The Incidence of Contrast-Induced Acute Kidney Injury in Patients on Dapagliflozin Undergoing Percutaneous Coronary Interventions

Abstract

Background:sodium glucose cotransporter 2 receptor inhibitor(SGLT2i) dapagliflozin protects the renal function of individuals with coronary artery disease (CAD) and reduces incidence of contrast-induced acute kidney injury (CI-AKI) among individuals having percutaneous coronary interventions (PCI).The purpose of this work was to assess the CI-AKI incidence acrossindividuals on dapagliflozin underwent PCI.

Methods: This single-center, prospective observational work had been conducted on 200 diabetic individuals ranging in age between 25 and 80 years old, both genders, with CAD were going to have elective coronary angiogram and PCI.We identified CI-AKI by the ESUR and KDIGO definition. Patients were divided into two equal groups: Group I:Type 2 diabetes mellitus(T2DM) were on dapagliflozin (SGLT2i) and group II: T2DM were on nonSGLT2i glucose-lowering drugs.

Results: CI AKI according toEuropean society of urogenital radiology(ESUR) and kidney disease improving global outcomescore were significantly higher among group II contrasted to group I ($P<0.05$). no significant correlations existed between contrast volume and creatinine post-PCI, estimated glomerular filtration rate (eGFR) post-PCI, high-density lipoprotein,total cholesterol, and hemoglobin A1c in both groups.Dapagliflozin use was significantly correlated with 76.2% risk reduction of AKI.Dapagliflozin usagehad been correlated with a 72.6% risk reduction of AKI but with borderline significance ($P = 0.064$).eGFR post-PCI was significantly greater among group I cootrasted to group II ($P <0.05$).

Conclusions: Regarding the predictors of AKI according to ESUR criteria, multivariate logistic regression analysis and demonstrated that using dapagliflozin was substantially correlated with 76.2% risk reduction of AKI controlling for age, sex, hypertension, smoking, and dyslipidemia.

Keywords: Contrast-Induced Acute Kidney Injury, Dapagliflozin, Percutaneous Coronary Interventions, Coronary Artery Disease

Introduction:

Revascularisation with percutaneous coronary intervention (PCI) has shown significant efficacy in decreasing death rates among individuals diagnosed with coronary artery disease (CAD)[1].

The contrast-induced nephropathy (CIN) incidence is rising amongst individuals with CAD, and the likelihood of this severe unfavourable incident is further heightened in individuals with type 2 diabetic mellitus (T2DM)[2].

AKI is often characterised as anepisode of abrupt decrease in kidney functioning and is termed CIN if it happens immediately following the introduction of intravenous contrast [3].

In order to establish a standardised definition of CIN, the AKI network mandates that at least one of three conditions must be fulfilled within two days following theintroduction of contrast media (CM): a higher than 0.3 mg/dl rise in the level of creatinine in the blood compared to baseline, a relative increase of at least 50% in serum creatinine levels compared to baseline, or a decrease in urine output to <0.5 mL/kg/h for a minimum of 6 hours [4].

Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are new treatmentsused to treat individuals with T2DM by selectively blocking the glucose reabsorption in the renal tubules [5].

Empirical evidence from recent real-world trials indicates that patients who use SGLT2 have a reduced likelihood of getting AKI and have a lesser decrease in estimated glomerular filtration rate (e-GFR) compared to individuals who use other glucose-lowering medications [6].

This suggests that SGLT2I may have reno-protective impacts against AKI in persons with T2DM.

The purpose of this work was toevaluate the frequency of CI-AKI across participants on Dapagliflozin who hadPCI.

Patients and Methods:

This prospective observational work had been conductedon 200 diabetic participants ranging in age between 25 and 80 years old,both genders, with CAD were going to have elective CA and PCI. The work had been conducted from January 2023 to January 2024 following approval from the Ethics CommitteeBenhaUniversity Hospitals, Qalyubia, Egypt.Each participant provided well-informed written consent.

The criteria for exclusion comprised individuals who had acute myocardial infarction necessary for emergent PCI, significant heart failure with a left ventricular ejection fraction of less than 35%, complicated coronary lesions requiring prolonged time for surgery or more than 400 ml of contrast agents, severe arrhythmia, severe hepatic or renal dysfunction, urinary tract infection, bad glycemic control (fasting blood glucose >130mg), hemodynamic instability and sensitivity to CM.

Participants had been allocatedinto two groupsequally:GroupI:T2DM were on dapagliflozin (SGLT2i) and Group II:T2DM were on nonSGLT2i glucose-lowering drugs.

Each participant had been exposed tocomplete taking of history, clinical examinations and radiological investigations [12 Lead electrocardiogram (ECG), baseline echocardiography andcoronary angiography].

12 Lead electrocardiogramwas done for every patient to detect the presence of any ischemic changes, brady or tachyarrhythmia and chamber enlargement.

Baseline echocardiographyfor the assessment of regional wall abnormalities, left ventricular systolic function, valvular affection, mechanical complications, or chamber dilatation.

Coronary angiographywas performed for all patients according to their clinical condition by the percutaneous femoral or radial approach by interventional cardiologists, who had been blinded to the group of participants. Angiograms were obtained for each coronary vessel in at least 2 projections and contrast volume was calculated.

We determined CI-AKI events utilizing a laboratory-based algorithm that adheres to the serum creatinine criteria established by the European Society of Urogenital Radiology (ESUR), that includes a rise in serum creatinine of ≥44.2 μmol/L or 0.5 mg/dL within 72 hours, or an elevate of ≥1.25 times the baseline value; henceforth referred to as CI-AKIESUR [7]. As part of a sensitivity analysis, we determined inpatient episodes of AKI utilizing the Kidney Disease: Improving Global Outcomes (KDIGO) serum creatinine criteria, which include an elevation in serum creatinine by ≥26.52 μmol/L (0.3 mg/dl) within 48 hours or an elevation in serum creatinine by ≥1.5 times the baseline value prior to CAG; this will be referred to as AKIKDIGO, along with the corresponding dates[8].

Upon admission, and subsequently at 24, 48, and 72 hours following coronary angiography, the kidney functioning tests (serum creatinine and urea nitrogen) for individuals with CAD were obtained and quantified using the VITROS5600 automatic biochemical immuno analyser (JNJ, New Jersey, US).

The result was the first AKI incident during the hospital stay.

Statistical analysis

Statistical analysis had been performed employing SPSS v26 (IBM Inc., Chicago, IL, USA). The Shapiro-Wilks test and histograms had been utilisedto evaluate the data distribution normality. Quantitative parametric factors had been displayed as mean and standard deviation (SD) and contrasted among both groups employing unpaired Student's t- test. Quantitative non-parametric factors had been displayed as median and interquartile range (IQR) and had beenanalysed by Mann Whitney-test. Qualitative parameters had been displayed as frequencies and percentages (%) and had been analysed utilizing the Chi-square test or Fisher's exact test when appropriate. A correlationamong different variables was done employing Pearson moment correlation equation.Multivariate regression was also utilised to

assess the correlation amongdependent and more independent variables. A two tailed P value < 0.05 was considered statistically significant.

Results:

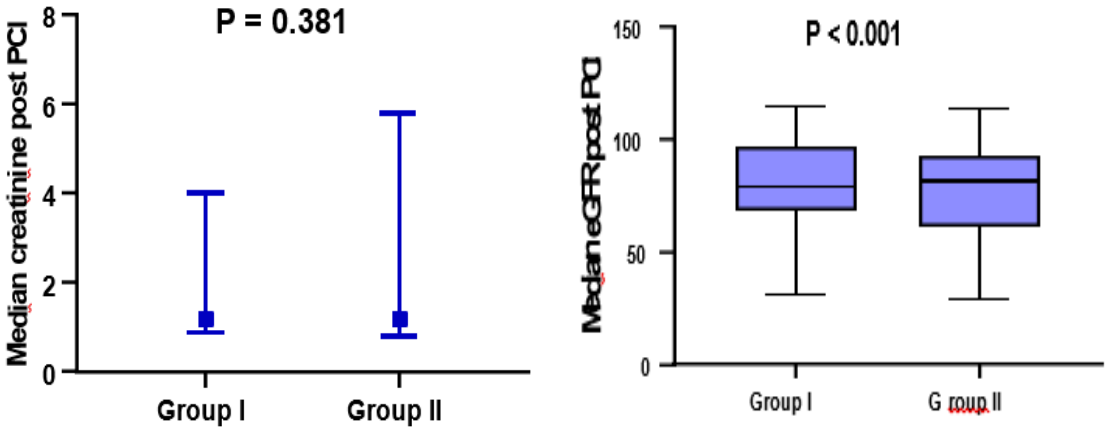
Demographic data and general featureswere insignificantly varied acrossthe two groups. **Table 1**

Table 1: Demographic data and general characteristics of the studied groups

		Group I (n = 100)	Group II (n = 100)	P
Age (years)		56±6	57±7	0.124
Sex	**Males**	77(77.0%)	75(75.0%)	0.741
	Females	23(23.0%)	25(25.0%)	
General characteristics	**Weight (kg)**	83±8	83±8	0.859
	HTN	44(44.0%)	47(47.0%)	0.670
	Smoking	49(49.0%)	51(51.0%)	0.777
	Dyslipidaemia	29(29.0%)	31(31.0%)	0.758
	Family history of IHD	16(16.0%)	18(18.0%)	0.707
	History of CKD	13(13.0%)	16(16.0%)	0.547
	Ejection fraction	55±6	55±6	0.875

Data are presented as mean ± SD or frequency (%). HTN: hypertension, IHD: ischemic heart disease; CKD: Chronic kidney disease.

Baseline (creatinine and eGFR) and creatinine post-PCI were insignificantly varied amongthe two groups. eGFR post-PCI was substantiallygreater in group I contrasted to group II (P <0.05). **Figure 1**



(A) **(B)**

Figure 1:(A) Creatinine and (B) estimated glomerular filtration rate level post-percutaneous coronary interventions in the studied groups

TC, HDL and HBA1C were insignificantly varied among both groups. **Table 2**

Table 2: Laboratory investigations of the studied groups

	Group I (n = 100)	Group II (n = 100)	P
TC	187±32	189±32	0.729
HDL	40±5	40±5	0.564
HBA1C	6.7±0.5	6.8±0.7	0.496

Data are presented as mean ± SD or median (IQR). * Significant P value <0.05. TC: total cholesterol, HDL: high-density lipoprotein; HBA1C: hemoglobin A1c.

CI AKI according to ESUR and KDIGO score were significantly higher among group IIcontrasted to group I (P<0.05). Contrast volume and need for dialysis were insignificantly varied among the two groups. **Table 3**

Table 3: Contrast volume and outcome in the studied groups

	Group I (n =100)	Group II (n =100)	P
Contrast volume	152±19	149±20	0.2
CI AKI (ESUR score)	3(3.0%)	11(11.0%)	**0.027***
CI AKI (KDIGO score)	3(3.0%)	10(10.0%)	**0.045***
Need for dialysis	1(1.0%)	2(2.0%)	0.497

Data are presented as mean ± SD or frequency (%). * Significant P value <0.05. CI AKI: contrast-induced acute kidney injury, ESUR score: European society of urogenital radiology, KDIGO score: kidney disease improving global outcomes.

There were no significant correlations between contrast volume and creatinine post-PCI, eGFR post-PCI, TC, HDL and HBA1C in both groups. **Table4**

Table 4: Correlation between contrast volume and other parameters in group I and II

	Group I (n =100)		Group II (n =100)	
	Contrast volume		Contrast volume	
	R	P	R	P
Creatinine post-PCI	0.035	0.726	0.004	0.969
eGFR post PCI	-0.009	0.931	0.0002	0.998
TC	0.045	0.657	0.079	0.437
HDL	-0.012	0.904	0.044	0.663
HBA1C	-0.016	0.871	0.067	0.509

r: correlation coefficient, eGFR: estimated glomerular filtration rate, PCI: percutaneous coronary intervention, TC: total cholesterol, HDL: high-density lipoprotein, HBA1C: hemoglobin A1c.

Multivariate logistic regression analysis was done to predict AKI according to ESUR and KDIGO criteria. According to ESUR criteria, dapagliflozin use was significantly associated with 76.2%, riskdecrease of AKI (OR = 0.238, 95% CI = 0.061 – 0.933, P = 0.039). According to KDIGO criteria,dapagliflozin usagehad been correlated with a 72.6% risk reduction of AKI but with borderline significance (P = 0.064). **Table 5**

Table 5: Multivariate logistic regression analysis to predict AKI according to ESUR and KDIGOcriteria

	ESUR criteria					KDIGO criteria				
	B	**S.E.**	**Wald**	**OR (95% CI)**	**P**	**B**	**S.E.**	**Wald**	**OR (95% CI)**	**P**
Age (years)	-0.042	0.045	0.889	0.958 (0.878-1.047)	0.346	-0.037	0.046	0.659	0.963(0.88-1.054)	0.417
Sex	1.929	0.61	10.017	6.885 (2.085-22.739)	**0.002***	1.748	0.619	7.984	5.742(1.708-19.301)	**0.005***
HTN	0.176	0.597	0.087	1.193(0.37-3.845)	0.768	0.022	0.614	0.001	1.022(0.307-3.402)	0.972
Smoking	0.037	0.614	0.004	1.038(0.311-3.458)	0.952	0.288	0.635	0.205	1.333(0.384-4.627)	0.65
Dyslipidaemia	0.572	0.611	0.878	1.772(0.536-5.865)	0.349	0.733	0.618	1.405	2.081(0.619-6.99)	0.236
Dapagliflozin use	-1.435	0.697	4.242	0.238(0.061-0.933)	**0.039***	-1.294	0.7	3.42	0.274(0.07-1.081)	0.064

* Significant P value <0.05. ESUR score: European society of urogenital radiology, KDIGO score: kidney disease improving global outcomes, HTN: hypertension, OR: Odds ratio, CI: Confidence interval, SE: Standard error, B: Regression coefficient.

Discussion

Acute coronary syndromes arise due to the sudden blockage of a coronary artery. Potential outcomes vary based on the extent and site of blockage and include unstable angina, ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and sudden cardiac arrest [9].

In patients with CAD, revascularisation via PCI has very successfully reduced mortality [1]. Concerning the laboratory results of the individuals under investigation, the baseline creatinine concentrations and eGFR were similar across the groups analysed. Post PCI, creatinine did not significantly differ, while eGFR was substantially greater in group I contrasted to group II ($P < 0.001$). Also, no substantial variations had been demonstrated among the studied groups regarding TC, HDL, and HBA1C. That agrees with Çabuk et al. [10] examined 345 individuals with T2DM. The baseline features (age, sex, medications and risk factors), laboratory results and administered contrast volume were similar between both groups.

As regards the contrast volume and outcome, the contrast volume was comparable between the studied groups. Group II exhibited significantly higher CI AKI according to ESUR

criteria and KDIGO criteriacontrasted to group I. No significant variation was reported in the need for dialysis.In alignment with our findings, Hua et al. [11]revealed thata reduction in the CI-AKI risk with SGLT2i usageexisted prior to and following propensity matching. Moreover, the CI-AKI incidence among individuals with CAD and diabetes had been decreased in the SGLT2 users' group, and SGLT2iutilisationhad been demonstrated to be an independent protective factor for the CIAKI incidence among participants following PCI.Also, Zhuo et al. [12] found that initiating a SGLT2i in older persons with T2DM2 was linked to a lower incidence of AKI in contrast to initiating a DPP-4 inhibitor or a GLP-1RA. Furthermore, Çabuk et al. [10] found that the administered contrast volume was similar among groups 1 and 2, correspondingly. They also revealed that contrast-associated AKI incidence was substantially higher among group II contrasted to group I, and the duration of hospital stay had been substantially prolonged in group II contrasted to in group.

As regard the predictors of AKI according to ESUR criteria, multivariate logistic regression analysis was done and revealed that using dapagliflozin was significantly correlated with 76.2% risk reduction of AKI (OR = 0.238, 95% CI = 0.061 – 0.933, P = 0.039), controlling for age, sex, hypertension, smoking, and dyslipidemia. Also, as regard the predictors of AKI according to KDIGO criteria, multivariate logistic regression analysis was done and demonstrated that The administration of dapagliflozin was linked to a 72.6% decrease in the incidence of AKI, however the statistical significance was just marginal (P = 0.064). It aligns with the results of Paolisso et al. [13] thatindividuals using SGLT2-I showed notably reduced creatinine levels 72 hours following PCI, in the two non-CKD and CKD groups. Significantly decreased overall incidence of CI-AKI had been seen in SGLT2-I consumers in contrast to non-SGLT2-I individuals (p = 0.022). Furthermore, this discovery was validated in individuals without chronic kidney disease (p = 0.040). In the group with CKD, patients using SGLT2-I maintained notably reduced creatinine levels upon discharge. Utilisation of

SGLT2-I was an independent predictor of lower incidence of CI-AKI (OR 0.356; 95%CI 0.134-0.943, p = 0.038).

The most plausible explanation for that discovery is that the primary cause of CI-AKI is a sudden and prolonged decrease in renal plasma flow, mostly affecting the outer medulla. The aforementioned effects may assist in the correction of volume depletion and expansion of IV volume by fluid administration. This, in turn, enhances the CMclearance, reduces the tubule lumen and vasa rectaCMconcentrations, and counteracts the stimulation of neurohormonal systems which cause medullary vasoconstriction[14].

Limitations of the study included that the follow up of participants had been limited for a relatively short period. So, we recommended that SGLT2is be used among diabetic patients undergoing elective coronary angiography due to suspected CAD, to decreased the CI-AKIrisk.including larger number of diabetic patients, and in different centers for better assessment of the effects of SGLT2is on the CI-AKI risk following coronary interventions.including other serum levels of other markers of CIAKI including cystatin C levels as alternative and reliable indicators of renal function.

Conclusions:

Regarding the predictors of AKI according to ESUR criteria, multivariate logistic regression analysis was done and revealed that using dapagliflozin was significantly associated with 76.2% risk reduction of AKI controlling for age, sex, hypertension, smoking, and dyslipidemia. Also, regarding the predictors of AKI according to KDIGO criteria, multivariate logistic regression analysis was done and revealed that dapagliflozin utilisation was correlated with a 72.6% risk reduction of AKI but with borderline statistical significance.

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