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

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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 about 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 was focused on examining how SGLT2i exposure impacts CI-AKI occurrence in patients with ST-segment 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. The study population included SGLT2i users (n = 130) and non-SGLT2i users (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 those treated. In a doubly robust inverse probability weighted regression model, in which covariates were balanced, CI-AKI risk was also found to be lower in the SGLT2i-user group (OR: 0.86 [0.76–0.98]; 95% CI; $P = 0.028$). In addition, ejection fraction, admission creatinine, albumin, and volume of contrast media were found to be independent predictors of CI-AKI in patients presenting with STEMI and undergoing pPCI.

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

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

INTRODUCTION

Primary percutaneous coronary intervention (pPCI) is a crucial treatment used in management of ST-segment 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 STEMI-related mortality rates [1]. However, a proportion of STEMI patients undergoing percutaneous coronary intervention procedures involving the use of contrast medium may experience acute kidney injury (AKI), so-called 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, amount of contrast medium administered, presence of diabetes, and pre-existing kidney disease. CI-AKI incidence can vary from

WHAT'S NEW?

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are a new generation of hypoglycemic drugs used in the treatment of patients with type 2 diabetes mellitus (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 about 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-segment elevation myocardial infarction (STEMI) who underwent pPCI. Our findings suggest a potential renoprotective role of SGLT2i in patients who were exposed to contrast media due to pPCI. The observed reduction in CI-AKI incidence highlights the importance of further investigation of the role of SGLT2i in renoprotection during PCI procedures.

1.3% to 33.3% [2]. However, this ratio is higher in diabetic patients compared to the general population [4, 5].

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are a new generation of hypoglycemic drugs used in the treatment of patients with type 2 diabetes mellitus (T2DM). These inhibitors function by specifically blocking 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 about the effect of SGLT2i on the incidence of CI-AKI in patients undergoing pPCI. Therefore, our research was focused on examining how SGLT2i impact CI-AKI occurrence in STEMI patients 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. In total, 1382 patients were reviewed, and 295 patients met the inclusion criteria. Study inclusion criteria were determined as patients with diabetes mellitus, who presented in the hospital with chest pain in the first 12 hours from the onset of symptoms, and who were diagnosed with STEMI (flowchart is shown in Figure 1). The study group was further divided into two subgroups: one with patients who had been on SGLT2i, including empagliflozin and dapagliflozin, and the other with patients who had not been on SGLT2i. The exposure time to the medicine, determined by electronic health records, had to last at least 6 months before pPCI. Study exclusion criteria were severe renal failure (estimated glomerular filtration rate <30 ml/min/1.73 m^2) on admission, having been treated with hemodialysis, history of CAD, and history of treatment with insulin. 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. Their 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 the 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 above the baseline value within 7 days [10].

Hypertension (HT) was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥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, except for 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, a 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 stenotic diameter exceeding 50% in major epicardial arteries. Coronary angiography was performed using a Siemens Artis floor angiography device. All patients underwent a pPCI procedure for culprit lesions. 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, a loading dose of ticagrelor or clopidogrel, and 70 U/kg unfractionated heparin before the procedure.

During hospitalization, all patients underwent post-procedural transthoracic echocardiography (Vivid 5 or

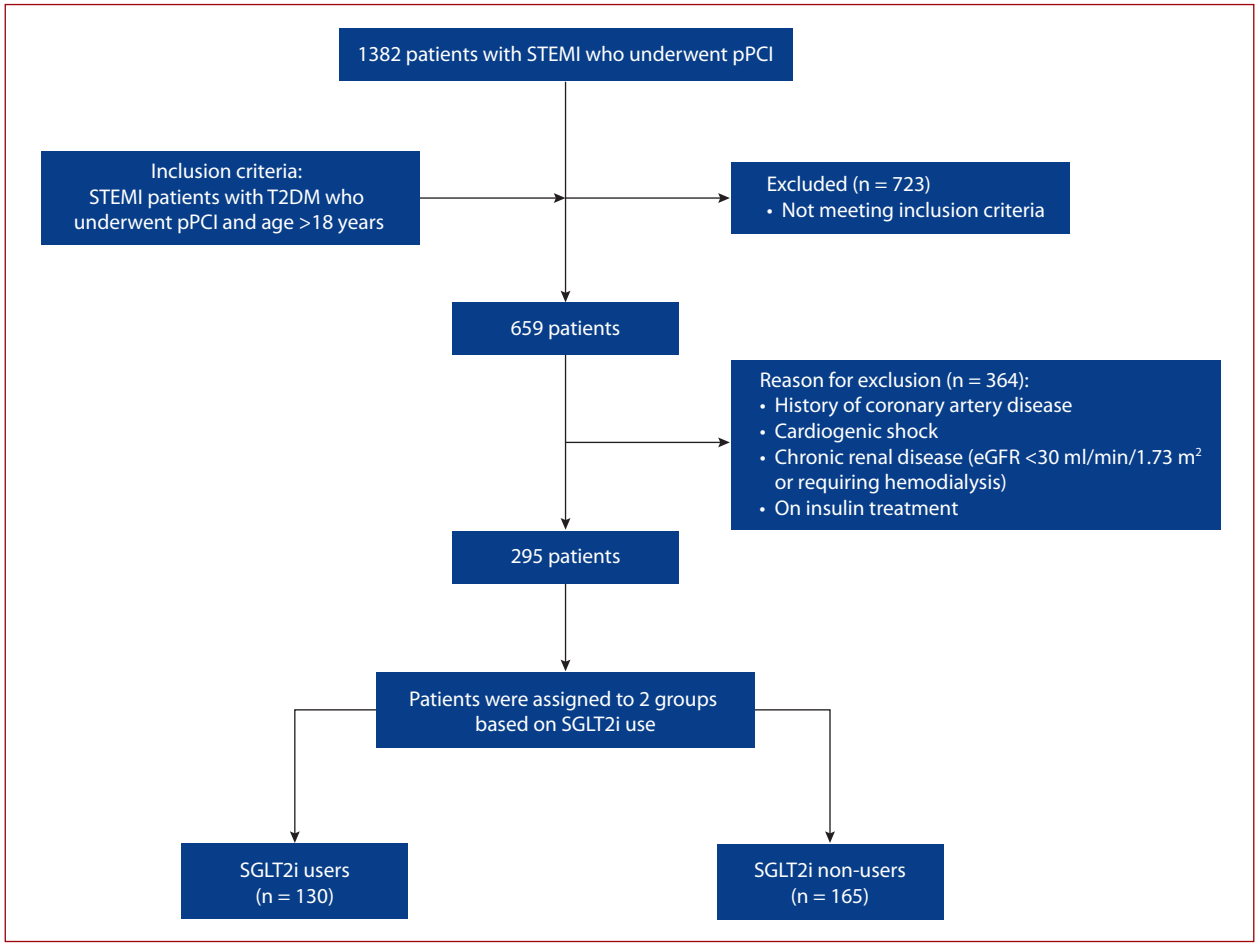

Figure 1. Consort flow diagram for inclusion in the study

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

Vivid 7; GE Vingmed Ultrasound AS, Horten, Norway). Left ventricular ejection fraction (LVEF) was calculated using the biplane Simpson method.

Statistical analysis and modeling

Normally distributed continuous data were expressed as mean and standard deviation values, whereas non-normally distributed data were expressed as medians and interquartile ranges, and categorical data were described as absolute and percentage values. Independent samples t-test and Mann-Whitney U test were used for comparisons of independent continuous data groups, and Pearson χ^2 or Fisher's exact tests were used for 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 those treated. Based on prior research and expert knowledge [13, 14], the following variables were chosen as covariates for logistic regression analysis to assess the impact on the outcome: SGLT2i treatment, age, sex, 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 model, including confounders such as age, sex, hypertension, Killip class, ejection fraction, prior ACEI/ARB use, prior metformin use, SGLT2i, number of prescribed OADs, albumin, admission creatinine, hemoglobin A1c, and contrast media volume was applied for double robustness. The model's coefficient was represented using odds ratio (OR), and CI was determined as 95%.

For all statistical analyses, 2-tailed probability (*P*) values of less than 0.05 were deemed to indicate statistical significance. All statistical analyses were performed using Jamovi and R 4.01 software (Vienna, Austria) with "ipw", "ggplot", "cobalt", and "rms" packages.

Table 1. Comparison of baseline clinical, demographic, and peri-procedural characteristics of the study population according to sodium-glucose cotransporter 2 inhibitors (SGLT2i) use

	Non-SGLT2i users (n = 165)	SGLT2i users (n = 130)	*P*-value
Demographic variables			
Age, years	61.4 (9.0)	58.5 (9.6)	0.008
Sex, 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 III vs. I–II, 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 for 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 for intravenous 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
Need for transfusion, n (%)	1 (0.6)	3 (2.3)	0.324
ICU stay duration, hours	24 (18–34)	30 (24–36)	<0.001
In-hospital stay duration, days	4 (3–5)	4 (3–4)	0.746

Continuous variables are given as means and standard deviations or medians and interquartile ranges ($25–75^{th}$)

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, intensive care unit; 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-segment elevation myocardial infarction; VT/VF, ventricular tachycardia/ventricular fibrillation; other — see Figure 1

RESULTS

The study population (n = 295) included SGLT2i users (n = 130) and non-users (n = 165). Baseline clinical, 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. The mean age was higher in non-users than in the 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 the non-user group ($P = 0.002$); HT, hyperlipidemia, anterior STEMI, Killip III vs. I–II, no-reflow, and need for re-coronary angiography were significantly more frequent in the SGLT2i-user group. There were no differences in the 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} (type of antiplatelet agent), stent throm-

Table 2. Comparison of baseline laboratory variables between sodium-glucose cotransporter 2 inhibitors (SGLT2i) users and non-users

Variables	Non-SGLT2i users (n = 165)	SGLT2i users (n = 130)	*P*-value
Glucose on admission, mg/dl	168 (136–249)	202 (146–290.5)	0.003
Glucose at 24 hours, 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 means and standard deviations or medians and interquartile ranges (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-SGLT2i users (n = 165)	SGLT2i users (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	91 (55.2)	74 (56.9)	
1	63 (38.2)	44 (33.8)	
2	11 (6.7)	12 (9.2)	0.597

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

bosis, CI-AKI, cardiopulmonary resuscitation, ventricular tachycardia/fibrillation, requirement of intravenous inotropic treatment, intensive care unit duration, duration of hospital stay, and in-hospital mortality between groups.

A comparison of laboratory parameters according to SGLT2i exposure is shown in Table 2. In the group of non-SGLT2i users, admission creatinine, peak creatinine, and high-density lipoprotein cholesterol levels were significantly higher. Glucose level on admission, glucose level at 24th hour, total protein, albumin, uric acid, glycated hemoglobin (HbA1c), total cholesterol, LDL-C, triglyceride, total bilirubin, and peak troponin levels as well as platelet count were significantly lower than in SGLT2i users. 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 the non-weighted and adjusted multivariable logistic regression model, CI-AKI risk was found to be lower in the SGLT2i-user group (OR, 0.23 [0.092–0.579; 95% CI; P = 0.001). Moreover, in the same model, the volume of contrast media used and albumin were found to be independent predictors of CI-AKI in 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 the doubly robust inverse probability weighted regression model, in which HT covariates, admission creatinine, sex, age, previous ACEI/ARB use, metformin use, and number of OADs were balanced (Figures 2 and 3), CI-AKI risk was also found to be lower in the 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 in patients presenting with STEMI and undergoing pPCI (OR, 0.99 [0.986–0.998], 95%

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

Variables	Inverse probability weighted model		
	Odds ratio	95% CI	*P*-value
Age	0.999	0.995–1.003	0.721
Sex	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

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

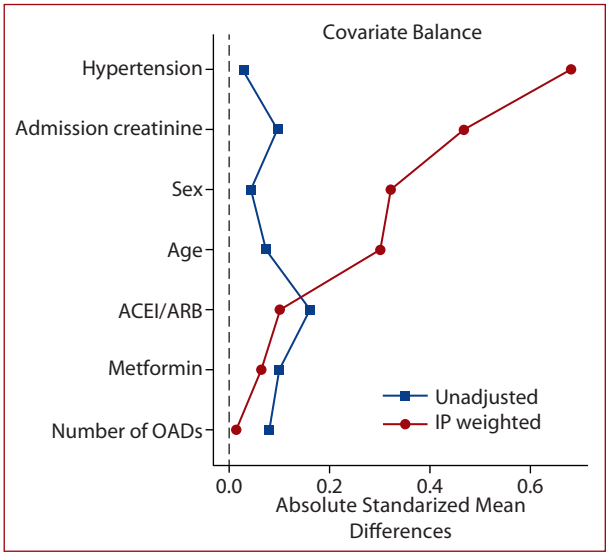

Figure 2. Covariate balancing after inverse probability (IP) weighting shown as absolute standardized mean differences

Abbreviations: OAD, oral antidiabetic drugs

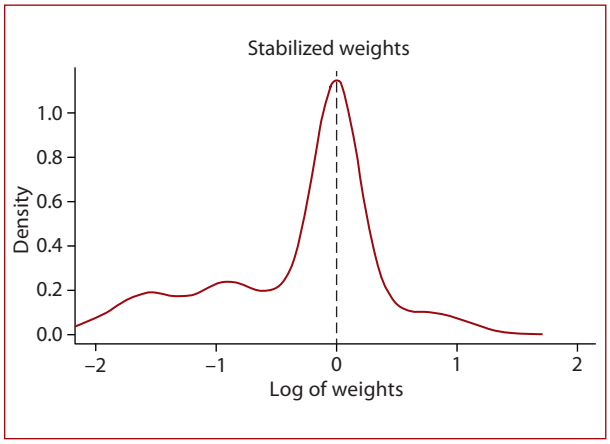

Figure 3. Stabilized weighting density plot between sodium-glucose cotransporter 2 inhibitor users and the non-user group

CI; *P* = 0.021 and OR, 1.27 [1.10–1.48], 95% CI; *P* = 0.003) (Table 4).

DISCUSSION

In contemporary cardiology practice, indications for using SGLT2i are growing after every single major clinical trial [15]. Treatment of T2DM, chronic renal disease (CKD), and chronic heart failure (HF) can be listed as the major indications for SGLTi [16]. Current guidelines support using SGLT2i after acute coronary syndrome, regardless of T2DM or LVEF level in HF to minimize the risk of worsening HF or cardiovascular mortality [1, 16, 17]. Beyond their glucose-lowering impact, these medications appear to have pleiotropic biological effects that cannot be solely attributed to the reduction in hyperglycemia. These effects include reduction in cardiovascular mortality, hospital admissions for HF, and adverse renal outcomes. The distinctive mechanism of action of SGLT2i, which involves enhanced renal glucose excretion resulting in a net energy loss, could also make SGLT2i good candidates for managing obesity, especially given its relationship with CAD and diabetes [18]. However, there are no sufficient data on the safety of using SGLT2i before and during pPCI in diabetic STEMI patients who have a high risk of CI-AKI. Our study represents an 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 STEMI patients who underwent pPCI. Our findings showed that in T2DM patients presenting with STEMI for the first time, the incidence of CI-AKI after pPCI was similar in 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 were exposed 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 to 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 developing CI-AKI. This effect size is clinically relevant and consistent with prior research that has demonstrated that SGLT2i have cardiovascular and renal advantages in patients 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 have proposed that initiating an SGLT2i is associated with a reduction in AKI when compared to other glucose-lowering strategies [25, 26]. Moreover, SGLT2i 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 in individuals using SGLT2i, supports the evidence that SGLT2i may have a more significant potential protective effect on kidney function in patients undergoing PCI. Hua et al. [13] demonstrated that the use of SGLT2i for more than 6 months before PCI provides renal protection in T2DM patients. Our results support these findings as our patients used the medication for at least 6 months prior to pPCI. Furthermore, investigating SGLT2i use 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 study supports the safety of using SGLT2i before coronary interventions and shows that there is no need to withhold SGLT2i 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 should be the subject of future research to assess whether the potential protective effects against AKI will be sustained.

Limitations

Despite these promising results, some limitations of our study 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 about 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 T2DM patients presenting with STEMI and undergoing pPCI. The observed reduction in CI-AKI incidence highlights the importance of investigating further the role of SGLT2i in renoprotection during pPCI procedures.

Article information

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