EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 10
Issue: 1
06-14
Year: 2023

THE FAVOURABLE EFFECTS OF SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS IN CHRONIC HEART FAILURE PATIENTS - THE FOURTH PILLAR OF HEART FAILURE MANAGEMENT

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Article Received on 25/10/2022 **Article Revised on 15/11/2022** **Article Accepted on 05/12/2022**

ABSTRACT

Background: The current global prevalence of heart failure is estimated at 64.34 million cases and 9.91 million years of disability as a result. Heart failure remains one of the most prevalent clinical syndromes associated with significant morbidity and mortality. **Objective:** The aim of our study was to determine whether Sodium-Glucose Cotransporter 2 inhibitors (SGLT2i) are useful for treating patients with chronic heart failure and their clinical benefits, especially their effect on preventing hospitalization due to worsening heart failure, reducing mortality, improving clinical status and quality of life among patients with heart failure. **Methods:** From March 2021 to May 2022, 126 randomized patients with chronic heart failure with reduced ejection fraction (HFrEF) were prospectively enrolled. Patients treated with standard optimal medical therapy and SGLT2 inhibitor empagliflozin were compared with an arm of the same size and matched by age and gender patients who were taking only a standard optimal medical therapy for HFrEF. **Results:** The mean duration of follow-up in the two treatment arms was 12 months. In the (SOMT + SGLT2i) arm, we evaluated the hemodynamic, metabolic, renal, and cardiac remodeling parameters upon initial evaluation and at the end of the follow-up after 12 months of treatment. A 6.3% increase in LVEF value was observed with SOMT + SGLT2i compared to SOMT alone ($p < 0.001$). Only the SOMT + SGLT2i treatment arm had significant improvement in LVMi from baseline with a mean reduction of -8,3g/m2. A reduction of -7.0 mL/m2 in LVESV index was observed in the first group treated with SOMT and SGLT2i compared to the SOMT arm ($p < 0.001$). LVEDV index was reduced by -9.5 mL/m2 with empagliflozin ($p < 0.001$). Th mean reduction in LAVi was - 4.1 mL/m2 ($p < 0.001$). In in the arm treated with SOMT + SGLT2i thew FMR (≥ II Grade) was reduced by -11% ($p < 0.001$). The values of systolic blood pressure, blood glucose and HbA1c decreased significantly in the SOMT + SGLT2i arm compared to the second arm (127.4 vs. 1121.1 mmHg, 6.4 vs. 5.6 mmol/L and 6.3 vs. 5.4 %) respectively; $p < 0.001$). The eGFR values increased considerably in the SOMT + SGLT2i arm compared to the SOMT arm by 9.7 mL/min/1.73 m2; ($p < 0.001$). A significant reduction of 2492.8 (pg/mL) in NT-pro-BNP levels was observed only in the SOMT + SGLT2i arm ($p < 0.001$). Over the course of one year, the mean KCCQ total symptom score increased 2.8 points more in the SOMT + SGLT2i group than in the SOMT group. In the arm SOMT + SGLT2i, the composite of cardiovascular death or worsening heart failure was lower in comparison with the control group (20.1 vs. 29.1%; P<0.001). There was a lower rate of worsening heart failure in the SOMT + SGLT2i arm compared to the SOMT group (15.1 vs 20.2%; P<0.001). Compared to the SOMT arm, the arm treated with SOMT + SGLT2i had a lower cardiovascular death rate (14.6 vs. 19.9%; P<0.001). **Conclusion:** Our study has demonstrated favourable changes on cardiac remodeling parameters (LVEF, LVMi, LVEDVi, LVESVi, LAVi), lower rate of hospitalization and cardiovascular death. When empagliflozin is administered to diabetic and nondiabetic HFrEF patients, LV volumes, LV mass, LV systolic function, functional capacity, and quality of life are significantly improved. A favourable reverse remodeling of the LV may explain the reduction in heart failure hospitalizations and mortality caused by SGLT2 inhibitors. In HFrEF patients, SGLT2 inhibitors are strongly recommended in guidelines. SGLT2 inhibitors have become a fourth pillar of chronic heart failure management based on the collective data of their efficacy.

KEYWORDS: Chronic heart failure, Sodium-glucose transporter 2 inhibitors (SGLT2i), Heart failure with reduced ejection fraction (HFrEF).

1. BACKGROUND

The current global prevalence of heart failure is estimated at 64.34 million cases and 9.91 million years of disability as a result. Heart failure remains one of the most prevalent clinical syndromes associated with significant morbidity and mortality. Heart failure patients with reduced ejection fraction are currently treated with beta-blockers, renin-angiotensin-aldosterone inhibitors (RAAS inhibitors), angiotensin receptor-nephrilysin inhibitors (ARNI), mineralocorticoid antagonists (MRA), diuretics, and digoxin to suppress neurohormones, reduce volume overload, and improve cardiac contractility. Although these drugs have substantial cardiovascular benefits, they also carry the risk of serious adverse effects, including hypotension, kidney dysfunction, and abnormal electrolytes. Moreover, patients are still at an increased risk of morbidity and mortality. Heart failure (HF) remains associated with a poor prognosis and suboptimal treatment options, highlighting the need for more effective treatment options. Sodium glucose transporter inhibitors are a relatively new class of medication used in the management of type 2 diabetes. In patients with chronic heart failure, sodium glucose cotransporter 2 inhibitors have emerged as a new foundational treatment. To advance outcomes in patients with HF, it is therefore crucial to identify novel therapeutic strategies for improving symptoms, reducing mortality, recurrent hospitalizations, and acute decompensation.

2. OBJECTIVE

The aim of our study was to determine whether SGLT2 inhibitors are useful for treating patients with chronic heart failure and their clinical benefits, especially their effect on preventing hospitalization due to worsening heart failure, reducing mortality, improving clinical status and quality of life (QOL) among patients with HF.

3. PATIENTS AND METHODS

A prospective study of 126 patients with chronic heart failure with reduced ejection fraction (HFrEF) was conducted from March 2021 to May 2022. The inclusion criteria for participating in the study were as follows: adult patients age ≥18 years with chronic HF, New York Heart Association (NYHA) functional class II/III/IV classification symptoms despite standard optimal medical therapy (SOMT), left ventricle ejection fraction (LVEF) of ≤40%, N-terminal pro–B-type natriuretic peptide (NT-proBNP) ≥ 600 pg/ml if EF ≤30%; ≥ 1000 pg/ml if EF 31-35%; ≥ 2500 pg/ml if EF >35%, HF hospitalization within 12 months, estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m2. The exclusion criteria were a history of hypersensitivity or intolerance to SGLT2, ACEI or ARB, eGFR <30 mL/min /1.73 m2, acute coronary syndrome stroke, or transient ischemic attack (TIA) within < 3 months, recent coronary revascularization, currently implanted LV assist device (LVAD), Cardiomyopathy based on infiltrative/accumulation diseases, hypertrophic cardiomyopathy, pericardial restriction, peripartum, cardiomyopathy caused by chemotherapy within 12 months, severe valvular heart disease, acute decompensated HF, implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy (CRT) within 3 months, dementia or inability to cooperate.

We randomized 126 patients with HFrEF into two groups of similar size (n = 63), each taking a standard optimal medical therapy for HFrEF according to the guidelines for chronic HF treatment. The first group represent patients treated with a standard optimal medical treatment for HFrEF (β-blockers, RAAS inhibitors, angiotensin receptor-nephrilysin (ARNI), MRA, diuretics and digoxin) and SGLT 2 inhibitors (Empagliflozin 10mg) as a new class of drugs, This group is named as (SOMT + SGLT2i). A second group of patients were treated with standard optimal heart failure medical treatment without adding empagliflozin 10mg (SGLT 2 inhibitor) during the entire 12-month follow-up period. This group is known as (SOMT).

At baseline, we conducted complete medical histories, physical examinations, electrocardiograms, transthoracic echocardiograms, blood analysis, renal function, and NT-pro-BNP tests for all participants. Simpson's method was used to estimate left ventricle ejection fraction (LVEF) from the apical four (A4C) and apical two (A2C) chamber views. Philips LV auto strain software was used to assess GLS in the 18 LV segments from the three standard apical views (4-chamber, 2-chamber, 3-chamber). The echocardiograms were performed with a phased-array echocardiography xMATRIX array transducer with PureWave crystal technology X51, Epiq 7 Philips ultrasound machine. These measurements were conducted in accordance with the latest cardiac chamber quantification guidelines.

To assess the effectiveness of SGLT 2 inhibitors as a new class of drugs in addition to standard OMT. On the initial visit, at the third and sixth months, and at the end of the follow-up in both arms, we assessed NYHA class, NT-pro-BNP, left ventricle ejection fraction (LVEF), cardiac remodeling parameters: left ventricle mass index (LVMi), left ventricle end diastolic volume index (LVEDVi), left ventricle end systolic volume index (LVESVi), left ventricular global longitudinal strain (LV GLS), left atrial volume index (LAVi) and functional mitral regurgitation ≥ II grade, and QOL. The mean duration of follow-up in the 2 groups was 12 months. The primary outcome of the study was the composite of a first episode of worsening heart failure or cardiovascular death. We defined an episode of worsening heart failure as an unplanned hospital admission due to worsening heart failure or an urgent hospital visit requiring intravenous treatment. We analyzed the composite of cardiovascular death or worsening heart failure, or worsening heart failure and cardiovascular death. SAS StatView 5.0® software was used for all statistical analyses.

4. RESULTS

126 patients with chronic heart failure with reduced ejection fraction (HFrEF) were prospectively enrolled from March 2021 to May 2022 year. The baseline characteristics of the randomized patients are shown in **Table 1.** A median age of 67.9 ± 7.5 years, 67% of patients were male, 65% of all patients had ischemic heart disease, 64% had arterial hypertension, 37% had diabetes mellitus, and 33% had chronic kidney disease. The eGFR was 65.4 mL/min/1.73 m2, the NT-pro-BNP was 5639.4 ± 3533.1. The etiology of heart failure, 67% ischemic and 33% non-ischemic. NYHA Classes: II in 45% III 39% and IV in 16% of patients. Other patient characteristics and medications at baseline were similar between treatment groups. The proportions of patients taking RAAS inhibitors (ACEIs, ARBs), ARNI, beta-blockers, MRA, diuretics, digoxin, CRT or ICD are shown in Table 1.

Table 1: Demographic and general characteristics of patients upon initial assessment in both arms.

Items	All (N = 126)	Group I (SOMT+ SGLT2i) (N = 63)	Group II (SOMT) (N = 63)	P value
Age (years)	67.9 ± 7.5	67.4 ± 7.9	67.7 ± 8.1	0.797
Male gender (%)	65	65	64	0.840
Body Mass Index (g/m^2)	27.3 ± 4.1	26.9 ± 4.2	27.1 ± 3.8	0.519
Systolic blood pressure (mmHg)	127.6 ± 7.5	127.4 ± 8.4	127.2 ± 8.6	0.209
Heart rate (bpm)	69.2 ± 8.4	68.8 ± 7.4	69.1 ± 6.3	0.512
Creatinine (µmol/L)	109 ± 37	110 ± 35	109 ± 41	0.773
Mean eGFR (mL/min/1.73 m^2)	65.4 ± 23.5	65.2 ± 22.3	64.9 ± 22.9	0.947
eGFR <60 mL/min/1.73 m2 (%)	21.6%	21.7%	21.5%	0.953
Blood glucose (mmol/L)	6.4 ± 1.5	6.4 ± 1.9	6.4 ± 1.2	0.543
HbA1c (%)	6.3 ± 1.6	6.3 ± 1.7	6.4 ± 1.6	0.756
NT-pro-BNP (pg/mL)	5639.4 ± 3533.1	5664.5 ± 3554.7	5614.4 ± 3511.4	0.836
NYHA Class (%)				
II	45	44.9	45.7	0.758
III	39	39.4	38.7	
IV	16	16.3	15.7	
Aetiologia of Heart Failure (%)				
Ischemic	67	68	66	0.851
Non-Ischemic	33	35	32	0.874
Comorbidities (%)				
Arterial Hypertension	64.4	64.8	63.9	0.836
Diabetes mellitus	37	37.4	36.7	0.843
Chronic kidney disease	33	34.1	31.9	0.972
Medications				
RAAS inhibitors (%)	46.4	46.9	45.8	0.826
ARNI (%)	53.6	53.3	53.9	0.782
Diuretics (%)	92	92.1	91.9	0.765
Beta-blockers (%)	71.7	68.5	74.8	0.742
MRA (%)	55.2	53.9	56.5	0.827
Digoxin (%)	36.5	36.7	36.3	0.423
CRT (%)	15.6	15.4	15.7	0.295
ICD (%)	12.1	12.3	11.9	0,934

eGFR: estimated glomerular filtration ratio, HbA1C: glycoside hemoglobin, NT-proBNP: N-terminal pro–B-type natriuretic peptide RAAS inhibitors: renin-angiotensin-aldosterone inhibitors; ARNI: angiotensin receptor-nephrilysin inhibitors, MRA: mineralocorticoid antagonist; CRT: cardiac resynchronization therapy, ICD: implantable cardiac defibrillator.

The Echocardiographic parameters in all patients and in both arms are shown in **Table 2**. The left ventricle mass index (LVMi) in all patients was 152.8 ± 9.8, left ventricle ejection fraction (LVEF) for all patients was 32.3 ± 5.7, left ventricle end diastolic volume index (LVEDVi) 117.70 ± 8.15, left ventricle end systolic volume index (LVESVi) 67.83 ± 6.23, left ventricular global longitudinal strain (LV GLS) 12.6 ± 2.9, left atrial volume index (LAVi) 53.8 ± 3.9, functional mitral regurgitation ≥ II grade was found in 43%.

Table 2: Echocardiographic parameters in all patients and in both arms.

Echocardiographic item	All (N = 126)	Group I (SOMT+ SGLT2i) (N = 63)	Group II (SOMT) (N = 63)	P value
LVEDVi (mL/m^2)	117.70 ± 8.15	117.17 ± 8.45	118.23 ± 7.84	0.834
LVESVi (mL/m^2)	67.83 ± 6.23	66.75 ± 5.34	68.91 ± 7.12	0.830
LVEF (%)	32.3 ± 5.7	32.7 ± 5.9	31.9 ± 5.4	0.781
LVMi (g/m^2)	152.8 ± 9.8	152.6 ± 8.9	153.1 ± 10.7	0.827
LV GLS (%)	12.6 ± 2.9	12.7 ± 2.8	12.5 ± 3.0	0.845
LAVi (mL/m^2)	53.8 ± 3.9	53.4 ± 3.7	54.2 ± 4.1	0.842
FMR (≥ II Grade) (%)	43	42	44	0.786

LVEDVi: left ventricular end-diastolic volume index, LVESVi: left ventricular end-systolic volume index, LVEF: left ventricular ejection fraction, LVMi: left ventricular mass index. LV GLS: left ventricular global longitudinal strain, LAVi: left atrial volume index, FMR: functional mitral regurgitation. Values mean ± SD.

Tolerability and adverse events

The study medication empagliflozin was stopped in 6 patients (9.5%) in the SOMT + SGLT2 arm. The most common adverse events of interest were those related to volume depletion and kidney impairment. The incidence of these adverse events did not differ significantly in both arms. No patients left the study voluntarily.

The hemodynamic, metabolic, renal, and cardiac remodeling parameters.

Based on the results of the initial evaluation and the end of the follow-up after 12 months treatment with SOMT + empagliflozin SGLT2i, **Table 3** summarizes the hemodynamic, metabolic, renal, and cardiac remodeling parameters in the SOMT + SGLT2i group. A 6.3% increase in LVEF value was observed with SOMT + SGLT2i compared to SOMT alone ($p < 0.001$). Only the SOMT + SGLT2i treatment arm had significant improvement in LVMi from baseline with a mean reduction of -8,3g/m2. A reduction of -7.0 mL/m2 in LVESV index was observed in the first group treated with SOMT and SGLT2i compared to the SOMT arm ($p < 0.001$). LVEDV index was reduced by -9.5 mL/m2 with empagliflozin ($p < 0.001$). Th mean reduction in LAVi was - 4.1 mL/m2 ($p < 0.001$). In in the arm treated with SOMT + SGLT2i thew FMR (≥ II Grade) was reduced by -11% ($p < 0.001$). There was no difference in LV GLS. The values of systolic blood pressure, blood glucose and HbA1c decreased significantly in the SOMT + SGLT2i arm compared to the second arm (127.4 vs. 1121.1 mmHg, 6.4 vs. 5.6 mmol/L and 6.3 vs. 5.4 %) respectively; $p < 0.001$). The eGFR values increased considerably in the SOMT + SGLT2i arm compared to the SOMT arm by 9.7 mL/min/1.73 m2; ($p < 0.001$). A significant reduction of 2492.8 (pg/mL) in NT-pro-BNP levels was observed only in the SOMT + SGLT2i arm ($p < 0.001$). Over the course of one year, the mean KCCQ total symptom score increased 2.8 points more in the SOMT + SGLT2i group than in the SOMT group.

Table 3: Hemodynamic, metabolic, renal, and cardiac remodeling parameters upon the initial evaluation and at the end of the follow-up after 12 months treatment in (SOMT + SGLT2i) arm.

Item	Baseline (N = 63)	Follow-up (N = 57)	Δ From Baseline
Systolic BP (mmHg)	127.4 ± 8.4	121.1 ± 14.6	6.3 ± 2.9
Blood glucose (mmol/L)	6.4 ± 1.9	5.6 ± 1.3	0.8 ± 0.5
HbA1c (%)	6.3 ± 1.7	5.4 ± 1.3	0.9 ± 0.7
NT-pro BNP (pg/mL)	5664.5 ± 3554.7	3121.2± 2456.3	2492.8 ± 131.6
eGFR (ml/min/1.73 m^2)	65.2 ± 22.3	74.9 ± 12.5	9.7 ± 4.1
LVMi (g/m2)	152.6 ± 8.9	144.3 ± 10.2	-8.3 ± 2.6
LVEF (%)	32.7 ± 5.9	38.2 ± 4.6	6.3 ± 2.2
LVEDVi (mL/m^2)	117.17 ± 8.45	109.14 ± 5.4	-9.5 ± 3.4
LVESVi (mL/m^2)	66.75 ± 5.34	56.23 ± 3.16	-7.0 ± 4.0
LV GLS (%)	12.7 ± 2.8	13.3 ± 1.7	0.6 ± 0.3
LAVi (mL/m^2)	53.4 ± 3.7	49.3 ± 2.1	-4.1± 2.5
FMR (≥ II Grade) (%)	42	31	11

HbA1C: glycoside hemoglobin, NT-proBNP: N-terminal pro–B-type natriuretic peptide, eGFR: estimated glomerular filtration ratio, LVMi: left ventricular mass index. LVEF: left ventricular ejection fraction, LVEDVi: left ventricular end-diastolic volume index, LVESVi: left ventricular end-systolic volume index, LV GLS: left ventricular global longitudinal strain, LAVi: left atrial volume index, FMR: functional mitral regurgitation.

The effects of SGLT2 inhibitor empagliflozin on the primary composite outcome, each of the individual mortality and hospital admission outcomes, and on urgent visits for worsening heart failure requiring intravenous treatment are shown in **Figure 1, 2 and 3**. In the arm SOMT + SGLT2i, the composition of cardiovascular death or worsening heart failure was lower in comparison with the control group (20.1 vs.

29.1%; P<0.001). Figure 1. There was a lower rate of worsening heart failure and hospitalization in the SOMT + SGLT2i arm compared to the SOMT group (15.1 vs 20.2%; P<0.001). Figure 2. Compared to the SOMT arm, the arm treated with SOMT + SGLT2i had a lower cardiovascular death rate (14.6 vs. 19.9%; P<0.001). Figure 3.

Figure 1. Composite of cardiovascular death or hospitalization

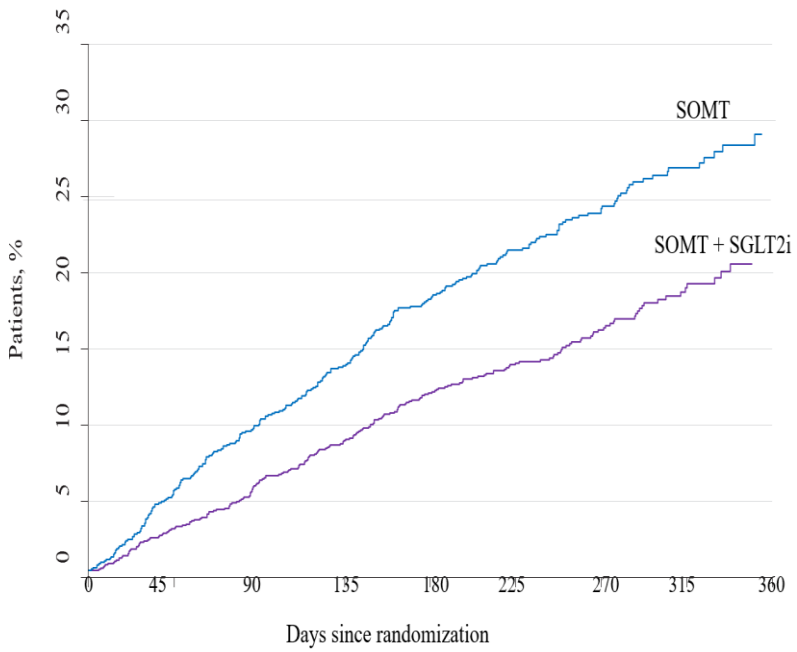
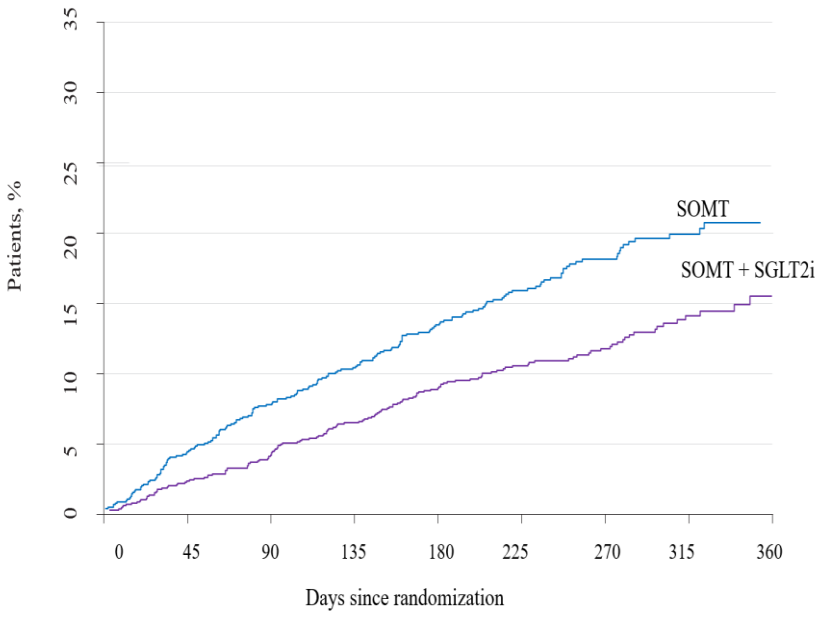
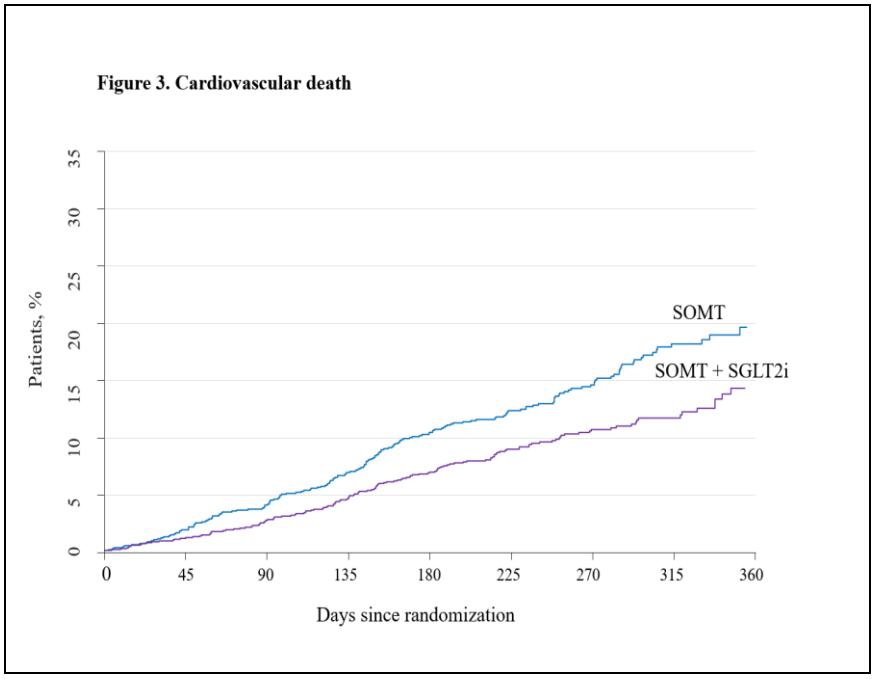


Figure 2. Worsening heart failure & hospitalization





5. DISCUSSION

Heart failure (HF) affects an estimated 1% to 2% of adults worldwide and is associated with reduced quality of life, high morbidity, mortality, and substantial financial burdens. Heart failure is still one of the leading causes of hospitalization and mortality worldwide despite current established treatments. A novel therapeutic target is therefore needed to improve the prognosis of patients with heart failure.[1,3]

Since the 1970s, heart failure (HF) management has evolved with advances in medical, device, and management strategies to collectively reduce morbidity and mortality. The key pillars of HF medical care have been RAAS inhibitors, ARNI, beta-blockers, and MRA. These therapies also carry the potential for serious adverse effects including hypotension, kidney dysfunction, and electrolyte abnormalities. To improve outcomes for patients with HF, it is crucial to identify novel therapeutic strategies to improve symptoms, reduce mortality, recurrent hospitalization, and acute decompensation. Empagliflozin's cardiovascular protective mechanism is complex, and part of it is still uncertain. Various mechanisms may be involved, including improved ventricular loading conditions, enhanced cardiac metabolism and bioenergetics, improved Na+/H+ exchange, sugar, and lipid metabolism, improved circulatory load, and enhanced cardiovascular system.[5,8,9,34]

The recent published studies, EMPEROR-Reduced (EMPagliflozin outcomE tRial in Patients With chrOnic heaRt Failure With Reduced Ejection Fraction) and DAPA-HF (Dapagliflozin And Prevention of Adverse-outcomes in Heart Failure) have demonstrated the benefit of SGLT2 inhibitors for treating patients with and without diabetes with HF by reducing the incidence of worsening heart failure and death in HF patients.[12,13,15] In the last several years, SGLT2 inhibitors have emerged as a new foundational therapy for patients suffering from heart failure with reduced ejection fraction (HFrEF). The most recent European and American guidelines include SGLT2 as a fourth class of medicine alongside the other three. The purpose of this is to establish the foundation for the management of heart failure.[8,9]

Empagliflozin has a cardioprotective effect on patients with HFrEF, according to our study. As well as improving ventricular loading conditions, cardiac metabolism, bioenergetics, and ventricular remodelling, SGLT2i has direct cardioprotective and antiarrhythmic effects. Our study has demonstrated favourable changes on cardiac remodeling parameters: (LVEF, LVMi, LVEDVi, LVESVi, LAVi) and FMR $\geq$ II grade. The systematic review and meta-analysis of randomized controlled trials have shown that the use of SGLT2 inhibitors was associated with an improvement in markers of cardiac function, confirming the importance of SGLT2 inhibition towards the reversal of cardiac remodeling.[20,21,27,28] Data published in the literature indicates that SGLT2 inhibition benefits people without diabetes or prediabetes as well. Heart failure patients with HFrEF, regardless of glycemic status, can benefit from them. Diabetes patients and those without diabetes responded similarly to empagliflozin in terms of blood pressure, HbA1C, eGFR, and NT-proBNP.[2,3,5,32]

Study investigators compared empagliflozin against placebo in patients with NYHA II-IV class and EF 40% or less in the EMPEROR-Reduced (EMPagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction) study to determine if it reduced CV death and hospitalization for HF. Overall, there was a 25% reduction in the combined risk of the

primary outcomes of CV death and hospitalization for HF regardless of diabetic status. DAPA-HF and EMPEROR-Reduced trials evaluated the effects of dapagliflozin and empagliflozin in patients with HFrEF, respectively. In both (DAPA-HF and EMPEROR-Reduced) trials, the risk reduction seen in their primary outcomes was principally driven by a reduction in hospitalizations for heart failure. Meta-analysis of both trials revealed consistent reductions in all endpoints of all-cause death, cardiovascular death, hospitalization for heart failure, or decline in renal function. According to clinical trials, SGLT2 inhibitors are effective in treating and preventing heart failure both in diabetics and non-diabetics. These studies led the US FDA to approve dapagliflozin and empagliflozin for heart failure in diabetics or non-diabetics.[10,12,15]

The EMPA-REG OUTCOME trial assessed the CV safety of empagliflozin in patients with type 2 diabetes (T2D) and atherosclerotic CV disease. The primary outcome of reduction in MACEs for the empagliflozin group yielded a 14% reduction in MACEs when compared with the placebo group. When empagliflozin was compared with placebo, the relative risk of CV deaths was reduced by 38%, the risk of all-cause deaths was reduced by 32%, and the risk of hospitalization for HF was reduced by 35%. The empagliflozin group also experienced a reduction in overall mortality. Additionally, empagliflozin significantly reduced CV death and hospitalizations for HF in patients with HFrEF regardless of T2D status.[16,17,18]

The three cardiovascular outcome trials of SGLT-2 inhibitors (EMPA-REG OUTCOME, CANVAS, and DECLARE-TIMI 58) enrolled significantly different patient populations with different ASCVD risks, but all demonstrated robust and consistent benefits in reducing hospitalizations for HF. A meta-analysis of three outcomes trials found that SGLT-2i significantly reduced the risk of cardiovascular death or hospitalization for HF by 23% and 31%, respectively. Secondary endpoints showed that SGLT2 inhibitors reduced total heart failure hospitalizations (inclusive of first and recurrent episodes) by 27%, urgent heart failure visits by 35%, and all-cause hospitalizations by 7%.[19,20,25]

Every day, evidence-based strategies for treating HF are being developed and expanded. ACC/AHA heart failure stages or NYHA heart failure classes should be familiar to clinicians caring for patients with HF or at risk of HF. Clinical guidelines from the ESC and ACC should be used to determine a patient's course of treatment, including use of SGLT2 inhibitors to prevent MACEs, such as CV death and recurrent hospitalizations for HF.[9,24,25,26]

6. CONCLUSION

Our study has demonstrated favourable changes on cardiac remodeling parameters (LVEF, LVMi, LVEDVi, LVESVi, LAVi), lower rate of hospitalization and cardiovascular death. When empagliflozin is administered to diabetic and nondiabetic HFrEF patients, LV volumes, LV mass, LV systolic function, functional capacity, and quality of life are significantly improved. A favourable reverse remodeling of the LV may explain the reduction in heart failure hospitalizations and mortality caused by SGLT2 inhibitors. Clinical trials have found that SGLT2 inhibitors significantly reduce the risk of cardiovascular death and hospitalization for heart failure among chronic heart failure patients. Regardless of the left ventricle ejection fraction, this is true. Recent evidence supports the pleiotropic effects of SGLT2i in reducing cardiovascular complications and hospitalizations in patients with and without diabetes by improving renal, cardiometabolic, and vascular function. In HFrEF patients, SGLT2 inhibitors are strongly recommended in guidelines. SGLT2 inhibitors have become a fourth pillar of chronic heart failure management based on the collective data of their efficacy.

ACKNOWLEDGEMENTS

The authors have no conflict of interest to declare.

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