	68.7±12.9	65.7±13.4	69.8±12.6	66±12.5	68±12.7	67.7±12
Gender – n (%)								
Female	335,98 (46)	150,061(44.1)	155,367(44.8)	139,826 (49.2)	90,676 (43.)	80,895 (48.4)	72,251 (48.2)	53,613 (48)
Male	398,157 (54)	190,209 (55.9)	191,295 (55.2)	144,428 (50.8)	115,633 (56)	86,237 (51.6)	77,795 (51.8)	58,047 (52)
Race – n (%)								
White	491,911 (67)	222,053 (65.3)	222,906 (64.3)	198,955 (70)	128,059 (62.1)	109,701 (65.1)	101,538 (67.7)	74,231 (66.5)
Black or African American	122,654 (17)	69,812 (20.5)	69,573 (20.1)	52,784 (18.6)	45,791 (22.2)	36,013 (21.5)	31,236 (20.8)	23,820 (21.3)
Asian	21,897 (3)	7,065 (2.1)	7,991 (2.3)	2,721 (1.0)	5,044 (2.4)	2,085 (1.2)	1,558 (1.0)	1.352 (1.2)
COPD – n (%)	69,613 (19)	79,965 (23.5)	77,417 (22.3)	74,149 (26.1)	52,016 (25.2)	46,529 (27.8)	46,232 (30.8)	36,064 (32.3)
CAD – n (%)	125,541 (34)	151,326 (44.5)	144,683 (41.7)	118.564 (41.7)	101,993 (49.4)	77,903 (46.6)	77,446 (51.6)	61,503 (55.1)
SGLT2i– n (%)								
Empagliflozin	6,293 (2)	8,581 (2.5)	11,773 (3.4)	9,213 (3.2)	8,023 (3.9)	8,155 (4.9)	6,214 (4.1)	5,966 (5.3)
Dapagliflozin	3,618 (1)	5,350 (1.6)	6,284 (1.8)	5,180 (1.8)	4,623 (2.2)	4,227 (2.5)	3,818 (2.5)	3,504 (3.1)
Canagliflozin	2,221 (1)	2,394 (0.7)	3,974 (1.1)	3,023 (1.1)	2,382 (1.2)	2,769 (1.7)	1,823 (1.2)	1,821 (1.6)
Ertugliflozin	112 (0.)	141 (0)	218 (0.1)	184 (0.1)	138 (0.1)	178 (0.1)	108 (0.1)	108 (0.1)
Total SGLT 2i – n (%)	**12,244 (1.6)**	**16,466 (4.8)**	**22,249 (6.4)**	**17,600 (6.1)**	**15,166 (7.3)**	**15,329 (9.1)**	**11,963 (7.9)**	**11,399 (10.2)**

Abbreviations: A: HF (heart failure), B: CKD (chronic kidney disease), C: DM type 2 (diabetes mellitus type 2), D: COPD (chronic obstructive pulmonary disease), E: CAD (coronary artery disease), F: SGLT2 inhibitors (sodium-glucose cotransporter-2 inhibitors).

*The total percentage of patients with HF will not add up to 100% since each patient with specific comorbidities would be counted more than once in the different subgroups.

Results

A total of 734,206 patients with HF were studied, with nearly half having type 2 diabetes mellitus and chronic kidney disease (47.2% and 46.3%, respectively). The use of SGLT2i among patients with HF remained low (1.6%). Likewise, among patients with HF + comorbidities, the rate of SGLT2i use also remained low (<11%). When compared to patients with HF without comorbidities, the group of patients with HF + comorbidities had lower rates of survival at one and five years after admission, except for HF + obesity subgroup.

Conclusions

The burden of comorbidities in patients with HF is high and may be associated with poorer clinical outcomes. Unfortunately, despite the potential clinical benefit, the overall rates of SGLT2i use remain low in patients with HF.

Bibliography

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