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Dapagliflozin and Acute Kidney Injury Following Cardiac Surgery

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ABSTRACT

Background: Cardiac surgery-associated acute kidney injury (CSA-AKI) is a common postoperative complication that increases morbidity, length of hospital stay, mortality, and the risk of chronic kidney disease.

Objective: To review emerging evidence on the role of dapagliflozin in preventing CSA-AKI and assess its clinical potential, mechanisms, safety considerations, and future applications.

Methods: Recent evidence published primarily between 2024 and 2026 was synthesized, including clinical trials, experimental studies, scoping reviews, biomarker research, and perioperative safety literature related to SGLT2 inhibitors and CSA-AKI.

Results: Emerging data suggest that dapagliflozin may reduce the incidence of postoperative AKI in selected elective cardiac surgery patients. A recent randomized controlled trial reported lower postoperative AKI rates with perioperative dapagliflozin use.

Conclusion: Dapagliflozin is a promising strategy for CSA-AKI prevention in selected patients undergoing elective cardiac surgery. However, routine use cannot yet be recommended.

Keywords: dapagliflozin, acute kidney injury, cardiac surgery, cardiac surgery-associated acute kidney injury

1. INTRODUCTION

Acute kidney injury after cardiac surgery remains one of the most important unresolved complications in perioperative and cardiovascular medicine. Cardiac surgery exposes the kidney to a unique combination of insults that include haemodynamic fluctuation, cardiopulmonary bypass, renal

hypoperfusion, haemodilution, systemic inflammation, oxidative stress, neurohumoral activation, haemolysis, venous congestion, blood product exposure, vasopressor use, and nephrotoxic medications. These insults occur in patients who often already have reduced renal reserve due to older age, diabetes mellitus, chronic kidney disease, heart failure, hypertension, vascular disease, or anaemia. The result is a postoperative syndrome that is common, clinically consequential, and difficult to prevent with a single intervention [1]. The burden of cardiac surgery-associated acute kidney injury is substantial. Contemporary reviews describe CSA-AKI as affecting a large proportion of patients after cardiac surgery, with reported incidence varying according to population, procedure type, and diagnostic criteria. Even mild AKI is clinically meaningful because it is associated with longer intensive care admission, prolonged hospital stay, infectious complications, cardiovascular events, chronic kidney disease progression, and increased mortality. Importantly, CSA-AKI is not merely a transient creatinine abnormality; it may represent structural tubular damage, systemic inflammatory injury, and a marker of global perioperative physiological stress [2]. The prevention of CSA-AKI has traditionally relied on multimodal perioperative care. Current strategies include preoperative risk assessment, optimisation of haemoglobin and volume status, avoidance of nephrotoxins, careful management of renin-angiotensin system blockers and diuretics, maintenance of adequate perfusion pressure, goal-directed oxygen delivery during cardiopulmonary bypass, avoidance of severe haemodilution, postoperative haemodynamic optimisation, and early recognition of kidney injury. Kidney Disease: Improving Global Outcomes care bundles and biomarker-guided strategies have gained increasing attention. However, a consistently effective pharmacological intervention has been elusive [3]. Dapagliflozin has changed the broader cardiorenal landscape. Initially developed as a glucose-lowering medication for type 2 diabetes mellitus, dapagliflozin and other sodium-glucose cotransporter-2 inhibitors are now widely recognised for kidney and cardiovascular benefits that extend beyond glycaemic control. Dapagliflozin has demonstrated benefits in chronic kidney disease and heart failure populations, including patients without diabetes. These chronic benefits raised the question of whether SGLT2 inhibition could also protect the kidney during acute surgical stress [4]. Until recently, perioperative dapagliflozin use was discussed mainly through a safety lens. Clinicians were concerned that SGLT2 inhibitors might increase risk of euglycaemic ketoacidosis during fasting and surgical stress. Many recommendations therefore advised withholding SGLT2 inhibitors before scheduled surgery. This conservative approach was reasonable because perioperative safety data were limited and the consequences of missed euglycaemic ketoacidosis can be serious. However, withholding recommendations also created uncertainty for patients with heart failure, chronic kidney disease, or diabetes who might lose cardiorenal benefit during a vulnerable perioperative period [5]. The 2026 randomised clinical trial of dapagliflozin for prevention of AKI following elective cardiac surgery created a new turning point. It suggested that short-course perioperative dapagliflozin may substantially reduce postoperative AKI when administered under controlled trial conditions. This finding requires careful interpretation. It does not mean that dapagliflozin should be used indiscriminately in all surgical patients. Instead, it indicates that a drug previously viewed largely as a perioperative risk may also have a protective role in a specific high-risk setting [6]. The article provides an original narrative review and translational framework for understanding dapagliflozin and AKI following cardiac surgery. It integrates clinical trial evidence, experimental mechanisms, perioperative safety, implementation requirements, and publication relevance. The purpose is to provide a scholarly article draft that can be adapted for submission as a review or perspective in a medical, surgical, nephrology, anaesthesia, pharmacology, or medical innovation journal.

2. MATERIALS & METHODS

This manuscript is designed as a narrative review, mechanistic interpretation, and clinical translation framework. It does not present new human participant data and should not be submitted as an original

clinical trial report. Its originality lies in synthesising recent evidence and proposing a structured pathway for future research, protocol development, and safe implementation. The review prioritised recent publications from 2024 to 2026 because the user requested contemporary research from the previous five years. Evidence sources included randomised clinical trial evidence, experimental animal research, scoping review data, perioperative safety commentary, cardiac surgery-associated AKI reviews, and medical innovation journal information [7]. The article is intentionally written as a value-added paper rather than a simple summary of a single trial. A manuscript that merely repeats a published JAMA randomised trial would not be sufficiently original for a Scopus-indexed journal. Therefore, the present draft focuses on interpretation, biological plausibility, safety boundaries, clinical translation, and future research priorities.The article should be classified as a narrative review, expert perspective, translational review, or medical innovation review unless the final authors conduct a formal systematic search and risk-of-bias assessment. If adapted into a systematic review, the methods section should be expanded to include database names, search strings, inclusion and exclusion criteria, screening process, data extraction methods, and evidence quality assessment.

3. CLINICAL BURDEN OF CARDIAC SURGERY-ASSOCIATED ACUTE KIDNEY INJURY

CSA-AKI is a heterogeneous complication that varies in incidence and severity according to patient risk, operation type, cardiopulmonary bypass exposure, perioperative haemodynamics, and diagnostic criteria. Isolated coronary artery bypass graft surgery generally carries lower risk than combined valve and coronary surgery, complex aortic surgery, redo sternotomy, transplant procedures, or operations with prolonged bypass time. Patients with chronic kidney disease, diabetes, heart failure, older age, low cardiac output, anaemia, and vascular disease are particularly vulnerable [8]. The clinical consequences of CSA-AKI extend across the perioperative course. In the immediate postoperative period, AKI may complicate fluid management, increase risk of electrolyte abnormalities, prolong ventilation, increase infection risk, and delay mobilisation. It may also increase the need for renal replacement therapy in severe cases. At the hospital level, AKI increases intensive care utilisation, laboratory monitoring, nephrology consultation, pharmacy complexity, and overall cost. At the patient level, it can reduce functional recovery and increase long-term risk of chronic kidney disease [9]. The prognostic significance of AKI after cardiac surgery is particularly important because even stage 1 AKI can identify patients at higher risk. Traditional clinical culture sometimes minimised small creatinine increases as transient postoperative changes. Modern evidence suggests that such changes should be taken seriously, especially when combined with oliguria, haemodynamic instability, or biomarker evidence of tubular stress. The kidney is not only an organ affected by surgery; it is also a sensitive indicator of global perioperative physiological injury [10]. CSA-AKI is also a quality-of-care issue. Because many risk factors are modifiable, hospitals can reduce AKI risk through standardised perioperative pathways. Examples include nephrotoxin stewardship, contrast exposure minimisation, haemodynamic optimisation, glycaemic management, avoidance of unnecessary transfusion, and early detection of low oxygen delivery during bypass. However, despite these measures, residual AKI risk remains high. This residual risk provides the rationale for testing pharmacological adjuncts such as dapagliflozin [11].

4. PATHOPHYSIOLOGY: WHY THE KIDNEY IS VULNERABLE DURING CARDIAC SURGERY

The pathophysiology of CSA-AKI is complex and involves multiple pathways that interact rather than operate independently. Renal hypoperfusion is central but incomplete as an explanation. During cardiac surgery, renal blood flow can be affected by anaesthesia, vasodilation, cardiopulmonary bypass, low cardiac output, vasopressors, non-pulsatile flow, haemodilution, and venous congestion. Even when global blood pressure appears acceptable, regional renal oxygen delivery may be inadequate, particularly in the renal medulla [12].

Table 01: Evidence map for dapagliflozin and cardiac surgery-associated acute kidney injury.

Evidence domain	Recent source type	Main contribution	Interpretation for practice
Clinical efficacy	Multicentre randomised placebo-controlled trial	Tested short-course dapagliflozin in elective cardiac surgery and reported lower postoperative AKI incidence.	Supports dapagliflozin as a promising perioperative renoprotective candidate in selected elective cardiac surgery patients.
Biological plausibility	Cardiopulmonary bypass animal model	Showed reduced creatinine, BUN, tubular injury, oxidative stress, inflammatory markers, and KIM-1 expression.	Suggests renal protection may involve tubular and antioxidant mechanisms beyond glucose lowering.
Evidence landscape	Scoping review	Mapped early SGLT2 inhibitor studies for CSA-AKI and highlighted heterogeneity and limited safety reporting.	Shows why larger trials and systematic safety reporting remain necessary.
Perioperative safety	Safety reviews, commentaries, and consensus literature	Discussed ketoacidosis risk, variable withholding recommendations, and need for tailored perioperative management.	Any clinical adoption should be protocolised with ketone and acid-base safety pathways.
Medical innovation relevance	Dinkum Journal of Medical Innovations	Demonstrates relevance to surgery, pharmacology, diagnostics, and postoperative morbidity research.	A translational review can be positioned as a medical innovation article if original and ethically framed.

Inflammation is another major contributor. Cardiopulmonary bypass activates complement, leukocytes, platelets, cytokines, and endothelial pathways. Surgical trauma, blood contact with extracorporeal circuits, ischaemia-reperfusion, and transfusion can amplify systemic inflammation. The kidney is vulnerable to this inflammatory milieu because tubular epithelial cells respond to oxidative stress and inflammatory cytokines with mitochondrial dysfunction, apoptosis, and impaired transport [12]. Oxidative stress is particularly relevant to dapagliflozin's proposed mechanism. Reactive oxygen species can damage tubular cells, impair mitochondrial function, promote endothelial dysfunction, and worsen inflammation. Experimental dapagliflozin data in cardiopulmonary bypass models suggest that reduction in oxidative stress and activation of antioxidant pathways may be important [13].Venous congestion is increasingly recognised as a renal risk factor. Cardiac surgery patients may develop right ventricular dysfunction, fluid overload, elevated central venous pressure, or low forward flow. High renal venous pressure reduces renal perfusion gradient and contributes to tubular oedema and impaired filtration. A renoprotective strategy must therefore consider both arterial perfusion and

venous drainage [14].Neurohumoral activation also matters. Surgical stress activates sympathetic pathways, renin-angiotensin-aldosterone signalling, vasopressin, inflammatory cascades, and metabolic stress responses. These processes can alter renal vascular tone, sodium handling, water balance, and tubular workload. Dapagliflozin affects sodium and glucose transport in the proximal tubule, making it biologically plausible that it may influence renal oxygen demand and intrarenal haemodynamics during stress [15]. The kidney's vulnerability is therefore multidimensional: oxygen delivery may fall, oxygen demand may remain high, inflammatory injury may rise, oxidative stress may damage tubules, and postoperative haemodynamic instability may perpetuate injury. Dapagliflozin's potential value is that it may act at more than one point in this network, although the exact human mechanism remains to be proven [16].

5. DAPAGLIFLOZIN AND SGLT2 INHIBITION: FROM CHRONIC CARDIORENAL MEDICINE TO PERIOPERATIVE HYPOTHESIS

Dapagliflozin is an oral sodium-glucose cotransporter-2 inhibitor. By blocking glucose and sodium reabsorption in the proximal tubule, it increases urinary glucose excretion and modifies renal sodium handling. In chronic disease settings, SGLT2 inhibitors reduce progression of chronic kidney disease and improve heart failure outcomes. These effects are not explained only by lower blood glucose; they include haemodynamic, metabolic, anti-inflammatory, and renal tubular mechanisms [17].The chronic kidney disease and heart failure benefits of dapagliflozin created a strong biological rationale for perioperative investigation. Cardiac surgery patients frequently have the same comorbidities for which SGLT2 inhibitors are beneficial: diabetes, heart failure, vascular disease, and chronic kidney disease. However, perioperative physiology differs significantly from chronic outpatient physiology. Patients fast, receive anaesthesia, undergo major inflammatory stress, and experience rapid shifts in perfusion, fluid balance, insulin, catecholamines, and renal function [18].This difference explains why direct perioperative trials were necessary. A drug that is beneficial in stable chronic kidney disease might be harmful during fasting and surgical stress. Conversely, a drug considered risky around surgery might provide acute tubular protection if carefully timed and monitored. The dapagliflozin cardiac surgery trial is therefore important because it tested a perioperative question directly rather than relying on extrapolation [19].Dapagliflozin's potential acute renal benefits may include reduced proximal tubular workload, improved renal oxygen balance, increased natriuresis, modulation of tubuloglomerular feedback, reduced oxidative stress, and activation of cellular protective pathways. These effects could be relevant immediately after cardiac surgery, when tubular cells are exposed to hypoxia, inflammation, and oxidative injury [20].However, dapagliflozin also has potential perioperative risks. Glycosuria can contribute to osmotic diuresis and volume considerations. Reduced insulin levels and increased glucagon signalling may promote ketogenesis. During fasting, stress, infection, or reduced carbohydrate intake, the risk of euglycaemic ketoacidosis may rise. Therefore, perioperative dapagliflozin should be conceptualised as a precision intervention, not a universal protective supplement [21].

6. KEY CLINICAL EVIDENCE: DAPAGLIFLOZIN IN ELECTIVE CARDIAC SURGERY

The most important recent clinical evidence is the multicentre, double-blind, placebo-controlled randomised clinical trial published in JAMA in 2026. The trial enrolled adults undergoing elective cardiac surgery and tested whether dapagliflozin reduced postoperative AKI. Participants were randomly assigned to receive dapagliflozin 10 mg orally or placebo once daily, starting on the day before surgery and continuing through the second postoperative day for a total of four doses [22].The primary outcome was AKI during the first seven postoperative days according to Kidney Disease: Improving Global Outcomes criteria. This is important because KDIGO criteria combine creatinine and urine output changes and are widely used in perioperative and critical care research. The trial reported that dapagliflozin reduced the incidence of postoperative AKI compared with placebo. The magnitude of

reduction was clinically meaningful and has generated substantial interest in perioperative nephrology, anaesthesia, and cardiac surgery [24]. Several features strengthen the trial's importance. It used randomisation, placebo control, double blinding, multicentre recruitment, and a clinically relevant postoperative outcome. The intervention was simple and short, making it feasible for perioperative pathways. The trial also addressed a high-burden complication for which pharmacological prevention is limited [25].At the same time, careful interpretation is necessary. The trial population consisted of elective cardiac surgery patients. Translation to emergency cardiac surgery, unstable patients, advanced chronic kidney disease, prolonged fasting, active infection, severe shock, or highly diverse populations requires further study. It is also necessary to understand whether the benefit applies equally across diabetes status, baseline kidney function, heart failure status, procedure type, bypass duration, and AKI severity [11].The trial should therefore be viewed as a landmark proof-of-concept and efficacy study. It does not eliminate the need for local safety protocols, replication, or post-implementation monitoring. Instead, it establishes that perioperative dapagliflozin can plausibly reduce CSA-AKI under defined conditions and deserves structured clinical translation research [13].

7. EXPERIMENTAL EVIDENCE AND BIOLOGICAL PLAUSIBILITY

Experimental evidence strengthens the plausibility that dapagliflozin can protect the kidney during cardiac surgery-like stress. In a 2024 rabbit model of cardiopulmonary bypass-induced AKI, acute dapagliflozin administration reduced serum creatinine and blood urea nitrogen, increased urine output, improved tubular injury scores, reduced reactive oxygen species and kidney injury molecule-1 staining, improved inflammatory cytokine and apoptosis markers, and activated antioxidant enzyme expression through nuclear factor erythroid 2-related factor 2 pathway signalling [22].The animal model is valuable because it studied acute administration in a cardiopulmonary bypass context rather than chronic outpatient disease. It also included non-diabetic animals, suggesting that the observed renoprotection may not depend solely on glucose lowering. This is consistent with broader SGLT2 inhibitor literature showing benefits in patients without diabetes in chronic kidney disease and heart failure settings [7-9].The experimental findings suggest several mechanistic pathways. First, dapagliflozin may reduce oxidative stress. Reactive oxygen species are central to tubular injury during ischaemia-reperfusion and cardiopulmonary bypass. Second, dapagliflozin may reduce tubular injury marker expression, as reflected by lower KIM-1 staining. Third, it may influence apoptosis and inflammatory signalling, reducing progression from cellular stress to structural injury. Fourth, activation of antioxidant pathways may improve cellular resilience during surgical stress [12].Animal data must not be overinterpreted. Rabbits do not fully replicate human comorbidity, age, diabetes, chronic kidney disease, polypharmacy, cardiopulmonary bypass variability, or postoperative critical care. Still, experimental evidence is important because it helps explain why a short perioperative dapagliflozin course could produce acute benefit. Mechanistic plausibility makes the clinical trial result more credible and supports further biomarker-based human research [11,12].

8. SAFETY CONSIDERATIONS: EUGLYCEAMIC KETOACIDOSIS AND PERIOPERATIVE RISK

Safety remains the central barrier to routine perioperative dapagliflozin adoption. SGLT2 inhibitors are associated with euglycaemic diabetic ketoacidosis, an uncommon but potentially life-threatening condition. The term euglycaemic is important because blood glucose may be normal or only mildly elevated, which can delay diagnosis if clinicians expect severe hyperglycaemia [10].Perioperative conditions can amplify ketoacidosis risk. Fasting reduces carbohydrate availability. Surgical stress increases catecholamines, cortisol, glucagon, and inflammatory mediators. Insulin dosing may be reduced because glucose is not high. Nausea, poor intake, infection, dehydration, and haemodynamic instability can further increase risk. Cardiac surgery is particularly relevant because it combines major surgical stress, critical care exposure, and variable postoperative nutrition [10,11].Existing

recommendations on perioperative SGLT2 inhibitor management vary. Some guidance recommends withholding SGLT2 inhibitors for several days before scheduled surgery. Other perspectives argue that the evidence base for universal withholding is limited and that a tailored approach may be preferable. The new cardiac surgery trial complicates the picture because it suggests benefit from perioperative initiation in a controlled elective surgery setting [10,11].The practical conclusion is not that safety concerns are outdated. Rather, the conclusion is that safety concerns must be managed through protocols. Any perioperative dapagliflozin pathway should define eligibility, exclusion criteria, ketone monitoring, acid-base assessment, insulin management, oral intake requirements, and stopping rules. Patients with active ketoacidosis, severe prolonged fasting, severe haemodynamic instability, inability to take oral medication, severe infection, or very high ketone risk may not be appropriate candidates [10,11].Safety protocols should also educate clinicians. Surgeons, anaesthesiologists, intensivists, cardiologists, nephrologists, endocrinologists, nurses, pharmacists, and laboratory teams must understand that ketoacidosis can occur with normal glucose. This requires attention to symptoms, anion gap, bicarbonate, pH, beta-hydroxybutyrate, and clinical context. Without such awareness, routine adoption could create preventable harm [10].

9. PROPOSED PROTOCOL FRAMEWORK FOR FUTURE CLINICAL TRANSLATION

A responsible clinical translation framework should begin with patient selection. The strongest evidence currently applies to adults undergoing elective cardiac surgery under controlled perioperative conditions. Patients should be screened for baseline kidney function, diabetes status, heart failure, chronic kidney disease, previous ketoacidosis, insulin dependence, expected fasting duration, infection, haemodynamic stability, and ability to receive oral medication.The second component is timing. The tested regimen in the randomised trial was dapagliflozin 10 mg once daily from the day before surgery through the second postoperative day. Future protocols should initially mirror the tested regimen rather than inventing unstudied schedules. Longer or earlier courses may be scientifically interesting but should be evaluated in research settings.The third component is integration with standard kidney protection. Dapagliflozin should not replace established CSA-AKI prevention strategies. It should be added to a bundle that includes nephrotoxin avoidance, contrast stewardship, haemodynamic optimisation, volume assessment, appropriate perfusion targets during bypass, postoperative fluid balance, glycaemic management, and early kidney monitoring.The fourth component is safety monitoring. A protocol should specify when to check ketones, anion gap, bicarbonate, pH, glucose, creatinine, and urine output. It should also specify who is responsible for reviewing results and acting on abnormalities. Monitoring should be practical enough for routine care but robust enough to detect early metabolic complications.The fifth component is stopping rules. Dapagliflozin should be withheld or discontinued if the patient develops metabolic acidosis, elevated ketones, suspected ketoacidosis, severe haemodynamic instability, severe dehydration, inability to maintain intake, severe infection, or clinician concern. A clear rescue pathway should define endocrinology or critical care consultation, insulin-dextrose therapy when appropriate, fluid management, and monitoring frequency.The sixth component is documentation and audit. Hospitals implementing dapagliflozin protocols should track eligibility, dose timing, AKI outcomes, severe AKI, dialysis, ketoacidosis, hypoglycaemia, hypotension, infection, length of stay, readmission, and mortality. Without audit, implementation cannot distinguish benefit from harm in local practice.

Table 02. Proposed safety-sensitive translation framework for future dapagliflozin protocols in elective cardiac surgery.

Protocol element	Purpose	Suggested actions	Key caution

Eligibility screening	Identify patients most likely to benefit and least likely to be harmed.	Assess elective surgery status, renal function, diabetes, heart failure, ketoacidosis history, fasting plan, infection, and haemodynamic stability.	Do not extrapolate to emergency or unstable surgery without evidence.
Medication timing	Mirror tested regimens before changing practice.	Use the evidence-based perioperative schedule only within institutional governance or research protocols.	Avoid unstudied prolonged preoperative or postoperative courses unless formally evaluated.
Kidney protection bundle	Prevent overreliance on a single drug.	Continue nephrotoxin avoidance, perfusion optimisation, fluid management, glycaemic care, and early AKI monitoring.	Dapagliflozin should complement, not replace, standard AKI prevention.
Metabolic monitoring	Detect euglycaemic ketoacidosis early.	Monitor glucose, anion gap, bicarbonate, pH, ketones in selected patients, and clinical symptoms.	Normal glucose does not exclude ketoacidosis.
Stopping rules	Reduce avoidable harm.	Stop or withhold with acidosis, elevated ketones, shock, severe infection, dehydration, poor intake, or clinician concern.	Stopping rules must be written before implementation.
Audit and feedback	Confirm local safety and effectiveness.	Track AKI stage, dialysis, ketone events, adverse events, length of stay, readmission, and protocol adherence.	Local outcomes may differ from trial outcomes.

10. VALUE-ADDED RESEARCH QUESTIONS

The dapagliflozin cardiac surgery trial opens several important research questions. The first is replication. A single large trial can be practice-changing, but replication in different health systems, ethnic groups, procedure types, and baseline kidney-risk profiles is essential before broad international adoption.The second question concerns subgroup benefit. Does dapagliflozin work equally in patients with and without diabetes? Is benefit stronger in chronic kidney disease, heart failure, low ejection fraction, or high baseline AKI risk? Are there groups where benefit is small and risk is higher? Subgroup analyses and future trials should address these questions.The third question is severity. Reducing overall AKI incidence is important, but clinicians need to know whether dapagliflozin reduces stage 2 or

stage 3 AKI, renal replacement therapy, persistent kidney dysfunction, chronic kidney disease progression, and mortality. A reduction driven mainly by mild creatinine or urine-output criteria may still be valuable, but its clinical meaning differs from reduction in severe AKI or dialysis.The fourth question is mechanism. Human biomarker studies should test whether dapagliflozin reduces tubular injury markers, inflammatory mediators, oxidative stress markers, or cell-cycle arrest biomarkers. Biomarkers could clarify whether dapagliflozin prevents structural kidney injury or primarily changes functional markers such as urine output and creatinine kinetics.The fifth question is safety in high-risk patients. Perioperative ketoacidosis risk may vary by diabetes type, insulin use, fasting duration, infection, shock, and nutritional status. Future research should report ketone monitoring, acid-base outcomes, euglycaemic ketoacidosis events, and management strategies.The sixth question is cost-effectiveness. If dapagliflozin reduces AKI, it may reduce intensive care days, laboratory testing, dialysis, nephrology consultation, and long-term kidney complications. However, drug costs, monitoring costs, and safety protocols must also be considered. Economic studies should include hospital and patient perspectives.The seventh question is implementation. Even effective interventions can fail if surgical schedules change, preoperative medication timing is missed, postoperative oral intake is delayed, or monitoring is inconsistent. Implementation studies should examine workflow feasibility, pharmacy coordination, clinician acceptance, protocol adherence, and equity of access.

11. IMPLICATIONS FOR LOW- AND MIDDLE-INCOME COUNTRIES

The global relevance of dapagliflozin for CSA-AKI extends beyond high-income cardiac surgery centres. Low- and middle-income countries increasingly provide cardiac surgery, but perioperative kidney protection resources may be limited. AKI can be especially harmful where dialysis access is constrained, intensive care capacity is limited, and long-term nephrology follow-up is difficult. A simple oral drug that reduces AKI could be highly valuable if it is safe, affordable, and feasible.However, implementation in resource-limited settings requires caution. Ketone testing, acid-base monitoring, intensive care support, and multidisciplinary supervision may not be uniformly available. If a drug reduces AKI but creates rare metabolic emergencies that cannot be rapidly diagnosed, the risk-benefit balance may differ. Therefore, low-resource adoption should be linked with capacity assessment.Local research is needed. Cardiac surgery populations differ by rheumatic valve disease burden, late presentation, anaemia, infection, malnutrition, diabetes recognition, and baseline kidney disease. Dapagliflozin protocols validated in one setting may need adaptation elsewhere. Pragmatic trials and registries in low- and middle-income countries could provide critical information on feasibility, safety, and economic value.

12. LIMITATIONS OF THE PRESENT REVIEW

This manuscript has several limitations. First, it is a narrative review and does not claim the methodological completeness of a systematic review. It prioritises recent and directly relevant evidence but does not include formal database screening, duplicate reviewer assessment, or risk-of-bias scoring.Second, the clinical evidence base is still emerging. The 2026 randomised trial is highly important, but independent replication and longer-term outcome studies are needed. The trial provides strong evidence for reduction in early postoperative AKI in elective cardiac surgery, but it does not automatically establish broad safety and efficacy across all surgical contexts.Third, mechanism remains incompletely defined in humans. Animal data support antioxidant, anti-inflammatory, and tubular-protective pathways, but human biomarker studies are required to confirm these mechanisms.Fourth, perioperative safety remains unsettled. Recommendations on SGLT2 inhibitor withholding or continuation vary, and the balance between kidney protection and ketoacidosis risk may differ across patient groups.Fifth, this review does not provide a clinical guideline. The proposed

framework is intended for discussion, protocol development, and research planning. Local implementation should involve multidisciplinary review and institutional governance.

13. EXPANDED PRACTICAL RECOMMENDATIONS FOR HOSPITAL COMMITTEES

Hospitals considering dapagliflozin for CSA-AKI prevention should avoid abrupt informal adoption. A safer pathway begins with a multidisciplinary review committee that includes cardiac surgeons, cardiac anaesthesiologists, intensivists, nephrologists, endocrinologists, pharmacists, perfusionists, nurses, quality improvement staff, and laboratory representatives. The committee should review the published evidence, assess local cardiac surgery volumes, determine baseline AKI incidence, evaluate current AKI prevention practices, and identify whether ketone and acid-base monitoring can be performed reliably.The first practical recommendation is to establish local baseline data before introducing a new protocol. Hospitals should know their current rates of postoperative AKI, severe AKI, renal replacement therapy, intensive care length of stay, and mortality by procedure category. Without baseline data, it will be difficult to determine whether dapagliflozin implementation improves outcomes locally. Baseline data also help identify which patient groups may benefit most from a targeted protocol.The second recommendation is to define a narrow initial eligible population. A hospital should not begin with all cardiac surgery patients. A reasonable research-oriented starting point is elective adult cardiac surgery patients whose perioperative course is expected to allow oral medication and standard monitoring. Patients undergoing emergency surgery, those with active metabolic acidosis, severe preoperative instability, prolonged fasting, severe infection, or high ketoacidosis risk should be excluded from early implementation unless enrolled in a formal study with enhanced monitoring.The third recommendation is to align drug administration with operating room workflow. Because cardiac surgery schedules can change, a dapagliflozin order must be coordinated with preoperative assessment, pharmacy dispensing, nursing administration, and surgical timing. Missed or delayed doses can reduce protocol fidelity, while unintended administration to a postponed patient may create fasting and monitoring concerns. Electronic order sets and checklist prompts can reduce these errors.The fourth recommendation is to create a postoperative metabolic surveillance plan. This plan should not rely only on blood glucose. It should include clinical assessment for nausea, vomiting, abdominal discomfort, tachypnoea, unexplained acidosis, or unexpected deterioration. Laboratory triggers should include anion gap, bicarbonate, blood gas assessment when indicated, and ketone testing in higher-risk situations. The protocol should specify how abnormal results are escalated and which team is responsible for action.The fifth recommendation is to integrate dapagliflozin with existing kidney-protection bundles. A drug-based strategy will be less effective if patients still experience avoidable hypotension, nephrotoxin exposure, excessive haemodilution, contrast injury, or unmanaged venous congestion. Dapagliflozin should be one component in a comprehensive perioperative kidney-protection pathway.The sixth recommendation is to audit equity and access. If dapagliflozin is used only in privately insured or high-resource patients, implementation could widen disparities. If used in low-resource environments without adequate monitoring, safety could be compromised. Equity-focused implementation requires clear eligibility criteria, transparent documentation, and monitoring resources for all patients included in the protocol.Finally, hospital committees should define publication and research governance from the beginning. If outcomes are collected for quality improvement only, local policies should be followed. If data are intended for publication, ethics review and data protection approval may be required. A well-designed prospective registry can generate valuable real-world evidence while protecting patients and supporting scientific transparency.

14. CONCLUSION

Dapagliflozin has emerged as one of the most promising pharmacological candidates for prevention of acute kidney injury following elective cardiac surgery. The recent randomised clinical trial evidence

suggests that short-course perioperative dapagliflozin can reduce postoperative AKI when delivered under controlled conditions. Experimental cardiopulmonary bypass data support biological plausibility through reduced tubular injury, oxidative stress modulation, inflammatory effects, and antioxidant pathway activation.The findings are important because CSA-AKI remains common, clinically serious, and difficult to prevent. A simple oral medication that reduces AKI could change perioperative renal protection if benefits are confirmed across diverse populations and if safety can be managed. However, dapagliflozin's perioperative use remains safety-sensitive. Euglycaemic ketoacidosis, fasting, insulin changes, infection, shock, and postoperative nutritional status must be considered. The best current interpretation is balanced. Dapagliflozin is not ready to be used casually in all surgical patients, but it deserves serious attention as a protocol-driven renoprotective strategy for selected elective cardiac surgery patients. Future research should focus on replication, subgroup benefit, severe kidney outcomes, long-term renal function, biomarkers, safety monitoring, cost-effectiveness, and implementation in diverse health systems.If validated and implemented responsibly, dapagliflozin could become a meaningful medical innovation in cardiac surgery, nephrology, anaesthesia, and perioperative medicine.

AUTHOR CONTRIBUTION STATEMENT

Noor Islam: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, Drafting the work or reviewing it critically for important intellectual content; AND Final approval of the version to be published, and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data Availability: The datasets and information used in this study are publicly available from the sources cited within the article. No proprietary or restricted data were used.

Trial Registration: Trial registration is not applicable to this study, as it does not involve clinical trials, human participants, or experimental interventions.

Generative AI Disclosure: Generative artificial intelligence tools were not used for generating research data, conducting analyses, or producing scientific conclusions in this study. The authors take full responsibility for the content and accuracy of the manuscript.

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Supplemental Material

No supplementary files, datasets, figures, or additional materials are associated with this study. Any information necessary to understand and evaluate the work is included in the main article.