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Effect of Sodium-Glucose Cotransporter 2 Inhibitors on Left Ventricular Ejection Fraction as Add on Therapy in Treatment of Heart Failure with Low Ejection Fraction

Dr. Israr Ahmad
MTI-Khyber Teaching Hospital, Peshawar. jayahmad570@gmail.com
Dr. Bughdad Khan
MTI-Khyber Teaching Hospital, Peshawar. drbughdad333@gmail.com
Dr. Muhammad Shahzaib
Khyber Medical College, Peshawar. shahzaibkmc2024@gmail.com
Dr. Mujahid
MTI-Khyber Teaching Hospital, Peshawar. drmujahidbuneri@gmail.com
Dr. Khushal Nadir
MTI-Khyber Teaching Hospital, Peshawar. khushhalhadi@gmail.com
Dr. Amjad Shahzad*
MTI-Khyber Teaching Hospital, Peshawar. Corresponding Author Email: janamjad147@gmail.com

Author Details

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Corresponding E-mails & Authors*:

Abstract

Objective: To compare mean left ventricular ejection fraction after treatment with sodium-glucose cotransporter 2 inhibitors versus placebo in treatment of heart failure with low ejection fraction. **Study Design:** Randomized controlled trial. **Duration and Setting:** This study was conducted from 15 May to 15 November 2025 at the Department of Medicine Khyber Teaching Hospital Peshawar. **Methodology:** Total 106 individuals between 40 and 70 years of age all confirmed to have heart failure with a left ventricular ejection fraction below 40% were included in the study. Participant were allocated into two arms through block randomization. One arm was treated with empagliflozin at a dose of 10 mg once daily in addition to conventional therapy where the comparison arm received a placebo alongside the same standard care. The difference in the average change in left ventricular ejection fraction between the two group was analyzed using an independent samples t-test. **Results:** Mean age was 61.81 ± 6.62 years in empagliflozin group and

59.49 ± 7.50 years in placebo group. ale patients constituted 66.0% and 79.2% respectively. Pre- treatment ejection fraction was 30.52 ± 3.69% in empagliflozin group and 31.98 ± 3.89% in placebo group. Post treatment values increased to 39.60 ± 4.09% and 34.98 ± 3.77% respectively. Mean improvement was significantly higher in empagliflozin group at 9.08 ± 1.92% compared to 2.99 ± 1.27% in placebo group ($p < 0.001$). **Conclusion:** Adding empagliflozin to routine treatment significantly increased left ventricular ejection fraction in patients suffering from heart failure with low ejection fraction.

Keywords: Cardiac output, Empagliflozin, Heart failure, Left ventricular function, Sodium-glucose cotransporter-2 inhibitors

INTRODUCTION

Heart failure with reduced ejection fraction abbreviated as HFrEF refers to a clinical entity wherein there is reduced ejection fraction and decreased forward output.[1] This occurs when the left ventricle of the heart fails to pump blood forward. This leads to a reduced ejection fraction and decreased forward output. The most common causes of HFrEF are ischemic heart disease, previous myocardial infarction, hypertension, dilated cardiomyopathy, and valvular heart disease.[2] With time the heart muscles become weakened and enlarged. The most common symptoms of HFrEF are dyspnea, orthopnea, paroxysmal nocturnal dyspnea, fatigue, peripheral edema, particularly swelling of the ankles, weight gain, and decreased exercise capacity.[3] The most common signs of HFrEF are elevated jugular venous pressure, bibasilar rales, displaced apical impulse, third heart sound, and hepatomegaly.[4]

The goal of heart failure with reduced ejection fraction treatment is to relieve symptoms, prevent decompensation, improve survival rates, and enhance the quality of life.[5] These goals are usually achieved through a combination of lifestyle and pharmacological interventions.[6] Patients with HFrEF should adopt measures that include sodium reduction, fluid reduction and monitoring, weight monitoring, exercise, vaccination and smoking cessation as well as optimizing blood glucose, blood pressure and lipid levels.[7] Diuretics, especially loop diuretics, are used to relieve congestion and edema; however, they do not provide any survival advantage and disease-modifying agents must be used.[8] Standard treatment for heart failure with reduced ejection

fraction (LVEF) mainly relies on evidence-based pharmacological therapy recommended in clinical guidelines. This regimen generally includes either an angiotensin-converting enzyme inhibitor, an angiotensin receptor blocker, or an angiotensin receptor–neprilysin inhibitor. These medications are commonly administered together with beta-blockers and mineralocorticoid receptor antagonists as part of the routine therapeutic approach.[9] Sodium-glucose cotransporter 2 inhibitor drugs a relatively new class of pharmacological agents, were originally designed to treat type 2 diabetes mellitus but subsequent studies showed that they were beneficial to heart failure patients regardless of their diabetic status.[10] SGLT2 inhibitor drugs are therefore now recognized as an important therapeutic option in the treatment of heart failure with reduced LVEF. SGLT2 inhibitor drugs reduce hospitalizations related to heart failure and improve symptoms of heart failure.[11] The mechanisms by which SGLT2 inhibitor drugs work include glucose metabolism, mild diuretic and natriuretic activity, reduction of preload and afterload, improvement of renal function, reduction of inflammation and oxidative stress and possibly improvement of myocardial energy metabolism.[12] With regard to left ventricular systolic function there are several studies that suggest that SGLT2 inhibitor drugs may improve LVEF over time.[13]

In the EMPA-HEART study empagliflozin a sodium-glucose-cotransporter-2 inhibitor given at a dose of 10 mg daily was evaluated as an additional therapy against placebo in patients with heart failure and reduced ejection fraction. At the start of the study the average LVEF in the empagliflozin group was 58.0 ± 7.5% and this value showed an increase to 59.1 ± 8.6% following treatment. In contrast participants receiving placebo had an initial mean ejection fraction of 55.5 ± 8.7% which declined over the study period to 54.3 ± 8.9%.[14]

There is a need for this study in Peshawar due to the lack of data regarding the effect of SGLT2 inhibitors on LVEF in patients with heart failure. There are differences in the pattern of disease, co-morbid conditions, and access to healthcare services, making it imperative for the effectiveness and safety of SGLT2 inhibitors in this patient group to be assessed.

METHODOLOGY

The study was conducted in the Department of Medicine Khyber Teaching Hospital Peshawar from 15 May 2025 to 15 November 2025. A randomized controlled trial design was applied in this study. Ethical permission was obtained from the hospital ethical review board before initiation of the study (786/DME/KMC, dated 05-12-2023) and all procedures were carried out according to institutional ethical guidelines. Sample size was calculated using WHO sample size calculator by keeping confidence level at 95%, absolute precision at 10% and power of study at 80%. The expected mean post-treatment LVEF was taken as 59.1±8.6 in sodium-glucose cotransporter 2 inhibitor group and 54.3±8.9 in placebo group.[14] The total number of participants in the study was 106, with 53 participants in each group according to the determined sample size calculation. The inclusion criteria for the participants in the study consisted of adults between 40 and 70 years of age, of both sexes, with a definite diagnosis of heart failure with reduced ejection fraction (HFrEF) less than 40%, and with symptoms of NYHA class IV. The severity of heart failure was assessed according to the New York Heart Association (NYHA) functional classification. This system categorizes patients into four classes based on the extent of symptoms and limitation of physical activity. Class I includes individuals who do not experience symptoms during routine daily activities. Class II comprises patients who develop mild symptoms with ordinary physical exertion. Class III refers to patients who experience symptoms with activities that are less than usual daily efforts. Class IV includes patients who have symptoms even while at rest. Patients not fitting into these categories are also included. LVEF was calculated through echocardiography by dividing stroke volume by end-diastolic volume and multiplying by 100 to obtain percentage. Patients with uncontrolled hypertension, pregnancy, renal impairment with estimated glomerular filtration rate less than 30 mL/min/1.73 m2 or liver disease with serum AST, ALT or alkaline phosphatase levels more than three times the upper limit of normal were excluded from the study. Before the commencement of the trial, all the participants who were eligible gave their written consent after being fully briefed about the purpose of the trial. The demographic data, such as age, gender, and the duration of the heart failure, were collected using a data collection form that was specifically designed for the purpose.

A detailed clinical history was obtained from each participant, followed by a complete physical examination. Initial laboratory investigations consisted of a complete blood count, liver function assessment, renal function evaluation, and measurement of serum electrolyte concentrations. Baseline echocardiography was conducted on all participants by a consultant cardiologist with at least five years of experience after completing fellowship training. Participants were divided into two groups using blocked randomization with computer software. Participants in Group A received 10 mg of empagliflozin orally once a day in addition to routine standard therapy, while those in Group B received a placebo in addition to routine treatment. Participants were followed up after four weeks, and echocardiography was conducted to determine LVEF. An improvement in LVEF was considered to be an increase in the post-treatment LVEF in comparison to the baseline LVEF after four weeks of treatment.

The collected information was coded and subsequently analyzed using the SPSS software, version 22. Quantitative variables including age, duration of heart failure, pre-treatment LVEF and post-treatment LVEF were expressed as mean and standard deviation. Categorical variables such as gender were presented as frequency and percentage. Comparison of change in LVEF between the two groups was done using independent t-test. Stratification was performed for age, gender and duration of heart failure to control effect modifiers and post stratification independent t-test was applied. A probability value of 0.05 or less was taken as statistical significance.

RESULTS

In empagliflozin group, the mean age was found to be 61.81 ± 6.62 years while placebo group showing 59.49 ± 7.50 years. The weight measurement was recorded as 86.42 ± 8.41 kg in empagliflozin patients compared with 83.76 ± 8.69 kg in placebo recipients. Height values were relatively similar, measuring 1.64 ± 0.05 m and 1.63 ± 0.05 m for empagliflozin and placebo groups respectively. Body mass index calculations revealed 32.15 ± 2.31 in empagliflozin arm versus 31.35 ± 2.54 in placebo arm. The duration of heart failure was documented as 16.23 ± 5.90 months for empagliflozin group and 16.87 ± 4.61 months for placebo group. Regarding gender distribution, male patients constituted 35 (66.0%) of empagliflozin group and 42 (79.2%) of placebo group,

whereas female patients were 18 (34.0%) and 11 (20.8%) in empagliflozin and placebo groups respectively as shown in Table-I.

Table-I: *Patient Demographics in Both Groups*

Variables	Empagliflozin n=53 Mean ± SD	Placebo n=53 Mean ± SD
Age (years)	61.81 ± 6.62	59.49 ± 7.50
Weight (kg)	86.42 ± 8.41	83.76 ± 8.69
Height (m)	1.64 ± 0.05	1.63 ± 0.05
BMI	32.15 ± 2.31	31.35 ± 2.54
HF Duration (months)	16.23 ± 5.90	16.87 ± 4.61
Gender	n (%)	n (%)
Male	35 (66.0%)	42 (79.2%)
Female	18 (34.0%)	11 (20.8%)

The LVEF parameters demonstrated notable variations between treatment arms. Pre-treatment LVEF measurements showed 30.52 ± 3.69% in empagliflozin group compared to 31.98 ± 3.89% in placebo group, with statistical significance observed at $t = -1.989$, $p = 0.049$. Following the treatment intervention, post-treatment LVEF values increased to 39.60 ± 4.09% in empagliflozin recipients while placebo group reached 34.98 ± 3.77%, yielding highly significant difference with $t = 6.051$, $p < 0.001$. The change in LVEF demonstrated substantial improvement, measuring 9.08 ± 1.92% in empagliflozin group in contrast to 2.99 ± 1.27% in placebo group, with remarkable statistical significance at $t = 19.21$, $p < 0.001$, as shown in Table-II.

Table-II: *Comparison of LVEF Parameters Between Both Groups*

LVEF Parameters	Empagliflozin n=53	Placebo n=53	t	P value
Pre-treatment LVEF (%)	30.52 ± 3.69	31.98 ± 3.89	-1.989	0.049*
Post-treatment LVEF (%)	39.60 ± 4.09	34.98 ± 3.77	6.051	<0.001*
Change in LVEF (%)	9.08 ± 1.92	2.99 ± 1.27	19.21	<0.001*

*Independent Sample t Test

Stratification analysis according to demographic factors revealed varied patterns in LVEF changes across subgroups. For age stratification of patients ⩽55 years, empagliflozin group with 11 patients showed mean change of 8.23 ± 2.24% while placebo group with 15 patients demonstrated 3.14 ± 1.43%, though not reaching statistical significance at p = 0.162. In patients aged >55 years, empagliflozin arm comprising 42 patients exhibited change of 9.3 ± 1.79% compared to placebo arm of 38 patients showing 2.94 ± 1.23%, with p value of 0.632. Gender-based stratification indicated that male patients receiving empagliflozin totaling 35 subjects achieved 9.32 ± 1.8% improvement versus 42 male placebo recipients with 3.12 ± 1.27% change, p = 0.239. Female participants numbered 18 in empagliflozin group demonstrated 8.62 ± 2.12% change while 11 female patients in placebo group showed 2.52 ± 1.23%, p = 0.171. Duration of heart failure stratification for patients with ⩽12 months duration showed empagliflozin group of 15 patients having 9.15 ± 1.92% change and placebo group of 9 patients with 2.56 ± 1.49%, p = 0.865. For heart failure duration >12 months, empagliflozin cohort of 38 patients presented 9.05 ± 1.95% improvement whereas placebo cohort of 44 patients exhibited 3.08 ± 1.23% change, p = 0.341, as shown in Table-III.

Table III: *Stratification of Change in LVEF with Respect to Demographic Factors in Both Groups*

Demographic Factors	Group		Change in LVEF (%)		p Value
			Mean	SD	
Age (years)	⩽55	Empagliflozin (n=11)	8.23	2.24	0.162
		Placebo (n=15)	3.14	1.43	
	>55	Empagliflozin (n=42)	9.3	1.79	0.632
		Placebo (n=38)	2.94	1.23	
Gender	Male	Empagliflozin (n=35)	9.32	1.8	0.239
		Placebo (n=42)	3.12	1.27	
	Female	Empagliflozin (n=18)	8.62	2.12	0.171
		Placebo (n=11)	2.52	1.23	
HF Duration (months)	⩽12	Empagliflozin (n=15)	9.15	1.92	0.865
		Placebo (n=9)	2.56	1.49	

	>12	Empagliflozin (n=38)	9.05	1.95	0.341
		Placebo (n=44)	3.08	1.23	

*Independent Sample t Test

DISCUSSION

The demographic characteristics in both groups showed male predominance with 35 (66.0%) males in empagliflozin group and 42 (79.2%) in placebo group. This gender distribution is consistent with epidemiological pattern of heart failure which is more prevalent in male population due to higher incidence of coronary artery disease and other cardiovascular risk factors in males. The mean age was 61.81 ± 6.62 years in empagliflozin group and 59.49 ± 7.50 years in placebo group, indicating that heart failure commonly affects elderly population because of age-related cardiac structural changes and accumulation of cardiovascular risk factors over time.

The pre-treatment LVEF showed 30.52 ± 3.69% in empagliflozin group versus 31.98 ± 3.89% in placebo group with $p = 0.049$, suggesting baseline comparability between groups. After treatment intervention, post-treatment LVEF increased to 39.60 ± 4.09% in empagliflozin group compared to 34.98 ± 3.77% in placebo group with highly significant $p < 0.001$. This substantial improvement can be explained by multiple mechanisms of SGLT2 inhibitors including reduction in preload and afterload, improvement in myocardial energetics, and decrease in oxidative stress which collectively enhances cardiac contractility and ventricular function. The change in LVEF (LVEF) was significantly higher in the empagliflozin group, where there was an improvement of 9.08 ± 1.92%, compared to 2.99 ± 1.27% in the placebo group ($p < 0.001$). This is because SGLT2 inhibitors have cardioprotective effects through the inhibition of the sodium-hydrogen exchanger in the myocardium, leading to reduced intracellular sodium and calcium overload. This improves cardiac function and prevents remodeling.

The present study findings revealed significant improvement in LVEF with empagliflozin treatment showing post-treatment LVEF of 39.60 ± 4.09% compared to 34.98 ± 3.77% in placebo group ($p < 0.001$), with change in LVEF being 9.08 ± 1.92% versus 2.99 ± 1.27% ($p < 0.001$). These results are consistent with findings of Yu *et al.* [15] who demonstrated in their meta-analysis of 21 randomized controlled trials that SGLT2

inhibitors improved LVEF significantly in heart failure patients with reduced EF subgroup with mean difference of 3.16% (95% CI 0.11 to 6.22; p=0.04). The similarity in results can be attributed to cardioprotective mechanisms of SGLT2 inhibitors through reduction in preload and afterload, improvement in myocardial energetics, and inhibition of sodium-hydrogen exchanger in myocardium which collectively enhances cardiac contractility and reduces ventricular remodeling. The findings also align with study by Satheesh *et al.* [16] who reported that LVEF increased from 42.6 ± 5.2% to 46.3 ± 7.9% in dapagliflozin group (p=0.002) in diabetic patients with acute myocardial infarction and left ventricular dysfunction. Both studies demonstrated significant improvement in LVEF with SGLT2 inhibitor therapy, though baseline LVEF was lower in current study (30.52 ± 3.69%) compared to Satheesh *et al.* (42.6 ± 5.2%), possibly because current study included more severe heart failure patients with lower EF. The improvement in LVEF in both studies can be explained by beneficial effects of SGLT2 inhibitors on left ventricular remodeling through reduction in intracellular sodium and calcium overload, leading to decreased myocardial oxidative stress and improved cardiac function. Tomasoni *et al.* [17] in their review reported that DAPA-HF trial showed 26% reduction in composite endpoint of cardiovascular death or worsening heart failure with dapagliflozin, while EMPEROR-Reduced trial demonstrated 25% reduction in cardiovascular death or hospitalization for heart failure with empagliflozin. Although current study focused on LVEF improvement rather than clinical endpoints, the significant change in LVEF observed (9.08 ± 1.92% in empagliflozin group) provides mechanistic explanation for reduced cardiovascular events reported in these large trials, as improvement in EF is associated with better cardiac output and reduced risk of heart failure progression.

Cheema *et al.* [18] conducted systematic review showing SGLT2 inhibitors reduced primary composite endpoint with risk ratio of 0.81 (95% CI: 0.76, 0.87) in HFpEF and HFmrEF patients, and improved quality of life with standardized mean difference of 0.13 (95% CI: 0.06, 0.20). Although current study population had HFrEF rather than HFpEF or HFmrEF, the magnitude of benefit observed in LVEF improvement suggests that SGLT2 inhibitors may have more pronounced effects in reduced EF phenotype compared to preserved EF, which is supported by Yu *et al.* [15] findings that SGLT2 inhibitors improved LVEF in HFrEF subgroup (MD 3.16%) but not in HFpEF subgroup (MD 0.19%). Yu *et al.* [15]

reported that SGLT2 inhibitors showed no significant effects on left ventricular mass index (MD -0.96 g/m²; p=0.27) or left ventricular end-diastolic volume index (MD 1.32 ml/m²; p=0.46) in overall analysis. However, Satheesh *et al.* [16] demonstrated significant decrease in left ventricular mass from 222.0 ± 48.4 g to 190.8 ± 48.2 g (p=0.0003) with SGLT2 inhibitors. The stratification analysis in current study revealed consistent improvement in LVEF across different age groups, gender, and heart failure duration, though statistical significance was not achieved in subgroup analyses. This finding is consistent with Cheema *et al.* [18] who reported no significant change in effects based on diabetes status (P interaction = 0.91) or EF diagnostic thresholds (P interaction = 0.57), suggesting that beneficial effects of SGLT2 inhibitors are relatively uniform across different patient subgroups. Abdelhady *et al.* [19] systematic review including 157,998 patients demonstrated that SGLT2 inhibitors reduced risk of hospitalization for heart failure or cardiovascular death in DECLARE-TIMI 58 trial (95% CI 0.73-0.95; p=0.005), while SOLOIST-WHF trial showed rate of primary endpoint was 51.0 in sotagliflozin group compared to 76.3 in placebo group (p<0.001). The improvement in LVEF observed in current study provides mechanistic basis for these clinical benefits, as enhanced EF leads to improved hemodynamics and reduced ventricular wall stress, thereby decreasing risk of heart failure decompensation and hospitalization. Maged *et al.* [20] reviewed EMPEROR-PRESERVED trial which found empagliflozin reduced primary composite outcome with hazard ratio of 0.79 (95% CI 0.69-0.90; p<0.001) in HFpEF patients, and PRESERVED-HF trial showed patients on dapagliflozin were 66% more likely to achieve improvement in 6-minute walk test distance. Although current study did not assess functional capacity or quality of life measures, the significant improvement in LVEF (9.08 ± 1.92%) suggests potential for functional improvement, as EF correlates with exercise capacity and quality of life in heart failure patients.

The present study is associated with certain limitations, which are discussed below. The present study was conducted in a single center, and it is possible that the results might not be generalizable to a wider population with heart failure. The sample size used in the present study is relatively small, with only 53 patients in each group, which could be a limiting factor in the stratified analysis, as indicated by the non-significant p-values. The long-term effects of empagliflozin on LVEF and clinical

outcomes cannot be assessed since the long-term follow-up is not mentioned in the present study. The present study does not mention the clinical outcomes such as hospitalizations related to heart failure, cardiovascular mortality, and quality of life, which are important patient-reported outcomes. Moreover, the present study does not mention the effects of empagliflozin on other parameters such as left ventricular mass, diastolic function, and biomarkers such as NT-proBNP, which would have provided a better understanding of the effects of the drug on the heart.

CONCLUSION

This current study shows that the addition of a sodium glucose cotransporter-2 inhibitor to the therapeutic management of heart failure with reduced EF results in a significant improvement in left ventricular systolic function. The increase in left ventricular EF in the empagliflozin group was much larger than in the placebo group, and the difference between the groups is highly statistically significant.

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Ethical Approval

Ethical permission for this study was taken from the concerned Ethical Committee. All procedure was carried out by following committee guideline and the principles of the Helsinki Declaration.

Patients' Consent

Written consent was obtained from all patient before inclusion in the study. Patient were informed that their personal information would remain confidential and that they had the right to withdraw at any stage.

Conflict of Interest

The author declares that there was no conflict of interest related to this research.

References

1. Desai N, Olewinska E, Famulska A, Remuzat C, Francois C, Folkerts K. Heart failure with mildly reduced and preserved EF: a review of disease burden and remaining

unmet medical needs within a new treatment landscape. *Heart Fail Rev.* 2024;**29**(**3**):631-662. DOI: https://doi.org/10.1007/s10741-024-10385-y.

2. Schwinger RHG. Pathophysiology of heart failure. *Cardiovasc Diagn Ther.* 2021;**11**(**1**):263-276. DOI: https://doi.org/10.21037/cdt-20-302.
3. Grigore M, Nicolae C, Grigore AM, Balahura AM, Păun N, Uscoiu G, *et al.* Contemporary perspectives on congestion in heart failure: bridging classic signs with evolving diagnostic and therapeutic strategies. *Diagnostics (Basel).* 2025;**15**(**9**):1083. DOI: https://doi.org/10.3390/diagnostics15091083.
4. Noguchi M, Kasai K, Honda S, Sakai C, Harimoto K, Kawasaki T. Jugular venous response for risk stratification in heart failure. *Cureus.* 2024;**16**(**4**):e58423. DOI: https://doi.org/10.7759/cureus.58423.
5. Docherty KF, McMurray JJV. Foundational drugs for HFrEF: the growing evidence for a rapid sequencing strategy. *Br J Cardiol.* 2022;**29**(**1**):2. DOI: https://doi.org/10.5837/bjc.2022.002.
6. Palaparthi EC, K P, Ignasimuthu A, N G, Sade N, Bade N, *et al.* Impact of lifestyle modifications along with pharmacological treatment of heart failure: a narrative review. *Cureus.* 2025;**17**(**4**):e81570. DOI: https://doi.org/10.7759/cureus.81570.
7. Chrysohoou C, Mantzouranis E, Dimitroglou Y, Mavroudis A, Tsioufis K. Fluid and salt balance and the role of nutrition in heart failure. *Nutrients.* 2022;**14**(**7**):1386. DOI: https://doi.org/10.3390/nu14071386.
8. Wu L, Rodriguez M, El Hachem K, Krittanawong C. Diuretic treatment in heart failure: a practical guide for clinicians. *J Clin Med.* 2024;**13**(**15**):4470. DOI: https://doi.org/10.3390/jcm13154470.
9. Ospina González OE, Llanos Mejía DC, Kaplinsky E, Barbagelata A, Perrone S. Emerging concepts in heart failure management and treatment: focus on current guideline-directed medical therapy for heart failure with reduced EF. *Drugs Context.* 2023;**12**:2022-6-4. DOI: https://doi.org/10.7573/dic.2022-6-4.
10. Seidu S, Alabraba V, Davies S, Newland-Jones P, Fernando K, Bain SC, *et al.* SGLT2 inhibitors – the new standard of care for cardiovascular, renal and metabolic protection in type 2 diabetes: a narrative review. *Diabetes Ther.* 2024;**15**(**5**):1099-1124. DOI: https://doi.org/10.1007/s13300-024-01550-5.

11. Cardoso R, Graffunder FP, Ternes CMP, Fernandes A, Rocha AV, Fernandes G, Bhatt DL. SGLT2 inhibitors decrease cardiovascular death and heart failure hospitalizations in patients with heart failure: a systematic review and meta-analysis. *EClinicalMedicine.* 2021;**36**:100933. DOI: https://doi.org/10.1016/j.eclinm.2021.100933.
12. Preda A, Montecucco F, Carbone F, Camici GG, Lüscher TF, Kraler S, *et al.* SGLT2 inhibitors: from glucose-lowering to cardiovascular benefits. *Cardiovasc Res.* 2024;**120**(**5**):443-460. DOI: https://doi.org/10.1093/cvr/cvae047.
13. Alcidi G, Pugliese R, Ioannoni S, Romano M, Palmieri G, Tabella E, *et al.* Improvement in left and right ventricular function after introduction of SGLT2 inhibitors in heart failure outpatients with reduced EF. *Clin Pract.* 2023;**13**(**6**):1303-1312. DOI: https://doi.org/10.3390/clinpract13060116.
14. Verma S, Mazer CD, Yan AT, Mason T, Garg V, Teoh H, *et al.* Effect of empagliflozin on left ventricular mass in patients with type 2 diabetes mellitus and coronary artery disease: the EMPA-HEART CardioLink-6 randomized clinical trial. *Circulation.* 2019;**140**(**21**):1693-1702. DOI: https://doi.org/10.1161/CIRCULATIONAHA.119.042375.
15. Yu YW, Zhang XM, Wang YH, Zhou Q, Huang Y, Zhai M, *et al.* Effect of sodium-glucose cotransporter 2 inhibitors on cardiac structure and function in type 2 diabetes mellitus patients with or without chronic heart failure: a meta-analysis. *Cardiovasc Diabetol.* 2021;**20**:25. DOI: https://doi.org/10.1186/s12933-020-01209-4.
16. Satheesh J, Rao MS, Ramachandran P, Samanth J. Effect of SGLT2 inhibitors on left ventricular function in patients with acute myocardial infarction and left ventricular dysfunction: a single-center randomized study. *J Appl Pharm Sci.* 2025;**15**(**10**):081-089. DOI: https://doi.org/10.7324/JAPS.2025.206239.
17. Tomasoni D, Fonarow GC, Adamo M, Anker SD, Butler J, Coats AJS, *et al.* Sodium-glucose co-transporter 2 inhibitors as an early, first-line therapy in patients with heart failure and reduced EF. *Eur J Heart Fail.* 2022;**24**(**3**):431-441. DOI: https://doi.org/10.1002/ejhf.2397.

18. Cheema HA, Shafiee A, Athar MMT, Rafiei MA, Mehmannavaz A, Jafarabady K, *et al.* Efficacy and safety of sodium-glucose cotransporter-2 inhibitors for heart failure with mildly reduced or preserved EF: a systematic review and meta-analysis of randomized controlled trials. *Front Cardiovasc Med.* 2023;**10**:1273781. DOI: https://doi.org/10.3389/fcvm.2023.1273781.

19. Abdelhady HA, Oumar Abakar A, Gangavarapu RR, Mahmud SA, Manandhar A, Sabir G, *et al.* Impact of sodium-glucose cotransporter-2 inhibitors on heart failure in patients with type 2 diabetes mellitus: a systematic review. *Cureus.* 2024;**16**(**9**):e68560. DOI: https://doi.org/10.7759/cureus.68560.

20. Maged R, Sinha M, Koneru HM, Sarwar H, Bandi VV, Tarar P, *et al.* Efficacy of sodium-glucose 2 transporter inhibitors in heart failure with preserved EF: a narrative review. *Cureus.* 2024;**16**(**9**):e69623. DOI: https://doi.org/10.7759/cureus.69623.