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Potential renoprotective effect of SGLT2 inhibitors against contrast-induced AKI in diabetic patients with STEMI undergoing primary PCI

Short title: SGLT2 inhibitors against contrast-induced acute kidney injury

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WHAT'S NEW?

Sodium glucose cotransporter 2 inhibitors (SGLT2i) are new generation of hypoglycemic drugs used in the treatment of patients with diabetes mellitus type 2 (T2DM). Several multicenter studies have demonstrated a significant reduction in the incidence of cardiovascular events, mortality rates, and worsening kidney disease in patients using SGLT2i. However, there is limited information available regarding the effect of SGLT2i on the incidence of contrast-induced acute kidney injury (CI-AKI) in patients undergoing primary percutaneous coronary intervention (pPCI). In our study, we investigated the potential protective effect of SGLT2i against CI-AKI in patients with ST-elevation myocardial infarction (STEMI) who underwent pPCI. This observation suggests a potential renoprotective role of SGLT2i in patients who had exposure to contrast media due to pPCI. The observed reduction in CI-AKI incidence highlights

the importance of further investigating the role of SGLT2i in renoprotection during PCI procedures.

ABSTRACT

Background: It has been demonstrated that there is a significant reduction in the incidence of cardiovascular events, mortality rates, and worsening kidney disease in patients using sodium glucose cotransporter 2 inhibitors (SGLT2i). However, there is limited information available regarding the effect of SGLT2i on the incidence of contrast-induced acute kidney injury (CI-AKI) in patients undergoing primary percutaneous intervention (pPCI).

Aims: Our research is focused on examining how SGLT2i exposure impact the occurrence of CI-AKI in patients with ST-elevation myocardial infarction (STEMI) and undergoing pPCI.

Results: This retrospective, single-center, case-control study included diabetic patients diagnosed with STEMI who underwent pPCI in a tertiary healthcare center between 2021 and 2022. Study population included patients with users of SGLT2i (n = 130) and patients with non-users of SGLT2i (n = 165). Inverse probability propensity score weighting and doubly robust estimation were performed to decrease bias and to balance covariate distribution for estimating average treatment for the treated. In doubly robust inverse probability weighted regression model in which covariates were balanced, CI-AKI risk was also found to be lower in SGLT2i user group (OR: 0.86 [0.76–0.98]; 95% CI; $P = 0.028$). In addition, ejection fraction, admission creatinine, albumin, volume of contrast media were found to be independent predictors of CI-AKI for patients presenting with STEMI and undergoing primary PCI.

Conclusion: Our study provides evidence supporting the potential protective effect of SGLT2i against CI-AKI in patients with diabetes presenting with STEMI and undergoing primary PCI.

Keywords: acute kidney injury, diabetes mellitus, primary percutaneous coronary intervention, renoprotection, SGLT2 inhibitor

INTRODUCTION

Primary percutaneous coronary intervention (pPCI) is a crucial treatment approach used in management of ST elevation myocardial infarction (STEMI), a severe and life-threatening manifestation of coronary artery disease (CAD) [1]. The main objective of pPCI is to minimize infarct size and reduce mortality rates associated with STEMI [1]. However, a proportion of patients with STEMI undergoing percutaneous coronary intervention procedures involving the use of contrast medium may experience acute kidney injury (AKI), specifically termed contrast-induced acute kidney injury (CI-AKI) [2]. CI-AKI ranks as the third most common cause of

hospital-acquired AKI [3]. The incidence of CI-AKI is closely related to the patient's baseline kidney function, the amount of contrast medium administered, the presence of diabetes, and pre-existing kidney disease. CI-AKI incidence can vary within a range from 1.3% to 33.3% [2]. However, this ratio is higher in diabetic patients contrast to general population [4, 5].

Sodium glucose cotransporter 2 inhibitors (SGLT2i) are new generation of hypoglycemic drugs used in the treatment of patients with diabetes mellitus type 2 (T2DM). These inhibitors function by specifically blocking the reabsorption of glucose in the renal tubules, leading to increased glucose excretion and lower blood glucose levels [6–8]. Several multicenter studies have demonstrated a significant reduction in the incidence of cardiovascular events, mortality rates, and worsening kidney disease in patients using SGLT2i [7–9]. However, there is limited information available regarding the effect of SGLT2i on the incidence of CI-AKI in patients undergoing pPCI. Therefore, our research is focused on examining how SGLT2i impact the occurrence of CI-AKI in patients with STEMI who are undergoing pPCI.

METHODS

Study design and population

This retrospective, single-center, case-control study included patients diagnosed with STEMI who underwent pPCI in Kartal Kosuyolu Heart and Research Hospital between 2021 and 2022. 1382 patients were reviewed and 295 patients were met the inclusion criteria. Study inclusion criteria were determined as having diabetes mellitus, having presented to the hospital with the complaint of chest pain in the first 12 hours of the onset of symptoms, and having been diagnosed with STEMI (Flowchart is shown in Figure 1). The study group was further divided into two subgroups: one comprised of patients who had been on SGLT2i including empagliflozin, dapagliflozin, and the other consisting of patients who had not been on SGLT2i. The exposure time of the medicine determined by electronical health records was at least 6 months prior pPCI. Study exclusion criteria were determined as having severe renal failure (estimated glomerular filtration rate <30 ml/min) at admission, having been treated with hemodialysis, history of CAD and history of insulin treatment. We excluded patients receiving insulin treatment to mitigate potential bias, as this group often presents with more advanced disease and its related complications, including severe kidney disease and atherosclerosis. Patients' baseline demographic, clinical characteristics and laboratory results were obtained from the hospital database. Patients' last laboratory results obtained from the national database before undergoing pPCI were used as baseline values. This study was conducted in accordance

with the Declaration of Helsinki and approved by Kartal Kosuyolu High Training and Research Hospital's Institutional Review Board.

Definitions

According to Kidney Disease Improving Global Outcomes (KDIGO) guidelines, CI-AKI is defined as a rise in creatinine level of ≥0.3 mg/dl (26.5 μmol/l) above the baseline value within 48 hours of contrast media exposure or an increase of at least 1.5 times the baseline value within 7 days [10].

Hypertension (HT) was defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg or the use of antihypertensive medications [11].

Hyperlipidemia was defined as total cholesterol levels >200 mg/dl, or low-density lipoprotein cholesterol (LDL-C) levels >116 mg/dl, or triglyceride levels >150 mg/dl, or the use of lipid-lowering drugs [12].

STEMI was defined as the presence of ST-segment elevation of at least 1 mm in two or more contiguous leads, with the exception of leads V1–V3, where the criteria for ST-segment elevation were ≥2 mm. In leads V3R, V4R and V7–V9, the ST-segment elevation was defined as at least 0.5 mm. Additionally, new onset left bundle branch block was included in the criteria for diagnosing STEMI. The manifestation of acute myocardial infarction was classified according to the Killip classification: Killip I, no evidence of heart failure; Killip II: heart failure; Killip III, severe heart failure or acute pulmonary edema; Killip IV, cardiogenic shock [1].

A diseased vessel was defined as the presence of a diameter stenosis exceeding 50% in major epicardial arteries. The coronary angiography was performed using a Siemens Artis floor angiography device. All patients underwent pPCI procedure for culprit lesion. Thrombolysis in myocardial infarction (TIMI) was defined as having the number of cine-frames needed for contrast to reach the standardized distal landmarks of coronary arteries. All patients were given aspirin, loading dose of ticagrelor or clopidogrel, and 70 U/kg unfractionated heparin before the procedure.

During hospitalization, all patients underwent postprocedural transthoracic echocardiography (Vivid 5 or Vivid 7; GE Vingmed Ultrasound AS, Horten, Norway). The left ventricular ejection fraction (LVEF) was calculated using the biplane Simpson method.

Statistical analysis and modelling

Normally distributed continuous data were expressed as mean and standard deviation values whereas non-normally distributed data were expressed as median and interquartile range, and categorical data were described as absolute and percentage values. Independent samples t-test and Mann–Whitney U test were used for the comparisons of independent continuous data groups, and Pearson's χ^2 or Fisher's exact test was used for the comparisons of categorical data groups.

In this study, inverse probability weighted propensity score weighting and doubly robust estimation were performed to decrease bias and to balance covariate distribution for estimating average treatment for the treated. Based on prior research and expert knowledge [13, 14], the following variables were chosen as covariates for the logistic regression analysis to assess the impact on the outcome condition being SGLT2i treatment: age, gender, hypertension, admission creatinine levels, prior use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACEI/ARB), previous use of metformin, and the number of prescribed oral antidiabetic drugs (OAD) excluding metformin. The probabilities derived from the model were utilized to compute stabilized inverse probability weights. These weights were subsequently applied to assess the impact of each individual's contribution to both AKI and the logistic regression model. Balance diagnostics of baseline covariates between treated and untreated subjects before and after propensity scoring were presented in terms of absolute standardized mean differences. Then, another regression modelling including confounders such as age, gender, hypertension, Killip class, ejection fraction, prior ACEI/ARB use, prior metformin use, SGLT2i, number of prescribed OAD's, albumin, admission creatinine, hemoglobin A1c and contrast media volume were applied for double robustness. Model's coefficient was represented using odds ratio (OR), and CI was determined as 95%.

For all statistical analyses, 2-tailed probability (*P*) values less than .05 were deemed to indicate statistical significance. All statistical analyses were performed using Jamovi and R 4.01 software (Vienna, Austria) with "ipw", "ggplot", "cobalt", "rms" packages.

RESULTS

The study population (n = 295) included patients with users of SGLT2i (n = 130) versus patients with non-users of SGLT2i (n = 165). Baseline clinic, demographic and peri-procedural characteristics in the whole population are shown in Table 1. The majority of users were on dapagliflozin (86, 66.15%). Dapagliflozin users all received a 10 mg dosage, while 7 (15.9%) of the empagliflozin users were prescribed 25 mg, and the remaining 37 (84.1%) were prescribed 10 mg. Mean age was higher in non-user of SGLT2i than in SGLT2i user group

(61.4 [9.0] years vs. 58.5 [9.6] years). Of 295 patients, 94 (31.7%) were female. While post PCI-LVEF was higher in non-user group of SGLT2i (P = 0.002); HT, hyperlipidemia, anterior STEMI, Killip 3 vs. 1–2, no-reflow and needing of re-coronary angiography were significantly higher in users of SGLT2i group. There were no differences in history of smoking, chronic obstructive pulmonary disease, peripheral artery disease, cerebrovascular disease, previous atrial fibrillation; total ischemic duration, post-TIMI flow, diseased vessel number, amount of contrast media, type of ADP_{P2Y12}, stent thrombosis, CI-AKI, cardiopulmonary resuscitation, ventricular tachycardia/fibrillation, requirement of intravenous inotropic treatment, intensive care unit duration, in-hospital duration and in-hospital mortality between groups.

The comparison of laboratory parameters according to exposure of SGLT2i was shown in Table 2. In non-users of SGLT2i group admission creatinine, peak creatinine and high-density lipoprotein cholesterol were significantly higher and glucose level at admission, glucose level at 24^{th} hour, total protein, albumin, uric acid, glycated hemoglobin (HbA1c), platelet count, total cholesterol, low-density lipoprotein cholesterol, triglyceride, total bilirubin and peak troponin were significantly lower than in users of SGLT2i group. The other intergroup comparisons of laboratory parameters are shown in Table 2.

Table 3 presents a comparison of the medications used in the study population. There were no significant differences between groups in terms of OAD use.

In non-weighted and adjusted multivariable logistic regression model, CI-AKI risk was found to be lower in SGLT2i user group (OR, 0.23 [0.092–0.579; 95 % CI; p = 0.001). Moreover, in the same model, volume of contrast media used and albumin were found to be independent predictors of CI-AKI for patients presenting with STEMI and undergoing pPCI (OR, 2.05 [1.30 – 3.23], 95% CI; P = 0.001) and OR, 2.23 (1.00–4.95, 95% CI; P = 0.048). Correspondingly, in doubly robust inverse probability weighted regression model in which covariates of HT, admission creatinine, gender, age, previous ACEI/ARB use, metformin use, and number of OADs were balanced (Figure 2 and 3), CI-AKI risk was also found to be lower in SGLT2i user group (OR, 0.86 [0.76–0.98], 95% CI; P = 0.028). In addition, LVEF and admission creatinine were found to be independent predictors of CI-AKI for patients presenting with STEMI and undergoing pPCI (OR, 0.99 [0.986–0.998], 95% CI; P = 0.021 and OR, 1.27 [1.10–1.48], 95% CI; P = 0.003) (Table 4).

DISCUSSION

In the contemporary cardiology practice, SGLT2i indications are growing after every single major clinical trial [15]. Treatment of T2DM, chronic renal disease (CKD), chronic heart failure

(HF) can be counted as the major indications of SGLTi [16]. Current guidelines support using SGLT2i after an ACS regardless of T2DM or HF regardless of LVEF to minimize the risk of worsening HF or CV mortality [1, 16, 17]. Beyond their glucose-lowering effects, these medications appear to have pleiotropic biological effects that cannot be solely attributed to the reduction of hyperglycemia. These effects include the reduction of cardiovascular mortality, hospitalizations due to HF, and significant renal outcomes. The distinctive mechanism of action, which involves enhanced renal glucose excretion resulting in a net energy loss, could also make SGLT2is appealing candidates for managing obesity, especially given their relationship with CAD and diabetes [18]. However, there is no sufficient data regarding the safety of using SGLT2i before and during the pPCI in diabetic STEMI patients who have high risk of CI-AKI. Our study represents the initial report of potential kidney-protective effects associated with SGLTi in this particular patient population.

In our study, we investigated the potential protective effect of SGLT2i against CI-AKI in patients with STEMI who underwent pPCI. Our findings revealed that among patients with T2DM presenting with STEMI for the first time, the incidence of CI-AKI after pPCI was similar between the group using SGLT2i and the group not using SGLT2i. However, we observed trends toward decreased risk of CI-AKI with SGLT2i use after propensity weighting.

This observation suggests a potential renoprotective role of SGLT2i in patients who had exposure to contrast media due to pPCI. The mechanism behind this protective effect may be multifaceted. SGLT2i have been previously shown to improve renal outcomes in patients with diabetes by promoting glycosuria, leading to reduced glucose and sodium reabsorption in the proximal tubules [15]. This diuretic effect may contribute for maintaining renal function during the critical period of contrast administration. Additionally, SGLT2i have been reported to have anti-inflammatory and anti-oxidative properties, which could counteract the pathways involved in CI-AKI development [19, 20]. The latest work by Huang et al. [21] showed that dapagliflozin, an SGLT2i, may ameliorate CI-AKI in vitro and *in vivo* by decreasing the hypoxia inducible factor (HIF)-1a/human epididymis protein 4 (HE4)/NF-κB signaling pathway [21].

Our study also demonstrated that the use of SGLT2i was associated with an approximately 20 % reduction in the odds of development of CI-AKI. This effect size is clinically relevant and consistent with prior research that has demonstrated that SGLT2i have cardiovascular and renal advantages in people with diabetes and cardiovascular disease [7–9]. Furthermore, our study provides valuable insights into the specific subset of T2DM patients undergoing pPCI, where the risk of CI-AKI is particularly pronounced.

Lately, multiple studies have presented some evidence indicating that SGLT2i do not raise the risk of AKI in patients diagnosed with T2DM or heart failure [22–24]. Additionally, some studies propose that initiating an SGLT2i is associated with a reduction in the AKI when compared to other glucose-lowering strategies [25, 26]. Moreover, SGLT2is have demonstrated a reduction in the odds of developing AKI in both randomized trials and real-world settings [27]. Nonetheless, there is a scarcity of studies investigating the impact of SGLT2i on the risk of CI-AKI in patients with CAD undergoing PCI. Our study, demonstrating a lower incidence of CI-AKI among individuals using SGLT2i, supports further evidence that SGLT2i may have a more significant potential protective effect on kidney function in patients undergoing PCI. Hua et al. demonstrated that the use of SGLT2i for more than 6 months prior to PCI provides renal protection in patients with T2DM [13]. This study is also supported by our findings, as our patients used the medication for at least 6 months prior to pPCI. Furthermore, investigating the use of SGLT2 inhibitors besides the conventional hydration therapies before coronary interventions in non-diabetic patients could be a subject of future research to assess whether the potential protective effects against contrast-induced damage persist.

The potential protective effect against CI-AKI reported in our investigation supports the safe use of SGLT2i before coronary interventions and eliminates the need for urge of withholding to decrease CI-AKI risk in diabetic STEMI patients. Not only in coronary interventions, but also in structural interventions such as transcatheter aortic valve implantation, AKI represents the most important predictor of post-procedural major adverse cardiovascular events and poor prognosis [28]. Therefore, investigating the use of SGLT2i in invasive cardiac procedures beyond coronary interventions could be a subject of future research to assess whether the potential protective effects against AKI prevails.

Limitations

Despite these promising results, some limitations should be acknowledged. First, the sample size was relatively small, which might have influenced the statistical power of our analyses. Further studies with larger cohorts are warranted to confirm our findings and explore potential subgroups that could benefit most from SGLT2i. Second, the specific SGLT2i agents and dosages used in our study varied among patients, and this heterogeneity might have influenced the outcomes. A comparative analysis of different SGLT2i would be valuable to identify potential differences in their renoprotective effects. Third, we did not have data regarding obesity status. Considering the association between obesity, CAD, and T2DM, data on body weight could have improved our analysis and results.

CONCLUSION

Our study provides evidence supporting the potential protective effect of SGLT2i against CI-AKI in patients with T2DM presenting with STEMI undergoing pPCI. The observed reduction in CI-AKI incidence highlights the importance of further investigating the role of SGLT2i in renoprotection during pPCI procedures.

Article information

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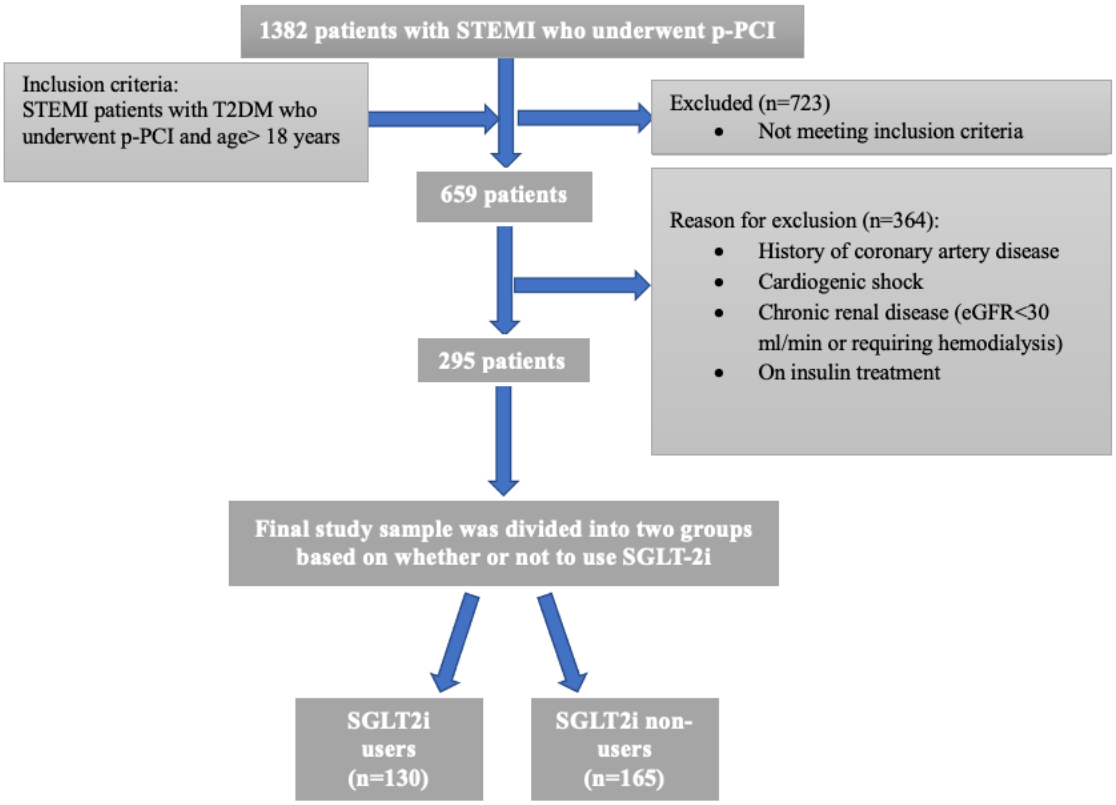

Figure 1. Consort flow diagram for inclusion to the study

Abbreviations: eGFR, estimated glomerular filtration rate; pPCI, primary percutaneous coronary intervention; SGLT2i, sodium glucose cotransporter 2 inhibitors; STEMI, ST-elevation myocardial infarction; T2DM, diabetes mellitus type 2

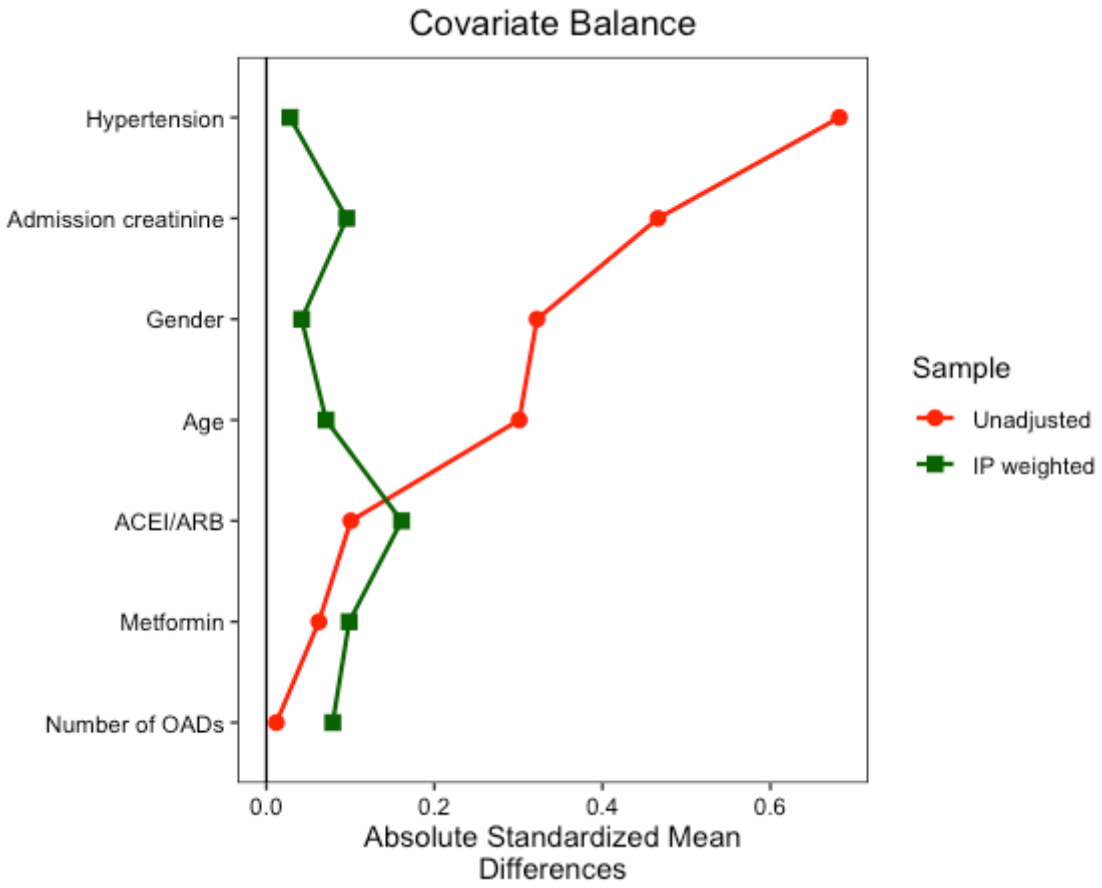

Figure 2. Covariate balancing after inverse probability (IP) weighting showed in absolute standardized mean differences

Abbreviation: OAD, oral antidiabetic drugs

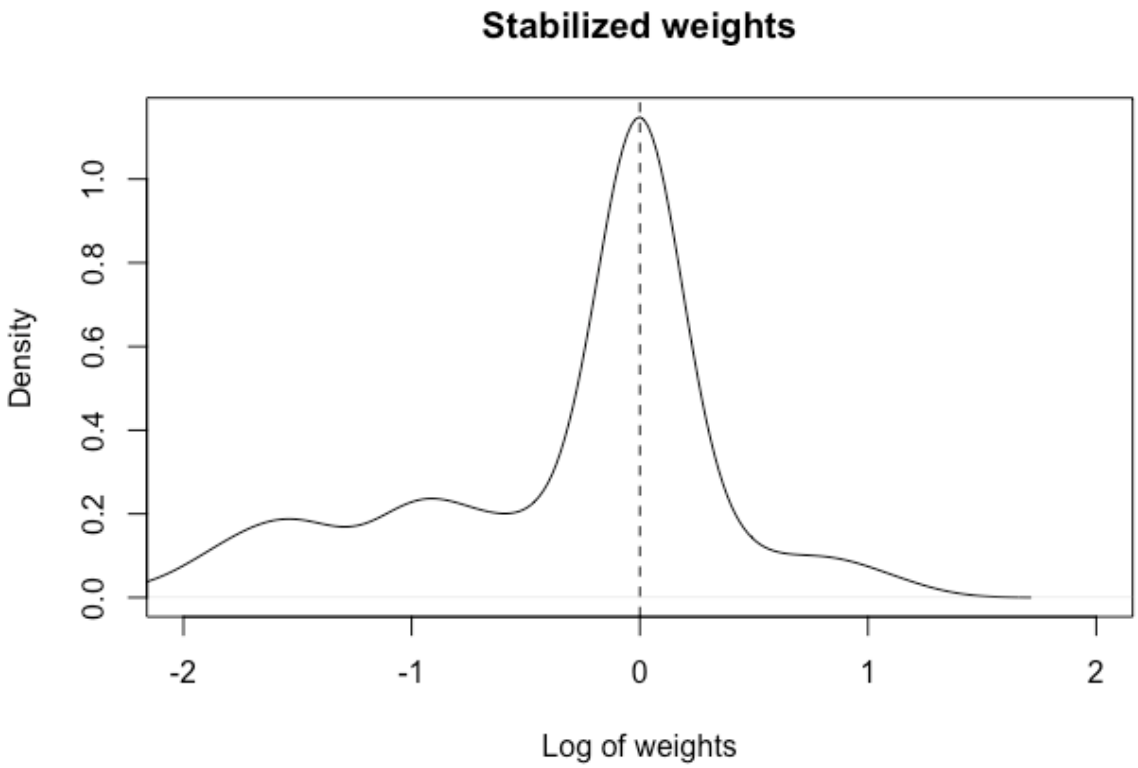

Figure 3. Stabilized weighting density plot between sodium glucose cotransporter 2 inhibitors user and non-user group

Table 1. Comparison of baseline clinical, demographic and peri-procedural characteristics of the study population according to use of SGLT2i

	Non-users of SGLT2i (n = 165)	**Users of SGLT2i (n = 130)**	***P*-value**
Demographic variables			
Age, years	61.4 (9.0)	58.5 (9.6)	**0.008**
Gender, male, n (%)	103 (62.4)	99 (76.1)	**0.012**
Smoking, n (%)	97 (58.8)	73 (56.2)	0.649
HT, n (%)	99 (60)	110 (84.6)	**<0.001**
COPD, n (%)	21 (12.7)	9 (6.9)	0.102
PAD, n (%)	13 (7.9)	14 (10.8)	0.393
CVD, n (%)	7 (4.2)	6 (4.6)	0.877
Hyperlipidemia, n (%)	61 (37)	76 (58.5)	**<0.001**
Previous AF, n (%)	13 (7.9)	8 (6.2)	0.567
CHA_2DS_2-VASc score	3.0 (2.0-4.0)	3.0 (3.0-4.0)	**0.021**
Procedural characteristics			
Type of ADP_{P2Y12}, n (%)			0.228
Clopidogrel	8 (4.8)	11 (8.5)	
Ticagrelor	155 (93.9)	115 (88.5)	
Prasugrel	2 (1.2)	4 (3.1)	
STEMI type, n (%) (Anterior STEMI)	35 (21.2)	60 (46.2)	**<0.001**
Killip 3 vs. 1–2, n (%)	3 (1.8)	14 (10.8)	**0.001**
Total ischemia duration, minutes	240 (120–600)	298.5 (174–556)	0.151
Diseased vessel number (>50% narrowing), n %			
1	67 (40.6)	55 (42.3)	0.668
2	65 (39.4)	54 (41.5)	
3	33 (20)	21 (16.2)	
Amount of contrast media, ml	265 (205–315)	290 (223.5–350)	0.122
No reflow, n (%)	16 (9.7)	23 (17.7)	**0.044**
Final TIMI flow, n (%)			
0	0	0	0.441
1	10 (6.1)	4 (3.1)	
2	16 (9.7)	11 (8.5)	

3	139 (84.2)	115 (88.5)	
Post-PCI characteristics			
Post PCI - EF	48 (42–57.5)	45 (37.5–55)	**0.002**
Need of re-CAG, n (%)	4 (2.4)	25 (19.2)	**<0.001**
Stent thrombosis, n (%)	2 (1.2)	4 (3.1)	0.411
CI-AKI, n (%)	41 (24.8)	22 (16.9)	0.099
CPR, n (%)	1 (0.6)	5 (3.8)	0.091
VT/VF, n (%)	7 (4.2)	5 (3.8)	0.864
Requirement of iv inotropic treatment, n (%)	6 (3.6)	13 (10)	0.027
In-hospital mortality, n (%)	4 (2.4)	4 (3.1)	0.735
Hemorrhagic events, n (%)	9 (5.5)	7 (5.4)	0.979
Needing of Transfusion, n (%)	1 (0.6)	3 (2.3)	0.324
ICU duration, hours	24 (18–34)	30 (24–36)	<0.001
In-hospital duration, days	4 (3–5)	4 (3–4)	0.746

Continuous variables are given as mean and standard deviation or median and interquartile range (25–75th)

Abbreviations: $ADP_{P2Y12,}$ adenosine diphosphate$_{P2Y12}$; AF, atrial fibrillation; CI-AKI, contrast induced acute kidney injury; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; CVD, cerebrovascular disease; HT, hypertension; ICU duration, intensive care unit duration; PAD, peripheral arterial disease; post-PCI EF, post-percutaneous coronary intervention ejection fraction; post-PCI TIMI flow, post-percutaneous coronary intervention thrombolysis in myocardial infarction flow; re-CAG, re-coronary angiography; STEMI, ST elevation myocardial infarction; VT/VF, ventricular tachycardia/ventricular fibrillation; other — see Figure 1

Table 2. Baseline laboratory variable comparison between users and non-users of SGLT2i

Variables	**Non-users of SGLT2i (n = 165)**	**Users of SGLT2i (n = 130)**	***P*-value**
Glucose at admission, mg/dl	168 (136–249)	202 (146–290.5)	**0.003**
Glucose at 24. hour, mg/dl	176 (130–222)	200.5 (158–282)	**<0.001**
Urea, mg/dl	25.7 (16–36.4)	26.5 (18–35)	0.801
Admission creatinine, mg/dl	0.84 (0.73–1.09)	0.80 (0.67–0.94)	**0.013**
Peak creatinine, mg/dl	0.95 (0.80–1.26)	0.88 (0.77–1.03)	**0.002**
Total protein, g/dl	6.3 (5.8–6.9)	7.3 (6.7–7.7)	**<0.001**
Albumin, g/l	3.9 (3.6–4.1)	4.1 (3.8–4.3)	**<0.001**
CRP, mg/l	5.6 (2.5–13.8)	6 (2.7–21.3)	0.517
Uric acid, mg/dl	5.6 (4.4–6.7)	6.3 (5.1–7.0)	**<0.001**

HbA1c, %	7.2 (6.5–8.6)	8.6 (7.1–10.3)	**<0.001**
WBC count, 10^3/μl	9.9 (8.6–12)	10.5 (8.1–14.9)	0.100
Hb, g/dl	13.3 (12.4–14.7)	13.8 (12.5–14.9)	0.433
Platelet count, 10^3/μl	245 (211.5–280)	295 (228–404.5)	**<0.001**
Neutrophil count, 10^3/μl	6.9 (5.6–9.1)	7.4 (5.1–11)	0.261
Lymphocyte count, 10^3/μl	2 (1.3–2.7)	2 (1.5–2.2)	**0.039**
Total Cholesterol, mg/dl	164 (146–206)	195.2 (161.4–220.9)	**<0.001**
HDL-C, mg/dl	35 (32–43)	21 (15.5–29)	**<0.001**
LDL-C, mg/dl	119 (89–142)	126 (101–154.2)	**0.024**
Triglyceride, mg/dl	161 (111–244.5)	194.5 (131.7–227)	**0.028**
Total bilirubin, mg/dl	0.49 (0.35–0.80)	0.90 (0.60–1.0)	**<0.001**
TSH, μIU/l	1.52 (0.84–3.04)	1.1 (1.0–1.5)	0.077
Peak troponin, ng/ml	0.8 (0.3–3.1)	3.4 (1.2–7.0)	**<0.001**

Continuous variables are given as mean and standard deviation or median and interquartile range (25–75th)

Abbreviations:

Hb, hemoglobin; CRP, C-reactive protein; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein; TSH, thyroid-stimulating hormone; WBC, white blood cell; other — see Figure 1

Table 3. Comparison of medications used in the study population.

Variables	**Non-users of SGLT2i (n = 165)**	**Users of SGLT2i (n = 130)**	***P*-value**
ACEI/ARB, n (%)	124 (75.2)	103 (79.2)	0.409
Metformin, n (%)	116 (70.3)	95 (73.1)	0.600
DPP4i, n (%)	57 (34.5)	52 (40)	0.335
GLP-1RAs, n (%)	0 (0)	1 (0.8)	0.441
Sulfonylurea, n (%)	28 (17)	15 (11.5)	0.189
Number of drugs excluding metformin, n (%)			0.597
0	91 (55.2)	74 (56.9)	
1	63 (38.2)	44 (33.8)	
2	11 (6.7)	12 (9.2)	

Abbreviations: ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers; DPP4-I, dipeptidyl peptidase 4 inhibitors; GLP-1Ras, glucagon like peptide-1 receptor agonists; other — see Figure 1

Table 4. Inverse probability weighted model of multivariable logistic regression analysis.

	Inverse probability weighted model		
Variables	**Odds ratio**	**95% CI**	***P*-value**
Age	0.999	0.995–1.003	0.721
Gender	0.873	0.765–0.995	0.052
HT	0.922	0.812–1.047	0.223
Killip class	1.221	0.959–1.554	0.114
Post PCI-EF	0.992	0.986–0.998	0.021
Albumin	1.072	0.906–1.269	0.419
Admission creatinine	1.274	1.099–1.476	0.003
HbA1c	1.028	0.985–1.072	0.208
Contrast volume (per 100 mL)	1.059	0.998–1.123	0.065
ACEI/ARB	0.891	0.773–1.026	0.121
Metformin	1.125	1.028–1.231	0.015
SGLT2i	0.863	0.762–0.978	0.028
Number of OADs	0.943	0.885–1.006	0.088

Abbreviationd: see Tables 1, 2, 3 and Figure 2