



Artificial intelligence in the management of acute kidney injury after cardiac surgery

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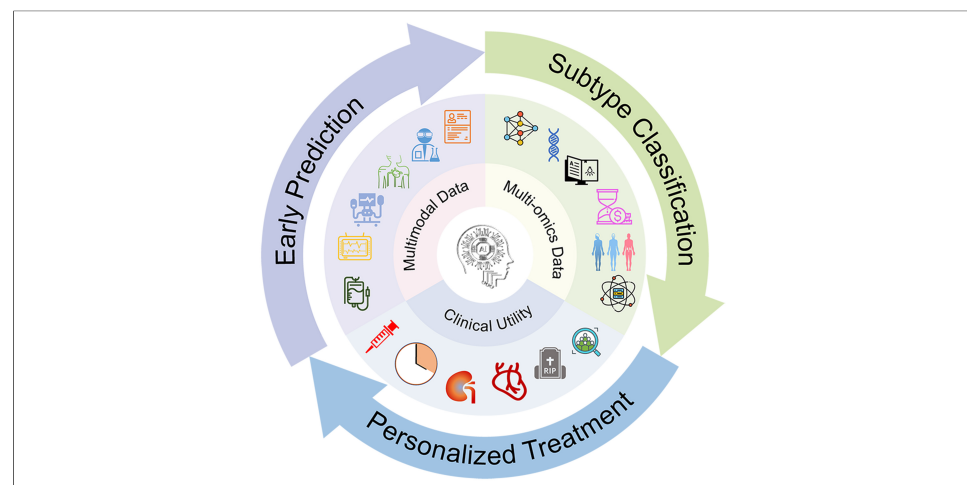
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Abstract

Acute kidney injury (AKI) is a common and serious complication after cardiac surgery, affecting 10%-40% of patients. It worsens patient outcomes and consumes significant healthcare resources. Its pathophysiology is complex and involves ischemia-reperfusion injury, inflammatory responses, and endothelial dysfunction. Artificial intelligence (AI) offers considerable potential to improve the management of this condition. AI models can integrate multimodal data, including preoperative clinical profiles, intraoperative hemodynamics, and postoperative laboratory values, thereby enabling early prediction of AKI. By identifying distinct clinical subtypes, AI may support personalized therapeutic strategies. Furthermore, it may improve prognostic assessments, allowing more precise risk stratification for both cardiac and renal outcomes. However, current applications face challenges, including inconsistent data quality, limited model interpretability, and high implementation costs. Existing models are also constrained by the range of variables they

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incorporate. Future technological advances may enable the analysis of a broader array of variables, potentially revealing novel biomarkers and clinically useful combinations of indicators. Such progress could advance precision medicine in this field, ultimately improving patient care and optimizing clinical workflows.

INTRODUCTION

Epidemiology and burden

According to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, postoperative acute kidney injury (PO-AKI) is defined as an increase in serum creatinine (Cr) of at least 0.3 mg/dL or 50% from baseline within 48 h after surgery, or a urine output of less than 0.5 mL/kg/h for at least 6 h^[1-3]. Cardiac surgery-associated acute kidney injury (CSA-AKI), also referred to as acute kidney injury (AKI) after cardiac surgery, is a common and serious complication of procedures such as coronary artery bypass grafting (CABG) and valve surgery^[4-6]. It poses a major threat to patient recovery and survival^[7-9] and places a substantial burden on healthcare systems^[10,11]. The reported incidence ranges from 10% to 40%^[12-15], and 2% to 5% of patients require renal replacement therapy (RRT)^[16,17]. Importantly, many of these patients subsequently develop chronic kidney disease (CKD) or end-stage renal disease (ESRD)^[14,18]. CSA-AKI is independently associated with a marked increase in both short- and long-term morbidity and mortality^[19]. For example, patients who develop AKI have been shown to have a threefold higher 30-day postoperative mortality rate than those who do not, along with hospital stays that are, on average, 5 days longer^[5] and substantially higher healthcare costs, reaching approximately \$40,000 per patient^[20,21].

Pathophysiology

The pathophysiology of CSA-AKI is complex^[12,22]. Cardiopulmonary bypass (CPB) is a key initiating factor in renal injury because it disrupts renal hemodynamic balance, causes ischemia and hypoxia in the renal medulla, and triggers oxidative stress^[23]. These effects are accompanied by rapid activation of the inflammatory cascade, with the release of cytokines such as tumor necrosis factor- α (TNF- α) and interleukin (IL)-6. At the same time, renal tubular epithelial cells undergo apoptosis in response to ischemia and hypoxia. Together, these processes contribute to ischemia-reperfusion injury. In addition, blood contact with the artificial surfaces of the bypass circuit activates the coagulation system, leading to the formation of numerous microthrombi that clog the renal microvasculature and impair renal perfusion. This process, combined with an imbalance in vasoactive mediators such as endothelin-1, exacerbates renal vasoconstriction and promotes microembolism and endothelial injury. In patients with postoperative low cardiac output, activation of the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system further increases renal vascular resistance and promotes sodium and water retention, creating a neurohormonal imbalance that further compromises renal function^[24,25].

Perioperative risk factors and the potential role of artificial intelligence

Risk factors for CSA-AKI are often classified into three stages: preoperative, intraoperative, and postoperative^[12,22]. Preoperative^[26] factors include advanced age (> 70 years), diabetes, CKD, and low left ventricular ejection fraction (LVEF < 35%). Intraoperative factors include prolonged CPB time and contrast exposure^[27,28]. Postoperative factors are more heterogeneous. They may include infectious shock, vasopressor requirement, and exposure to nephrotoxic medications such as vancomycin and non-steroidal anti-inflammatory drugs (NSAIDs)^[12]. One study^[29], for example, found that severe hyperglycemia within 24 h of intensive care unit (ICU) admission after cardiac surgery increased the risks of AKI within 7 days, as well as ICU mortality, and in-hospital mortality.

The severity of this complication and its complex origins underscore the urgent need for improved management strategies. This is where artificial intelligence (AI) may play an important role^[30,31]. AI has the capacity to integrate diverse data streams, including preoperative patient characteristics, real-time

intraoperative hemodynamics, and high-granularity postoperative ICU monitoring data^[32]. This makes it a powerful tool for developing predictive models that provide early warning of CSA-AKI. Furthermore, the integration of AI with cluster analysis can facilitate the identification of patient phenotypes, which may guide individualized intervention strategies, such as goal-directed fluid therapy and the targeted use of anti-inflammatory agents. Continued advances in AI, coupled with large-scale multicenter clinical studies, may further optimize perioperative renal protection and lead to new breakthroughs in the prevention and treatment of this condition.

Literature search strategy

For this narrative review, we systematically searched PubMed, Embase, Web of Science, and the Cochrane Library for articles published through March 2026. We used a combination of Medical Subject Headings terms and keywords, including “acute kidney injury,” “AKI,” “cardiac surgery-associated AKI,” “CSA-AKI,” “cardiac surgical procedures,” “cardiopulmonary bypass,” and “heart surgery,” together with terms such as “artificial intelligence,” “machine learning,” “deep learning,” “predictive model,” “neural network,” “random forest,” and “gradient boosting.” Our search included both pediatric and adult populations.

We included studies that evaluated AI applications in the management of postoperative CSA-AKI, including risk prediction, subtype classification, diagnostic assistance, prognostic assessment, and clinical decision support. All included studies were published in peer-reviewed journals and reported original data with clear model-performance metrics. We excluded editorials, commentaries, conference abstracts, case reports, and non-English articles. Studies not focused on cardiac surgery or AI were also excluded. We manually screened the reference lists of included articles to identify additional relevant studies.

Our search identified many potentially relevant articles. After screening titles, abstracts, and full texts, we selected the primary studies that met all eligibility criteria. Their key features are summarized in [Table 1](#). The remaining articles informed the background, theoretical framework, and discussion sections of this review. The overall framework of the review is illustrated in [Figure 1](#).

AI-DRIVEN CSA-AKI EARLY PREDICTION: FROM DATA INTEGRATION TO CLINICAL TRANSLATION

The disease burden of CSA-AKI and the urgency of early prediction

AKI after cardiac surgery poses a significant risk to patients during the perioperative period. Studies have shown that it is independently associated with higher in-hospital mortality, with the highest odds of death observed in patients who require acute dialysis^[20]. More importantly, a substantial proportion of these patients may progress to CKD. A systematic review found that PO-AKI is associated with an increased risk of long-term mortality, particularly in patients with persistent renal impairment compared with those whose kidney function recovers to baseline levels^[22,65]. Patients with AKI have longer hospital stays, incur higher medical costs, and require long-term nephrology follow-up, thereby placing a substantial burden on healthcare systems^[17]. Early identification of high-risk patients, followed by timely intervention, has been shown to reduce the incidence of AKI by 40%, mitigate progression to ESRD, and lower healthcare expenditures. This is important from both individualized-care and socioeconomic perspectives^[66].

Traditional risk scores have long been used to predict CSA-AKI. Common examples include the Cleveland Clinic Score (CCS) and the European System for Cardiac Operative Risk Evaluation (EuroSCORE)^[67,68]. However, these scores typically rely on relatively static preoperative and intraoperative data. They do not incorporate real-time postoperative biomarkers or other dynamic postoperative variables. This limits their ability to accurately predict early-onset CSA-AKI, thereby delaying treatment adjustments and ultimately affecting patient outcomes^[34].

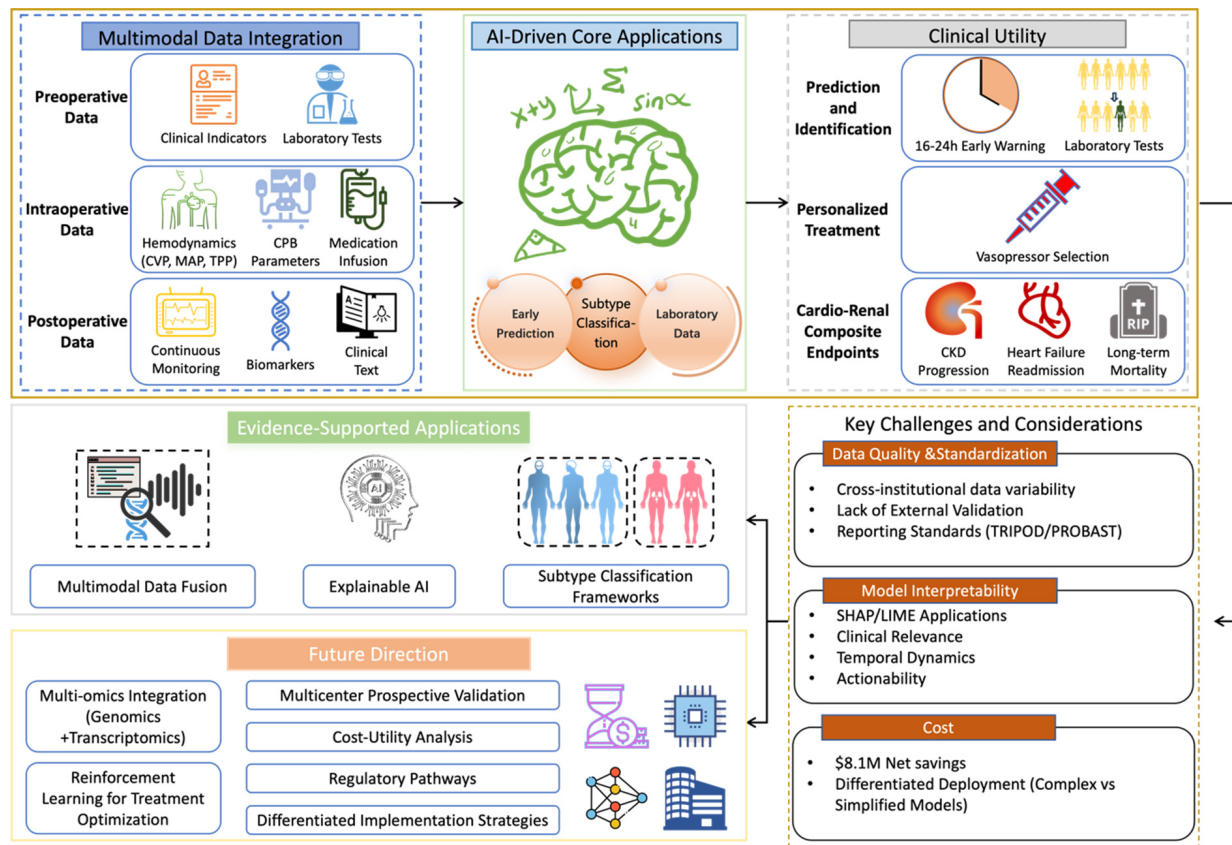


Figure 1. Artificial intelligence in cardiac surgery-associated acute kidney injury management: a comprehensive framework. Figure 1 illustrates the multidimensional framework of AI applications in CSA-AKI management. The framework is organized into six core layers: (1) multimodal data integration, encompassing preoperative, intraoperative, and postoperative data sources; (2) AI-driven core applications, including early prediction, subtype classification, and prognostic assessment, with representative studies and performance metrics; (3) clinical utility, highlighting key outcomes such as early warning, personalized treatment, and cardio-renal composite endpoints; (4) key challenges and considerations for clinical translation, including data quality, model interpretability, and implementation costs; (5) evidence-supported applications; and (6) future research directions. AI: Artificial intelligence; CSA-AKI: cardiac surgery-associated acute kidney injury; CVP: central venous pressure; MAP: mean arterial pressure; TPP: tissue perfusion pressure; CPB: cardiopulmonary bypass; CKD: chronic kidney disease; TRIPOD: Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis; PROBAST: Prediction model Risk Of Bias ASsessment Tool; SHAP: SHapley Additive exPlanations; LIME: local interpretable model-agnostic explanations.

In contrast, a machine learning (ML)-based model developed by Penny-Dimri *et al.* using preoperative and intraoperative data outperformed traditional risk scores in predicting the need for postoperative RRT^[35]. Their Gradient Boosting Machine (GBM) algorithm achieved an area under the curve (AUC) of 0.85 (0.01) on the receiver operating characteristic (ROC) curve, outperforming the CCS, which achieved an AUC of 0.81 (0.004). In 2020, Tseng *et al.*^[33] used ML to integrate a wide range of data, including demographic characteristics, preoperative laboratory results, medications, and intraoperative hemodynamic time-series data. They tested several algorithms, including random forest (RF) and extreme gradient boosting (XGBoost). The RF model, which incorporated intraoperative variables, achieved the highest AUC. Kalisnik *et al.*^[34] applied AI specifically to the early detection of CSA-AKI. By tracking serial changes in Cr and estimated glomerular filtration rate (eGFR), their “Detect-A(K)I” model detected CSA-AKI within 12 h after surgery with high accuracy, sensitivity, and specificity.

Despite these promising results, several methodological limitations warrant consideration. Many studies selectively report performance metrics, focusing heavily on AUC while giving limited attention to calibration, clinical utility, and real-world feasibility. For example, the GBM model developed by

Table 1. Representative studies on artificial intelligence in cardiac surgery-associated acute kidney injury management

Number	Author	Title	Category	AI application domains
1	Tseng et al. ^[33] (2020)	Prediction of the development of acute kidney injury following cardiac surgery by machine learning	Predictive models	Early prediction (RF+XGBoost, AUC 0.839)
2	Kalishnik et al. ^[34] (2022)	Artificial intelligence-based early detection of acute kidney injury after cardiac surgery	Predictive models	Early detection within 12 h (AUC 0.88, accuracy 82.1%)
3	Penny-Dimri et al. ^[35] (2021)	Machine learning algorithms for predicting and risk profiling of cardiac surgery-associated acute kidney injury	Predictive models	Risk stratification for RRT (GBM AUC 0.85)
4	Thongprayoon et al. ^[36] (2022)	Explainable preoperative automated machine learning prediction model for cardiac surgery-associated acute kidney injury	Predictive models	Preoperative autoML with SHAP/LIME explainability
5	Li et al. ^[37] (2023)	Development and validation of a machine learning predictive model for cardiac surgery-associated acute kidney injury	Predictive models	CatBoost model, NT-proBNP as key predictor
6	Gao et al. ^[38] (2023)	An explainable machine learning model to predict acute kidney injury after cardiac surgery	Predictive models	XGBoost with SHAP, eGFR and ICU Cr as top features
7	Jiang et al. ^[39] (2023)	Interpretable machine learning models for early prediction of acute kidney injury after cardiac surgery	Predictive models	LR for any AKI (AUC 0.812), GBC for severe AKI (AUC 0.86)
8	Song et al. ^[40] (2024)	Machine learning-based prediction of off-pump coronary artery bypass grafting-associated acute kidney injury	Predictive models	GBDT for OPCABG-AKI (AUC 0.861), insulin use as top predictor
9	Zhong et al. ^[41] (2025)	Causal deep learning for real-time detection of cardiac surgery-associated acute kidney injury: derivation and validation in seven time-series cohorts	Predictive models	Causal deep learning (REACT) across 7 cohorts, 16.35 h earlier detection
10	Baloglu et al. ^[42] (2026)	Performance of supervised machine learning models for cardiac surgery-associated acute kidney injury in children: multicenter retrospective cohort study	Predictive models	4-center pediatric study, model performance variability (AUC 0.64-0.83)
11	Ryan et al. ^[43] (2023)	Machine learning for dynamic and early prediction of acute kidney injury after cardiac surgery	Predictive models	Ensemble ML on MIMIC-IV, 89% cases predicted before clinical detection
12	Lee et al. ^[44] (2018)	Derivation and validation of machine learning approaches to predict acute kidney injury after cardiac surgery	Predictive models	GBM best (AUC 0.78), online risk calculator
13	Luo et al. ^[45] (2023)	Machine learning-based prediction of acute kidney injury following pediatric cardiac surgery	Predictive models	XGBoost in 3 centers, AUC 0.912 (internal)/0.889 (external)
14	Shao et al. ^[46] (2023)	Development, external validation, and visualization of machine learning models for predicting occurrence of acute kidney injury after cardiac surgery	Predictive models	RF best in external validation, SHAP visualization
15	Sun et al. ^[47] (2025)	Explainable machine learning models for early prediction of acute kidney injury after cardiac surgery	Predictive models	Ensemble model AUC 0.856, SVM external validation AUC 0.847
16	Chen et al. ^[48] (2025)	Artificial intelligence-driven prediction of acute kidney injury following acute type a aortic dissection surgery in a chinese population	Predictive models	LightGBM for ATAAD, AUC 0.874, web application
17	Ranucci et al. ^[49] (2024)	The multifactorial dynamic perfusion index: a predictive tool of cardiac surgery associated acute kidney injury	Predictive models	MDPI integrating preoperative risk and CPB quality, AUC 0.769
18	Thongprayoon et al. ^[36] (2022)	Explainable preoperative automated machine learning prediction model for cardiac surgery-associated acute kidney injury	Explainable AI studies	SHAP and LIME for patient-specific predictions
19	Li et al. ^[37] (2023)	Development and validation of a machine learning predictive model for cardiac surgery-associated acute kidney injury	Explainable AI studies	SHAP identified positive/negative associations with clinical variables
20	Tseng et al. ^[33] (2020)	Prediction of the development of acute kidney injury following cardiac surgery by machine learning	Explainable AI studies	SHAP summary and dependence plots for RF model

21	Zeng <i>et al.</i> ^[50] (2024)	An interpretable machine learning model to predict off-pump coronary artery bypass grafting-associated acute kidney injury	Explainable AI studies	SHAP-based feature importance, intraoperative urine volume top
22	Ejmalian <i>et al.</i> ^[51] (2022)	Prediction of acute kidney injury after cardiac surgery using interpretable machine learning	Explainable AI studies	LIME and Shapley methods, confirmed Cr, CPB time, BS, Alb as top features
23	Han <i>et al.</i> ^[52] (2025)	Care guided by tissue oxygenation and haemodynamic monitoring in off-pump coronary artery bypass grafting (Bottomline-CS)	Multimodal data integration	Tissue oxygenation + hemodynamic monitoring for early warning
24	Li <i>et al.</i> ^[53] (2025)	Integration of machine learning and large language models for screening and identifying key risk factors of acute kidney injury after cardiac surgery	Multimodal data integration	LLM-simulated expert judgment enhanced risk factor selection
25	Wang <i>et al.</i> ^[54] (2025)	Leveraging large language models for preoperative prevention of cardiopulmonary bypass-associated acute kidney injury	Multimodal data integration	LLM-extracted semantics from clinical text, multimodal fusion AUC 0.9201
26	Karway <i>et al.</i> ^[55] (2023)	Development and external validation of multimodal postoperative acute kidney injury risk machine learning models	Multimodal data integration	Structured data + CUI features from notes, AUC 0.82
27	Han <i>et al.</i> ^[56] (2024)	Machine learning with clinical and intraoperative biosignal data for predicting cardiac surgery-associated acute kidney injury	Multimodal data integration	High-resolution intraoperative biosignals improved AUC from 0.767 to 0.840
28	Milam <i>et al.</i> ^[57] (2023)	Derivation and validation of clinical phenotypes of the cardiopulmonary bypass-induced inflammatory response	Subtype classification	K-means identified 3 phenotypes; α phenotype had highest inflammatory/kidney biomarkers
29	Zhao <i>et al.</i> ^[58] (2024)	Development and validation of LCMM prediction algorithms to estimate recovery pattern of postoperative AKI in type A aortic dissection	Subtype classification	LCMM identified early recovery (51.8%) and late/no recovery (48.2%)
30	Giles <i>et al.</i> ^[59] (2024)	Prediction of acute kidney injury after cardiac surgery with combined arterial and venous intrarenal doppler	Subtype classification	Hierarchical clustering identified 3 intrarenal Doppler subtypes; high-risk subtype had higher AKI risk
31	Li <i>et al.</i> ^[60] (2020)	A novel machine learning algorithm, Bayesian networks model, to predict the high-risk patients with cardiac surgery-associated acute kidney injury	Subtype classification	Bayesian networks revealed different variable relationships for AKI and severe AKI
32	Fan <i>et al.</i> ^[61] (2023)	Clinical characteristics and risk factors of cardiac surgery associated-acute kidney injury progressed to chronic kidney disease in adults	Prognostic assessment	19.1% progressed to CKD; risk prediction model AUC 0.859
33	Chen <i>et al.</i> ^[62] (2023)	A novel predictive model for poor in-hospital outcomes in patients with acute kidney injury after cardiac surgery	Prognostic assessment	IL-16, IL-8, Δ SCr predicted RRT/death, AUC 0.947
34	Huang <i>et al.</i> ^[63] (2023)	Development and validation of clinical prediction models for acute kidney injury recovery at hospital discharge in critically ill adults	Prognostic assessment	Cardiac surgery subgroup showed acceptable recovery prediction (AUC 0.71)
35	Chen <i>et al.</i> ^[64] (2020)	Novel blood cytokine-based model for predicting severe acute kidney injury and poor outcomes after cardiac surgery	Prognostic assessment	Cytokine model (IFN- γ , IL-16, MIP-1 α) C-statistic 0.86-0.87

RF: Random forest; XGBoost: extreme gradient boosting; AUC: area under the curve; RRT: renal replacement therapy; GBM: Gradient Boosting Machine; autoML: automated ML; ML: machine learning; SHAP: SHapley Additive exPlanations; LIME: local interpretable model-agnostic explanations; NT-proBNP: N-terminal pro-B-type natriuretic peptide; eGFR: estimated glomerular filtration rate; ICU: intensive care unit; Cr: creatinine; LR: logistic regression; AKI: acute kidney injury; GBDT: gradient-boosting decision tree; OPCABG-AKI: off-pump coronary artery bypass grafting-associated acute kidney injury; MIMIC-IV: medical information mart for intensive care IV; SVM: support vector machine; ATAAD: acute type A aortic dissection; MDPI: multifactorial dynamic perfusion index; CPB: cardiopulmonary bypass; BS: blood sugar; Alb: albumin; Bottomline-CS: better outcome through tissue oxygenation monitoring linked with intervention in cardiac surgery; LLM: large language model; CUI: concept unique identifier; LCMM: latent class mixture modeling; CKD: chronic kidney disease; IL: interleukin; IFN: interferon; MIP: macrophage inflammatory protein.

Penny-Dimri *et al.* lacked calibration assessment and decision-curve analysis^[35]. The XGBoost model developed by Tseng *et al.* was derived from a single-center cohort and lacked external validation^[33]. The “Detect-A(K)I” model, although highly accurate, depends on serial Cr measurements that may not be feasible in all clinical settings and also requires validation in more diverse populations^[34].

Table 2. Multimodal data types and storage formats in cardiac surgery perioperative period

Phase	Category	Data type	Examples	Storage format	References
Preoperative	Lab tests	Cardiac function markers	Serum creatinine (Cr), N-terminal pro-B-type natriuretic peptide (NT-proBNP)	Electronic health record (EHR) system (structured database)	[71-73]
	Imaging data	Cardiac structure analysis	Left ventricular ejection fraction (LVEF), coronary CT angiography (CTA)	Picture archiving and communication system (PACS) (DICOM format)	[74-78]
Intraoperative	Hemodynamic monitoring	Real-time waveform data	Invasive blood pressure (IBP, 100 Hz Sampling), central venous pressure (CVP)	Anesthesia information management system (AIMS) (time-series database)	[79,80]
	Medication infusion	Vasoactive drug delivery	Epinephrine infusion rate ($\mu\text{g/kg/min}$), heparin concentration monitoring	Smart infusion pump system (temporal log)	[81,82]
Postoperative	Continuous monitoring	Organ function dynamics	Pulse contour cardiac output (PiCCO), mixed venous oxygen saturation (SvO_2)	ICU central monitoring system (High-frequency streaming data)	[52,79,83-85]
	Biomarkers	Tissue injury evaluation	Troponin I (cTnI), neutrophil gelatinase-associated lipocalin (NGAL)	Laboratory information system (LIS) (numerical reporting system)	[73,86,87]

More recent multicenter studies have begun to address these issues by reporting a more comprehensive set of performance metrics. For instance, Baloglu *et al.* evaluated 40 ML models across four pediatric cardiac surgery centers^[42]. They reported not only AUC but also calibration and decision-curve analyses, showing that a model with good discrimination may still be poorly calibrated. Similarly, Zhong *et al.* developed a causal deep learning (DL) model, called REACT, using seven international cohorts comprising more than 63,000 patients^[41]. They provided calibration plots and decision-curve analysis, demonstrating substantial net benefit across a range of risk thresholds and an average lead time of more than 16 h before clinical detection. These studies highlight the need for rigorous external validation and comprehensive performance assessment before any model is deployed clinically.

Integration and characterization of multimodal data for cardiac surgery

Multimodal data refers to information collected in multiple forms or modalities, often from different sources or sensors^[69]. In the context of cardiac surgery, these data may include physiological time-series data, medical imaging, laboratory results, clinical notes, bioelectrical signals^[70], and medication infusion records [Table 2]. The integration and analysis of these datasets enable researchers to obtain more comprehensive information, thereby providing high-dimensional feature support for AI modeling^[88].

Several studies support the value of this approach in CSA-AKI. For example, Han *et al.* developed an early warning system that fused intraoperative tissue oxygen monitoring data with hemodynamic parameters, helping maintain stable tissue oxygen levels and reducing postoperative complications^[52]. Li *et al.* integrated structured electronic health record (EHR) data with a large language model (LLM), to simulate expert clinical judgment. This approach identified 18 key risk factors for PO-AKI and improved model interpretability^[53]. Karway *et al.* demonstrated that combining structured data, such as demographics, vital signs, and laboratory results, with concept unique identifiers (CUIs), extracted from unstructured clinical notes improved AKI prediction in a multicenter cohort, increasing the AUC from 0.79 to 0.82^[55]. Adding high-frequency intraoperative biosignals, such as perfusion pressure waveforms, progressively improved model performance, with the AUC rising from 0.767 with preoperative data alone to 0.840 when postoperative data were included^[56].

Looking ahead, integrating multi-omics data, including genomics, transcriptomics, and proteomics, with real-time physiological monitoring could enable truly dynamic and personalized risk stratification. Preliminary studies have already identified associations between specific genetic polymorphisms such as

Table 3. Classification and characteristics of AKI subtypes after cardiac surgery

Dimension	Subtype	Characteristics	Related factors/biomarkers
Etiology & pathophysiology	Ischemia-reperfusion injury ^[22,102,103]	Renal tubular epithelial cell apoptosis, elevated oxidative stress biomarkers	Intraoperative hypoperfusion, prolonged CPB; NGAL, KIM-1
	Inflammation-driven ^[100,104,105]	Systemic inflammatory response syndrome (SIRS), elevated inflammatory cytokines	Sepsis/postoperative infection; IL-6, IL-8, TNF- α
	Endothelial dysfunction ^[106-108]	Increased vascular permeability, elevated ANG-2/ANG-1 ratio	Risk of postoperative multiorgan failure
Biomarker features	Tubular stress ^[109-111]	Cell cycle arrest	Urinary [TIMP-2]·[IGFBP7] > 0.3
	Tubular injury ^[112-115]	Acute tubular necrosis, linked to persistent AKI and CKD progression	Elevated urinary NGAL or KIM-1
Clinical course & recovery	Risk factor subtype ^[58,61,116,117]	Distinct risk factors for persistent severe AKI (septic shock, catecholamine use, comorbidities)	Cardiac surgery-specific risk factors

AKI: Acute kidney injury; CPB: cardiopulmonary bypass; NGAL: neutrophil gelatinase-associated lipocalin; KIM-1: kidney injury molecule-1; IL: interleukin; TNF: tumor necrosis factor; ANG: angiotensin; [TIMP-2]·[IGFBP7]: tissue inhibitor of metalloproteinases-2 and insulin-like growth factor-binding protein 7; CKD: chronic kidney disease.

those in IL-6 and Apolipoprotein E (APOE), and the risk of CSA-AKI^[89,90]. However, the clinical utility of this approach in dynamic prediction models has not yet been established and requires prospective validation in large, multicenter cohorts. Future work should focus on hypothesis-driven studies that test specific integrative frameworks, rather than exploratory multi-omics analyses that lack a clear mechanistic basis.

CLASSIFICATION OF CSA-AKI SUBTYPES: FROM RESOLVING HETEROGENEITY TO PRECISE INTERVENTION

AKI after cardiac surgery: challenges posed by heterogeneity

AKI after cardiac surgery is a highly heterogeneous clinical syndrome. Despite the shared exposure to cardiac surgery, this heterogeneity is evident in its complex pathophysiology, which involves interacting mechanisms such as ischemic injury, inflammation, and nephrotoxin exposure. It is also reflected in its diverse clinical presentations, which vary widely in severity, disease trajectory, and effects on other organs^[14,91-94]. In clinical practice, the effectiveness of traditional one-size-fits-all approaches, such as standard fluid protocols or simple avoidance of nephrotoxins, is limited because these strategies ignore this heterogeneity. This likely explains why several randomized controlled trials (RCT) of such interventions have failed to meet their primary endpoints^[95-97]. For instance, one RCT of perioperative spironolactone not only failed to reduce the incidence of KDIGO-defined AKI but also was associated with a significantly increased AKI risk, with no benefit in secondary outcomes such as the need for RRT, ICU length of stay, or mortality. Therefore, establishing a personalized therapeutic framework based on multidimensional omics data and real-time physiological monitoring will be critical for overcoming current therapeutic limitations^[94,98].

Subtype classification

In medicine, personalized therapy is defined as the development of targeted intervention strategies informed by multidimensional features. These features may include the patient's genome, pathophysiological mechanisms, clinical phenotype, and biomarkers^[99]. A clinical phenotype refers to the observable characteristics of a disease. By contrast, a subtype is a more specific subgroup of patients defined by shared features such as etiology, biomarkers, treatment response, or prognosis^[100]. The goal of subtyping is to identify groups with similar underlying disease mechanisms, thereby paving the way for targeted therapeutic interventions^[101]. Current approaches to subtyping CSA-AKI can be organized into three dimensions: etiology and pathophysiology, biomarker profiles, and clinical course with recovery patterns [Table 3].

From an etiologic and pathophysiologic standpoint, one subtype is driven by ischemia-reperfusion injury. This subtype is linked to intraoperative hypoperfusion and prolonged CPB and is characterized by renal tubular epithelial cell apoptosis and elevated oxidative stress markers, such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1)^[103,118]. Animal models have shown that sepsis or postoperative infection can trigger an inflammation-driven phenotype consistent with systemic inflammatory response syndrome (SIRS). This phenotype is characterized by marked elevations in cytokines such as IL-6, IL-8, and TNF- α ^[119]. An endothelial dysfunction subtype has also been described, featuring increased vascular permeability and a higher angiopoietin (ANG)-2/ANG-1 ratio, which correlated with an elevated risk of postoperative multiorgan failure^[106,120]. In terms of biomarker profiles^[113], one subtype reflects tubular stress and is identified by a urinary product of tissue inhibitor of metalloproteinases-2 and insulin-like growth factor-binding protein 7 ([TIMP-2]·[IGFBP7]) greater than 0.3. This finding indicates cell cycle arrest and is commonly observed in the early postoperative period^[109,114,121-124]. Another subtype is a tubular injury phenotype, marked by elevated urinary NGAL or KIM-1 levels and reflecting acute tubular necrosis as well as an increased risk of persistent AKI and progression to CKD^[112,115]. Finally, subtypes can also be defined by clinical course and recovery patterns. For example, the risk factors for persistent severe AKI after cardiac surgery, such as septic shock, catecholamine use, and comorbidities, are distinct from those observed in non-cardiac surgery populations^[125].

Based on the aforementioned subtype classification system, the precise identification of patient populations with distinct pathophysiological characteristics is key to advancing personalized treatment. AI models provide an efficient quantitative tool for subtype-driven therapeutic decision-making by integrating multidimensional biomarker and clinical data. The inflammation-endothelial injury classification system for sepsis-associated AKI (SA-AKI), proposed by Bhatraju *et al.*, may offer a useful framework for CSA-AKI^[107]. Both conditions share key biomarker patterns and demonstrate heterogeneity in treatment response. For example, the elevated ANG-2/ANG-1 ratio and IL-8 levels observed in some CSA-AKI subtypes are also characteristic of the sepsis AKI-SP2 subtype, suggesting that the classification by Bhatraju *et al.* could be adapted for this population. In terms of treatment, vasopressin shows efficacy in the sepsis AKI-SP1 subtype, while its use in cardiac surgery patients with vasoplegia similarly improves renal perfusion^[107,126]. The three-variable model by Bhatraju *et al.*, incorporating ANG-2/ANG-1, IL-8, and soluble TNF receptor-1 (sTNFR-1), retains discriminative power in CSA-AKI. By enabling dynamic biomarker monitoring, AI can help identify these subtypes early, optimize the timing of interventions, and leverage these pathophysiological links to guide more precise treatment.

However, despite these promising mechanistic insights and potential avenues for personalized therapy, the direct clinical applicability of such subtype-classification frameworks in cardiac surgery populations remains to be rigorously established. Several important caveats warrant consideration. First, most studies to date, including those by Milam *et al.*^[57] and Zhao *et al.*^[58], have derived subtypes from retrospective, often single-center cohorts without prospective validation. The generalizability of these phenotypes across diverse surgical settings and patient populations is therefore uncertain. Second, the inherent overlap among pathophysiological subtypes poses a significant challenge for real-time classification. For instance, a single patient may simultaneously exhibit features of both ischemia-reperfusion injury and inflammation-driven injury, complicating assignment to a discrete therapeutic category. Third, AKI is a dynamic process, and subtype membership may evolve over the course of illness, necessitating serial assessments rather than reliance on a single baseline classification.

PROGNOSTIC EVALUATION OF CARDIAC AND RENAL FUNCTION: FROM MULTIDIMENSIONAL INDICATORS TO PRECISE STRATIFICATION

Prognostic evaluation after CSA-AKI now extends well beyond the immediate postoperative period and focuses on long-term, multi-organ outcomes. Although 40% to 60% of patients achieve complete renal recovery according to KDIGO criteria^[9], survivors remain at significantly higher risks of CKD, ESRD, heart failure, and premature death. The concept of cardiorenal syndrome (CRS), as defined by the Acute Dialysis Quality Initiative (ADQI), consensus, captures the bidirectional pathophysiologic interactions between the heart and kidneys^[127,128]. This framework provides a rationale for including both cardiac and renal markers in prognostic models. Modern prognostic models have moved beyond static outcome measures toward a more dynamic, multidimensional approach. Key domains now include the timing of renal recovery, which is an independent prognostic factor, with delayed recovery linked to progressively worse long-term kidney outcomes^[116].

The inclusion of perioperative hemodynamic parameters such as central venous pressure (CVP)^[129], oxygen delivery (DO₂)^[52], tissue perfusion pressure (TPP)^[81], and intrarenal Doppler indices^[59] has improved AKI risk prediction. Tracking temporal trajectories of biomarkers such as inflammatory cytokines provides better prognostic information than a single static measurement^[62,64]. Molecular subphenotyping has identified distinct AKI subgroups that respond differently to targeted therapies, highlighting the potential for predictive enrichment and more personalized treatment^[107]. AKI survivors require prolonged surveillance for multi-organ complications, including cardiovascular events, stroke, dementia, sepsis, and malignancy^[130]. Importantly, pre-existing CKD independently predicts both ischemic and bleeding events after complex percutaneous coronary intervention and doubles the risk of contrast-induced AKI^[131]. This underscores that cardiac and renal outcomes are inseparable and that composite endpoints provide a more complete picture of a patient's overall prognosis^[92].

CHALLENGES AND FUTURE RESEARCH DIRECTIONS FOR AI IN CSA-AKI MANAGEMENT

Current challenges in AI implementation

AI models rely on large, high-quality datasets, but real-world data are often inconsistent. Variability in data collection standards and equipment accuracy across institutions can compromise data quality and reliability. Certain complex models such as DL networks can be highly accurate, but their internal decision-making processes are often opaque. This lack of interpretability, the so-called “black box” problem, can erode clinician trust and limit clinical adoption. Finally, integrating AI into clinical workflows requires substantial investments in personnel, infrastructure, and funding. These include both one-time costs, such as hardware upgrades and system integration, and recurring costs, such as data governance, model maintenance, and personnel training^[132-134]. These challenges, including data quality, interpretability, generalizability, and cost, are not unique to this field but are particularly relevant in this context. They currently limit the broader adoption and further development of AI for managing CSA-AKI.

Future research priorities

Enhancing model interpretability

Among these barriers, the lack of interpretability is perhaps the most significant. Recent advances in explainable AI (XAI) offer tools to address this. For instance, Thongprayoon *et al.*^[36] applied SHapley Additive exPlanations (SHAP) and local interpretable model-agnostic explanations (LIME) to an automated ML (autoML) model for preoperative prediction of CSA-AKI, thereby providing patient-specific explanations for the key risk factors identified. Li *et al.*^[37] used SHAP to show that preoperative blood urea nitrogen, prothrombin time, and age were positively associated with CSA-AKI, whereas platelet count and albumin were negatively associated. These findings align well with established clinical knowledge. Similarly,

Tseng *et al.*^[33] used SHAP dependence plots to show how intraoperative urine output and red blood cell transfusion influenced their model's predictions. Ejmalian *et al.*^[51] found that combining SHAP with LIME provided robust interpretability, confirming that Cr, CPB time, and albumin were among the most important predictors. Based on these studies, we propose that effective XAI for CSA-AKI should meet several criteria. First, it should demonstrate clinical relevance, with identified features aligning with known pathophysiology. Second, it should demonstrate decision consistency, meaning that model outputs correlate with expert clinical judgment. Third, it should capture temporal dynamics by explaining how time-varying parameters, such as hemodynamic variables, contribute to changing risk. Fourth, it should offer actionability, with explanations suggesting potential interventions, such as adjusting fluids or titrating vasopressors. Future research should focus on integrating these tools directly into clinical workflows to build trust and enable real-time decision support.

Multicenter validation and generalizability

Most AI research in this area is still based on single-center studies or small-scale trials^[135]. Future work must prioritize prospective, multicenter trials with predefined protocols, external validation in diverse populations, and comprehensive performance metrics, including calibration and decision-curve analysis. Strict adherence to established guidelines, such as Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD)^[136] and the Prediction model Risk Of Bias ASsessment Tool (PROBAST)^[137] will be essential for ensuring transparency and reproducibility.

Multi-omics integration

Currently, AI models for predicting and managing CSA-AKI have largely focused on proteomic and metabolomic data^[138]. Future research should integrate other omics layers, such as genomics and transcriptomics, to enrich model inputs and potentially improve predictive accuracy. Analyzing these multi-omics datasets could reveal complex biological pathways and provide deeper insights into AKI pathophysiology, paving the way for interventions targeted to specific disease mechanisms.

Standardization, regulatory pathways, and implementation

To move these tools from research into clinical practice, an international consensus on standardized definitions for CSA-AKI and cardiorenal composite endpoints is urgently needed. This would enable meaningful cross-study comparisons and support regulatory approval. Early engagement with regulatory agencies can help define acceptable performance thresholds and ensure compliance with relevant medical device regulations. Implementation science frameworks should be used to systematically identify barriers to and facilitators of AI-tool adoption across the full range of healthcare settings, from large tertiary cardiac centers to smaller community hospitals. Formal economic evaluations, including cost-utility analyses based on quality-adjusted life years (QALYs) are also needed to guide reimbursement decisions and health policy. Preliminary evidence is promising, with one cost-sensitive model estimating net savings of around eight million dollars through optimized resource allocation and a reduction in complications^[139].

Differentiated implementation strategies will be key to ensuring equitable access. High-resource settings might deploy complex multimodal models such as REACT^[41], whereas resource-limited environments could use simpler, preoperative models such as autoML tools^[36]. This tailored approach can help ensure that the benefits of AI-enhanced perioperative care are available to all patients.

CONCLUSIONS

In summary, AI has shown considerable promise in managing AKI after cardiac surgery, with preliminary advances in prediction, treatment guidance, and prognostic assessment. By integrating multimodal data, these models can detect early signs of CSA-AKI, thereby enabling timely intervention. They can also help

tailor treatment plans through more precise subtype classification and improve prognostic accuracy for both cardiac and renal outcomes, thereby guiding postoperative care. However, significant challenges remain. These include inconsistent data quality across institutions, the opacity of many AI models, which limits clinical trust, high implementation costs that restrict access, and the failure to incorporate many variables likely to be critical to the pathophysiology of this condition. Future advancements hinge on optimizing AI algorithms, establishing standardized, high-quality databases, and fostering interdisciplinary collaboration. Priorities include developing interpretable AI systems, integrating broader clinical variables to identify novel biomarkers or combinations, and refining data governance frameworks. These efforts aim to advance precision medicine for AKI after cardiac surgery, ultimately transforming perioperative care and improving patient outcomes in this patient population.

DECLARATIONS

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Authors' contributions

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Contributed to the discussion and analysis: Yang J, Wang Y, Zhang J, Xing L, Zhou P, Chen P, Ni H, Yu Y

Acquired the funding and supervised the study: Zhang Z

Availability of data and materials

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AI and AI-assisted tools statement

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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