

Synergistic Renoprotection of SGLT2 Inhibitors and ACEi/ARB Against Contrast-Induced Nephropathy in PCI: A Prospective Observational Study

Kareem Ali Maher

Kafrelsheikh University

Mohamed Shokry Fahmy

Kafrelsheikh University

Osama Abouelfetouh Elshaer

`osama.med_0296@med.kfs.edu.eg`

Kafrelsheikh University

Ramy Magdy Elgamal

Kafrelsheikh University

Reda Nabil Dawoud

Kafrelsheikh University

Dina Ahmed Abdelmoneim

Kafrelsheikh University

Khaled Ramadan Elsayed

Kafrelsheikh University

Mohamed Elsayed Abdelfattah

Kafrelsheikh University

Reda Biomy

Kafrelsheikh University

Mohamed Kamal Salama

Kafrelsheikh University

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Abstract

Background: Contrast-induced nephropathy (CIN) is a common complication of percutaneous coronary intervention (PCI). Despite renoprotective effects of sodium–glucose cotransporter-2 inhibitors (SGLT2i), evidence on chronic SGLT2i use—particularly its synergy with renin–angiotensin system (RAS) blockade—in CIN prevention remains limited.

Methods: This cohort study enrolled 249 PCI patients between August 2024 and December 2025. Patients were stratified by chronic SGLT2i use (126 users, 123 non-users). CIN was defined as a ≥ 0.5 mg/dL or $\geq 25\%$ increase in creatinine within 48 hours. All procedures used low-osmolar non-ionic contrast. Multivariate logistic regression was used to identify predictors of CIN

Results: Baseline and procedural characteristics were comparable, except for higher diabetes and heart failure rates among SGLT2i users. Chronic SGLT2i use was associated with smaller creatinine rises (ΔCr 0.05 [0.02–0.07] vs. 0.08 [0.00–0.16] mg/dL, $p < 0.001$) and smaller eGFR declines (ΔeGFR -3.30 [-5.50 to 1.40] vs. -5.20 [-9.10 to 0.15] mL/min/1.73 m², $p = 0.009$). CIN occurred less often (7.1% vs. 16.3%, $p = 0.025$). Multivariate analysis showed SGLT2i (OR 0.37, 95% CI 0.15–0.92, $p = 0.032$) and ACEi/ARB use (OR 0.15, 95% CI 0.06–0.41, $p < 0.001$) were protective. Dual therapy provided greatest renoprotection, especially in chronic kidney disease.

Conclusion: In this study, chronic SGLT2i therapy was associated with reduced CIN incidence and attenuated post-PCI renal decline. Concomitant ACEi/ARB therapy provided synergistic renoprotection, in CKD. These findings support SGLT2i continuation during contrast exposure and highlight value of dual SGLT2i–RAS blockade. Randomized trials are warranted.

Introduction

Contrast-induced nephropathy (CIN), or contrast-induced acute kidney injury (CI-AKI), remains a frequent and prognostically significant complication of percutaneous coronary intervention (PCI). Its incidence ranges from 7–15% overall, increasing to 20–30% in high-risk patients, including those with diabetes, heart failure, or chronic kidney disease [1]. As the third leading cause of hospital-acquired acute kidney injury, CIN is independently associated with prolonged hospitalization, accelerated CKD progression, and increased short- and long-term mortality and major adverse cardiovascular events [2–4].

CIN is a multifactorial process driven by renal vasoconstriction, medullary hypoxia, oxidative stress, tubular toxicity, and inflammation. Standard preventive measures, including hydration and contrast minimization, remain insufficient in high-risk patients. Sodium–glucose cotransporter-2 inhibitors (SGLT2i), recommended with Grade 1A evidence by the 2024 KDIGO CKD guideline and endorsed by ESC (2023) and AHA/ACC/HFSA (2022), exert hemodynamic, metabolic, and anti-inflammatory effects—reducing intraglomerular pressure, improving oxygen efficiency via ketone metabolism, and inhibiting the NLRP3 inflammasome—that may directly attenuate contrast-induced renal injury [5–7].

Accumulating observational studies and meta-analyses support a renoprotective role for SGLT2 inhibitors against CIN. Meregildo-Rodriguez et al. reported a 63% relative risk reduction (RR 0.37), while a dedicated AMI/PCI meta-analysis by Li et al. demonstrated a 45% reduction [8, 9]. Similarly, the multicentre SGLT2-I AMI PROTECT registry showed significantly lower CIN rates with chronic SGLT2i use (5.4% vs. 13.1%), with the greatest benefit observed in patients with CKD [10].

However, findings remain inconsistent. Short-term SGLT2i initiation may increase post-contrast AKI risk (Zang et al.; Yang et al.), whereas chronic use—particularly in stable settings—appears protective or neutral [11, 12]. These discrepancies likely reflect differences in treatment duration, baseline renal function, and concomitant therapies such as ACE inhibitors or ARBs. Consequently, high-quality prospective real-world data are limited, particularly regarding the safety of continued SGLT2i therapy, potential synergy with renin–angiotensin system blockade, and the prognostic role of inflammatory markers.

This prospective observational study of 249 patients undergoing PCI therefore evaluated whether chronic SGLT2i therapy is independently associated with attenuated post-procedural renal-function decline and lower CIN incidence, with dedicated subgroup analyses by CKD status and combined ACEi/ARB + SGLT2i use.

Patients and Methods

This prospective observational cohort study was conducted at the Department of Cardiology of a tertiary university hospital. Participants were recruited between August 2024 and December 2025. The study was approved by the institutional Research Ethics Committee (IRB No: KFSIRB200-298) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrolment, and the study adhered to the STROBE reporting guidelines for observational research.

A total of 355 patients undergoing percutaneous coronary intervention (PCI) were initially screened. After applying predefined inclusion and exclusion criteria, 260 patients were enrolled and classified according to baseline SGLT2 inhibitor use to SGLT2 inhibitor users and non-users (130 each). During follow-up, 11 patients were excluded due to incomplete outcome data or loss to follow-up (4 in the SGLT2i group and 7 in the non-SGLT2i group). The final analysis therefore included 126 SGLT2i users and 123 non-users.

Eligible participants were adults (≥ 18 years) undergoing coronary angiography with or without PCI. Both patients with normal renal function and those with CKD (defined as $\text{eGFR} < 60 \text{ mL/min/1.73 m}^2$ for ≥ 3 months) were included, irrespective of diabetes or heart failure status [13]. Patients receiving SGLT2 inhibitors as part of routine care, as well as non-users, were eligible. Written informed consent was obtained from all participants.

Exclusion criteria included baseline acute kidney injury or prior contrast-induced nephropathy, advanced renal impairment (eGFR < 30 mL/min/1.73 m²) or need for renal replacement therapy, and hemodynamic instability (e.g., acute decompensated heart failure or cardiogenic shock). Patients with conditions affecting renal function or oxygenation (e.g., severe anemia or active malignancy), recent exposure to nephrotoxic agents, insufficient data, or active/recent urinary tract infection were also excluded.

All patients underwent detailed history taking and comprehensive clinical examination prior to PCI. Baseline demographic characteristics, cardiovascular risk factors, comorbidities, and current medications were systematically recorded.

Baseline laboratory investigations were obtained within 24 hours prior to contrast exposure, including serum creatinine. Estimated glomerular filtration rate (eGFR) was calculated using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation [14].

All patients received standard pre-procedural care according to institutional protocols. Adequate hydration was encouraged, with oral fluid intake recommended whenever feasible. Intravenous isotonic saline hydration was administered at the discretion of the treating physician, particularly in patients at increased risk for contrast-induced nephropathy. Potentially nephrotoxic medications were withheld prior to the procedure when clinically appropriate.

PCI was performed according to standard institutional practice. Vascular access was obtained via either the radial or femoral approach, based on operator preference and patient-specific anatomical considerations. A low-osmolar, non-ionic iodinated contrast agent was used in all procedures. To minimize procedural variability and operator-related bias, all procedures were performed by a single experienced interventional cardiologist.

Renal function was reassessed 48 hours following contrast exposure through repeat measurement of serum creatinine and calculation of eGFR to evaluate post-procedural changes and detect contrast-induced nephropathy.

Contrast-induced nephropathy (CIN) was defined as an absolute increase in serum creatinine of ≥ 0.5 mg/dL or a relative increase of $\geq 25\%$ from baseline within 48 hours following contrast exposure, in the absence of alternative causes of acute kidney injury [15].

Sample size was estimated based on the reported CIN incidence after PCI (1.3–33.3%). Using the midpoint (17.3%) as a conservative estimate, with a 95% confidence level ($Z = 1.96$) and 7% margin of error, the minimum required sample size was calculated at approximately 112 patients per group. To account for potential dropouts and incomplete data, the target was increased to 130 patients per group.

Statistical analysis was performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Normality was assessed using the Shapiro–Wilk test. Continuous variables are presented as mean $\pm$ standard deviation (SD) or median (interquartile range [IQR]) as appropriate, while categorical variables are expressed as frequencies and percentages. Between-group comparisons were conducted

using the independent samples t-test or Mann–Whitney U test, and categorical variables were analyzed using the chi-square or Fisher’s exact test. For comparisons involving more than two groups, one-way ANOVA with Bonferroni post hoc correction or the Kruskal–Wallis test with Bonferroni-adjusted pairwise comparisons was applied as appropriate. Effect sizes were calculated using Cohen’s d, rank-biserial correlation (r), and Cramér’s V.

Independent predictors of contrast-induced nephropathy (CIN) were identified using univariate logistic regression followed by multivariate analysis including variables with $p < 0.05$. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Model performance was assessed using the Hosmer–Lemeshow test, Nagelkerke R^2 , and classification accuracy, with a probability cut-off of 0.20 to improve sensitivity. Changes in renal function (Δ creatinine and Δ eGFR) were analyzed using appropriate two-group and multi-group tests as described above to evaluate the effects of SGLT2 inhibitor use, CKD status, and combined treatment strategies. A two-tailed p-value < 0.05 was considered statistically significant.

Results

A total of 355 patients undergoing percutaneous coronary intervention (PCI) were consecutively screened between August 2024 and December 2025. After applying predefined inclusion and exclusion criteria, 260 patients were enrolled into SGLT2 inhibitor users and non-users (130 each). Eleven patients were excluded due to incomplete 48-hour renal data or loss to follow-up (4 vs. 7), yielding a final cohort of 249 patients (126 vs. 123).

Baseline characteristics were largely comparable between groups, including age, sex, body mass index, smoking status, hypertension, blood pressure, hemoglobin, platelet count, lipid profile, baseline renal function (serum creatinine 1.11 vs. 1.12 mg/dL, $p = 0.968$; eGFR 73.5 vs. 72.0 mL/min/1.73 m², $p = 0.342$), and concomitant medications (Tables 1–3). However, SGLT2 inhibitor users had a higher prevalence of diabetes mellitus (54.0% vs. 37.4%, $p = 0.009$) and heart failure (29.4% vs. 10.6%, $p < 0.001$), along with lower left ventricular ejection fraction (53.0% [50.0–61.0] vs. 59.0% [54.0–64.0], $p < 0.001$).

Table 1
Baseline Clinical and Demographic Characteristics of the Study Population

Variable	SGLT2i users (n = 126)	SGLT2i non-users (n = 123)	P value	Effect size
Age (years)	57.0 [52.0–62.0]	60.0 [53.0–65.0]	0.127	r = 0.10
Sex (Male %)	97 (77.0%)	85 (69.1%)	0.161	V = 0.09
BMI (kg/m ²)	26.93 ± 3.80	27.59 ± 3.87	0.170	d = 0.17
Smoking	37 (29.4%)	29 (23.6%)	0.301	V = 0.07
Diabetes mellitus (DM)	68 (54.0%)	46 (37.4%)	0.009	V = 0.17
Hypertension (HTN)	74 (58.7%)	74 (60.2%)	0.818	V = 0.02
SBP (mmHg)	136.38 ± 14.38	134.89 ± 13.85	0.407	d = 0.11
DBP (mmHg)	80.00 [73.00–89.00]	82.00 [74.00–88.00]	0.449	r = 0.05
Ejection Fraction (EF, %)	53.00 [50.00–61.00]	59.00 [54.00–64.00]	< 0.001	r = 0.28
Heart Failure	37 (29.4%)	13 (10.6%)	< 0.001	V = 0.24
Heart Failure category			0.761	V = 0.11
- HFpEF	13 (35.1%)	6 (46.2%)		
- HFmrEF	8 (21.6%)	2 (15.4%)		
- HFrEF	16 (43.2%)	5 (38.5%)		
No. of CKD Patients	30 (23.8%)	33 (26.8%)	0.584	V = 0.04

Data are presented as mean ± standard deviation (SD) for normally distributed variables and median (interquartile range [IQR]) for non-normally distributed variables, as assessed by the Shapiro–Wilk test, or as number (percentage) for categorical variables. Between-group comparisons were performed using the independent samples t-test or Mann–Whitney U test for continuous variables and the chi-square test for categorical variables. Effect sizes are reported as Cohen’s d, rank-biserial correlation (r), and Cramér’s V, interpreted as small (0.1), moderate (0.3), and large (0.5). A two-tailed p-value < 0.05 was considered statistically significant.

Procedural characteristics were similar between groups, including vascular access, number of implanted stents, contrast volume (148 [115–193] vs. 146 [111–192] mL, p = 0.980), and procedure time (72 [60–89] vs. 74 [57–97] minutes, p = 0.566) (Table 2). SGLT2 inhibitor use was associated with significantly smaller increases in serum creatinine (Δ Cr 0.05 [0.02–0.07] vs. 0.08 [0.00–0.16] mg/dL, p < 0.001) and

smaller declines in eGFR (– 3.30 [– 5.50 to 1.40] vs. –5.20 [– 9.10 to 0.15] mL/min/1.73 m², p = 0.009) at 48 hours (Table 3).

Table 2
Baseline Laboratory, Medication Use, and Procedural Characteristics

Variable	SGLT2i users (n = 126)	SGLT2i non-users (n = 123)	P value	Effect size
Beta-blockers	107 (84.9%)	102 (82.9%)	0.668	V = 0.03
ACE inhibitors / ARBs	66 (52.4%)	64 (52.0%)	0.956	V = 0.00
Calcium channel blockers (CCB)	47 (37.3%)	44 (35.8%)	0.802	V = 0.02
Haemoglobin (g/dL)	12.65 ± 1.50	12.75 ± 1.44	0.594	d = 0.07
WBCs (×10 ³ /μL)	6.80 [5.60–8.10]	7.20 [5.30–8.50]	0.599	r = 0.03
Platelets (×10 ³ /μL)	239.52 ± 50.68	234.82 ± 47.09	0.283	d = 0.10
Total Cholesterol (mg/dL)	199.0 [165.75–225.0]	203.0 [175.0–232.0]	0.189	r = 0.08
Triglycerides (mg/dL)	177.76 ± 47.40	174.76 ± 41.68	0.597	d = 0.06
HDL (mg/dL)	49.0 [38.0–59.0]	52.0 [44.5–59.0]	0.204	r = 0.08
LDL (mg/dL)	111.72 ± 31.69	116.45 ± 30.64	0.233	d = 0.15
Procedure time (min)	72 [60–89]	74 [57–97]	0.566	r = 0.04
Contrast volume (mL)	148 [115–193]	146 [111–192]	0.980	r = 0.002
Number of stents			0.471	V = 0.08
1 Stent	40 (31.7%)	34 (27.6%)		
2 Stents	63 (50.0%)	59 (48.0%)		
3 Stents	23 (18.3%)	30 (24.4%)		

Data are presented as mean ± standard deviation (SD), median (interquartile range [IQR]), or number (percentage), as appropriate. Between-group comparisons were performed using the independent samples t-test or Mann–Whitney U test for continuous variables and the chi-square test for categorical variables. Effect sizes are expressed as Cohen’s d, rank-biserial correlation (r), and Cramér’s V. A two-tailed p-value < 0.05 was considered statistically significant.

Table 3
Changes in Renal Function and Incidence of Contrast-Induced Nephropathy

Variable	SGLT2i users (n = 126)	SGLT2i non-users (n = 123)	P value	Effect size
Creatinine (mg/dL)				
Baseline	1.11 [0.97–1.24]	1.12 [0.96–1.29]	0.968	r = 0.003
Post-procedure	1.16 [0.99–1.38]	1.23 [0.97–1.45]	0.312	r = 0.06
Δ Creatinine	0.05 [0.02–0.07]	0.08 [0.00–0.16]	< 0.001	r = 0.25
Range (Baseline)	0.71–1.97	0.76–1.96		
Range (Post)	0.71–2.13	0.81–2.59		
eGFR (mL/min/1.73 m ²)				
Baseline	73.5 [59.0–85.0]	72.0 [56.5–83.0]	0.342	d = 0.12
Post-procedure	68.0 [56.0–86.0]	64.0 [50.0–80.5]	0.094	r = 0.11
Δ eGFR	-3.30 [-5.50 to 1.40]	-5.20 [-9.10 to 0.15]	0.009	r = 0.17
Range (Baseline)	35–125	32–107		
Range (Post)	33–121	23–108		
Clinical Renal Outcomes				
Incidence of CIN	9 (7.1%)	20 (16.3%)	0.025	V = 0.14

Data are presented as median (interquartile range [IQR]) or number (percentage), as appropriate. Between-group comparisons were performed using the Mann–Whitney U test for continuous variables and the chi-square test or *Fisher’s exact test for categorical variables when appropriate. Effect sizes are reported as rank-biserial correlation (r) and Cramér’s V. A two-tailed p-value < 0.05 was considered statistically significant.

The incidence of contrast-induced nephropathy (CIN) was significantly lower among SGLT2 inhibitor users (7.1% vs. 16.3%, p = 0.025). The prevalence of pre-existing CKD was similar between groups (23.8% vs. 26.8%, p = 0.584). In multivariate logistic regression analysis, SGLT2 inhibitor use was independently associated with a reduced risk of CIN (OR 0.37, 95% CI 0.15–0.92, p = 0.032), while ACE inhibitor/ARB use showed a stronger protective effect (OR 0.15, 95% CI 0.06–0.41, p < 0.001). Higher baseline white blood cell count (OR 1.23, p = 0.019) and lower baseline eGFR (OR 0.97 per unit increase, p = 0.007) were independent predictors of CIN. The model demonstrated good calibration (Hosmer–Lemeshow p > 0.05), moderate explanatory power (Nagelkerke R² = 0.245), and 83.1% classification accuracy at a 0.20 cut-off (Table 4).

Table 4
Univariate and Multivariate Logistic Regression for Prediction of CIN (n = 249)

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Demographics				
Age	0.969 (0.929–1.009)	0.129	—	—
Sex (Male)	0.796 (0.343–1.846)	0.595	—	—
Height	0.981 (0.945–1.018)	0.303	—	—
Weight	1.455 (0.039–54.958)	0.840	—	—
BMI	0.950 (0.858–1.052)	0.322	—	—
Clinical History				
Diabetes	1.310 (0.603–2.843)	0.495	—	—
HTN	0.962 (0.438–2.113)	0.924	—	—
Smoking	0.868 (0.353–2.138)	0.759	—	—
Hemodynamic				
SBP	0.993 (0.966–1.021)	0.616	—	—
DBP	1.023 (0.987–1.061)	0.214	—	—
Laboratory Findings				
Haemoglobin	0.960 (0.738–1.250)	0.763	—	—
WBCs	1.241 (1.057–1.457)	0.009	1.23 (1.03–1.45)	0.019
Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression analysis. Variables with $p < 0.05$ in univariate analysis were included in the multivariate model. The multivariate model was statistically significant ($\chi^2 = 33.44$, $p < 0.001$) and demonstrated moderate explanatory power (Nagelkerke $R^2 = 0.245$). Model performance was further assessed using the Hosmer–Lemeshow goodness-of-fit test. Using a probability cut-off of 0.20, the model achieved an overall classification accuracy of 83.1%, with sensitivity of 48.3% and specificity of 87.7%, indicating balanced and clinically relevant predictive performance.				

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Platelets	1.001 (0.993–1.009)	0.896	—	—
Total Cholesterol	1.003 (0.993–1.014)	0.575	—	—
LDL	1.009 (1.000–1.018)	0.058	—	—
HDL	1.002 (0.989–1.014)	0.778	—	—
Triglycerides	0.994 (0.964–1.024)	0.678	—	—
Cardiac / Procedural				
EF (%)	1.007 (0.964–1.052)	0.762	—	—
Number of Stents	1.306 (0.756–2.254)	0.339	—	—
Contrast Volume	0.994 (0.985–1.002)	0.140		
PCI Time	0.998 (0.982–1.014)	0.798		
Renal Function				
Baseline Creatinine	8.473 (2.173–33.044)	0.002	—	—
Baseline eGFR	0.972 (0.950–0.995)	0.015	0.97 (0.94–0.99)	0.007
Medications				
ACE/ARB	0.240 (0.079–0.516)	< 0.001	0.15 (0.06–0.41)	< 0.001
SGLT2 inhibitor	0.194 (0.173–0.909)	0.023	0.37 (0.15–0.92)	0.032
Calcium Channel Blocker	1.069 (0.481–2.377)	0.869		
Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression analysis. Variables with $p < 0.05$ in univariate analysis were included in the multivariate model. The multivariate model was statistically significant ($\chi^2 = 33.44$, $p < 0.001$) and demonstrated moderate explanatory power (Nagelkerke $R^2 = 0.245$). Model performance was further assessed using the Hosmer–Lemeshow goodness-of-fit test. Using a probability cut-off of 0.20, the model achieved an overall classification accuracy of 83.1%, with sensitivity of 48.3% and specificity of 87.7%, indicating balanced and clinically relevant predictive performance.				

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Beta-blocker	0.908 (0.325–2.541)	0.854		
Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression analysis. Variables with $p < 0.05$ in univariate analysis were included in the multivariate model. The multivariate model was statistically significant ($\chi^2 = 33.44$, $p < 0.001$) and demonstrated moderate explanatory power (Nagelkerke $R^2 = 0.245$). Model performance was further assessed using the Hosmer–Lemeshow goodness-of-fit test. Using a probability cut-off of 0.20, the model achieved an overall classification accuracy of 83.1%, with sensitivity of 48.3% and specificity of 87.7%, indicating balanced and clinically relevant predictive performance.				

Table . Univariate and Multivariate Logistic Regression for Prediction of CIN (n = 252)

Subgroup analysis demonstrated a more pronounced protective effect of SGLT2 inhibitors in patients with CKD (Table 5). The CKD-only group exhibited the greatest increase in creatinine (0.2285 ± 0.2403 mg/dL), whereas SGLT2 inhibitor users with CKD showed significantly smaller changes (0.0867 ± 0.2004 mg/dL; mean difference -0.1418 mg/dL, $p = 0.008$). In patients without CKD, the difference between SGLT2 inhibitor users and non-users was smaller and not statistically significant (mean difference -0.0321 mg/dL, $p = 1.000$).

Table 5
Subgroup Analysis of Serum Creatinine Changes by CKD Status and SGLT2 Inhibitor Use

Subgroup	SGLT2i	Δ Creatinine (Mean $\pm$ SD)	Mean Difference	P value
No CKD	No	0.0769 ± 0.1483		
	Yes	0.0448 ± 0.1578	-0.0321	1.000
CKD	No	0.2285 ± 0.2403		
	Yes	0.0867 ± 0.2004	-0.1418	0.008

Data are presented as mean $\pm$ standard deviation (SD). Within each CKD stratum, comparisons between SGLT2 inhibitor users and non-users were performed using independent samples t-tests. Mean difference represents the difference in Δ creatinine between SGLT2 inhibitor users and non-users within each subgroup.

Combined therapy with ACE inhibitors/ARBs and SGLT2 inhibitors resulted in the least deterioration in renal function (Δ Cr H = 19.91, $p < 0.001$; Δ eGFR H = 13.64, $p = 0.003$), with Bonferroni-adjusted pairwise comparisons confirming superiority of the combination over no-treatment (group 1 vs. 4: $p < 0.001$ for Δ Cr and $p = 0.001$ for Δ eGFR) and over ACE inhibitor/ARB monotherapy (group 4 vs. 3: $p = 0.015$ for Δ Cr) (Table 6).

Table 6
Renal Function Changes by Medication Combination (Kruskal–Wallis Test with Bonferroni-Adjusted Pairwise Comparisons)

Outcome	Kruskal–Wallis H (df = 3)	P value	Significant Comparisons (Bonferroni-adjusted)
Δ eGFR (mL/min/1.73m ²)	13.64	0.003	1 vs 4 (0.001)
Δ Creatinine (mg/dL)	19.91	< 0.001	4 vs 1 (< 0.001) • 4 vs 3 (0.015)

Data are presented as median (interquartile range [IQR]) for non-normally distributed variables. Comparisons across medication groups were performed using the Kruskal–Wallis test, followed by Bonferroni-adjusted pairwise comparisons. The Kruskal–Wallis H statistic and corresponding p-values are reported.

Medication groups were defined as follows: (1) neither ACE inhibitor/ARB nor SGLT2 inhibitor, (2) SGLT2 inhibitor only, (3) ACE inhibitor/ARB only, and (4) combined therapy (ACE inhibitor/ARB + SGLT2 inhibitor). Chronic kidney disease (CKD) was defined as baseline estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m². All tests were two-tailed, and a p-value < 0.05 was considered statistically significant.

Discussion

Contrast-induced nephropathy (CIN) remains a frequent and prognostically important complication of percutaneous coronary intervention (PCI). In this prospective observational study of 249 eligible patients, chronic SGLT2 inhibitor (SGLT2i) therapy was independently associated with a substantial reduction in CIN incidence (7.1% vs. 16.3%; $p = 0.025$) and attenuated post-procedural renal-function decline (median ΔCreatinine 0.05 vs. 0.08 mg/dL, $p < 0.001$; median ΔeGFR – 3.30 vs. –5.20 mL/min/1.73 m², $p = 0.009$). Multivariate logistic regression confirmed SGLT2i use as an independent protective factor (OR 0.37, $p = 0.032$), with an even stronger association for ACE inhibitor/ARB therapy (OR 0.15, $p < 0.001$). Dual therapy with both agents conferred additive renoprotection, yielding the smallest deteriorations in creatinine and eGFR (Kruskal–Wallis $p < 0.001$). The benefit was particularly pronounced in patients with chronic kidney disease (CKD)—the highest-risk subgroup—where SGLT2i users showed significantly smaller creatinine increases than non-users (0.0867 ± 0.2004 vs. 0.2285 ± 0.2403 mg/dL; mean difference – 0.1418 mg/dL, $p = 0.008$), despite higher baseline diabetes and heart-failure prevalence among SGLT2i users and balanced procedural characteristics.

This protective effect is clinically important, as CIN remains the third leading cause of hospital-acquired acute kidney injury and is associated with significant morbidity and mortality. In a cohort of 696 patients with acute myocardial infarction undergoing PCI, Sun et al. reported a CIN incidence of 15.8%, which independently predicted long-term mortality over 2.8 years [3]. Similarly, Ng et al., in a large cohort of 34,576 patients undergoing first PCI, showed that severe CI-AKI was associated with a 1.92-fold

increased risk of major adverse cardiovascular events at 5 years, with progressively increasing risk over time [2].

Our findings align with and extend the growing evidence that SGLT2 inhibitors confer consistent nephroprotection against CIN in PCI patients. Meta-analyses by Meregildo-Rodriguez et al. and Li et al. reported significant risk reductions (RR 0.37 and 0.55, respectively), supporting a class-wide benefit [8, 9]. This is reinforced by observational studies across high-risk populations: Nardi et al. reported markedly lower CIN rates in heart failure patients, Özkan et al. demonstrated similar reductions in diabetic NSTEMI patients, and Hua et al. observed lower rates in diabetic CAD cohorts [16–18]. Notably, the CIN incidence in our control group (16.3%) closely matches published benchmarks, supporting the external validity of our findings. Overall, the observed > 50% reduction in CIN with SGLT2 inhibitor use highlights a clinically meaningful and practical strategy to reduce renal injury and its downstream cardiovascular consequences.

Chronic SGLT2 inhibitor use appears particularly beneficial in patients with CKD undergoing PCI—the subgroup at highest risk for CIN. In the SGLT2-I AMI PROTECT registry, SGLT2i use was associated with lower post-procedural creatinine and a significantly reduced CIN incidence (5.4% vs 13.1%; OR 0.36), with consistent benefits observed in both CKD and non-CKD patients. Notably, CKD patients receiving SGLT2i maintained lower creatinine levels at discharge, highlighting a targeted effect in those with reduced renal reserve [10]. These findings closely align with our subgroup analysis, where SGLT2i therapy markedly attenuated creatinine rise in CKD patients despite comparable procedural characteristics.

However, a more cautious perspective emerges when considering short-term SGLT2i initiation, particularly in acutely ill or high-risk CKD patients. Heyman et al. suggested that the combination of contrast media and newly initiated SGLT2i may exacerbate medullary hypoxia, with propensity-matched data showing an increased risk of contrast-associated nephropathy largely confined to new users rather than chronic therapy [19]. Accordingly, temporary withholding in unstable, high-risk patients has been proposed.

Consistent with this, Yang et al. reported higher CIN rates with short-term (< 2 weeks) dapagliflozin initiation (14.2% vs 7.0%; OR 2.31), while Zang et al. similarly observed increased post-contrast AKI, particularly among new users compared with long-term users (20.5% vs 3.4%) [11, 12]. These findings contrast with our results and highlight the importance of treatment duration and clinical context, suggesting that the renal effects of SGLT2 inhibitors may differ substantially between acute initiation and chronic stable use.

These discrepancies compared with our findings likely reflect key differences in treatment exposure and study design. In our cohort, patients were on chronic, stable SGLT2i therapy, whereas prior studies focused on recent initiation, a period characterized by a transient hemodynamic dip in eGFR that may increase vulnerability to acute insults. Additionally, our prospective design, single-operator standardization, and balanced procedural characteristics reduce confounding inherent to retrospective analyses.

Taken together, these findings suggest that the renal effects of SGLT2 inhibitors are highly context-dependent. While short-term initiation in unstable or high-risk patients may warrant caution, chronic therapy appears safe to continue and may confer meaningful protection—particularly in patients with CKD—supporting the avoidance of routine discontinuation around the time of coronary angiography.

Mechanistically, SGLT2 inhibitors reduce proximal tubular sodium and glucose reabsorption, enhancing tubuloglomerular feedback and inducing afferent arteriolar vasoconstriction, thereby lowering intraglomerular pressure and hyperfiltration. As highlighted by Yang et al., this results in an initial, reversible dip in eGFR—once considered nephrotoxic but now recognized as a protective adaptation that reduces filtration workload and medullary oxygen demand [12]. This mechanism may explain why early initiation can transiently increase vulnerability, whereas chronic therapy associated with reduced risk in the setting of contrast exposure.

In the setting of contrast-induced injury—where medullary hypoxia is central—these effects may be particularly protective. Contrast media increase blood viscosity, promote vasoconstriction, and generate oxidative stress, further compromising medullary oxygen balance. By reducing baseline oxygen demand, SGLT2 inhibitors may enhance renal tolerance to hypoxic stress [20]. Additionally, they induce a metabolic shift toward more efficient ketone utilization and exert anti-inflammatory and antioxidative effects, including inhibition of the NLRP3 inflammasome and pro-inflammatory cytokines. Experimental data support these mechanisms, as Chung et al. demonstrated that dapagliflozin attenuates contrast-induced tubular injury and inflammasome activation, translating into a significantly lower risk of post-PCI dialysis [21].

A notable finding of our study is the identification of baseline white blood cell count as an independent predictor of CIN (OR 1.23), consistent with Masoomi et al., who reported a similar association in STEMI patients (OR 2.03) [22]. Despite differences in population and setting, both studies support a central role of systemic inflammation in susceptibility to contrast-induced kidney injury.

Mechanistically, contrast media trigger tubular inflammation through cytokine release, leukocyte recruitment, and oxidative stress, amplifying tubular damage. Elevated WBC count may therefore reflect a primed inflammatory state that increases vulnerability to injury. In this context, the anti-inflammatory effects of SGLT2 inhibitors—including suppression of the NLRP3 inflammasome—may contribute to their renoprotective profile. Clinically, WBC count emerges as a simple, accessible risk marker, while inflammation itself represents a potential therapeutic target [23].

Perhaps the most clinically relevant finding is the synergistic renoprotective effect of combined ACE inhibitor/ARB and SGLT2 inhibitor therapy. Dual therapy was associated with significantly less deterioration in both creatinine and eGFR compared with monotherapy or no treatment, with ACEi/ARB use showing an even stronger protective association than SGLT2i alone in multivariate analysis. While prior studies have evaluated these agents individually, their combined effect in CIN has not been specifically explored. Our prospective design, multivariate adjustment, and subgroup analyses strengthen the validity of this observation.

Mechanistically, this synergy is plausible: ACE inhibitors reduce intraglomerular pressure via efferent arteriolar dilation, whereas SGLT2 inhibitors act through afferent vasoconstriction mediated by tubuloglomerular feedback. Together, they may more effectively reduce glomerular pressure and filtration workload, thereby lowering tubular oxygen demand. In addition, both classes exert complementary anti-inflammatory and antioxidative effects, further supporting their combined renoprotective potential [24].

Taken together, our findings support current guideline recommendations, including the 2024 KDIGO CKD guideline and the 2023 ESC/2022 AHA/ACC/HFSA heart failure guidelines, which position SGLT2 inhibitors as cornerstone therapy in CKD and heart failure. By demonstrating that chronic SGLT2i use attenuates CIN risk—particularly in patients with CKD and those receiving combined therapy—our study suggests that continuation of a guideline-directed therapy may be safe during PCI in eligible patients [5, 6].

This study has several strengths, including its prospective design with consecutive patient enrolment, adherence to STROBE guidelines, and standardized procedural protocol performed by a single experienced operator, thereby minimizing variability. The cohort reflects real-world practice, including patients with varying renal function and comorbidities, and was supported by comprehensive baseline assessment, a standardized CIN definition, and robust multivariate and subgroup analyses.

However, limitations should be acknowledged. As a single-center observational study conducted in Egypt, residual confounding cannot be excluded and generalizability to other populations may be limited. Follow-up was restricted to 48 hours, preventing assessment of longer-term renal outcomes or persistent AKI. SGLT2i type, dose, and duration of therapy were not standardized (although all users were on chronic stable treatment). Very high-risk patients (eGFR < 30 mL/min/1.73 m² or hemodynamic instability) were excluded. Additionally, the modest sample size may limit detection of rare events

Conclusion

In this prospective observational study of 249 patients undergoing PCI, chronic SGLT2 inhibitor therapy was independently associated with a substantial reduction in contrast-induced nephropathy (7.1% vs. 16.3%; OR 0.37, 95% CI 0.15–0.92) and attenuated renal-function decline, with additive benefit from concomitant ACE inhibitor/ARB therapy (OR 0.15). Protection was most pronounced in patients with chronic kidney disease—the highest-risk subgroup—despite greater baseline diabetes and heart-failure prevalence among SGLT2i users. Baseline white blood cell count emerged as a novel inflammatory predictor of CIN.

These real-world findings reinforce current guideline recommendations (2024 KDIGO CKD Grade 1A; 2023 ESC/2022 AHA/ACC/HFSA heart failure guidelines) and provide procedural reassurance that chronic SGLT2 inhibitor therapy, ideally combined with renin–angiotensin system blockade, should be continued rather than withheld around contrast exposure. Larger multicenter randomized trials are needed to confirm dual-therapy synergy and inflammation-guided risk stratification.

Abbreviations

ACEi
Ace inhibitors
AKI
Acute kidney injury
AMI
Acute myocardial infarction
CI
Confidence intervals
CI-AKI
Contrast-induced acute kidney injury
CIN
Contrast-induced nephropathy
CKD
Chronic kidney disease
CKD-EPI
Chronic Kidney Disease Epidemiology Collaboration
eGFR
Estimated glomerular filtration rate
IQR
Interquartile range
IRB
Institutional Research Ethics Committee
NSTEMI
Non-ST Segment Elevation Myocardial Infarction
OR
Odds ratios
PCI
Percutaneous coronary intervention
RAS
Renin–angiotensin system
RR
Relative risk
SD
Standard deviation
SGLT2i
Sodium–glucose cotransporter-2 inhibitors
WBC
White blood cell

Declarations

Ethics approval and consent to participate:

This study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Kafrelsheikh University (IRB No: KFSIRB200-298). All clinical procedures involving human participants complied with the ethical standards established by the 1964 Declaration of Helsinki and its subsequent amendments. Written informed consent was obtained from all individual participants prior to enrolment.

Consent for publication:

Not applicable.

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Author Contribution

K.A.M., M.S.F., and R.M.E. conceptualized the study framework and oversaw the methodological design. R.N.D., D.A.A., and K.R.E. managed patient data acquisition and conducted the primary clinical investigations. M.E.A. and O.A.E. performed the formal statistical analysis and developed the visual data representations. R.B. and M.K.S. drafted the initial manuscript. Furthermore, all authors engaged in critical revisions of the text to enhance its intellectual content. All authors read and approved the final manuscript.

Data Availability

Availability of data and materials The specific datasets generated and analyzed throughout this prospective investigation are not maintained in a public repository to strictly protect patient confidentiality and adhere to institutional privacy guidelines. However, interested researchers may request access to the de-identified clinical data by contacting the corresponding author directly, provided the request is reasonable and scientifically sound.

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