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EMPAGLIFOZIN ON CARDIAC ENERGETICS AND FUNCTION

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Background Type 2 diabetes (T2D) is associated with an increased risk of heart failure (HF) and cardiovascular (CV) mortality. Sodium–glucose-cotransporter-2 (SGLT2) inhibitors reduce the risk of major adverse CV events and hospitalization for HF in T2D patients with high cardiovascular risk, despite only a modest improvement in glycaemic control. Restoring cellular energy homeostasis and reversing adverse cardiac remodelling in diabetes have been speculated as a potential metabolic modulatory effect of SGLT2 inhibitors leading to their beneficial CV outcomes. Myocardial energy deficient states can be detected non-invasively by 31-phosphorus magnetic resonance spectroscopy (31P-MRS).

Objectives Utilising cardiovascular magnetic resonance imaging (CMR) and 31P-MRS in a single centre longitudinal cohort study, we aimed to investigate the effects of the selective SGLT2 inhibitor empagliflozin on myocardial energetics, function, perfusion, and myocardial cellular volume in patients with T2D.

Methods Eighteen consecutive T2D patients who were commenced on empagliflozin in cardiometabolic optimisation clinics underwent CMR and 31P-MRS scans before and after twelve-week empagliflozin treatment, and plasma N-terminal

Abstract 154 Table 1 Changes in clinical parameters after empagliflozin treatment

Variable	Baseline (n=18)	Follow up (n=18)	P value
BMI, kg/m ²	29 ± 4	27 ± 4	0.09
Heart rate, bpm	66 ± 10	60 ± 9	0.02
Systolic blood pressure, mmHg	134 ± 13	120 ± 13	0.001
Diastolic blood pressure, mmHg	79 ± 7	74 ± 6	0.01
Hemoglobin, g/L	140 ± 17	142 ± 19	0.17
Haematocrit, L/L	0.43 ± 0.05	0.44 ± 0.05	0.03
Total cholesterol, mmol/L	4.4 ± 1.2	4.5 ± 1.5	0.6
HDL, mmol/L	1.36 ± 0.37	1.28 ± 0.35	0.06
LDL, mmol/L	2.31 ± 1.13	2.11 ± 1.23	0.3
TG, mmol/L	2.46 ± 1.63	2.32 ± 1.26	0.7
Creatinine, umol/L	77 ± 22	81 ± 19	0.4
eGFR, ml/min/1.73m ²	71 ± 37	70 ± 36	0.5
HBA1c, mmol/mol	60 ± 13	56 ± 9	0.3
Insulin, pmol/L	139 ± 126	175 ± 143	0.4
NT- proBNP, ng/L	199 [IQR:40-1289]	118 [IQR:58-409]	0.05
Medications			
Metformin, n (%)	15 (83)	15 (83)	1
Sulphonylurea, n (%)	2 (11)	2 (11)	1
Gliptin, n (%)	1 (6)	1 (6)	1
Thiazolidendiones, n (%)	0 (0)	0 (0)	1
Aspirin, n (%)	13 (72)	13 (72)	1
Statin, n (%)	18 (100)	18 (100)	1
ACEI, n (%)	12 (66)	12 (66)	1
ARB, n (%)	6 (33)	6 (33)	1

Values are means (SD) or median (IQR) for continuous variables and number (%) for categorical variables. BMI indicates body mass index; kg, kilograms; n, number; bpm, beats per minute; mmHg, millimeters of mercury; g/L, gram per Liter; HDL, high density lipoprotein; mmol/L, millimoles per litre; LDL, low density lipoprotein; TG, triglyceride; eGFR, estimated-glomerular filtration rate; ml/min/1.73m², millilitre per minute per (1.73square meters); pmol/L, picomoles per litre; NT-pro BNP, N-terminal pro hormone B-type natriuretic peptide; ACEI, Angiotensin converting enzyme inhibitor; ARB, Angiotensinreceptor blocker.

Abstract 154 Figure 1

Abstract 154 Table 2 Changes in CMR findings with empagliflozin treatment

Variable	Baseline (n=18)	Follow up (n=18)	P value
LV end diastolic volume (ml)	164 ± 50	149 ± 38	0.02
LV end diastolic volume index (ml/m ²)	86 ± 27	79 ± 21	0.02
LV end systolic volume (ml)	83 ± 45	65 ± 39	0.001
LV end systolic volume index (ml/m ²)	44 ± 25	35 ± 21	0.001
LV stroke volume (ml)	81 ± 20	84 ± 16	0.39
LV ejection fraction (%)	52 ± 13	59 ± 15	0.001
LV mass (g)	119 ± 33	109 ± 29	0.06
LV mass index (g/m ²)	61 ± 15	56 ± 12	0.07
LV mass to LV end diastolic volume (g/ml)	0.76 ± 0.27	0.75 ± 0.18	0.6
RV end diastolic volume (ml)	151 ± 34	155 ± 32	0.5
RV end diastolic volume index (ml/m ²)	79 ± 19	83 ± 24	0.3
RV end systolic volume (ml)	71 ± 25	76 ± 27	0.4
RV end systolic volume index (ml/m ²)	38 ± 15	41 ± 22	0.4
RV stroke volume (ml)	78 ± 11	80 ± 12	0.7
RV ejection fraction (%)	53 ± 9	53 ± 11	0.9
Peak circumferential strain (%)	-17.4 ± 4.1	-18.8 ± 4.9	0.3
Global longitudinal strain (%)	-10.2 ± 2.9	-13.1 ± 4.1	0.01
Peak diastolic circumferential strain rate (1/s)	1 ± 0.2	1.1 ± 0.3	0.4
Peak diastolic longitudinal strain rate (1/s)	0.7 ± 0.2	0.7 ± 0.2	0.9
LA maximum volume (ml)	63 ± 2	57 ± 17	0.2
LA ejection fraction (%)	48 ± 13	48 ± 15	0.2
Mean T1 (ms)	1285 ± 104	1310 ± 42	0.6
Extra-cellular volume (%)	24 ± 3	25 ± 3	0.1
Cell volume (ml/m ²)	92 ± 30	84 ± 27	0.04
MBF rest (ml/g/min)	0.62 ± 0.3	0.66 ± 0.3	0.4
MBF stress (ml/g/min)	1.6 ± 0.5	1.4 ± 0.3	0.08
MPRI	2.9 ± 1.5	2.3 ± 0.8	0.06

Values are means (SD) or median (IQR) for continuous variables and number (%) for categorical variables. LV indicates left ventricular; ml, milliliter; ml/m², milliliters per square meter of body surface area; g, gram; g/m², gram per square meter of body surface area; LVEF, left ventricular ejection fraction; RV, right ventricular; LA, left atrium; MBF, myocardial blood flow; ms, milliseconds; MPRI, myocardial perfusion index.

pro hormone B-type natriuretic peptide (NT-proBNP) levels were measured. (Table 1) Ten controls with no diabetes underwent an identical 31P-MRS and CMR protocol on a single visit.

Results When compared to controls, patients with T2D showed: lower myocardial energetics (1.52 ± 0.40 vs 2.20 ± 0.5 , $p=0.0005$), lower stress myocardial blood flow (1.60 ± 0.50 vs 2.10 ± 0.50 , $p=0.02$) and lower left ventricular ejection fraction ($52 \pm 13\%$ vs $63 \pm 4\%$, $p=0.01$). Treatment with empagliflozin led to significant improvements in myocardial energetics (PCr/ATP: 1.52 to 1.76, $p=0.009$). This was accompanied by a relative 13% improvement in left ventricular ejection fraction ($p=0.001$), 3% improvement in global longitudinal strain ($p=0.01$), 61% reduction in NTproBNP ($p=0.05$), and 9% reduction in myocardial cell volume ($p=0.04$). No significant change in myocardial blood flow or diastolic strain was detected (table 1).

Conclusions Empagliflozin improves myocardial energetics and function, reduces myocardial cellular volume, and reduces NT-proBNP levels in patients with T2D (figure 1). This study, by using the myocardial phosphocreatine to ATP ratio to monitor the early energetic response of the heart to treatment, and

CMR to monitor structural and functional changes, provides significant novel insights into potential mechanisms by which empagliflozin exerts its beneficial cardiovascular effects.

Conflict of Interest NONE

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PERICORONARY ADIPOSE TISSUE ATTENUATION, LOW ATTENUATION PLAQUE BURDEN AND 5-YEAR RISK OF MYOCARDIAL INFARCTION

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Introduction Pericoronary adipose tissue (PCAT) attenuation has emerged as a surrogate marker of pericoronary inflammation. To date, no studies have compared the impact of pericoronary adipose tissue (PCAT) attenuation and quantitative plaque burden on cardiac outcomes. We aimed to establish the relative merits of these approaches to risk prediction and hypothesised that the combination of PCAT attenuation and quantitative plaque burden measures could provide additive and improved prediction of myocardial infarction in patients with stable chest pain.

Methods In a post-hoc analysis of a randomized controlled trial, we investigated the association between the future risk of fatal or non-fatal myocardial infarction and PCAT attenuation measured from CT coronary angiography using multivariable Cox regression models including plaque burden, obstructive coronary disease and cardiac risk score

Abstract 155 Table 1 PCAT attenuation and quantitative plaque burden in patients with and without subsequent myocardial infarction

	No event	Event	p value
Plaque burden (%)	38.9 [0 to 49.2]	50.1 [43.0 to 53.8]	<0.001
Noncalcified plaque burden (%)	35.4 [0 to 45.3]	42 [37.39 to 48.95]	<0.001
Low-attenuation plaque burden (%)	4.1 [0 to 6.7]	7.4 [4.8 to 9.1]	<0.001
Calcified plaque burden (%)	0.39 [0 to 2.69]	3.18 [0.9 to 7.97]	<0.001
PCAT-RCA (HU)	-76.0 ± 7.8	-72.5 ± 8.3	0.009
PCAT-LAD (HU)	-77.0 ± 7.8	-76.2 ± 8.6	0.5432
PCAT-LCx (HU)	-73.3 ± 7.7	-71.6 ± 7.3	0.3345
Agatston CACS (Agatston Units)	19 [0 to 218]	283 [59 to 1041]	<0.001
Obstructive disease	416 (25%)	19 (51%)	<0.001
Cardiovascular risk score (%)	18 ± 11	22 ± 12	0.039

Median [interquartile interval], mean ± standard deviation or number (%).

CACS, coronary artery calcium score; HU, Hounsfield units; PCAT, Pericoronary adipose tissue attenuation.