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Original article

The effect of Treatment with SGLT2 Inhibitor on Right Ventricular Function in Heart Failure and Low Ejection Fraction patients

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Abstract

Background: This study investigates the effects of SGLT2 inhibitors on right ventricular (RV) function in patients with heart failure and reduced ejection fraction (HFrEF). SGLT2 inhibitors, initially used for Type 2 diabetes, have become a first-line therapy for heart failure, improving both short-term (e.g., diuresis, volume reduction) and long-term outcomes (e.g., structural remodeling, reduced fibrosis, lower hospitalization, and mortality rates). The research highlights their potential benefits in enhancing RV function and overall heart failure management. **Methods**: The study involved 100 HFrEF patients, divided into two groups: one received SGLT2 inhibitors alongside optimal medical therapy (OMT) for 3 months, while the other received only OMT. Comprehensive assessments included clinical evaluations, laboratory tests, and echocardiographic measurements (2D TTE and speckle tracking echocardiography) to assess RV function. **Results**: showed significant improvements in RV function in the OMT + SGLT2 group compared to the OMT-only group, with mean absolute changes in key parameters such as TAPSE (+2.2 mm), FAC (+12%), TR V max (-1.1 m/s), PASP (-23 mmHg), and RV free-wall strain (+7.5%). Multivariate regression analysis confirmed that OMT + SGLT2 significantly improved RV function compared to OMT alone. **Conclusion**: adding SGLT2 inhibitors to OMT significantly improves RV function in HFrEF patients, highlighting the potential benefits of SGLT2 inhibitors beyond their effects on glycemic control.

Keywords: SGLT2 Inhibitor, Right Ventricular Function, Heart Failure, Low Ejection Fraction.

Introduction

Since the main use of sodium-glucose cotransporter-2 inhibitors (SGLT2i) is for diabetic patients, as they are unique type of drugs that reduce glucose reabsorption in the renal proximal tubules, enhancing urinary glucose excretion; hence reducing plasma glucose level without any insulin-dependent mechanism. Now recent studies revealed its efficacy on patients with co-morbidity of Type 2 Diabetes Mellitus and heart failure (1, 2).

SGLT2i (empagliflozin and dapagliflozin), are now revolutionary therapy in heart failure with reduced ejection fraction patients (HFrEF) (3) regardless the glycemic status of the patient and are considered as A1 class drug according to the 2021 European Society of Cardiology Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure (ESC) (4, 5). About the specific mechanism of SGLT2i in Heart Failure, many studies are suggesting that they affect the cardiac cell through ion transport mechanisms, pro-inflammatory and oxidative process resulting in controlling calcium-sodium homeostasis within metabolic and mitochondrial pathways. These mechanisms are considerable as if any disturbance occurs within it results in diastolic dysfunction, endothelial dysfunction, cardiac stiffness, and cardiac arrhythmias that together contribute to heart failure (6).

This impact of SGLT2i on patients with HFrEF was based on the EMPEROR-preserved trial studies and DELIVER trials that assured reaching the lowest mortality and hospitalization rate in patients with HFrEF (7, 8). After meticulous research, we found that the majority of the studies have demonstrated the impact of SGLT2i on the left ventricle function and only few studies undertook the effect of SGLT2i on the right ventricle (9, 10).

The purpose of this study was to evaluate the effect of treatment with SGLT2 inhibitor on right ventricular function in heart failure patients and low ejection fraction patients who underwent optimal medical therapy (OMT).

Patients and methods

This prospective (single center) study included 100 patients diagnosed with HFrEF defined as "a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood **(Heidenreich et al., 2022).**

The study was carried out at Cardiology Departments at Benha University Hospital, during the period (5/ 2023–11/2023).

An informed written consents were obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

Inclusion criteria were patients aged 18 years or older with verified LVEF < 40%,

diagnosed with HFrEF according to the ESC guidelines with impaired RV function beside HFrEF who already needed to receive background optimal guideline-directed OMT at the highest tolerated daily doses of medications, including (Angiotensin Receptor Neprilysin Inhibitor—ARNi (sacubitril-valsartan), beta-blocker (BB), and the mineralocorticoid receptor antagonist (MRA), and those with a functional symptom severity class II and III, as assessed by the New York Heart Association (NYHA) scale.

Exclusion criteria were patients with disease affecting Rt side (significant pulmonary hypertension, COPD), with severe aortic stenosis, acute coronary syndrome, with transient ischemic attack (TIA), or acute ischemic stroke, with history of previous coronary artery bypass surgery (CABG) Or previous percutaneous coronary intervention, with history of an artificial heart valve, symptomatic hypotension, with hepatic and renal dysfunction, active malignancy, those under the use of hormone replacement therapy, chemotherapy, or immunotherapy, pregnancy, or breastfeeding, with diabetes mellitus treated with DPP4 inhibitors and GLP receptor agonists were excluded from the study because of possible interactions with the structure and function of the myocardial and patients who were unable to provide informed consent or declined to participate in the study were not enrolled.

Grouping: Patients were selected and divided into two equal groups: **The OMT + SGLT2 inhibitor group:** 50 patients received the SGLT2 inhibitor (either empagliflozin or dapagliflozin. mg once daily) in addition to background OMT for 3 months' time. **The OMT control group:** 50 patients received background OMT without the addition of SGLT2i.

All studied cases were subjected to the following: Detailed history taking, including [age, gender, and history of diabetes mellitus, hypertension, hyperlipidemia, cigarette smoking, and family history of premature CAD, previous ischemic stroke or TIA and symptoms of HF]. **Full clinical examination, including [**weight, height, body mass index (BMI), heart rate, systolic blood pressure, diastolic blood pressure, and signs of heart failure general & local examination to exclude decompensation]. **Routine laboratory investigations [**fasting blood glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and renal function tests& Electrolytes].

Echocardiography:

Conventional transthoracic, tissue doppler and two-dimensional speckle tracking echocardiography were performed to all patients using a Philips, Epic 7C machine, with the 5.5 X transducer S5-1 probe with simultaneous ECG signal. Patients were examined in the left lateral decubitus position. All echocardiographic

examinations were performed according to the guidelines and recommendations of the American society of echocardiography (ASE) and European association of cardiovascular imaging (EACVI) and recorded offline (11).

1. 2D Conventional TTE evaluation of RV function (RVF) was conducted through measuring tricuspid annular plane systolic excursion (TAPSE), Fractional area change (FAC), TR velocity, pulmonary artery systolic pressure (PASP). LV end-diastolic and end-systolic volumes were to calculate left ventricular ejection fraction (LVEF) using modified biplane Simpson's method in the apical four chamber and apical two chamber views. Ejection fraction is the fraction of the end –diastolic volume that is ejected with each beat; that is, stroke volume (SV) divided by end diastolic volume. Stroke volume = end-diastolic volume – end systolic volume (12).

2. Speckle tracking echocardiography was done: many of the software tools and imaging technique designed for assessing of LV function can be adapted for RV function through the RV unique anatomy. So 2D and 3D echo can measure RV size, wall thickness and function, however RV strain is increasingly used to evaluate RV function.

3. Speckle -tracking echo was done to assess RV strain and contractility.

4. Images of the RV were obtained from dedicated RV-focused apical four-chamber views. End of systole was identified by pulmonary valve closure detected on pulsed-wave Doppler tracing of the RV outflow tract, whereas end of diastole was defined as the peak of the R-wave in electrocardiogram. In the case of the presence of intraventricular conduction delay, end of diastole was detected manually as tricuspid valve closure from the continuous wave Doppler profile of tricuspid regurgitation. The automatically generated region of interest (ROI) was manually adjusted in terms of width and orientation in order to include the entire RV myocardium, without the pericardium. The ROI consisted of both the IVS and RV free wall. Afterwards, detailed analysis of RV free-wall longitudinal strain using RV software. (19)

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Statistical analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The distribution of quantitative data was tested by Kolmogorov-Smirnov test of normality and was found non-parametric. So, the quantitative data were presented as mean, standard deviations and ranges when parametric and median with interquartile range (IQR) when nonparametric qualitative variables were presented as number and percentages.

The comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test when the expected count in any cell found less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using independent t-test. Multivariate linear regression analyses were done to predict different follow-up echo parameters. The regression coefficients with 95% confidence intervals were calculated. All statistical tests were two-sided. P values less than 0.05 were considered significant.

Results

The studied groups were comparable regarding the general characteristics (age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking, and family history of CAD) and all clinical characteristics (systolic and diastolic blood pressure, heart rate, and body mass index). LDL levels were significantly different between the OMT + SGLT2 and OMT groups, with the OMT + SGLT2 group showing higher LDL levels (128 ± 27 mg/dL) compared to the OMT group (116 ± 22 mg/dL) (P = 0.015). Other parameters, including total cholesterol, triglycerides, fasting blood sugar (FBS), and estimated glomerular filtration rate (eGFR), were not significantly different between the two groups. **Table 1**

In the assessment of baseline cardiac function parameters, the OMT + SGLT2 and OMT groups were comparable. Left ventricular ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), fractional area change (FAC), tricuspid regurgitation velocity maximum (TR V max), pulmonary artery systolic pressure (PASP) and right ventricle free wall strain (RV FWS) were all comparable between the two groups. **Table 2**

In the evaluation of follow-up right ventricular function, significant differences were observed between the OMT + SGLT2 and OMT groups. The right ventricle free wall strain (RV FWS) and fractional area change (FAC) were significantly higher in the OMT + SGLT2 group compared to the OMT group ($P < 0.00001$ and $P<0.001$, respectively). Similarly, tricuspid regurgitation velocity maximum (TR V max) and pulmonary artery systolic pressure (PASP) were significantly lower in the OMT + SGLT2 group, with TR V max was 2 ± 0.4 m/s versus 3.1 ± 0.3 m/s ($P < 0.001$) and PASP was 27 ± 6 mmHg versus 49 ± 8 mmHg ($P < 0.001$). TAPSE showed a trend towards significance ($P = 0.065$) but was not statistically significant. **Table 2**

The study shows the effect of SGLT2 inhibitors on RV function in patient with HFrEF not parallel to LV systolic function.

The study included patients with HFrEF who were randomized into two groups:

- **The OMT + SGLT2 inhibitor group**: patients received the

SGLT2 inhibitor in addition to background OMT.

- **The OMT control group**: patients received background OMT without the addition of SGLT2i.

Patients who were randomized to OMT+SGLT2 experienced a significant improvement in all RV functional echocardiographic parameters from baseline to 3 months follow up, as reflected in the mean absolute changes as follows: TAPSE (2.2 mm, p<0.001), FAC (12%, p<0.001), TR V max (-1.1m/s, p<0.001), PASP (-23mmHg, p<0.001), RV FWS (7.5%, p<0.001). On the other hand, the improvement from baseline to 3 months follow up in the OMT group was significant only for TAPSE (1.8 mm, p<0.01), while the FAC, TR V max, PASP and RV FWS were all associated with numerical improvement but failed to reach statistical significance. **Table 3**

Multivariate linear regression analysis was done to predict follow-up echo parameters using the OMT + SGLT2. It revealed that OMT + SGLT2 was associated with 0.375 increase in TAPSE (B = 0.375, 95% CI = -0.018 - 0.769, P = 0.061), 10.923 increase in FAC (B = 10.923, 95% CI = 8.25 – 13.595, P <0.001), 1.052 decrease in TR V max (B =-1.052, 95% CI = -1.187 - -0.917, P < 0.001), and 21.839 decrease in PASP (B = -21.839, 95% CI = -24.527 - -19.151, P < 0.001) compared to OMT alone, controlling for age, gender, hypertension, diabetes, dyslipidemia, smoking, family history of CAD, and intervention. **Table 4**

Table 1 : General and clinical characteristics and laboratory findings of the studied groups

			OMT + SGLT2 (n = 50)	OMT (n = 50)	P-value
Age (years)		**Mean ±SD**	62 ±6	63 ±6	0.595
Sex	**Males (%)**	**n (%)**	31 (62)	31 (62)	1.0
	Females(%)	**n (%)**	19 (38)	19 (38)	
Hypertension (%)		**n (%)**	38 (76)	39 (78)	0.812
Diabetes mellitus (%)		**n (%)**	25 (50)	23 (46)	0.689
Dyslipidaemia (%)		**n (%)**	26 (52)	28 (56)	0.688
Smoking (%)		**n (%)**	20 (40)	20 (40)	1.0
Family history of CAD (%)		**n (%)**	17 (34)	15 (30)	0.668
Systolic blood pressure(mmHg)		**Mean ±SD**	122 ±16	120 ±16	0.664
Diastolic blood pressure(mmHg)		**Mean ±SD**	69 ±7	68 ±8	0.792
Heart rate(bpm)		**Mean ±SD**	69 ±8	69 ±9	0.858
Body mass index (kg/ m^2)		**Mean ±SD**	25 ±4	26 ±4	0.897
Total cholesterol(mg/dl)		**Mean ±SD**	212 ±32	207 ±27	0.425
Triglycerides(mg/dl)		**Mean ±SD**	206 ±27	204 ±28	0.792
LDL (mg/dl)		**Mean ±SD**	128 ±27	116 ±22	**0.015***
FBS (mg/dl)		**Mean ±SD**	134 ±41	144 ±43	0.235
eGFR(ml/min/1.73 m^2)		**Mean ±SD**	76 ±8	77 ±8	0.747

SD: Standard deviation; CAD: Coronary artery disease; LDL: Low-density lipoprotein; FBS: Fasting blood sugar; eGFR: Estimated glomerular filtration rate. *: statistically significant as P value <0.05

blood pressure unit: millimeters of mercury(mmHg), heart rate unit: beats per minute (bpm), total cholesterol unit: milligrams per deciliter(mg/dL), triglycerides unit: milligrams per deciliter(mg/dL), LDL unit: milligrams per deciliter(mg/dL), FBS unit: milligrams per deciliter(mg/dL), eGFR unit:(mL/min/1.73 m2

Table 2: Baseline and follow-up echo findings of the studied groups

		OMT + SGLT2 (n = 50)	OMT (n = 50)	P-value
Baseline				
LVEF (%)	**Mean ±SD**	32 ±5	32 ±5	0.567
TAPSE (mm)	**Mean ±SD**	10.9 ±0.6	11 ±0.7	0.792
FAC (%)	**Mean ±SD**	35 ±7	35 ±8	0.895
TR V max(m/s)	**Mean ±SD**	3.1 ±0.4	3 ±0.4	0.381
PASP (mmHg)	**Mean ±SD**	50 ±10	49.4 ±9	0.505
RV FWS (%)	**Mean ± SD**	18.1±3.9	16.1±2.5	0.083
Follow-up				
TAPSE (mm)	**Mean ±SD**	13.1 ±1.1	12.8 ±0.8	0.065
FAC (%)	**Mean ±SD**	47 ±6	37 ±7	**<0.001***
TR V max(m/s)	**Mean ±SD**	2 ±0.4	3.1 ±0.3	**<0.001***
PASP (mmHg)	**Mean ±SD**	27 ±6	49 ±8	**<0.001***
RV FWS (%)	**Mean ± SD**	-25.6±2.5	-16.9±2.6	**<0.00001***

SD: Standard deviation; LVEF: Left ventricular ejection fraction; TAPSE: Tricuspid annular plane systolic excursion; FAC: Fractional area change; TR V max: Tricuspid regurgitation velocity maximum; PASP: Pulmonary artery systolic pressure. *: statistically significant as P value <0.05
RV Fws. unit: percentage (%), TAPSE unit: millimeters(mm), LV EF unit: percentage (%), FAC unit: percentage (%), TR V max unit: meters per second (m/s), PASP unit: millimeters of mercury (mmHg)

Table 3: Absolute changes in RV echocardiographic parameters at baseline and 3 months follow up, stratified by the type of treatment received

RV parameters	**OMT+SGLT2**				**OMT**			
	Baseline	**Follow up**	**Absolute change**	**P value**	**Baseline**	**Follow up**	**Absolute change**	**P value**
TAPSE (mm)	10.9	13.1	2.2	**<0.001**	11	12.8	1.8	**<0.01**
FAC (%)	35	47	12	**<0.001**	35	37	2	0.104
TRVmax(m/s)	3.1	2	-1.1	**<0.001**	3	3.1	0.1	0.372
PASP(mmHg)	50	27	-23	**<0.001**	49.4	49	-0.4	0.421
RV FWS(%)	-18.1	-25.6	7.5	**<0.001**	-16.1	-16.9	0.8	0.386

LVEF: Left ventricular ejection fraction; TAPSE: Tricuspid annular plane systolic excursion; FAC: Fractional area change; TR V max: Tricuspid regurgitation velocity maximum; PASP: Pulmonary artery systolic pressure.
RV Fws. unit: percentage (%), TAPSE unit: millimeters(mm), LV EF unit: percentage (%), FAC unit: percentage (%), TR V max unit: meters per second (m/s), PASP unit: millimeters of mercury (mmHg)

Table 4: Multivariate linear regression analysis to predict follow-up echo parameters using the OMT + SGLT2

	B (95% CI)	**P-value**
TAPSE (mm)		
Age (years)	-0.002 (-0.033 - 0.03)	0.906
Sex	0.045 (-0.369 - 0.459)	0.830
Hypertension	-0.067 (-0.54 - 0.406)	0.780
Diabetes mellitus	-0.366 (-0.77 - 0.038)	0.075
Dyslipidemia	-0.048 (-0.449 - 0.352)	0.812
Smoking	-0.037 (-0.444 - 0.37)	0.859
Family history of CAD	-0.085 (-0.521 - 0.351)	0.701
Intervention	0.375 (-0.018 - 0.769)	0.061
FAC(%)		

Age (years)	0.065 (-0.149 - 0.28)	0.546
Sex	-0.777 (-3.588 - 2.033)	0.584
Hypertension	1.944 (-1.266 - 5.154)	0.232
Diabetes mellitus	0.513 (-2.229 - 3.256)	0.711
Dyslipidemia	-0.246 (-2.964 - 2.473)	0.858
Smoking	1.62 (-1.143 - 4.383)	0.247
Family history of CAD	-0.241 (-3.201 - 2.719)	0.872
Intervention	10.923 (8.25 - 13.595)	**<0.001***
TR V max(m/s)		
Age (years)	0.007 (-0.004 - 0.018)	0.189
Sex	0.009 (-0.133 - 0.151)	0.898
Hypertension	0.01 (-0.152 - 0.172)	0.903
Diabetes mellitus	-0.203 (-0.341 - -0.065)	0.004
Dyslipidemia	-0.138 (-0.275 - -0.001)	0.048
Smoking	0.069 (-0.07 - 0.209)	0.325
Family history of CAD	-0.059 (-0.209 - 0.09)	0.432
Intervention	-1.052 (-1.187 - -0.917)	**<0.001***
PASP(mmHg)		
Age (years)	0.206 (-0.01 - 0.421)	0.061
Sex	0.459 (-2.367 - 3.285)	0.748
Hypertension	0.973 (-2.255 - 4.201)	0.551
Diabetes mellitus	-2.973 (-5.731 - -0.215)	0.035
Dyslipidemia	-2.854 (-5.588 - -0.12)	0.041
Smoking	0.791 (-1.988 - 3.57)	0.573
Family history of CAD	-0.924 (-3.901 - 2.053)	0.539
Intervention	-21.839 (-24.527 - -19.151)	**<0.001***

*Significant P-value; CI: Confidence interval; CAD: Coronary artery disease; TAPSE: Tricuspid annular plane systolic excursion; FAC: Fractional area change; TR V max: Tricuspid regurgitation velocity maximum; PASP: Pulmonary artery systolic pressure.

blood pressure unit: millimeters of mercury(mmHg), heart rate unit: beats per minute (bpm), total cholesterol unit: milligrams per deciliter(mg/dL), triglycerides unit: milligrams per deciliter(mg/dL), LDL unit: milligrams per deciliter(mg/dL), FBS unit: milligrams per deciliter(mg/dL), eGFR unit:(mL/min/1.73 m2)

RV Fws. unit: percentage (%), TAPSE unit: millimeters(mm), LV EF unit: percentage (%), FAC unit: percentage (%), TR V max unit: meters per second (m/s), PASP unit: millimeters of mercury (mmHg)

Discussion

SGLT2 inhibitors, first identified as anti-diabetic drugs, are now recommended by both diabetes and heart failure guidelines. SGLT2 inhibitors inhibit sodium-glucose transport proteins in the nephron, unlike SGLT1 inhibitors that perform a similar function in the intestinal mucosa (12).

Patients included in the 2 groups were comparable regarding the general characteristics (age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking, and family history of CAD) and all clinical characteristics (systolic and diastolic blood pressure, heart rate, and body mass index).

This is in agreement with Mustapic & co-workers, (13) who reported that the baseline characteristics of the patients randomized to OMT+SLGT2i vs. OMT

alone did not significantly differ concerning the age, sex, NYHA functional class, renal function, etiology of cardiomyopathy, relevant comorbidities (HTN, DM, dyslipidemia, and atrial fibrillation), and mean daily dose or distribution of the chronic HF-related therapies.

As regard the laboratory findings, LDL levels were significantly different between the OMT + SGLT2 and OMT groups, with the OMT + SGLT2 group showing higher LDL levels compared to the OMT group (P = 0.015). Other parameters, including total cholesterol, triglycerides, FBS, and eGFR, were not significantly different between the two groups.

This is in agreement with Louise & the co-workers (14) who showed that SGLT2i treatment increased total cholesterol by 0.09 mmol/L, LDL cholesterol by 0.08 mmol/L, and high-density lipoprotein (HDL) cholesterol by 0.06 mmol/L, while it reduced triglycerides by 0.10 mmol/L. For higher SGLT2-inhibitor doses, there was a nominally higher non-significant effect on lipids and lipoproteins. In Asian compared to non-Asian populations, a slightly larger increase in HDL cholesterol and a decrease in triglycerides were observed, but with similar results for total and LDL cholesterol.

Regarding the baseline echo findings, the OMT + SGLT2 and OMT groups were comparable. LVEF, TAPSE, FAC, TR V max, and PASP were all comparable between the two groups. However, in the evaluation of follow-up right ventricular function, significant differences were observed between the OMT + SGLT2 and OMT groups. RV free wall strain and FAC was significantly higher in the OMT + SGLT2 group (P < 0.001). Similarly, TR V max and PASP were significantly lower in the OMT + SGLT2 group (P < 0.001). TAPSE showed a trend towards significance (P = 0.065) but was not statistically significant.

This is in agreement with Mustapic & co-workers, (13) who reported that, they were similar in the baseline echocardiographic parameters reflecting the left ventricular systolic, diastolic function and echocardiographic parameters of the right ventricular systolic function.

Alexios et al. (15) found that SGLT2i improved left ventricular systolic function in a sample of real-world diabetic patients, as shown by the changes in LVEF and LVEDV with a trend towards right ventricular function improvement demonstrated by the TAPSE increase.

Also, Çamcı & co-workers (16) found that SGLT2 inhibitor treatment provided significant improvement in NYHA classification, NT-pro BNP levels, LVEF, FAC, TAPSE, RV MPI, mPAP and PASP.

As well as Alcidi G, & co-workers (17) who showed that addition of SGLT2 inhibitors to the optimized therapy for HFrEF was associated with significant

improvement of RV free wall longitudinal strain at 3 & 6 months follow up (as relative changes of RV FWS from baseline to 3 & 6 months follow up were: -13.5±22.6 vs. 10.9±22.3; respectively with p value< 0.05).

However, that was disconcordant with a post HOC analysis of the EMPA-HEART CardioLink-6 trial in patients with type II diabetes mellitus and CAD, which showed no differences in the RV mass index, RV volume, and RV EF measured by CMR after 6 months of empagliflozin compared with placebo (16). This difference mostly due to different types of population.

The exact pathophysiological mechanisms explaining these results waits to be elucidated. However, the beneficial role of SGLT2i in reducing the extent of pulmonary hypertension and RV remodeling can be explained by their multifactorial and pleiotropic effects. SGLT2i have metabolic, vascular, and hemodynamic effects. They reduce body weight due to renal caloric loss by glycosuria, have beneficial effects on the cardiac metabolism, and improve the cardiac energetics (17). They also reduce myocardial oxidative stress, and by inhibiting the myocardial sodium-hydrogen exchanger 1 (NHE1), they the reduce cytoplasmic sodium and calcium levels. The combination of the different mechanisms prevents cardiac remodeling. Due to the mechanism of osmotic diuresis, the initial volume depletion results in a decrease in the pulmonary pressure within the first few days after the initiation of the treatment (18).

The limitations of the current study were the relatively small sample size, and the short follow-up duration.

Therefore, larger cohort with longer follow-up are recommended to validate our findings.

Conclusion

We can safely conclude that SGLT2 inhibitors significantly improve the right ventricular function in patients with heart failure and reduced ejection fractions who receive OMT. The improvement of RV function is independent on LV function improvement.

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