Received: 11 April 2022 | Revised: 16 June 2022 | Accepted: 3 July 2022

DOI: 10.1111/echo.15424

Echocardiography WILEY

ORIGINAL ARTICLE

Effects of 3 months of treatment with empagliflozin on left ventricle global longitudinal strain and myocardial mechano-energetic effiency

İbrahim Etem Dural MD[1] | Alper Sarı MD[2] | İbrahim Ersoy MD[1]

[1]Afyonkarahisar Health Sciences University, Department of Cardiology, Afyonkarahisar, Turkey

[2]Afyonkarahisar Health Sciences University, Department of İnternal Medicine, Afyonkarahisar, Turkey

Correspondence
İbrahim Etem Dural, MD, Afyonkarahisar Science of Health University, Faculty of Medicine, Department of Cardiology, Afyonkarahisar. Selçuklu Mahallesi, No:1534, Afyonkarahisar, Turkey.
Email: iedural@hotmail.com

Abstract

Purpose: Sodium glucose transporter-2 (SGLT-2) inhibitors are employed in the treatment of cardiovascular diseases such as heart failure and coronary artery disease. In the present study, we aimed to investigate how Empagliflozin in SGLT 2 inhibitors affects cardiac contraction and pump efficiency in patients who have Diabetes Mellitus (DM) without cardiovascular disease.

Methods: The conventional echocardiographic records and biochemical values of 62 patients who had DM without a history of cardiovascular disease were evaluated before using Empagliflozin. The myocardial mechano-energetic (MME) activity and index, and global longitudinal strain (GLS) were also calculated. After 3 months of Empagliflozin use, the tests were repeated and compared with previous data. A $p < .05$ was considered statistically significant.

Results: Left ventricular GLS and MME efficiency were found to be significantly higher after treatment (-17.71 ± 2.12, -19.15 ± .71; $p < .001$ and 62.14 ± 18.21, 72.24 ± 26.57; p: .019).

Conclusion: An increase was detected in left ventricular longitudinal strain and MME efficiency after using Empagliflozin for 3 months in patients with DM. This result suggests that Empagliflozin improves left ventricular pump efficiency and contraction.

KEYWORDS
empagliflozin, global longitudinal strain, myocardial mechano-energetic effiency

1 | INTRODUCTION

Diabetes Mellitus (DM) is the most important risk factor for cardiovascular diseases. On a global scale, the prevalence of DM is estimated to be 8.4% in adults aged 18–99 in 2017 and will increase to 9.9% in 2045. According to the present databases, it is already known that there are approximately 415 million diabetic patients in the world.[1] Type 2 diabetes constitutes 90% of all DM patients.[2] Macrovascular and microvascular complications of DM cause increased mortality in patients. Providing primary prophylaxis of DM before cardiovascular disease develops has been one of the main problems of cardiology in this respect.[3]

The main purpose of medical treatment in DM is blood sugar regulation and reduction of complications. Sodium glucose transporter-2 (SGLT-2) inhibitors, which have been used frequently in recent years, have taken their place in the treatment of coronary artery disease and heart failure. However, their primary prophylactic efficacy prior to the development of cardiovascular events is not clear.[4]

Global longitudinal strain (GLS) is the most important parameter predicting myocardial systolic and diastolic functions in cardiovascular events. Today, evaluating preclinical myocardial functions with two-dimensional speckle tracking echocardiography has become important for patients who have cardiovascular risk factors.[5] It is now included in routine evaluation, especially for patients who receive cardiotoxic

chemotherapy.[6] GLS was also found to be associated with cardiovascular events in DM patients who do not have a history of cardiovascular complications.[7]

The myocardial mechano-energetic efficiency (MME) method has been used in recent years to provide important information on the structure, functions, and oxygen consumption of the myocardium. It has come to the forefront as an effective method in predicting preclinical cardiovascular events.[8] MME has also been found to be associated with cardiovascular events in DM patients.[9]

In the present study, the purpose was to evaluate myocardial functions before and after the use of Empagliflozin, which is used to predict preclinical cardiovascular events, in GLS, MME, and DM patients. The detection of improvement in myocardial structure and functions in GLS and MME, and the use of these drugs in primary prophylaxis for DM patients who do not have a history of cardiovascular events will strengthen the idea.

2 | METHODS

2.1 | Patients

For this study, 62 patients aged over 18 in the internal medicine outpatient evaluated at 2021. Newly diagnosed or followed-up DM patients who did not use empagliflosin were included in the study. Patients who were previously on oral anti-diabetic and/or insulin therapy or those with fasting blood glucose measured at least twice ≥126 mg/dl, or hemoglobin A1C (HbA1c) ≥6.5%, or the 2-h plasma glucose value ≥200 mg/dl after a 75-g oral glucose tolerance test, and/or in a patient with classic symptoms of hyperglycemia a random plasma glucose ≥200 mg/dl were considered DM. Patients with any of the following conditions were excluded: heart failure (typical symptoms and signs, depressed left ventricular ejection fraction [EF], and elevated natriuretic peptides); valvular heart disease (hemodynamically significant regurgitation/stenosis); coronary heart disease (history of percutaneous intervention or coronary artery bypass graft surgery); atrial fibrillation or any arrhythmia; chronic renal and hepatic disease; a history of malignancy; or a suboptimal echo window.

Echocardiographic and biochemical data of the patients were collected before Empagliflosin use. The examinations of the patients were repeated 3 months after the use of Empagliflosin.

2.2 | Standard echocardiographic measurements

In the standard echocardiographic examination, patients were placed in the left lateral decubitus position using a Phillips Echocardiography machine with a 2.5 MHz transducer. Images were acquired from apical four-chamber, two-chamber, and three-chamber views using two-dimensional (2D), M-mode, color Doppler, continuous-wave Doppler, and pulse-wave Doppler according to recommendations in the American Society of Echocardiography (ASE) guidelines.[10] The left ventricle (LV) and left atrium (LA) dimensions were evaluated in M-mode during LV diastole from 2D parasternal images. The sample volume of pulsed-wave Doppler was taken at the mitral leaflets' tip level from the apical four-chamber view for mitral inflow velocity assessment. The peak mitral inflow in early diastole (E wave), the late diastolic atrial filling velocity (A wave), their ratio (E/A ratio), mitral deceleration time (DecT), and aortic ejection time (ET) parameters were measured. The sample volume with measurements of myocardial systolic (S'), early (E′), and late (A′) diastolic velocities were applied at the septal and lateral sides of the mitral annulus using pulsed-wave tissue Doppler imaging (TDI) to assess myocardial velocities. All the TDI measures were obtained by averaging values at the septal and lateral mitral annulus. LV isovolumic contraction time (IVCT) and isovolumic relaxation time (IVRT) were acquired from the pulse wave Doppler traces.

2.3 | Speckle-tracking echocardiography evaluation

A specific software package, QLAB version 13 (Advanced Quantification Software version 6; Phillips), was used to perform the speckle tracking echocardiography (STE) analysis from the apical and parasternal short-axis offline images at a frame rate of 70–90 frames/s. Three consecutive cardiac cycles were apical four-chamber, two-chamber, three-chamber views, and parasternal short-axis basal, mid, and apical views were recorded. They averaged[13] in Digital Imaging and Communications in Medicine (DICOM) format for offline STE analysis by an experienced cardiologist. Images were acquired at end-expiration during breath hold.

Records were examined in the region of interest (ROI) tab; then, the views were drawn to include the entire myocardium. The ROI thickness was the same in all the patients independently from LV hypertrophy.

The first step in this process was to mark the mitral annulus endocardial borders and apex on the apical two-, three-, and four-chamber images. Second, automatic tracing was performed. Endocardial borders were reviewed during end-systolic frames, and images were settled in motion for tracking confirmation. Areas that cannot be tracked were excluded. Third, peak systolic strain was measured and averaged for determining GLS. Before conducting radial strain analysis, the anatomical structures were marked manually as anterior, inferior, and interventricular parts on the short-axis basal, mid, and apical images and endocardial borders were determined by software. Then, borders were again reviewed during end-systolic frames, and images were settled in motion for tracking confirmation. Peak systolic global circumferential strain (GCS) and global radial strain (GRS) values were calculated by averaging from analyzed ventricular segments. The software could track 95% of segments longitudinal for GLS and 93% for GRS and GCS, respectively. Finally, a bullseye image showing LV whole-strain parameters was obtained.

2.4 | Myocardial mechanoenergetic calculation

The mechanical efficiency of a system is the ratio between the work done and the corresponding energy consumption. To estimate the

MME, two factors are required: work and energy consumption Therefore, external myocardial work, which may be expressed as stroke work (SW), is calculated from systolic blood pressure (SBP) times stroke volume (SV) and converted in gram-meters by multiplying with .0144. In addition, we calculated SV using the Doppler time velocity integral of the LV outflow tract and 2-dimensional echocardiographic cross-sectional area measured in parasternal long-axis view.[11] The myocardial energy consumption (MVO_2) is calculated as SBP times HR. Therefore, MME can be expressed as the optimal amount of blood pumped with one heartbeat in 1 sn. Therefore, the MME can be formulated as follows:

$$MME = \frac{SW}{MVO_2} = \frac{SBP \times SV}{SBP \times HR} = \frac{SV}{HR}$$

MMEi estimates the optimal amount of blood pumped with each gram of LV mass in 1 sn. It can be calculated as MME divided by left ventricular mass (LVM)[12,13] and formulated below:

$$MMEi = \frac{MME}{LVM}$$

2.5 | Statistical analyses

Statistical Package for Social Science (SPSS) (IBM, SPSS, Inc., Chicago, Illinois) version 26.0 package program was used for the analysis. The Kolmogorov-Smirnov test was used to test the distribution of numeric variables. The descriptive data were summarized as the percentage frequency for categorical variables and the mean ± standard deviations (SD) or median 25–75 interquartile Range (IQR) for continuous variables.

Variable differences between baseline and 3 months after Empagliflosin treatment in paired observations were compared using the Wilcoxon rank test. For comparing serial changes in laboratory and echocardiographic parameters, a repeated measures ANOVA test was used. The analyzes followed an "intention-to-treat" approach, in which all patients were assigned to their appropriate group according to the treatment initially prescribed. A $p < .05$ was considered a statistically significant result.

2.6 | Ethical considerations

The local Ethics Committee approved the study protocol (approval date and number are 16/04/2021 and 2021/5). The study was conducted in compliance with the good clinical practices protocol and Declaration of Helsinki principles.

3 | RESULTS

In our study a total of 62 patients were enrolled. The mean age (SD) was 55.8 (±10.1) years, and there were 28 men (45%) and 34 women (55%). The most frequent comorbid disease was hypertension (64.5%).

TABLE 1 Basal characteristics of the study population

Factor	Group, *n* (%)
Age (years) (SD)	55.8 (10.1)
Sex (F/M)	34/28(54.8%/45.2)
Concomitant diseases, *n* (%)	
Hypertension	40 (64.5%)
Hyperlipidemia	25 (40.3%)
Smoking	7 (11.3%)
Beta-blockers	15(24.1%)
Ca^{+2}- Ch. blockers	8(12.9%)
Anti-RAS	26 (41.9%)
Diuretics	19 (30.6%)
Insulin	18 (29%)
OAD	56 (90.3%)

Abbreviations: AF, Atrial fibrillation; Anti-RAS, Renin-angiotensin blockers; Ca+2- Ch. Blockers, Calcium channel blockers; F, Female; M, Male; OAD, Oral anti-diabetics; SD, Standard deviation.

TABLE 2 Blood and anthropometric measurements of the study population

	Baseline	3-month	*p*-Value
Glucose	207.68 (69.79)	197.81 (48,72)	**<.001**
BUN (mmol/L)	13.89 (5.42)	12.73 (4.38)	.162
Creatinin (mg/dl)	.83 (.20)	.79 (.21)	.742
GFR	82.49 (15.35)	94.89 (15.51)	.853
HbA1c	8.92 (1.42)	8.51 (1.05)	**<.001**
AST (U/L)	24.74 (14.08)	26,54(11.32)	.768
ALT (U/L)	27.76 (15.48)	26,62(10.87)	.845
Hemoglobin (g/dl)	14.53 (1.75)	13,98(2,11)	.664
WBC (m/mm^3)	8.77 (2.34)	8.43(2.56)	.918
Platelet (m/mm^3)	245.66(67.43)	276.53(75.18)	.516
Heart rate	76.76 (11.06)	74.47 (9.08)	**.016**
Weight (kg)	88.00 (18.29)	86.59 (19.23)	.130
BMI	41.66 (8.09)	33.53 (7.13)	**<.001**
SBP (mmHg)	130.79 (17.59)	129.11 (15.80)	**.006**
DBP (mmHg)	81.81 (11.01)	80.74 (12.22)	0,084

Note: Data are expressed as number (%) or mean ± SD.
Abbreviations: ALT, Alanine transaminase; AST, Aspartate transaminase (U/L); BMI, Body mass index; BUN, Blood urea nitro; DBP, Diastolic blood pressure; GFR, Glomerular filtration rate; SBP, systolic blood pressure; WBC, White blood cell.
A $p < .05$ was considered a statistically significant result.

Baseline characteristics, blood and anthropometric measurements of study population are given Table 1.

The results, as shown in Table 2, indicate that plasma glucose, HbA1c, and body mass index (BMI) were significantly lower after treatment (all $p < .001$).

TABLE 3 2D, M-mode and Doppler echocardiographic measurements of the study population

	Baseline	3-month	*p*-Value
GLS (%)	−17.71 (2.12)	−19.15 (.71)	**<.001**
MME (%)	62.14 (18.21)	72.24 (26.57)	**.019**
MMEi (ml/secxg)	.35 (.13)	.40 (.09)	**.032**
RWT	.43 (.08)	.46 (.07)	.246
LVD volume (ml/m^2)	112.64 (24.67)	106.18 (24.22)	.164
LVS volume (ml/m^2)	33.67 (8.79)	34.63 (11.52)	.917
LV EF (%)	62.23 (4.60)	63.17 (5.30)	.117
LVM (g/m^2)	189.81 (57.61)	195.85 (41.10)	.239
LVMi	96.32 (29.89)	101.68 (25.12)	.324
SV (ml/m^2)	77.86 (19.16)	88.51 (30.71)	**.034**
SW	142.37 (38.63)	160.94 (61.83)	**.045**
MVO$_2$ (j/g/min)	10069.03 (2195.62)	9623.06 (1715.55)	**.002**
E (cm/sn)	59.52 (13.59)	62.79 (14.67)	.119
A (cm/sn)	83.08 (12.79)	84.06 (10.57)	.368
DecT (msn)	223.24 (54.76)	222.02 (53.79)	**.024**
E/A ratio	.76 (.19)	.82 (.90)	.568
E/E' ratio	9.52 (1.26)	9.33 (2.00)	.700
IVRT (msn)	54.27 (9.88)	51.08 (6.81)	**0,012**
IVCT (msn)	93.04 (23.39)	82.91 (16.18)	**.024**

Note: Data are expressed as number (%) or mean ± SD.
Abbreviations: DecT, Deceleration time; GLS, Global longitudinal strain; IVCT, Isovolumic contraction time; IVRT, Isovolumic relaxation time; LV EF, Left ventricular ejection fraction; LVD, Left ventricular diastolic; LVM, Left ventricular mass; LVMi, Left ventricular mass index; LVS, Left ventricular systolic; MME, Myocardial mechanoenergetic efficiency; MMEi, Myocardial mechanoenergetic efficiency index; MVO$_2$, Myocardial energy consumption; RWT, Relative wall thickness; SV, Stroke volume; SW, Stroke work.
A $p < .05$ was considered a statistically significant result.

Table 3 shows the echocardiographic changes of the study group. Left ventricular GLS, MME and MMEi tend to increase significantly with empagliflosin treatment (-17.71 ± 2.12, -19.15 ± .71; $p < .001$ and 62.14 ± 18.21, 72.24 ± 26.57; *p*: .019 and .35 ± .13, .40 ± .09; *p*: .032).

4 | DISCUSSION

In the present study, it was shown that left ventricular GLS and myocardial energetic efficiency increased after 3 months of use of Empagliflozin in DM patients who did not have a history of cardiovascular disease.

The risk of cardiovascular disease in Type 2 DM patients is increased two to four times when compared to non-diabetics, and 65%–70% of these patients die because of macrovascular complications as coronary artery disease, peripheral artery disease, cerebrovascular disease.[14] On the other hand, the developments in the treatment of DM gained a serious momentum especially in the millennium and many new drugs have been brought into use in this respect. Some of these are drugs are those that inhibit the SGLT-2 molecule. These drugs ensure glucose excretion from the kidney by inhibiting the sodium-glucose channels in the proximal tubule.[15]

SGLT2 inhibitors, which are also called "glucoretics" or "gliflozins," are antidiabetic agents that are effective by inhibiting SGLT2, which is the transporter responsible for reabsorption of approximately 90% of the filtered glucose load in the kidney proximal tubules, and by preventing glucose reabsorption from the kidney and causing glycosuria, osmotic diuresis and natriuresis. It was shown that they improve diastolic functions with their natriuresis, diuresis, and glycosuria effects, as well as reducing afterload and preload. It has been shown that they reduce hospitalization and mortality in patients with heart failure whether diabetic or not.[16]

DM contributes to myocardial fibrosis and myocardial stiffness by causing structural changes in myocardial contractile proteins and collagen composition.[17] Left ventricular longitudinal contraction develops from hypoperfusion and contraction of subendocardial fibers, which are more susceptible to myocardial fibrosis.[18] For this reason, LV longitudinal dysfunction develops in the earliest stages of diabetic cardiomyopathy. Impaired calcium metabolism, increased oxidative stress, increased renin angiotensin aldosterone activation, mitochondrial dysfunction, and impaired substrate metabolism are the causes of cardiomyopathy.[19] In the present study, it was shown that Empagliflozin could improve global longitudinal contraction with its positive effects on the increased RAA system and impaired substrate

metabolism. The study of Chulian et al., with fewer cases, supports the fact that SGLT-2 inhibitors increase GLS.[20]

Cardiac metabolism depends on aerobic oxidation. The continuous energy provided by this oxidation, creates MME activity along with left ventricular structure and function.[21–22] The activity that corresponds to 1-gram myocyte per second is called the mechano-energetic efficiency index (MMEi). Glucose fatty acids and ketone bodies are used in the aerobic oxidation of the heart. Losses occur in this oxidation phase with the impaired glucose regulation in diabetes. This causes decreased mechano-energetic efficiency of the heart in patients with DM.[23] It was shown that SSGLT 2 inhibitors increase the utilization of ketone bodies, an energy substrate. In this way, it was considered to increase the decreasing mechano-energetics. In a study conducted with dapagliflozin, it was shown that MME was increased.[24] In the present study, it was shown that the MME and MMEi also increased after empagliflozin use.

MME and left ventricular GLS were associated with preclinical cardiovascular events.[25] An idea about the prognosis of the disease can be obtained and can be used in the follow-up of treatment with these tests, which are predictive of diabetic cardiomyopathy and coronary artery disease. Improvement in cardiac functions is expected after treatment because SGLT 2 inhibitors reduce cardiac fibrosis, improve cardiac substrate metabolism, and reduce arterial stiffness.[26] These drugs, which cause improvement in both systolic and diastolic functions in patients who are followed up with heart failure, have also started to be investigated in patients with normal systolic functions. In the present study, it was observed that Empagliflozin increased mechano-energetic efficiency and GLS in patients with normal systolic functions without cardiovascular disease. We obtained similar results with Empagliflozin in the study that was conducted by Oldgren et al. with dapagliflozin.[24]

4.1 | Limitations

The biggest limitation of the present study was that it was not a randomized-controlled study and it did not have a high sample size. Also, the evaluation of mechano-energetic efficiency was not made with scintigraphic methods, which is the gold standard method, but with echocardiography, which is more common and practical.

5 | CONCLUSION

In the study, it was shown that Empagliflozin improved GLS and MME, which are the predictors of cardiovascular events. Empagliflozin seems to improve the left ventricular pump efficiency and contraction.

ACKNOWLEDGEMENTS

We have not received any funding and grant

CONFLICT OF INTEREST

All authors declare that they have no conflict of interest

ORCID

İbrahim Etem Dural MD https://orcid.org/0000-0003-4005-4858

İbrahim Ersoy MD https://orcid.org/0000-0002-9553-8801

REFERENCES

1. Cho NH, Shaw JE, Karuranga S, et al. IDF diabetes atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract;*. 2018;138:271-281.
2. Levy NK, Orzeck-Byrnes NA, Aidasani SR, et al. Transition of a text-based insulin titration program from a randomized controlled trial into real-world settings: implementation study. *J Med Internet Res;*. 2018;20(3).
3. Viigimaa M, Sachinidis A, Toumpourleka M, Koutsampasopoulos K, Alliksoo S, Titma T. Macrovascular complications of type 2 diabetes mellitus. *Curr Vasc Pharmacol;*. 2019;18(2):110-116.
4. Zannad F, Ferreira JP, Pocock SJ, et al. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. *Lancet;*. 2020;396(10254):819-829.
5. Potter E, Marwick TH. Assessment of left ventricular function by echocardiography: the case for routinely adding global longitudinal strain to ejection fraction. *JACC Cardiovasc Imaging;*. 2018;11(2P1):260-274.
6. Oikonomou EK, Kokkinidis DG, Kampaktsis PN, Amir EA, Marwick TH, Gupta D. Assessment of prognostic value of left ventricular global longitudinal strain for early prediction of chemotherapy-induced cardiotoxicity: a systematic review and meta-analysis. *JAMA Cardiol;*. 2019;4(10):1007-1018.
7. Pararajasingam G, Heinsen LJ, Larsson J, et al. Diabetic microvascular complications are associated with reduced global longitudinal strain independent of atherosclerotic coronary artery disease in asymptomatic patients with diabetes mellitus: a cross-sectional study. *BMC Cardiovasc Disord*. 2021;21(1).
8. Tran P, Maddock H, Banerjee P. Myocardial fatigue: a mechano-energetic concept in heart failure. *Curr Cardiol Rep*. 2022;30. Published online March.
9. Vanessa Fiorentino T, Miceli S, Succurro E, Sciacqua A, Andreozzi F, Sesti G. Depressed myocardial mechano-energetic efficiency in subjects with dysglycemia. *Diabetes Res Clin Pract;*. 2021;177:108883.
10. Porter TR, Mulvagh SL, Abdelmoneim SS, et al. Clinical applications of ultrasonic enhancing agents in echocardiography: 2018 American society of echocardiography guidelines update. *J Am Soc Echocardiogr*. 2018;31(3):241-274.
11. Dubin J, Wallerson DC, Cody RJ, Devereux RB. Comparative accuracy of Doppler echocardiographic methods for clinical stroke volume determination. *Am Heart J*. 1990;120(1):116-123.
12. De Simone G, Izzo R, Losi MA, et al. Depressed myocardial energetic efficiency is associated with increased cardiovascular risk in hypertensive left ventricular hypertrophy. *J Hypertens;*. 2016;34(9):1846-1853.
13. De Simone G, Chinali M, Galderisi M, et al. Myocardial mechano-energetic efficiency in hypertensive adults. *J Hypertens:*. 2009;27(3):650-655.
14. Booth GL, Kapral MK, Fung K, Tu JV. Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. *Lancet;*. 2006;368(9529):29-36.
15. Brown E, Heerspink HJL, Cuthbertson DJ, Wilding JPH. SGLT2 inhibitors and GLP-1 receptor agonists: established and emerging indications. *Lancet;*. 2021;398(10296):262-276.
16. Zelniker TA, Wiviott SD, Raz I, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. *Lancet*. 2019;393(10166):31-39.

17. Mizushige K, Yao L, Noma T, et al. Alteration in left ventricular diastolic filling and accumulation of myocardial collagen at insulin-resistant prediabetic stage of a type II diabetic rat model. *Circulation;*. 2000;101(8):899-907.
18. Hansen A, Johansson BL, Wahren J, Von Bibra H. C-peptide exerts beneficial effects on myocardial blood flow and function in patients with type 1 diabetes. *Diabetes*. 2002;51(10):3077-3982.
19. Spector KS. Diabetic cardiomyopathy. *Clin Cardiol;*. 1998;21(12):885-887.
20. Gamaza-Chulián S, Díaz-Retamino E, González-Testón F, et al. Effect of sodium-glucose cotransporter 2 (SGLT2) inhibitors on left ventricular remodelling and longitudinal strain: a prospective observational study. *BMC Cardiovasc Disord;*. 2021;21(1):1-11.
21. Succurro E, Miceli S, Fiorentino TV, et al. Sex-specific differences in left ventricular mass and myocardial energetic efficiency in non-diabetic, pre-diabetic and newly diagnosed type 2 diabetic subjects. *Cardiovasc Diabetol;*. 2021;20(1).
22. Ersoy İ, Demir FA. Obstructive sleep apnea is associated with depressed myocardial mechanoenergetics. *J Clin Ultrasound*. 2022;50(2):162-169.
23. Mancusi C, De Simone G, Best LG, et al. Myocardial mechano-energetic efficiency and insulin resistance in non-diabetic members of the Strong Heart Study cohort. *Cardiovasc Diabetol;*. 2019;18(1).
24. Oldgren J, Laurila S, Åkerblom A, et al. Effects of 6 weeks of treatment with dapagliflozin, a sodium-glucose co-transporter-2 inhibitor, on myocardial function and metabolism in patients with type 2 diabetes: a randomized, placebo-controlled, exploratory study. *Diabetes, Obes Metab;*. 2021;23(7):1505-1517.
25. Ersoy I, "Using speckle-tracking echocardiography to evaluate subclinical left ventricular dysfunction in patients with obstructive sleep apnea syndrome." *Int J Cardiovasc Acad*; 2021;7(1) 26-32.
26. Ikonomidis I, Pavlidis G, Thymis J, et al. Effects of glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter-2 inhibitors, and their combination on endothelial glycocalyx, arterial function, and myocardial work index in patients with type 2 diabetes mellitus after 12-month treatment. *J Am Heart Assoc;*. 2020;9(9).

How to cite this article: Dural İE, Sarı A, Ersoy İ. Effects of 3 months of treatment with empagliflozin on left ventricle global longitudinal strain and myocardial mechano-energetic effiency. *Echocardiography*. 2022;1-6.
https://doi.org/10.1111/echo.15424