Effect of Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors on Left Ventricular Remodelling and Longitudinal Strain: A Prospective Observational Study

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Abstract

Background: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) lower cardiovascular events in type 2 diabetes mellitus (T2DM) patients, although the mechanisms underlying these benefits are not clearly understood. Our aim was to study the effects of SGLT2i on left ventricular remodelling and longitudinal strain.

Methods: Between November 2019 and April 2020, we included 52 patients with T2DM ≥18 years old, with HbA1c between 6.5% and 10.0%, and estimated glomerular filtration ≥45 ml/min/1.73 m^2. Patients were classified into SGLT2i group and control group, according to prescribed treatment by their referring physician. Conventional and speckle tracking echocardiography were performed by blinded sonographers, at baseline and after 6 months of treatment.

Results: Among the 52 included patients (44% females, mean age 66.8±8.6 years, mean HbA1c was 7.40±0.7%), 30 patients were prescribed SGLT2i and 22 patients were classified as control group. Mean change in indexed left ventricular mass (LVM) was -10.85±3.31 g/m^2 (p=0.003) in the SGLT2i group, and +2.34±4.13 g/m^2 (p=0.58) in the control group. Absolute value of Global Longitudinal Strain (GLS) increased by a mean of 1.29±0.47 (p=0.011) in the SGLT2i group, and 0.40±0.62 (p=0.34) in the control group. We did not find correlations between changes in LVM and GLS, and other variables like change in HbA1c.

Conclusions: Among patients with T2DM, SGLT2i were associated with a significant reduction in indexed LVM and a significant increment in longitudinal strain measured by speckle tracking echocardiography, which may explain in part the clinical benefits found in clinical trials.

Background

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a recent and fast growing class of oral anti-hyperglycaemic agents available to treat patients with type 2 diabetes [1]. They function through a novel mechanism by reducing renal tubular glucose reabsorption, and produce a reduction in blood glucose without stimulating insulin release. When compared with other oral anti-hyperglycaemic agents, SGLT2 inhibitors have demonstrated non-inferiority along with additional metabolic benefits of weight loss and blood pressure lowering [2]. In addition, SGLT2 inhibitors have been shown to improve cardiovascular outcomes in type 2 diabetes mellitus (T2DM) trials [3–6]. The mechanisms underlying the clinical cardiovascular beneficial effects, especially on heart failure, are not fully understood and have been the subject of various studies and publications [7, 8].

Reverse ventricular remodelling refers to a “more-normal” chamber geometry restoration [9]. Several pharmacological treatments such as angiotensin-converting enzyme (ACE) inhibitors [10], beta-blockers [11, 12] and mineralcorticoid receptor antagonists [13], have been shown to promote reverse ventricular remodelling, with reductions in left ventricular mass (LVM) and volume and improved left ventricular systolic function. These changes are consistently associated with reductions in morbidity and mortality.

As a result, some authors advocate that reverse remodelling can serve as a valid surrogate endpoint for clinical outcomes in studies of new therapies [14].

Furthermore, Global Longitudinal Strain (GLS) determined by Speckle Tracking technique is a surrogate of left ventricular systolic function [15]. Clinical studies of the effects of SGLT2 inhibitors on myocardial deformation parameters are scarce [16, 17]. Although LV longitudinal strain was previously measured by cardiac magnetic resonance [18], to our knowledge, there are no studies estimating GLS by speckle tracking echocardiography in patients treated with SGLT2 inhibitors.

We hypothesised that the SGLT2 inhibitors effects on left ventricular remodelling may play a role in the underlying mechanisms through which SGLT2 inhibitors reduce the risk of heart failure in people with diabetes. Our aim was to study the effects of SGLT2 inhibitors on left ventricular remodelling and function in patients with T2DM. Our results might enable us to better understand how SGLT2 inhibitors influences cardiovascular outcomes in the clinical setting.

Methods

Study design and participants

This was a prospective observational study conducted in a single-centre in Jerez de la Frontera (Spain). Patients were recruited from the endocrinology outpatient department. Fifty-two consecutive diabetic patients with at least 18 years of age and glycated haemoglobin level between 6.5% and 10.0% were prospectively included between November 2019 and April 2020. The exclusion criteria were: a history of type 1 diabetes mellitus, current SGLT2 inhibitor or glucagon-like peptide receptor agonist use, an estimated glomerular filtration rate < 45 ml/min/1.73 m2, acute coronary syndrome the last 2 months, previous cardiac surgery, pregnant women, New York Heart Association IV symptoms of heart failure, greater than moderate valvular disease, or suboptimal echocardiographic acoustic window.

Clinical decisions on medical management were made by the referring physician based on clinical data and co-morbidities at baseline visit, according to current recommendations [19].

Data collection and follow-up

Clinical, anthropometric, analytical and echocardiographic assessments were performed at baseline and after 6 months of follow-up. Arterial blood pressure was also estimated during the initial visit. According to the prescribed treatment at this point, patients were classified into SGLT2 inhibitors group or control group. The same sonographers, who were blinded to clinical data, baseline echocardiographic data and prescribed treatment, performed both echocardiographic examinations.

Variables

The primary outcome endpoint was the change in ventricular remodelling and function between initial and follow-up echocardiographic assessment.

Standard echocardiographic examination

Two-dimensional transthoracic echocardiographic and Doppler studies were obtained with clinical ultrasound machines equipped with 2.5 to 3.5 MHz transducers (iE33 Phillips Medical Systems, The Best, The Netherlands). All tests were conducted by two experienced sonographers, who were blinded to the clinical data and prescribed treatment. Baseline echocardiographic examination was performed during the first 7 days after inclusion to the study.

Left ventricular chamber dimension and wall thicknesses were measured, and left ventricular mass was calculated according to the American Society of Echocardiography guidelines [20]. Left ventricular hypertrophy (LVH) was defined as indexed left ventricular mass of 95 g/m^2 or greater for women and 115 g/m^2 or greater for men [20]. The relative wall thickness (RWT) was calculated as the ratio of posterior wall thickness/left ventricular diastolic radius, independently of the presence of LVH. A ratio of 0.42 or greater indicated concentric left ventricular geometry. End-diastolic and end-systolic left ventricular volumes were estimated and left ventricular ejection fraction (EF) was assessed by the modified Simpson's Biplane Method. To assess diastolic function, the following mitral Doppler pulse and tissue Doppler variables were measured: early (E) and late (A) diastolic filling velocity, E/A ratio, septal (septal e') and lateral (lateral e') early mitral annular tissue velocity. We also calculated the E/e' ratio.

According to LVVi (cut off value 75 mL/m2), LVMi (cut off value 115 g/m2 in men and 95 g/m2 in women), and RWT, patients were classified into 8 geometric patterns. Normal ventricle was considered as normal LVMi, normal LVVi, and RWT between 0.32 and 0.42. Dilated and hypertrophied ventricles were classified, according to RWT, as eccentric hypertrophy (RWT < 0.32), mixed hypertrophy (RWT > 0.42), or dilated hypertrophy (RWT 0.32–0.42). Nondilated ventricles with RWT > 0.42 are categorized as having concentric remodelling or concentric hypertrophy, based on the value of LVMi. Dilated ventricles with normal LVMi and RWT < 0.32 are described as eccentric remodelling. Patients were classified into 8 geometric remodelling patterns according to the end-diastolic left ventricular volume (LVV) (cut-off value 75 ml/m^2), LVH and RWT [21] (Figure 1).

Strain analyses

Myocardial strain was measured using Speckle Tracking echocardiography. To assess LV, longitudinal strain the endocardial and epicardial borders were traced in the apical two-, three- and four-chamber echocardiographic view on an end-diastolic frame. The software then automatically divided the myocardium into 17 segments. Peak systolic strain was estimated for each segment, and then GLS was calculated from the average of the 17 segments values. All images were stored electronically and LV strain was analyzed off-line with 2D Speckle Tracking software (QLab 10).

Statistical analysis

Data were expressed as mean ± standard deviation for continuous variables, and were compared using the unpaired *t*-test. Categorical variables were expressed as percentages and were compared using chi-

square analysis or the Fisher exact test. Comparison of variables between baseline and 6 months after treatment were made using the paired test or Wilcoxon signed-rank test. Comparisons between changes in indexed LVM, GLS and other continuous variables were calculated by Pearson correlation.

Analyses followed an intention-to-treat approach, where all the patients were included in their corresponding group according to the initial prescribed treatment.

Differences were considered significant at p values<0.05. For data analysis, the statistical program SPSS version 20.0 (SPSS Inc., Chicago, Illinois) was used.

Results

Baseline characteristics

A total of 52 patients (29 males and 23 females) were included in the study after exclusion of 2 patients because of suboptimal acoustic window. Mean age of the patients was 66.8±8.6 years, mean duration of diabetes was 104±101 months, mean glycated haemoglobin was 7.40±0.7%. Of the participants, 65% had arterial hypertension, 13% were current smokers, 54% had dyslipidaemia, and 4 patients (8%) had coronary artery disease. At baseline, 29% were on DPP-4 inhibitors, 27% on insulin, 79% on metformin, 75% on RAAS inhibitors (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) and 9% on beta-blockers.

Of the total sample, 30 patients were prescribed SGLT2 inhibitors (67% empagliflozin, 17% dapagliflozin, 10% canagliflozin, 7% ertugliflozin), whilst the remaining 22 patients were included in the “control” group. Basal clinical characteristics of both groups are summarized in Table 1, and echocardiographic characteristics in Table 2. Patients prescribed SGLT2 inhibitors had significantly higher glycated haemoglobin and worse GLS, however, we did not find any other differences in basal characteristics between both groups.

Left ventricular remodelling was similar in both groups during the initial examination: concentric remodelling was the most frequent finding in the SGLT2 and control group (40.0% vs. 45.5%), concentric hypertrophy (27% vs. 27%) and normal geometry (23% vs. 27%).

Outcome

At 6-month visit, 3 patients in the SGLT2 group had stopped this treatment during the follow-up (one patient one month after the first visit and two patients 5 months after the baseline examination) because of minor side effects. SGL2 inhibitors were initiated in the control group, as indicated by their referring physician (1, 3 and 5 months after the initial assessment).

Mean change in the indexed LVM from baseline to the 6-month visit was -10.85±3.31 g/m^2 (p= 0.003) in the SGLT2 group, and +2.34±4.13 g/m^2 (p=0.58) in the control group (Figure 2). Absolute value of GLS increased by a mean of 1.29±0.47 (p=0.011) from baseline to the 6-month examination in the SGLT2

group, and 0.40±0.62 (p=0.34) in the control group (Figure 3). Table 3 and 4 summarize the changes from baseline to 6-month visit.

Ventricular remodelling classification did not change significantly in the control group after 6 months of follow-up. Nevertheless, 7 patients in the SGLT2 group changed from concentric hypertrophy to concentric remodelling due to a significant reduction in the indexed left ventricular mass (Figure 4 and 5), indicating that the concentric hypertrophy decreased during the follow-up (from 33% to 10%, p=0.006).

Glycated haemoglobin decreased in both groups: in SGLT2 patients from 7.8±0.9% at baseline, to 5.8±2.7% during the 6-month visit (-1.9±2.8%, p=0.001), in the control group from 6.9±1.0% to 5.9±2.5% (-1.0±2.5%, p=0.07).

Glomerular filtration did not change significantly in the control group (from 85.2±29.0 to 82.6±28.9, p=0.47), whilst there was a non-significant increase in patients treated with SGLT2 inhibitors (from 87.6±32.0 to 90.6±29.9, p=0.19).

We failed to find any correlations between changes in LVM, GLS, septal e' and other variables (Table 5).

Discussion

The main findings of this study were that the addition of SGLT2 inhibitors to standard anti-hyperglycaemic treatment in people with T2DM was associated with: 1) a significant decrease in indexed LVM; 2) an improvement in left ventricular GLS assessed by speckle tracking echocardiography.

Although SGLT2 inhibitors have demonstrated a reduction in heart failure outcomes [3–6], even in nondiabetic patients [22] mechanisms to explain the cardiovascular benefits of these drugs are not clearly understood. Our data support the theory that the benefits of SGLT2 inhibitors are, at least in part, mediated via a mechanism independent of its glucose-lowering activity.

LV hypertrophy is a strong determinant of cardiovascular outcomes and mortality in the general population [23] and also in people with T2DM [24]. Several studies showed previously significant reductions in LVM in mice with [25] and without T2DM [26, 27]. In clinical research, two small-sized-sample studies found that empagliflozin [28] and canagliflozin [29] reduced LVM, although these studies were not controlled by placebo. Verma et al [30] showed that mean LVM regression assessed by cardiac magnetic resonance after 6 months of treatment with empagliflozin in patients with coronary artery disease was 2.6 g/m^2. Similarly, treatment with dapagliflozin reduced LVM measured by cardiac resonance [31]. In our study, we found a higher reduction in LV hypertrophy, probably due to different inclusion criteria, higher baseline LVM and overestimation of LV hypertrophy by echocardiography [32].

LVM reduction supposed a change in ventricular remodelling classification in SGLT2 inhibitors patients that could have an impact on cardiovascular outcomes [33].

One of the strengths of our study was that, to our knowledge, this is the first clinical study to show an improvement in absolute value of GLS estimated by speckle tracking echocardiography in patients treated with SGLT2 inhibitors. Speckle tracking echocardiography is a relatively new method used to measure systolic myocardial function, with higher prognostic value than LV ejection fraction [15].

Several studies observed that diabetic patients have lower absolute GLS values despite normal LV ejection fraction [34, 35]. Other authors suggested that GLS by speckle tracking echocardiography may detect changes in systolic function earlier than conventional methods [36], which could explain why other studies did not find differences in LV ejection fraction in T2DM patients [28–30].

Garcia-Ropero et al [37] found that empagliflozin improved myocardial deformation estimated by speckle tracking echocardiography in an ischemic non-diabetic porcine model. However, clinical studies of the effects of SGLT2 inhibitors on myocardial deformation parameters are lacking. Tanaka et al [38] showed a GLS enhancement in patients treated with dapagliflozin, with similar results to our study, although this study was not a placebo-controlled one.

The mechanisms of the beneficial effects of SGLT2 inhibitors on cardiac remodelling and function are not completely understood. Improved glycaemic control and hypotensive effects seem unlikely, given that their benefits would have taken years. Other hypotheses like intravascular volume reduction, inhibition in the Na/H exchanger, tissue oxygenation improvement via increased haematocrit have been proposed [39]. It has also been postulated that SGLT2 inhibitors may increase myocardial energy supply and metabolic efficiency, thereby, improving myocardial performance. Santos-Gallego et al [40] showed that empagliflozin switched myocardial fuel utilization away from glucose towards other molecules like ketone bodies, free fatty acids and branched-chain amino acid that improved myocardial energetics.

Although other authors demonstrated that SGLT2 inhibitors improve diastolic function in T2DM patients [29, 41, 42] we achieved a significant improvement only on septal e' values, probably due to our reduced sample size.

In our opinion, our main limitation was the non-randomized design of our study that hampered the establishment of a cause-effect relationship between SGLT2 inhibitors and positive effects on LV mass and function. However, there is a biologic plausibility for a relation between our results and the positive clinical impact of SGLT2 inhibition on patients with heart failure and reduced ejection fraction both with and without T2DM [43]. Other limitations of our study were the short duration of the follow-up and the reduced number of patients. These limitations made it difficult to obtain statistically significant differences in other variables. However, despite the limited number of patients and relatively short follow-up, it seems that there are large differences in significant variables between the groups. Finally, although cardiac magnetic resonance is the gold standard for cardiac chambers volume and mass assessment, we preferred the use of echocardiography due to a more widespread use. On the other hand, one strength of the study was that it evaluated the effects of SGLT2 inhibitors on LV mass and function in real-world settings. It included a patient population that may be more representative of the non-selective population

normally used in randomised controlled trials and provided evidence that the treatment may exert positive effects in the every day practice.

Conclusions

The present study showed that T2DM patients treated with SGLT2 inhibitors displayed positive effects on left ventricular remodelling due to a reduction in LVM, and LV longitudinal function assessed by speckle tracking echocardiography. These findings could explain the beneficial effects on cardiovascular outcomes seen in clinical trials.

Abbreviations

GLS, global longitudinal strain; LVM, left ventricular mass; SGLT2, sodium-glucose contransporter 2; T2DM, type-2 diabetes mellitus.

Declarations

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Availability of data and materials

The datasets used/and analysed during the current study are available from the corresponding author on reasonable request.

Author's contributions

Study design, data collection, data analysis, interpretation of results, drafting of manuscript: Sergio Gamaza Chulián. Data collection, interpretation of results, reviewing the manuscript: Enrique Díaz Retamino. Data collection, database design, data analysis, reviewing the manuscript: Fátima González Testón. Data collection, reviewing the manuscript, major corrections to the manuscript: José Carlos Gaitero, María José Castillo, Raquel Alfaro, Elías Rodríguez. Reviewing the manuscript, major corrections to the manuscript: Jesús Oneto. Study design, data collection, interpretation of results, critical reviewing the manuscript: Antonio Martín Santana.

Ethics approval and consent to participate

The Ethics Committee of our institution (Hospital de Jerez de la Frontera) approved the study protocol used in this work. All the participants gave their consent to participate in the study.

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests.

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Tables

TABLE 1. Basal clinical characteristics in SGLT2i and control group.

Variable	SGLT2i (n=30)	Control (n=22)	*p* value
Female, n (%)	13 (43%)	10 (45%)	0.88
Age (years)	65.7±8.7	68.2±8.5	0.32
Arterial hypertension	18 (60%)	16 (73%)	0.34
Smokers	6 (20%)	1 (4%)	0.22
Dyslipidaemia	16 (53%)	12 (54%)	0.93
Coronary disease	3 (10%)	1 (4%)	0.33
Metformin	23 (77%)	18 (82%)	0.74
DPP4 inhibitors	8 (27%)	7 (32%)	0.68
Insulin	9 (30%)	5 (23%)	0.56
RAAS inhibitors	21 (70%)	17 (77%)	0.56
Beta-blockers	3 (10%)	2 (9%)	0.89
Aldosterone antagonist	2 (7%)	0 (0%)	0.50
GF≥60 ml/min/1.73 m^2	12 (43%)	11 (50%)	0.24
Glycated haemoglobin	7.78±0.94	6.97±0.44	0.002
Diabetes duration (months)	87±97	128±105	0.14
BMI (kg/m^2)	30.5±6.8	28.9±4.7	0.33
GF (ml/min/1.73 m^2)	92.6±40.8	86.7±28.9	

DPP4: Dipeptidyl peptidase-4; RAAS: Renin-angiotensin-aldosterone system; GF: Glomerular filtration; BMI: Body Mass Index.

TABLE 2. Basal echocardiographic characteristics in SGLT2i and control group.

Variable	SGLT2i (n=30)	Control (n=22)	*p* value
LV end-diastolic diameter (mm)	46.9±5.0	44.5±4.3	0.08
LV end-diastolic volume (ml)	103.3±40.0	97.0±25.7	0.52
LV indexed end-diastolic volume (ml/m^2)	52.6±18.9	50.2±9.7	0.59
LV end-systolic volume (ml)	40.7±26.5	33.9±8.5	0.19
LV ejection fraction (%)	62.9±8.2	64.6±5.8	0.43
LV ejection fraction<50%	2 (7%)	0 (0%)	0.50
E wave (cm/s)	72.2±25.5	64.2±19.7	0.22
A wave (cm/s)	82.8±18.9	87.5±19.2	0.41
LA indexed volume (ml/m^2)	31.9±9.8	28.7±9.1	0.23
Lateral e' (cm/s)	8.3±2.2	8.3±3.2	0.95
Septal e' (cm/s)	5.9±1.4	5.8±1.2	0.73
E/A ratio	0.83±0.39	0.81±0.26	0.80
E/e' ratio	10.5±3.6	9.8±2.4	0.40
LV indexed mass (g/m^2)	98.5±27.9	90.8±21.0	0.28
RWT	0.47±0.07	0.49±0.08	0.29
GLS	-17.8±2.9	-19.6±2.5	0.02

LV: Left ventricular; LA: Left Atrial; RWT: Relative Wall Thickness; GLS: Global Longitudinal Strain.

TABLE 3. Changes from baseline to 6-month visit in SGLT2 patients.

	Baseline	6-month	Δ from baseline	*p*
Indexed LVM (g/m^2)	98.5±27.9	87.6±18.4	-10.8±3.3	0.003
LV end-diastolic volume (ml)	103.3±40.0	100.8±34.0	-2.5±5.0	0.62
LV end-diastolic diameter (mm)	46.9±5.0	45.7±4.3	-1.2±0.67	0.09
LV ejection fraction (%)	62.9±8.2	62.6±8.4	-0.4±1.5	0.81
RWT	0.47±0.07	0.46±0.06	-0.01±0.01	0.44
GLS	-17.8±2.9	-19.1±3.1	1.29±0.47	0.01
LA indexed volume (ml/m^2)	31.9±9.8	31.2±9.9	-0.75±1.28	0.56
E/A ratio	0.81±0.39	0.92±0.52	0.10±0.05	0.07
Lateral e' (cm/s)	8.31±2.19	9.07±2.57	0.76±0.47	0.12
Septal e' (cm/s)	5.91±1.37	6.57±1.60	0.66±0.25	0.01
E/e' ratio	10.5±3.6	10.0±3.9	-0.52±0.53	0.34

LVM: Left Ventricular Mass; LV: Left Ventricular; RWT: Relative Wall Thickness; GLS: Global Longitudinal Strain; LA: Left Atrial.

TABLE 4. Changes from baseline to 6-month visit in control group.

	Baseline	6-month	Δ from baseline	*p*
Indexed LVM (g/m^2)	90.8±21.0	88.5±22.5	-2.3±4.1	0.58
LV end-diastolic volume (ml)	97.0±25.7	96.2±26.2	-0.8±4.7	0.86
LV end-diastolic diameter (mm)	44.5±4.3	45.0±4.2	0.4±0.8	0.57
LV ejection fraction (%)	64.6±5.8	64.4±4.6	-0.2±1.3	0.89
RWT	0.49±0.08	0.47±0.10	-0.02±0.02	0.35
GLS	-19.6±2.5	-20.0±2.4	-0.4±0.6	0.34
LA indexed volume (ml/m^2)	28.7±9.1	28.9±8.5	0.3±1.4	0.85
E/A ratio	0.81±0.26	0.73±0.20	-0.08±0.04	0.05
Lateral e' (cm/s)	8.26±3.24	8.35±2.35	0.09±0.73	0.90
Septal e' (cm/s)	5.78±1.22	5.95±1.26	0.16±0.23	0.48
E/e' ratio	9.79±2.44	9.10±2.36	-0.69±0.68	0.32

LVM: Left Ventricular Mass; LV: Left Ventricular; RWT: Relative Wall Thickness; GLS: Global Longitudinal Strain; LA: Left Atrial.

Table 5. Univariate correlates of change in indexed LVM, GLS and septal e' vs. baseline and changes in variables.

	Δ indexed LVM		**Δ GLS**		**Δ septal e'**	
Variable	r	*p*	r	*p*	r	*p*
Age (years)	-0.06	0.69	0.22	0.11	-0.11	0.46
Basal glycated haemoglobin	-0.16	0.25	-0.19	0.17	0.13	0.36
Δ glycated haemoglobin	-0.06	0.65	-0.10	0.46	0.23	0.08
Duration of diabetes (months)	0.01	0.92	-0.01	0.93	-0.18	0.21
GF (ml/min/1.73 m^2)	0.07	0.62	-0.26	0.06	0.23	0.12
Δ GF (ml/min/1.73 m^2)	-0.09	0.55	-0.04	0.78	0.15	0.36
SBP (mmHg)	-0.18	0.21	0.21	0.13	0.20	0.16
DBP (mmHg)	-0.12	0.39	-0.09	0.53	-0.07	0.63
LV ejection fraction (%)	-0.04	0.78	0.02	0.90	-0.03	0.82

LVM: Left Ventricular Mass; GLS: Global Longitudinal Strain; Δ: Change from baseline to 6-month visit; GF: Glomerular filtration; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LV: Left Ventricular

Figures

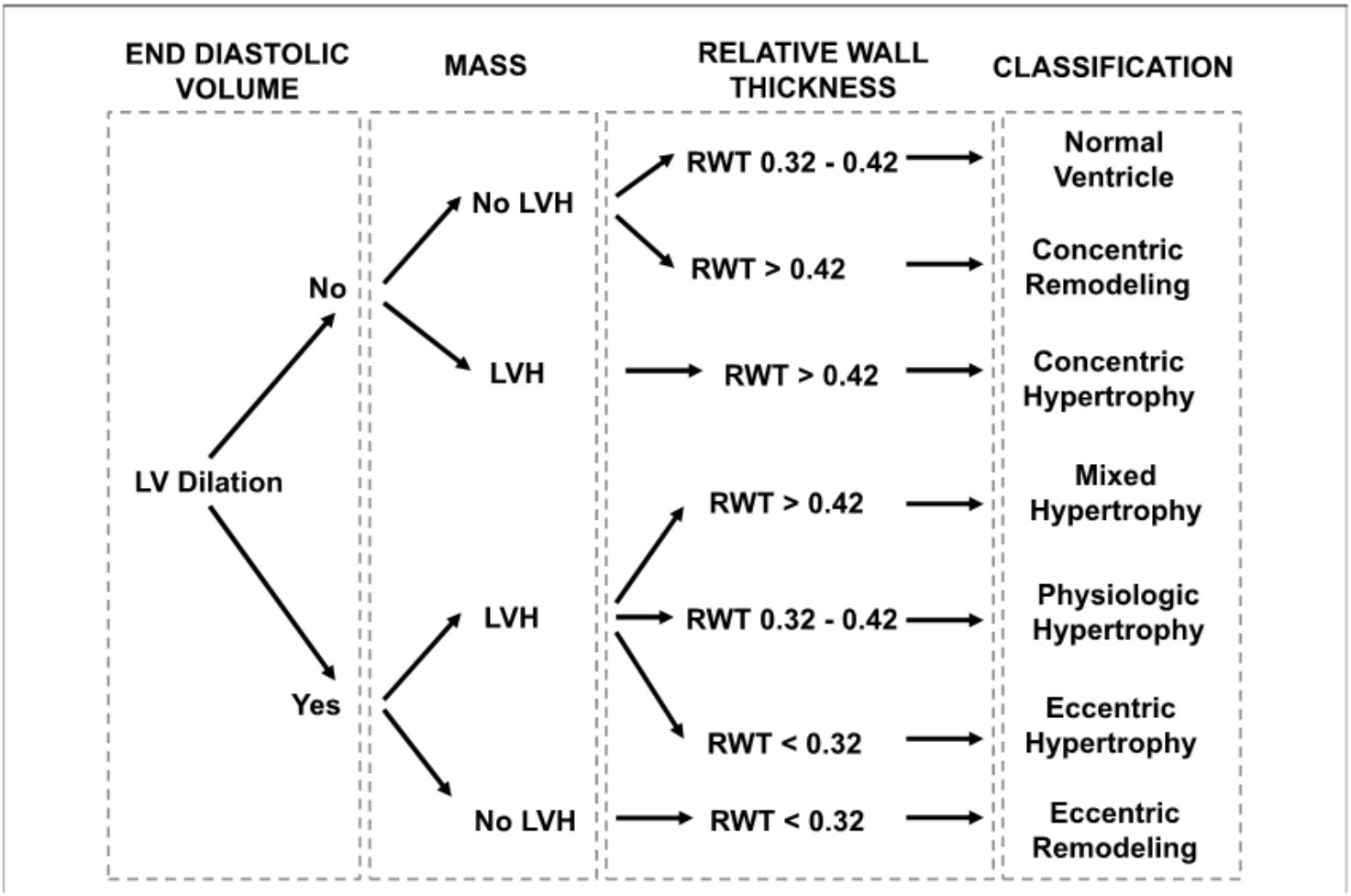

Figure 1

Left ventricular remodelling classification.

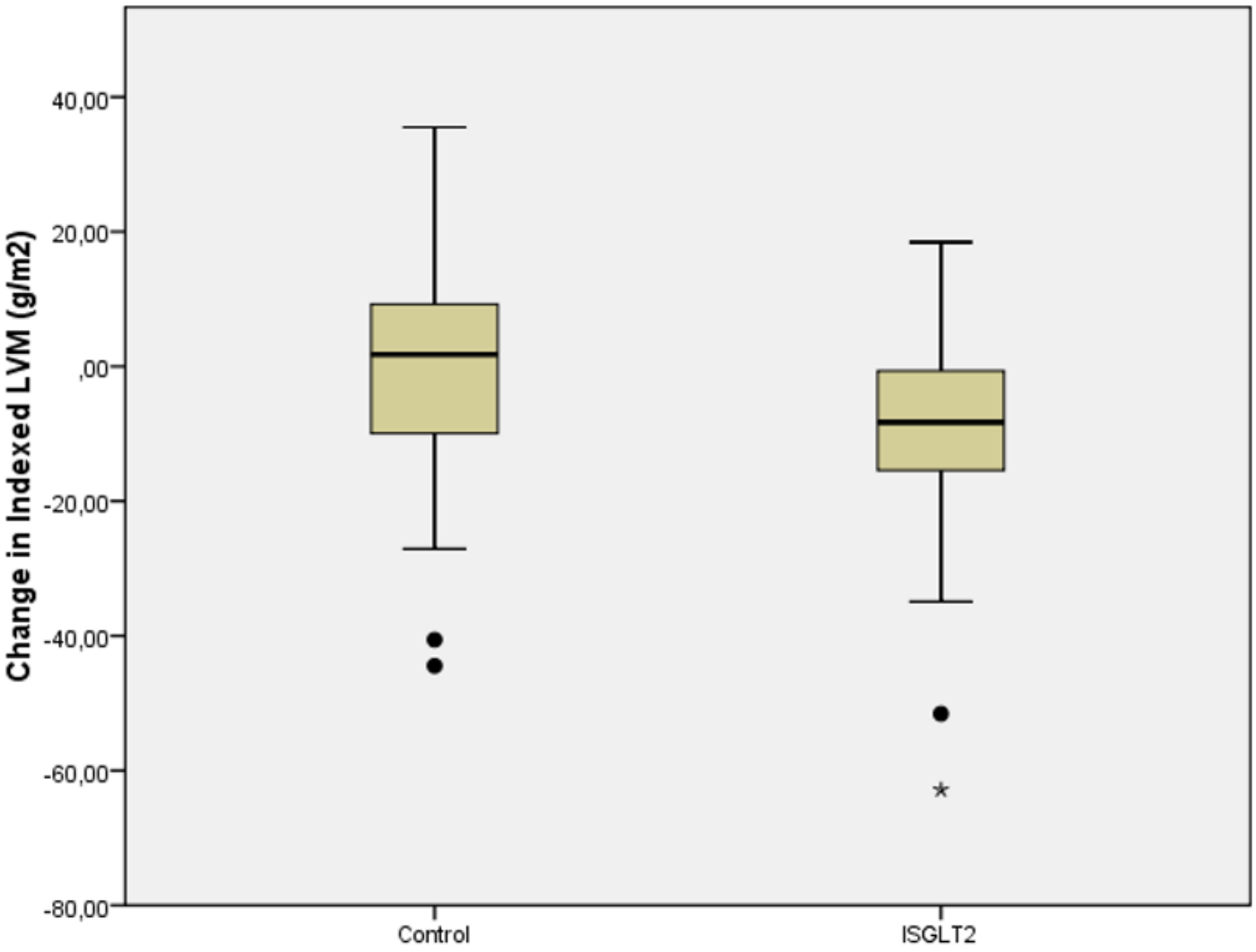

Figure 2

Change in indexed LVM from baseline to 6-month visit.

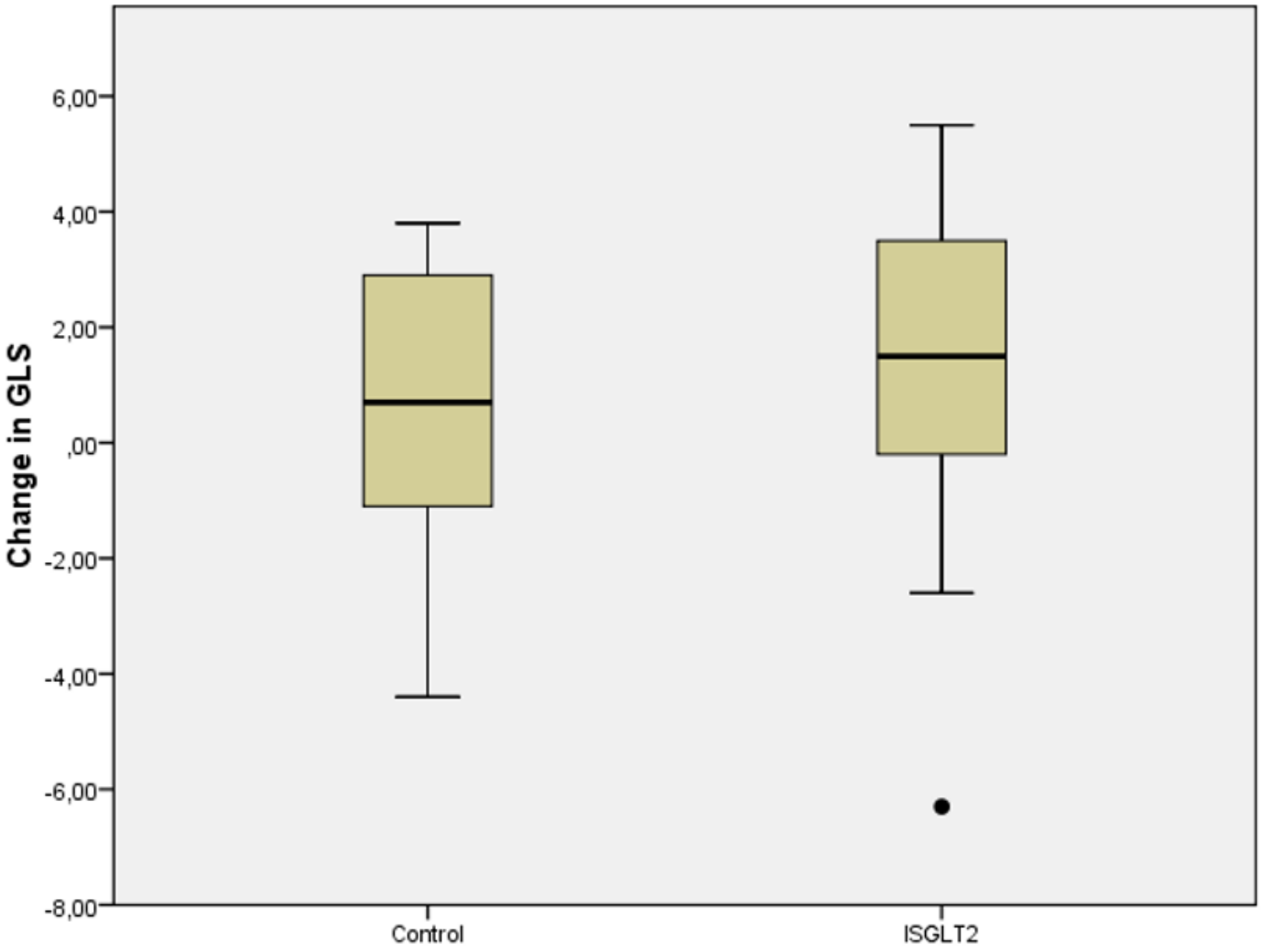

Figure 3

Change in GLS from baseline to 6-month visit.

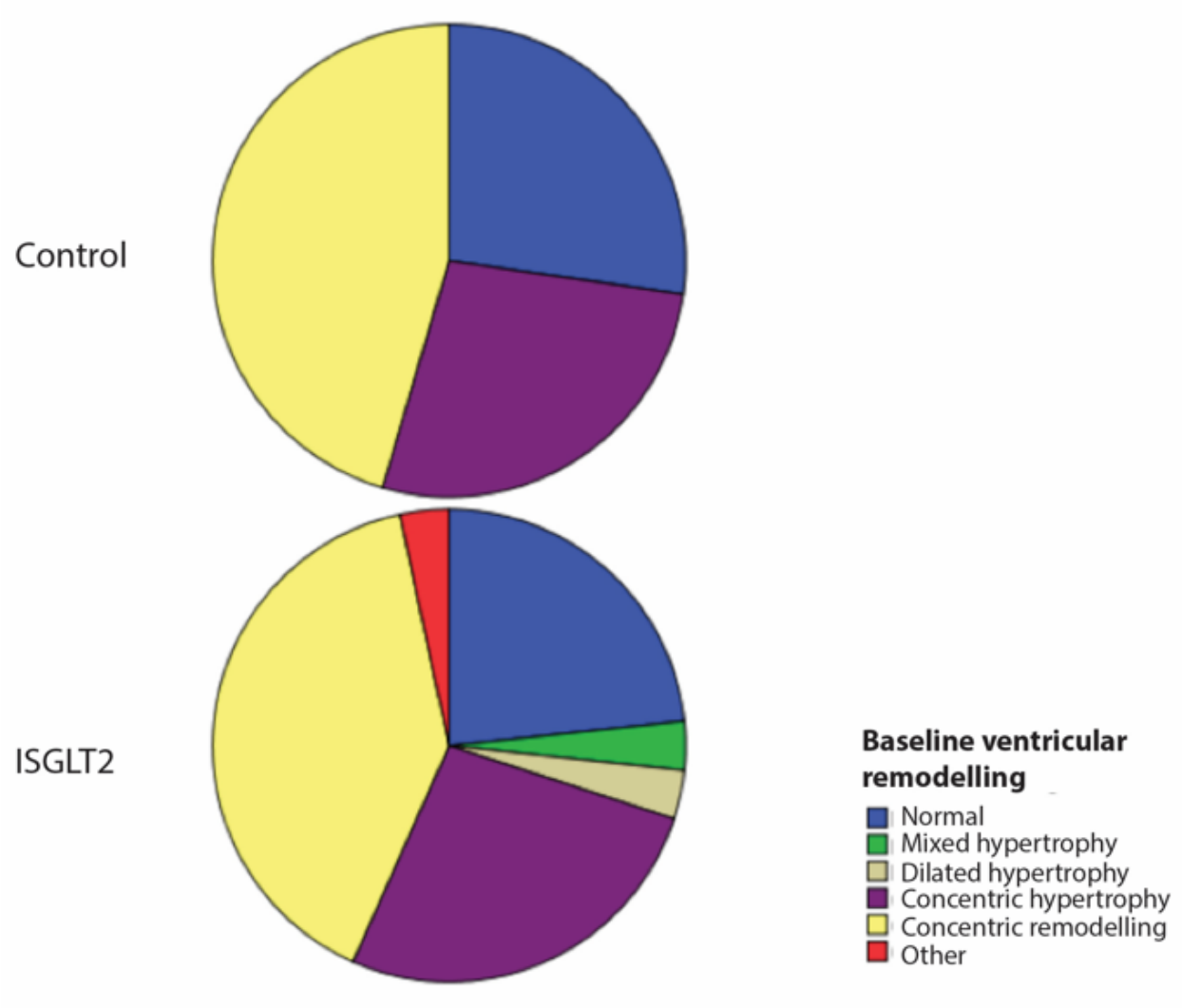

Figure 4

Baseline ventricular remodelling in control and SGLT2 groups.

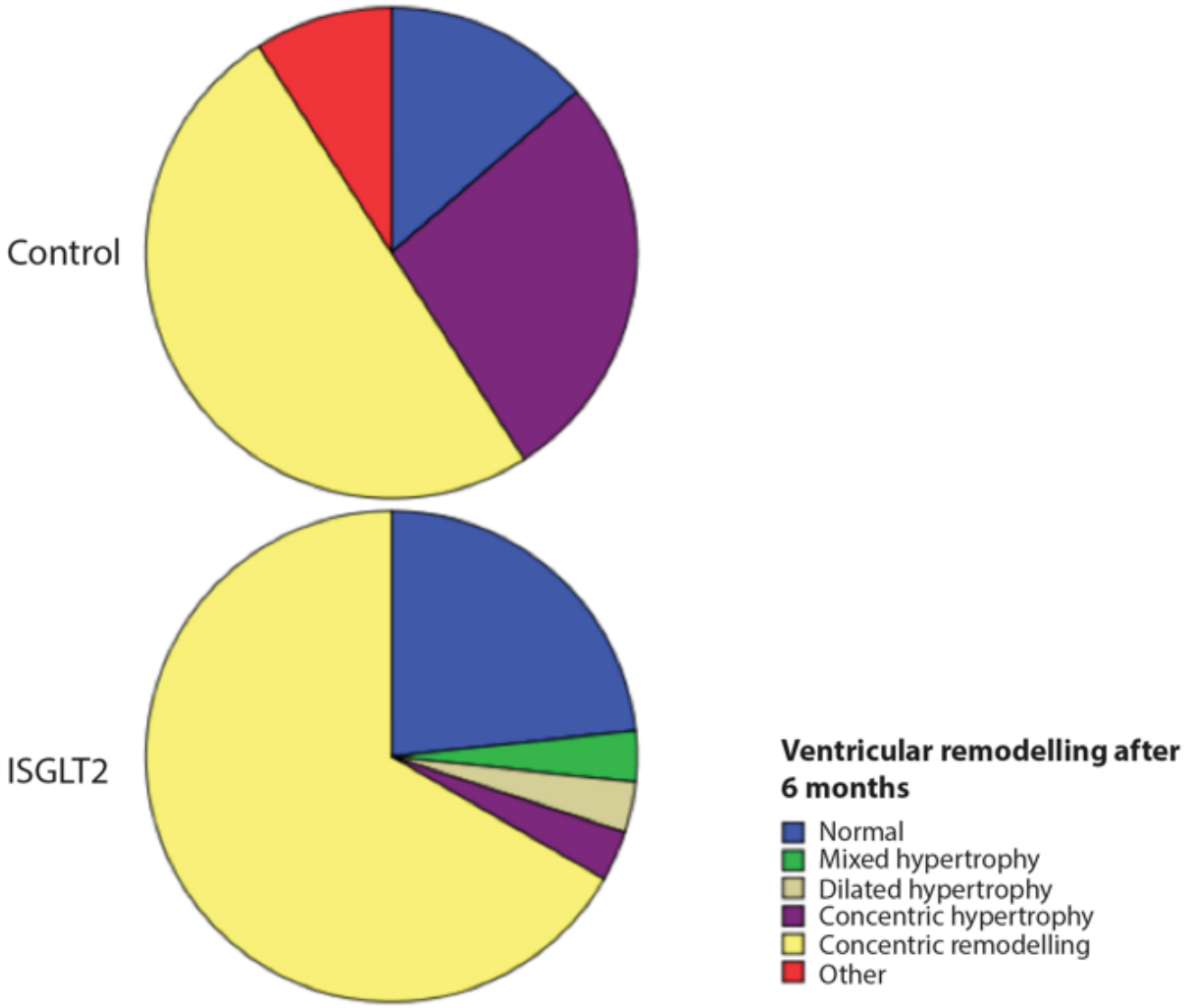

Figure 5

Ventricular remodelling after 6 months of follow-up in control and SGLT2 groups.