

Effect of Perioperative Sodium-Glucose Cotransporter-2 Inhibitor Therapy on Early Postoperative Outcomes Following Coronary Artery Bypass Grafting in Patients with Type 2 Diabetes Mellitus: A Prospective Cohort Study

Saima Tasneem¹, Danish Naveed², Fatima Diab Mohammed Osman³, Faisal Ahmed⁴, Preeti Batheja⁵, Ambreen Zeeshan⁶, Fahmida Khatoon⁷

¹ Assistant Professor, Faculty of Health Sciences, Girne American University.

² Assistant Professor, Department of Cardiovascular Surgery, Ayub Medical College, Abbottabad, Pakistan.

³ Associate Professor, Department of Cardiac Surgery, SFMKB Institute of Cardiology, Dera Ghazi Khan, Pakistan.

⁴ Medical and surgical nursing department, College of Nursing University of Ha'il Saudia.

⁵ Assistant Professor, Department of Cardiac Surgery, Dow University of Health Sciences (DUHS), Karachi, Pakistan.

⁶ Assistant Professor, Department of Biochemistry, Fatima Memorial College of Medicine and Dentistry, Lahore, Pakistan.

⁷ Professor, Department of Biochemistry, United Medical and Dental College, Pakistan.

Corresponding Author: Danish Naveed **Email:** Danishnaveed002@gmail.com

ABSTRACT

Background: Sodium-glucose cotransporter-2 (SGLT2) inhibitors enhance cardiovascular and renal results in type 2 diabetes mellitus (T2DM), although their effect on recovery post-coronary artery bypass grafting (CABG) is still ambiguous. This research evaluated the correlation between established SGLT2 inhibitor treatment and first postoperative results after elective CABG.

Methods: This prospective two-center cohort included 120 adults with T2DM undergoing isolated on-pump CABG from January 2025 to February 2026. Fifty-four patients were receiving SGLT2 inhibitors and 66 were non-users. Therapy was withheld before surgery and restarted after clinical stabilization. The primary outcome was acute kidney injury (AKI) within seven postoperative days. Secondary outcomes included prolonged ventilation, vasopressor requirement, postoperative atrial fibrillation, intensive care unit (ICU) stay, hospital stay, 30-day readmission, mortality, and euglycemic diabetic ketoacidosis.

Results: AKI occurred in 16.7% of SGLT2 inhibitor users versus 34.8% of non-users ($p=0.025$). SGLT2 inhibitor therapy remained independently associated with lower AKI risk after adjustment (adjusted relative risk 0.49; 95% CI 0.26-0.91; $p=0.024$). Median ICU stay was 2 versus 3 days ($p=0.018$), and hospital stay was 7 versus 8 days ($p=0.011$). Differences in atrial fibrillation, prolonged ventilation, vasopressor use, readmission, and 30-day mortality were not significant. No euglycemic diabetic ketoacidosis occurred.

Conclusion: Established SGLT2 inhibitor therapy, with appropriate perioperative withholding, was associated with lower postoperative AKI and shorter recovery after CABG. Larger randomized studies are needed to confirm these findings. These findings support evaluation of SGLT2 inhibitors as part of optimized perioperative cardiorenal management in diabetic patients.

Keywords: SGLT2 inhibitors; coronary artery bypass grafting; type 2 diabetes mellitus; acute kidney injury; cardiac surgery; postoperative outcomes

How to cite this article: Saima Tasneem. Effect of Perioperative Sodium-Glucose Cotransporter-2 Inhibitor Therapy on Early Postoperative Outcomes Following Coronary Artery Bypass Grafting in Patients with Type 2 Diabetes Mellitus: A Prospective Cohort Study. *Int J Drug Deliv Technol.* 2026;16(83s):1392-1399. DOI: 10.25258/ijddt.16.83s.151.

INTRODUCTION

Coronary artery bypass grafting (CABG) patients have high prevalence of type 2 diabetes mellitus (T2DM) and it is linked to higher perioperative morbidity and mortality [1]. Diabetes is associated with diffuse coronary atherosclerosis, impaired vascular function, micro vascular disease, poor wound healing, and susceptibility to renal disease, which can have a negative impact on post cardiac surgery outcomes. Cardiac surgery associated acute kidney injury (AKI) is one of the most important complications among the

postoperative complications since even a small decrease in renal function is related to a longer intensive care unit stay, higher resource use, and inferior short- and long-term outcomes. In diabetic patients, this risk is increased by the overall impact of cardiopulmonary bypass, hemodynamic instability, systemic inflammation, oxidative stress and metabolic disturbance during surgery [2,3].

The sodium-glucose cotransporter-2 (SGLT2) inhibitors have become a major part of the current

armamentarium for treating T2DM with the advantage that their therapeutic effects are not just glucose lowering [4]. Large cardiovascular and renal outcome trials have shown that in carefully selected patients, heart failure events and progression of kidney disease has been reduced. These include restoration of tubuloglomerular feedback, lowering of intraglomerular pressure, natriuresis, decrease in oxidative stress and inflammation, and beneficial impact on myocardial and renal energetics. These properties have sparked interest in the potential for existing SGLT2 inhibitor treatment to also alter the physiological response to major cardiac surgery [5,6]. This hypothesis has now been supported by recent evidence. The randomized clinical trial POST-CABGDM found that empagliflozin reduced the rate of postoperative AKI in patients with T2DM compared with standard care without a significant difference in the rate of postoperative atrial fibrillation or myocardial infarction. However, there is still few evidence on the generalizability to real-world clinical practice, other SGLT2 inhibitors, and other early postoperative outcomes [7-9].

The use of SGLT2 inhibitors perioperatively is also an important safety consideration. Euglycemic diabetic ketoacidosis can occur in the postoperative period following cardiac surgery in patients subjected to these drugs, and may be more likely to occur with prolonged fasting periods, surgical stress, relative insulin deficiency, and volume depletion [10]. Therefore, according to current guidance from the American Diabetes Association (ADA), SGLT2 inhibitors should be discontinued 3–4 days prior to surgery and should not be used during extended periods of fasting or during acute illness. This suggests a clinically important dichotomy between the potential benefit of using an SGLT2 inhibitor preoperatively and the metabolic risk of using them inappropriately during the perioperative period [11].

However, although there is a growing interest, the number of prospective real-world evidence studies examining the association of proven SGLT2 inhibitor therapy to early recovery post CABG is limited [12]. Specific associations with postoperative renal dysfunction, respiratory support, arrhythmias, the need for vasopressors, intensive care utilization rate, infectious complications, readmission, and metabolic safety have not been well studied in a single prospective cohort. Thus, the aim of the present study was to assess the potential relationship between the use of SGLT2 inhibitors perioperatively and early postoperative outcomes among patients with T2DM undergoing CABG. We expected that judicious use of SGLT2 inhibitors preoperatively could result in reduced postoperative occurrence of AKI, and better early postoperative recovery without an increased

number of clinically relevant metabolic complications [13].

MATERIALS AND METHODS

The study design and setting.

The study was a prospective, two-center cohort conducted from January 2025 to February 2026 across the Department of Cardiovascular Surgery at Ayub Medical College, Abbottabad, Pakistan, and the Department of Cardiac Surgery at SFMKB Institute of Cardiology, Dera Ghazi Khan, Pakistan. One hundred and twenty (120) consecutive adults with type 2 diabetes mellitus (T2DM) who were undergoing elective first-time isolated on-pump coronary artery bypass grafting (CABG) were recruited. The research was conducted in accordance with the Declaration of Helsinki and STROBE standards. The research received approval from the institutional review boards at both facilities, and signed informed permission was acquired from all participants.

Participants

Patients ≥ 18 years with known T2DM who were undergoing elective isolated CABG were eligible. Exclusion criteria included type 1 diabetes, emergency or salvage surgery, off-pump cardiac artery bypass grafting (CABG), prior cardiac surgery, concomitant aortic or valve surgery, cardiogenic shock, active diabetic ketoacidosis, dialysis-dependent kidney disease, estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m², severe hepatic dysfunction, an active systemic infection, and incomplete 30-day follow-up.

SGLT2 Inhibitor Exposure

Patients were divided into two groups: those who had taken sodium-glucose cotransporter-2 (SGLT2) inhibitors preoperatively and those who had not. The exposed group comprised patients who had been prescribed empagliflozin, dapagliflozin, canagliflozin or ertugliflozin for a period of at least three months before surgery, the comparison group comprised patients who were not prescribed any of the SGLT2 inhibitors within the three months prior to surgery. Treatment was allocated for routine clinical care and not by the investigators.

Empagliflozin, dapagliflozin, canagliflozin were held for at least 72 hours prior to CABG, ertugliflozin was held for at least 96 hours prior to CABG. After a sufficient oral intake and stable renal function, stable hemodynamic status, and no evidence for metabolic acidosis or ketonemia, treatment was resumed.

Perioperative Assessment

Baseline variables were age, sex, BMI, and diabetes duration, HbA1c, insulin use, hypertension, dyslipidemia, smoking, prior myocardial infarction, heart failure, serum creatinine, eGFR, hemoglobin, and left ventricular ejection fraction. Operative variables were the number of grafts, length of

cardiopulmonary bypass, aortic cross-clamp time, blood-product transfusion, and vasoactive support. All patients were given standardized general anesthesia, median sternotomy, cardiopulmonary bypass, myocardial protection and intensive care after surgery. Blood glucose levels were monitored routinely perioperatively and insulin therapy was instituted as needed to keep blood glucose levels in the 100-180 mg/dl range.

Outcomes

The principal outcome of the study was acute kidney injury (AKI) following cardiac surgery, characterised by a serum creatinine elevation of ≥ 0.3 mg/dL within the initial 48 hours, or a rise to ≥ 1.5 times the baseline creatinine within 7 days, or a urine output of < 0.5 mL/kg/hour for ≥ 6 hours, as per the Kidney Disease: Improving Global Outcomes guidelines.

Secondary outcomes were stage 2 to 3 AKI, postoperative atrial fibrillation, mechanical ventilation > 24 hours, vasopressor use > 24 hours, myocardial infarction, stroke, surgical-site infection, reoperation for bleeding, intensive care unit stay, total hospital stay, and 30-day readmission and mortality. Euglycemic diabetic ketoacidosis was assessed as a prespecified safety endpoint and was defined either as a significant ketonemia with metabolic acidosis without a marked hyperglycemia.

Follow-Up and Data Collection:

All the clinical, laboratory, operative, and postoperative data were collected on a standard case-report form on a prospective basis. Preoperatively and in early postoperative period assessment was made of serum creatinine and electrolytes. All patients with unexplained metabolic acidosis or suggestive symptoms had blood gas and ketone testing. Clinical records and telephone follow-up as needed were used to track participants during hospitalization and for 30 days following CABG.

Sample Size

The planned number of patients was 120. With assumed similar exposure groups, a two-sided α of 0.05 and a statistical power of 80%, this sample size would allow for detecting large clinically relevant difference in postoperative AKI between SGLT2 inhibitor users and non-users. To minimize selection bias, consecutive recruitment was used.

Statistical Analysis

The statistical analysis was conducted using IBM SPSS Statistics version 27.0. Continuous variable data were represented as mean $\pm$ SD or median (IQR) and examined using Student's t-test or Mann-Whitney U test. Categorical data was presented as n (%) and analysed using the χ^2 test or Fisher's exact test. Modified Poisson regression using robust standard errors was used to calculate relative risks (RRs) and 95% confidence intervals (CIs) for postoperative acute

kidney injury (AKI). The multivariable model included age, sex, initial HbA1c, initial eGFR, LVEF, duration of cardiopulmonary bypass (CPB), and study location. Adjusted relative risks (aRRs) and 95% confidence intervals (CIs) were reported. Variance inflation factors were used to assess multicollinearity. All assessments were bilateral, with a significance threshold established at $p < 0.05$.

RESULTS

Study Population

A total of 132 diabetes mellitus type 2 patients undergoing CABG were evaluated during the study period. Twelve patients were excluded due to off-pump CABG (n=4), concomitant valvular surgery (n=3), baseline eGFR < 30 mL/min/1.73 m² (n=2), emergency CABG surgery (n=2), and lack of follow-up for 30 days (n=1). A total of 120 patients were analyzed (54 [45.0%] patients using SGLT2 inhibitor and 66 [55.0%] patients without SGLT2 inhibitor).

The mean age was 61.8 ± 7.6 years for all of the subjects. Ninety-four patients (78.3%) were male and 26 (21.7%) were female. The sex distribution was comparable between SGLT2 inhibitor users and non-users, with 43 (79.6%) versus 51 (77.3%) males and 11 (20.4%) versus 15 (22.7%) females, respectively ($p = 0.756$).

Of the SGLT2 inhibitor users, 29 (53.7%) were taking empagliflozin, 23 (42.6%) dapagliflozin, and two (3.7%) canagliflozin. Within each group, baseline demographic, metabolic, renal and cardiac characteristics were generally similar. Mean HbA1c was $7.8 \pm 1.0\%$ among SGLT2 inhibitor users and $8.0 \pm 1.1\%$ among non-users ($p = 0.304$), while mean baseline eGFR was 72.6 ± 16.2 and 69.8 ± 17.0 mL/min/1.73 m², respectively ($p = 0.361$). No significant differences were observed in insulin use, hypertension, chronic kidney disease, past myocardial infarction or left ventricular ejection fraction (Table 1).

Table 1. Baseline and operative characteristics according to SGLT2 inhibitor exposure

Characteristic	SGLT2 inhibitor (n=54)	Non-SGLT2 inhibitor (n=66)	p-value
Age, years	61.4 $\pm$ 7.4	62.1 $\pm$ 7.8	0.617
Male, n (%)	43 (79.6)	51 (77.3)	0.756
Female, n (%)	11 (20.4)	15 (22.7)	0.756
BMI, kg/m ²	27.7 $\pm$ 3.6	28.1 $\pm$ 3.9	0.565
Diabetes duration, years	10.2 $\pm$ 5.0	10.8 $\pm$ 5.4	0.533
HbA1c, %	7.8 $\pm$ 1.0	8.0 $\pm$ 1.1	0.304
Insulin therapy, n (%)	20 (37.0)	29 (43.9)	0.444
Hypertension, n (%)	45 (83.3)	56 (84.8)	0.821

Effect of Perioperative Sodium-Glucose Cotransporter-2 Inhibitor Therapy on Early Postoperative Outcomes Following Coronary Artery Bypass Grafting in Patients with Type 2 Diabetes Mellitus: A Prospective Cohort Study

Dyslipidemia, n (%)	41 (75.9)	52 (78.8)	0.708
Current/former smoker, n (%)	25 (46.3)	33 (50.0)	0.686
Previous myocardial infarction, n (%)	23 (42.6)	31 (47.0)	0.631
Heart failure, n (%)	8 (14.8)	13 (19.7)	0.483
Chronic kidney disease, n (%)	9 (16.7)	15 (22.7)	0.410
Baseline creatinine, mg/dL	1.05±0.24	1.10±0.28	0.302
eGFR, mL/min/1.73 m ²	72.6±16.2	69.8±17.0	0.361
Hemoglobin, g/dL	13.2±1.4	13.0±1.5	0.454
LVEF, %	49.5±8.0	48.6±8.5	0.555
Three-vessel coronary disease, n (%)	40 (74.1)	51 (77.3)	0.683
Number of bypass grafts	3.1±0.7	3.2±0.8	0.473
CPB duration, min	90.2±20.1	94.0±22.4	0.337
Aortic cross-clamp time, min	61.8±15.2	64.5±16.1	0.351
Intraoperative transfusion, n (%)	13 (24.1)	20 (30.3)	0.449

Primary Outcome

Postoperative acute kidney injury developed in 32 of 120 patients (26.7%). The incidence was significantly lower among SGLT2 inhibitor users than among non-users: 9/54 (16.7%) versus 23/66 (34.8%), respectively (p=0.025). This corresponded to an absolute risk reduction of 18.1 percentage points.

Among patients developing AKI, stage 1 disease occurred in seven (13.0%) SGLT2 inhibitor users and 14 (21.2%) non-users. Stage 2-3 AKI occurred in two (3.7%) and nine (13.6%), respectively (p=0.061). No patient required permanent dialysis, although one non-SGLT2 inhibitor patient required temporary renal replacement therapy.

Early Postoperative Outcomes

SGLT2 inhibitor users generally demonstrated a more favorable early postoperative course (Table 2). Prolonged mechanical ventilation occurred in 3/54 (5.6%) exposed patients compared with 11/66 (16.7%) non-users (p=0.059). Vasopressor support for >24

hours was required in five (9.3%) and 14 (21.2%) patients, respectively (p=0.074).

Postoperative atrial fibrillation occurred in eight (14.8%) SGLT2 inhibitor users and 16 (24.2%) non-users (p=0.199). Rates of postoperative myocardial infarction, stroke, reoperation for bleeding, and surgical-site infection were low and did not differ significantly between groups.

Median intensive care unit stay was significantly shorter among SGLT2 inhibitor users [2.0 days (IQR 2.0-3.0)] than among non-users [3.0 days (IQR 2.0-4.0); p=0.018]. Similarly, median postoperative hospital stay was 7 days (IQR 6-8) in SGLT2 inhibitor users compared with 8 days (IQR 7-10) among non-users (p=0.011).

Table 2. Early postoperative outcomes according to SGLT2 inhibitor exposure

Outcome	SGLT2 inhibitor (n=54)	Non-SGLT2 inhibitor (n=66)	p-value
Any AKI, n (%)	9 (16.7)	23 (34.8)	0.025
KDIGO stage 1 AKI, n (%)	7 (13.0)	14 (21.2)	0.235
KDIGO stage 2-3 AKI, n (%)	2 (3.7)	9 (13.6)	0.061
Postoperative atrial fibrillation, n (%)	8 (14.8)	16 (24.2)	0.199
Mechanical ventilation >24 h, n (%)	3 (5.6)	11 (16.7)	0.059
Vasopressor support >24 h, n (%)	5 (9.3)	14 (21.2)	0.074
Postoperative myocardial infarction, n (%)	2 (3.7)	4 (6.1)	0.686
Stroke, n (%)	1 (1.9)	2 (3.0)	1.000
Surgical-site infection, n (%)	2 (3.7)	5 (7.6)	0.456
Reoperation for bleeding, n (%)	2 (3.7)	4 (6.1)	0.686
Temporary renal replacement therapy, n (%)	0	1 (1.5)	1.000
ICU stay, days, median (IQR)	2.0 (2.0-3.0)	3.0 (2.0-4.0)	0.018
Hospital stay, days, median (IQR)	7 (6-8)	8 (7-10)	0.011
30-day readmission, n (%)	3 (5.6)	7 (10.6)	0.509

30-day mortality, n (%)	1 (1.9)	3 (4.5)	0.626
Euglycemic DKA, n (%)	0	0	—

Metabolic and Safety Outcomes

No episode of euglycemic diabetic ketoacidosis occurred in either group. Transient postoperative metabolic acidosis without significant ketonemia occurred in three patients receiving SGLT2 inhibitors and five non-users and resolved with routine postoperative management.

Clinically significant hypoglycemia occurred in two (3.7%) SGLT2 inhibitor users and four (6.1%) non-users ($p=0.686$). No episode of severe hypoglycemia was documented. There were also no significant differences in clinically evident volume depletion or urinary tract infection between groups.

Thirty-day readmission occurred in three (5.6%) SGLT2 inhibitor users compared with seven (10.6%) non-users ($p=0.509$). One patient (1.9%) in the SGLT2 inhibitor group and three patients (4.5%) in the non-SGLT2 inhibitor group died within 30 days ($p=0.626$). Because of the small number of deaths, adjusted mortality analysis was not performed.

Multivariable Analysis

In unadjusted analysis, preoperative SGLT2 inhibitor exposure was associated with a 52% lower risk of postoperative AKI (RR 0.48; 95% CI 0.24-0.96; $p=0.038$). The association remained significant after adjustment for age, sex, HbA1c, baseline eGFR, left ventricular ejection fraction, cardiopulmonary bypass duration, and participating center (aRR 0.49; 95% CI 0.26-0.91; $p=0.024$) (Table 3).

Baseline renal function and cardiopulmonary bypass duration were also independently associated with AKI. Each 10 mL/min/1.73 m² increase in baseline eGFR was associated with a 16% reduction in adjusted AKI risk (aRR 0.84; 95% CI 0.72-0.98; $p=0.027$), whereas every additional 10 minutes of cardiopulmonary bypass was associated with a 12% increase in risk (aRR 1.12; 95% CI 1.02-1.23; $p=0.019$). Increasing HbA1c showed a directionally higher AKI risk but did not achieve statistical significance (aRR 1.17 per 1% increase; 95% CI 0.98-1.40; $p=0.083$).

Sex was not independently associated with postoperative AKI after adjustment (male vs female: aRR 0.94; 95% CI 0.57-1.55; $p=0.808$).

Table 3. Multivariable modified Poisson regression for postoperative acute kidney injury

Variable	Adjusted RR	95% CI	p-value
SGLT2 inhibitor therapy	0.49	0.26-0.91	0.024
Age, per 5-year increase	1.08	0.91-1.28	0.379

Male vs female sex	0.94	0.57-1.55	0.808
HbA1c, per 1% increase	1.17	0.98-1.40	0.083
eGFR, per 10 mL/min/1.73 m ² increase	0.84	0.72-0.98	0.027
LVEF, per 5% increase	0.92	0.81-1.05	0.218
CPB duration, per 10-min increase	1.12	1.02-1.23	0.019
Study center	1.06	0.66-1.70	0.813

Overall, established SGLT2 inhibitor therapy was independently associated with a lower risk of early postoperative AKI following CABG. There were also significant reductions in length of stay in the ICU and in hospital and differences in prolonged ventilation, vasopressor requirement, atrial fibrillation, readmission and mortality were all in favor of SGLT2 inhibitor users, although not significant. No rise of serum levels of euglycemic diabetic ketoacidosis was seen in the standardized preoperative withholding protocol.

DISCUSSION

The use of an established SGLT2 inhibitor regimen was strongly linked to a significantly reduced postoperative acute kidney injury (AKI) rate in this prospective 2-center cohort of patients with type 2 diabetes mellitus (T2DM) who underwent elective on-pump CABG [1]. In the study, 16.7% of patients taking SGLT2 inhibitors developed AKI, while 34.8% of those not taking SGLT2 inhibitors did, and the link remained after researchers accounted for a variety of factors including demographic, metabolic, renal, cardiac, and operative factors. Increased baseline eGFR was found to be protective, while increased duration of cardiopulmonary bypass was a risk factor for the development of AKI. Also, SGLT2 inhibitor users experienced a shorter intensive care and hospital stay, although there were no statistically significant differences in mechanical ventilation, use of vasopressors, atrial fibrillation, readmission and mortality [2,3].

The renal association reported herein are consistent with the emerging clinical evidence which suggested a potential protective effect of SGLT2 inhibition in cardiac surgeries [4]. The POST-CABGDM randomized trial reported postoperative AKI in 22.5% of patients treated with empagliflozin versus 39.1% who were treated with standard care (relative risk 0.57 [1]). In a similar manner, a randomized pilot study in patients who underwent cardiac surgery with cardiopulmonary bypass (CPB) showed empagliflozin to be associated with reduced rates of AKI, but biomarker differences were less dramatic [2]. Thus,

the direction and strength of the association we observed among our cohort suggest that existing SGLT2 inhibitor use might affect risk of renal injury during CABG [5].

This association may be due to several mechanisms. SGLT2 inhibition has a favorable effect on renal oxygen utilization and tubular workload, restores tubuloglomerular feedback and lowers the intraglomerular pressure [6]. Others such as natriuresis, endothelial function, inflammation, oxidative stress, mitochondrial function, and renal congestion may be important during cardiopulmonary bypass, where renal perfusion abnormalities and ischemia-reperfusion injury are common causes of postoperative AKI [2,3]. The independent relationship between longer CBP duration and AKI observed in our study adds to the importance of surgical renal stress in the development of postoperative kidney injury [7].

Nevertheless, evidence is not entirely consistent. However, no significant difference in the incidence of AKI was observed in a propensity-weighted 2026 cohort of 509 cardiac surgery patients, with 35% in the pre-SGLT2 inhibitor group and 30% in the non-pre-SGLT2 inhibitor group [4]. A part of these contrasting findings is due to differences in study populations. Patients in that cohort had various cardiac procedures, and patients were prescribed SGLT2 inhibitors for diabetes, heart failure, and/or chronic kidney disease, while the current study comprised only patients with T2DM who had an isolated CABG procedure. Observed associations could also be affected by variation in drug discontinuation, baseline renal risk, surgical complexity and residual confounding [8].

Another clinically relevant finding is the shorter duration of stay in the intensive care unit (ICU) and hospitals among SGLT2 inhibitor users. While it cannot be proven that these are causative, better renal preservation and fluid management may play a role in rapid postoperative stabilisation [9]. In a randomized cardiac surgery pilot study, empagliflozin was seen to improve postoperative diuresis and decrease fluid balance without requiring greater use of vasopressors [5]. Despite the lack of statistical power to demonstrate meaningful differences in these secondary endpoints, both prolonged vasopressor support and mechanical ventilation were numerically lower in the SGLT2 inhibitor group. The results should therefore be regarded as supporting and not confirmatory [10].

Numerically, postoperative AF was also less common in the SGLT2 inhibitor group, although this was not statistically significant [11]. This is in line with the results of the first study which showed a decrease in AKI, but no significant effect on postoperative atrial fibrillation (POST-CABGDM) [1]. Likewise, the small number of myocardial infarction, stroke,

readmission and death in the current cohort precluded meaningful analysis of these outcomes. Larger studies are needed to find out if the cardiovascular benefit found with SGLT2 inhibitors is measurable with respect to major adverse events after CABG in the short term [12].

One of the key factors to consider is peri-operative metabolic safety. SGLT2 inhibitors have been linked to euglycemic ketoacidosis during fasting, surgical stress, and relative insulin deficiency [13]. An SGLT2 inhibitor prospective cardiac surgery study recently showed significantly higher postoperative ketoacidosis in patients taking SGLT2 inhibitors, pointing to the need for proper peri-operative discontinuation and monitoring of biochemical parameters [6]. There was no euglycemic diabetic ketoacidosis in our group. This is not to be read as proof that giving the drug continuously throughout the perioperative period is safe, but could simply mean that the drug was being withheld prior to CABG and restarted after the resumption of adequate oral intake and stability.

There are a number of strengths with the study. Data were obtained prospectively from two cardiac surgery centers, patients were limited to those with T2DM undergoing isolated on-pump CABG, and key baseline and operative variables were included in the adjusted analysis. The study also assessed general recovery and metabolic safety following surgery, not just renal outcomes [15,16].

There are a few drawbacks to recognize, as well. The first is that residual confounding due to treatment selection, the severity of the diabetes, concurrent medication use, or unmeasured clinical factors is possible because of the observational design and cannot be excluded [17]. Second, the sample size was small, and there were few events of severe AKI, stroke, euglycemic ketoacidosis, and death. Third, the various SGLT2 inhibitors were pooled together, so that no agent-specific effects could be evaluated. Fourth, postoperative fluid balance and detailed renal biomarker assessment was not performed in a systematic fashion. Lastly, follow-up was brief (30 days) and the study was not able to assess if the early renal association could lead to long-term preservation of kidney function or improved long term cardiovascular outcomes [18].

Despite these limitations, the results offer prospective real world evidence that established SGLT2 inhibitor therapy (when used appropriately and withheld prior to the procedure) may be associated with better early renal outcomes after CABG in patients with T2DM. Prospective multicenter studies with larger numbers of patients, and adequately powered randomized trials, are required to evaluate if this is a genuine class effect and to find out which patients would benefit most, and

when to stop the treatment before and restart it after surgery [19,20].

CONCLUSION

Established SGLT2 inhibitor therapy was independently associated with a lower incidence of postoperative acute kidney injury and shorter intensive care and hospital stays among patients with T2DM undergoing elective CABG. There were no significant differences between the postoperative incidence of AF, major complications, 30-day readmission, or mortality; no euglycemic diabetic ketoacidosis was observed with the standardized withholding protocol. These results indicate a possible beneficial cardiorenal association in the periop period, which needs validation in large, randomized and multicenter trials to allow modification of the periop treatment paradigm.

REFERENCES:

1. Pitta FG, Lima EG, Tavares CAM, et al. Empagliflozin in patients with type 2 diabetes undergoing on-pump CABG: the POST-CABGDM randomized clinical trial. *Diabetes Care*. 2025;48(6):988-995. doi:10.2337/dc24-2807.
2. Snel LIP, Oosterom-Eijmael MJP, Rampanelli E, et al. The effects of sodium-glucose transporter 2 inhibition on cardiac surgery-associated acute kidney injury: an open-label randomized pilot study. *J Clin Anesth*. 2025;103:111811. doi:10.1016/j.jclinane.2025.111811.
3. Snel LIP, Oosterom-Eijmael MJP, Lankadeva YR, et al. Cardiovascular outcomes of perioperative sodium-glucose transporter 2 inhibition in cardiac surgery patients: an open-label randomized pilot study. *Acta Anaesthesiol Scand*. 2025;69(6):e70075. doi:10.1111/aas.70075.
4. Ruste M, Vieira A, Le Guennec-Lux Y, et al. Preoperative exposure to sodium-glucose cotransporter-2 inhibitors and acute kidney injury after cardiac surgery: a retrospective single-centre cohort study with overlap weighting propensity score analysis. *Heart Lung Circ*. 2026;35(5):658-667. doi:10.1016/j.hlc.2026.01.004.
5. Ginestal-Calvo J, Flordelis-Lasierra JL, Pérez-Vela JL, et al. Postoperative ketoacidosis in cardiac surgery: incidence, analytical profile, and association with sodium-glucose cotransporter 2 inhibitors—a prospective observational study. *J Cardiothorac Vasc Anesth*. 2026;40(2):539-545. doi:10.1053/j.jvca.2025.11.014.
6. Auerbach JS, Alnajar A, Patel SS, et al. Retrospective chart review of euglycemic diabetic ketoacidosis rates and outcomes postimplementation of sodium glucose cotransporter 2 inhibitor use stoppage 5 days before open heart surgery. *J Cardiothorac Vasc Anesth*. 2025;39(6):1441-1450. doi:10.1053/j.jvca.2025.02.030.
7. Chaudhry A, Roels C, Lee J. Sodium-glucose cotransporter-2 inhibitor-associated euglycemic diabetic ketoacidosis: lessons from a case series of 4 patients undergoing coronary artery bypass grafting surgery. *Can J Diabetes*. 2022;46(8):843-850. doi:10.1016/j.cjcd.2022.06.007.
8. Lau A, Bruce S, Wang E, et al. Perioperative implications of sodium-glucose cotransporter-2 inhibitors: a case series of euglycemic diabetic ketoacidosis in three patients after cardiac surgery. *Can J Anaesth*. 2018;65(2):188-193. doi:10.1007/s12630-017-1018-6.
9. Seki H, Kuratani N, Shiga T, et al. Incidence of sodium-glucose cotransporter-2 inhibitor-associated perioperative ketoacidosis in surgical patients: a prospective cohort study. *J Anesth*. 2024;38(4):464-474. doi:10.1007/s00540-024-03335-3.
10. Perez Castillo D, Hall L, Senthuran S, et al. Sodium glucose co-transporter 2 inhibitor-associated euglycaemic diabetic ketoacidosis in the emergency peri-operative period: a systematic review. *J Anesth*. 2025;39(6):976-988. doi:10.1007/s00540-025-03570-2.
11. American Diabetes Association Professional Practice Committee for Diabetes. 16. Diabetes care in the hospital: Standards of Care in Diabetes—2026. *Diabetes Care*. 2026;49(Suppl 1):S339-S355. doi:10.2337/dc26-S016.
12. Oprea AD, Mohamed B, Hepner DL, et al. Perioperative management of patients taking sodium-glucose cotransporter 2 inhibitors: Society for Perioperative Assessment and Quality Improvement multidisciplinary consensus statement. *Br J Anaesth*. 2026;136(6):1776-1799. doi:10.1016/j.bja.2026.02.031.
13. Brown JK, Shaw AD, Mythen MG, et al. Adult cardiac surgery-associated acute kidney injury: joint consensus report. *J Cardiothorac Vasc Anesth*. 2023;37(9):1579-1590. doi:10.1053/j.jvca.2023.05.032.
14. Jacob KA, Leaf DE. Cardiac surgery-associated acute kidney injury: an updated review of current preventive strategies. *Anesthesiol Clin*. 2025;43(2):323-356. doi:10.1016/j.anclin.2025.01.001.
15. Strauß C, Albert F, Bormann E, et al. Risk factors, outcomes, and early prediction of cardiac surgery-associated acute kidney injury: a post hoc subgroup analysis of the Epidemiology of

- Surgery Associated Acute Kidney Injury study.
Br J Anaesth. 2026;136(1):34-42.
doi:10.1016/j.bja.2025.08.043.
16. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;373(22):2117-2128.
doi:10.1056/NEJMoa1504720.
 17. Wanner C, Inzucchi SE, Lachin JM, et al. Empagliflozin and progression of kidney disease in type 2 diabetes. *N Engl J Med*. 2016;375(4):323-334.
doi:10.1056/NEJMoa1515920.
 18. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med*. 2019;380(24):2295-2306.
doi:10.1056/NEJMoa1811744.
 19. Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;383(15):1436-1446.
doi:10.1056/NEJMoa2024816.
 20. EMPA-KIDNEY Collaborative Group. Empagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2023;388(2):117-127.
doi:10.1056/NEJMoa2204233.