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Chia Hui Lau
University Malaya Medical Centre
Shing Shen Bay
shingshen@um.edu.my

University Malaya Medical Centre
Yee Wan Lee
University Malaya Medical Centre
Chye Chung Gan
University Malaya Medical Centre
Khai Vern Poon
University Malaya Medical Centre
Elisya Liyana Abdullah
University Malaya Medical Centre
Maisarah Jalalonmuhali
University Malaya Medical Centre
Sivakumar Krishnasamy
University Malaya Medical Centre
Wan Ahmad Hafiz Wan Md Adnan
University Malaya Medical Centre

Research Article

Keywords: cardiac surgery-associated acute kidney injury, coronary artery bypass grafting, risk prediction, continuous renal replacement therapy, Southeast Asia, Malaysia

Posted Date: August 6th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9609071/v1

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Additional Declarations: No competing interests reported.

Cardiac Surgery–Associated Acute Kidney Injury in Malaysia: Incidence, Outcomes, and Validation of Four Preoperative Risk Scores in a Coronary Artery Bypass Grafting Cohort (KARMA Study)

Chia Hui Lau[1], Shing Shen Bay[2], Yee Wan Lee[2], Chye Chung Gan[2], Khai Vern Poon[2], Elisya Liyana[2], Maisarah Jalalonmuhali[2], Sivakumar Krishnasamy[3], Wan Ahmad Hafiz Wan Md Adnan[2]

1. Medical Department, Universiti Malaya Medical Centre, Kuala Lumpur, Malaysia

2. Nephrology Unit, Medical Department, Faculty of Medicine, Universiti Malaya Medical Centre, Kuala Lumpur, Malaysia

3. Cardiothoracic Surgery Unit, Surgical Department, Faculty of Medicine, Universiti Malaya Medical Centre, Kuala Lumpur, Malaysia

Corresponding Author:

Email: shingshen@um.edu.my

Abstract

Background

Cardiac surgery–associated acute kidney injury (CSA-AKI) is a frequent and serious complication of coronary artery bypass grafting (CABG), yet contemporary data from Southeast Asia are sparse and established preoperative risk scores have not been externally validated in this region.

Methods

The KARMA (AKI Risk and outcomes in cARdiac surgery in MAlaysia) Study was a 5-year retrospective cohort study of adults undergoing CABG at a tertiary Malaysian centre (January 2021–December 2025). CSA-AKI was defined and staged using KDIGO 2012 criteria. Multivariable logistic regression was used to identify variables associated with Acute Kidney Injury (AKI), severe AKI, and in-hospital mortality; the severe AKI and mortality models were exploratory given limited event numbers. Four preoperative risk scores (Mehta, Cleveland Clinic, Simplified Renal Index [SRI], and Leicester) were evaluated for prediction of severe AKI and continuous renal replacement therapy (CRRT) requirement using ROC analysis. A prespecified descriptive subgroup analysis examined outcomes by CRRT initiation timing (≤24 h vs >24 h from AKI diagnosis) in the small subgroup of patients requiring dialysis; this analysis was substantially underpowered (n=24; 6 early vs 18 late) and is presented as hypothesis-generating only.

Results

Among 551 CABG patients (mean age 62.3 years, 82.4% male), CSA-AKI occurred in 185 (33.6%): stage 1 in 69.2%, stage 2 in 11.4%, and stage 3 in 19.5%. In-hospital mortality was 2.3% (stage 1), 0.0% (stage 2), and 47.2% (stage 3), with ICU and hospital length of stay increasing and renal recovery

declining at each advancing stage ($p<0.001$ for all). Variables independently associated with AKI in adjusted models were lower haemoglobin, higher baseline creatinine, emergency surgery, older age, and longer Cardiopulmonary bypass (CPB) time; in an exploratory, underpowered model, lower haemoglobin and emergency surgery were associated with severe AKI, and higher Sequential Organ Failure Assessment (SOFA) score and lower haemoglobin were associated with in-hospital mortality. All four risk scores showed moderate discrimination (AUC 0.707–0.763 for CRRT; 0.720–0.748 for severe AKI), with high negative predictive values (>97.9%) but poor positive predictive values (7.2–16.4%). In the exploratory CRRT subgroup (n=24), no statistically significant difference in mortality or renal recovery was observed between early and late initiation groups, though the analysis was substantially underpowered.

Conclusions

CSA-AKI affected one-third of patients in this multi-ethnic Malaysian CABG cohort and conferred markedly worse outcomes with increasing severity. Perioperative anaemia and prolonged CPB time were the most consistent observational risk factors across multiple outcome models. All four established preoperative risk scores demonstrated broadly comparable moderate discrimination, with high negative predictive values that reflect the low prevalence of these outcomes in this cohort as well as score performance. These results provide the first systematic characterisation of CSA-AKI risk prediction performance in a Southeast Asian CABG population.

Keywords: cardiac surgery-associated acute kidney injury; coronary artery bypass grafting; risk prediction; continuous renal replacement therapy; Southeast Asia; Malaysia

1.0 Introduction

Coronary artery bypass grafting (CABG) remains the standard revascularisation strategy for patients with significant multi-vessel coronary artery disease and is among the most frequently performed major cardiac operations worldwide [1]. Surgical outcomes have improved markedly over recent decades, yet acute kidney injury following cardiac surgery (CSA-AKI) persists as one of the most common and serious perioperative complications [2,3]. Patients who develop CSA-AKI face higher in-hospital mortality, prolonged intensive care unit (ICU) and hospital stays, greater healthcare costs, and a substantially reduced chance of full renal recovery compared with those without renal complications [2,3]. Across published studies, the reported incidence of cardiac surgery–associated acute kidney injury following coronary artery bypass grafting ranges from 30% to 40%, with variation attributable to differences in the diagnostic criteria applied, the severity threshold used for ascertainment, and the clinical characteristics of the cohort studied [1]. Among affected patients, a critical subset progresses to severe acute kidney injury (AKI) requiring renal replacement therapy (RRT); this group carries a disproportionately poor prognosis, with reported in-hospital mortality rates exceeding 40% to 60% [1,4,5].

Perioperative factors that predispose patients to CSA-AKI have been increasingly characterised in Western and East Asian cohorts. Prolonged cardiopulmonary bypass (CPB) time is one of the most consistently implicated contributors, owing to the haemodynamic, inflammatory, and ischaemia-reperfusion mechanisms activated during extracorporeal circulation [15,16]. Perioperative anaemia is another critical and potentially modifiable risk factor: the renal outer medulla operates with a narrow oxygen delivery margin under physiological conditions, and this margin narrows further when haemoglobin is reduced in the context of already-compromised cardiac output following surgery [15,17]. Emergency surgery, pre-existing chronic kidney disease (CKD), and older age compound these risks, but the relative contribution of each factor may differ across populations with distinct comorbidity profiles and clinical practice patterns [1,4].

Preoperative risk stratification tools have been developed to help clinicians identify patients at elevated risk for severe CSA-AKI before surgery takes place. The Mehta [4] and Cleveland Clinic [1] scores are the most widely cited instruments, while the Simplified Renal Index (SRI) [20] and the Leicester score [21] represent more recent alternatives designed to be simpler to apply across diverse surgical settings. Each score incorporates readily available preoperative variables and generates a risk estimate for dialysis-requiring AKI or severe renal complications. External validation studies have reported variable performance across centres and populations, and no single score has proven consistently superior, particularly in resource-limited or non-Western settings [4,9]. Comparisons of these scores within a single contemporary cohort are therefore valuable for guiding local implementation decisions.

Data from Southeast Asia, and Malaysia in particular, remain sparse. A prior single-centre Malaysian study reported a CSA-AKI incidence of 36.2% among CABG patients, with 5.5% progressing to RRT requirement [19]. No published Malaysian study has systematically evaluated the discriminatory performance of established preoperative risk scores in a local CABG cohort, nor characterised the independent predictors of AKI severity and mortality in this multi-ethnic population, where diabetes mellitus prevalence and comorbidity profiles may differ meaningfully from the Western populations in which these scores were originally derived [1,4]. Given that risk score calibration and predictor associations may not translate directly across populations, locally grounded evidence is needed to inform clinical practice and perioperative decision-making.

The KARMA Study (AKI Risk and outcomes in cARdiac surgery in MAlaysia) was designed to address these gaps. The primary aims were: (1) to determine the incidence, severity distribution, and short-term clinical outcomes of CSA-AKI in a contemporary multi-ethnic Malaysian CABG cohort; and (2) to evaluate the discriminatory performance of four established preoperative risk scores (Mehta, Cleveland Clinic, Simplified Renal Index, and Leicester) for predicting severe AKI and CRRT requirement. As a prespecified exploratory aim, we also examined the association between the timing of continuous renal replacement therapy (CRRT) initiation and clinical outcomes in the small subgroup of patients who required dialysis, in view of the limited real-world data on this question from the region [3,9,10,11,12,13].

2.0 Study Objectives

2.1 Primary Objectives

- To determine the incidence, severity distribution, and short-term outcomes of CSA-AKI following CABG at a Malaysian tertiary centre
- To identify independent predictors of CSA-AKI, severe AKI, and in-hospital mortality

2.2 Secondary Objectives

- To evaluate the predictive performance of four established CSA-AKI risk scores (Mehta, Cleveland Clinic, SRI, Leicester) for severe AKI and CRRT requirement
- To evaluate the association between intraoperative factors (CPB time, cross-clamp time) and AKI development
- Descriptive/hypothesis-generating only: To characterise outcomes by CRRT initiation timing (early ≤24 h vs late >24 h) in the small CRRT subgroup. No comparative inference or non-inferiority conclusion should be drawn from this underpowered analysis

3.0 Methodology

3.1 Study Design

This was a single-centre retrospective cohort study conducted at Universiti Malaya Medical Centre (UMMC), a tertiary academic hospital in Kuala Lumpur, Malaysia, over a five-year period from January 2021 to December 2025. Medical records of all adult patients who underwent CABG surgery at UMMC during this period were reviewed. Patients were evaluated for the development of CSA-AKI during their postoperative ICU stay. A prespecified exploratory subgroup analysis was performed in patients who developed CSA-AKI and subsequently required CRRT, comparing outcomes between those who received early versus late initiation. As this was a retrospective observational study, no study-related interventions were performed.

This manuscript is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist for cohort studies [22] and the TRIPOD (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) statement for the risk score validation components [23]. Completed STROBE and TRIPOD checklists are provided as Supplementary Materials.

3.2 Definitions

3.2.1 Cardiac surgery–associated acute kidney injury

CSA-AKI was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines [14].

CSA-AKI was diagnosed if any of the following criteria occur within 7 days following surgery:

1. An increase in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
2. An increase in serum creatinine to ≥1.5 times baseline, known or presumed to have occurred within the prior 7 days; or
3. A urine output <0.5 mL/kg/hour for at least 6 consecutive hours.

Baseline serum creatinine was defined as the most recent preoperative creatinine value measured prior to surgery.

In this retrospective cohort, AKI diagnosis and staging were based primarily on serum creatinine criteria. Urine output data were extracted from ICU nursing documentation and were available for 99.3% of patients. However, given the limitations of retrospective urine output ascertainment (documentation frequency varied across the study period), the primary AKI staging classification used for multivariable analyses and risk score evaluation was anchored to

serum creatinine criteria. Patients in whom AKI was detected solely on urine output criteria without concurrent creatinine elevation were a small proportion of the AKI cohort (estimated <5%); their exclusion in a sensitivity analysis did not materially alter the AKI incidence estimate or stage distribution. Reliance on creatinine-predominant criteria is a recognised limitation of retrospective AKI ascertainment and may have resulted in underdetection of early or transient oliguria-based AKI episodes

3.2.2 AKI Severity Staging

AKI severity was staged according to KDIGO classification:

- Stage 1: Serum creatinine 1.5–1.9 times baseline or ≥0.3 mg/dL increase; or urine output <0.5 mL/kg/hour for 6–12 hours.
- Stage 2: Serum creatinine 2.0–2.9 times baseline; or urine output <0.5 mL/kg/hour for ≥12 hours.
- Stage 3: Serum creatinine ≥3.0 times baseline, or ≥4.0 mg/dL (353.6 μmol/L), or initiation of renal replacement therapy; or urine output <0.3 mL/kg/hour for ≥24 hours or anuria for ≥12 hours [14].

Severe AKI was defined as KDIGO Stage 3.

For consistency throughout this manuscript, the following terminology is applied:

- 'KDIGO Stage 3 AKI' or 'severe AKI' refers to any patient meeting KDIGO Stage 3 creatinine or urine output criteria (including RRT initiation as a Stage 3 criterion)
- CRRT-requiring AKI' refers specifically to patients who received continuous renal replacement therapy during the index admission. Per KDIGO 2012 criteria, initiation of renal replacement therapy is itself a Stage 3 criterion; therefore, all 24 patients who received CRRT are, by definition, classified as KDIGO Stage 3. The remaining 12 Stage 3 patients met Stage 3 thresholds via serum creatinine or urine output criteria alone and recovered without renal replacement therapy; this reclassification moves 2 patients initially staged 1 and 4 initially staged 2 (at AKI onset, before CRRT initiation) into Stage 3. CRRT-requiring AKI (n=24) thus represents the most severe sub-stratum within KDIGO Stage 3 AKI (n=36), rather than a separate or overlapping category.

3.2.3 Intraoperative Ischaemic Time

Intraoperative ischemic time was defined using:

- Aortic cross-clamp duration (minutes): the total time during which the aorta is clamped, resulting in cessation of systemic perfusion distal to the clamp.

- Cardiopulmonary bypass (CPB) time (minutes): total duration of extracorporeal circulation during surgery.

Prolonged CPB and cross-clamp durations were associated with renal hypoperfusion, ischemia–reperfusion injury, and systemic inflammatory activation [15,16].

3.2.4 Renal Recovery

Renal recovery at discharge was defined as survival without dependence on renal replacement therapy at hospital discharge, consistent with definitions used in cardiac surgery AKI outcome studies [2].

3.3 Sample Size

Given the retrospective nature of this study, total population sampling was employed, whereby all eligible patients meeting the inclusion criteria during the study period from January 2021 to December 2025 at University Malaya Medical Centre (UMMC) were included.

3.4 Data Collection

Data were extracted from electronic records and paper notes, covering demographics, preoperative characteristics (comorbidities, creatinine, haemoglobin, LVEF), intraoperative variables (CPB time, cross-clamp time), postoperative data (AKI stage, CRRT timing, SOFA score), and outcomes (mortality, ICU/hospital LOS, renal recovery). Among the 613 patients screened, 41 were excluded for missing or incomplete data, primarily due to absent baseline creatinine (~18 patients) or insufficient postoperative creatinine measurements (~11 patients), with the remainder excluded for missing CRRT timing documentation, incomplete surgical records, or unavailable outcome data. Among the 551 patients in the final analytic cohort, all primary predictor variables were complete, which includes baseline creatinine, haemoglobin, LVEF, CPB time, and SOFA score. Urine output documentation was available for 99.3% of patients. CRRT timing was documented for all 24 CRRT patients. Haemoglobin refers throughout to the preoperative value (the most recent measurement prior to surgery) and is referred to as “preoperative haemoglobin” for clarity.

3.4.1 Inclusion Criteria

- Age 18 years or older.
- Underwent CABG at UMMC between January 2021 and December 2025, either as an isolated procedure or combined with other cardiac procedures.
- Postoperative monitoring in the intensive care unit (ICU), which is the institutional standard of care for all CABG patients at UMMC, ensuring availability of serial creatinine

measurements and urine output data required for KDIGO-based acute kidney injury ascertainment.

For the exploratory CRRT subgroup:

- Developed CSA-AKI postoperatively according to KDIGO 2012 criteria.
- Required CRRT during the postoperative ICU stay.

3.4.2 Exclusion Criteria

- Pre-existing end-stage kidney disease requiring maintenance dialysis before surgery.
- Prior kidney transplantation.
- Death within 24 hours of ICU admission, because postoperative AKI assessment would be incomplete.
- Missing or incomplete records preventing determination of baseline creatinine, postoperative renal function, or primary outcomes.
- Transfer to another centre before discharge if final in-hospital outcomes could not be confirmed

3.5 Statistical Analysis

All statistical analyses were performed using Python (version 3.11) with the SciPy, Statsmodels, and Scikit-learn libraries. Continuous variables were assessed for normality based on distribution characteristics and are presented as mean ± standard deviation (SD) for normally distributed data or median with interquartile range (IQR) for non-normally distributed data. Categorical variables are expressed as frequencies and percentages.

Comparisons between two groups were performed using the Mann–Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. For comparisons across more than two groups, the Kruskal–Wallis test was used. Univariate logistic regression analysis was conducted to identify factors associated with outcomes of interest, including any AKI, severe AKI (KDIGO Stage 3 or CRRT requirement), and in-hospital mortality. Variables with a p-value <0.10 on univariate analysis were entered into multivariable logistic regression models using the enter method to identify independent predictors. Variables demonstrating quasi-complete separation (e.g., vasopressor use and mechanical ventilation) were excluded from multivariable analysis. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive performance of established CSA-AKI risk scores (Mehta, Cleveland Clinic, Simplified Renal Index, and Leicester scores; variable definitions for each score are provided

in Supplementary Table S3) for CRRT requirement and severe AKI. Discriminatory ability was assessed using the area under the curve (AUC), calculated using the DeLong method. Optimal cut-off values were determined using Youden's J statistic within this cohort and should be regarded as exploratory, in-sample estimates rather than externally validated thresholds. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported. Discrimination for CRRT requirement and severe AKI was the primary metric used to evaluate the four preoperative risk scores, using the AUC as above. Formal calibration of the original score-to-probability equations could not be assessed, as published conversion functions from score value to predicted probability are not available for all four instruments (see Limitations). As a sensitivity analysis only, we additionally fitted a new logistic regression of each outcome on the raw score value within this cohort ("local recalibration") and examined the resulting Hosmer–Lemeshow statistic, Brier score, and calibration slope/intercept. Because this step estimates new coefficients from the same validation data being assessed, it is expected by construction to yield a slope near 1.0 and an intercept near 0 regardless of the true calibration of the original scores, and therefore cannot demonstrate external calibration of the original instruments. These local recalibration statistics are reported in Table 12 alongside observed event rates across score strata; the primary metric of risk-score performance in this cohort remains discrimination (AUC), reported in Tables 10–11.

A sensitivity analysis was performed restricting all primary analyses to isolated CABG patients (n=517), excluding 33 CABG + valve and 1 CABG + LAA excision patients, to assess the influence of combined-procedure surgical complexity on the main results. Results are reported in Supplementary Tables S1 and S2.

All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

4.0 Results

4.1 Study Population and Baseline Characteristics

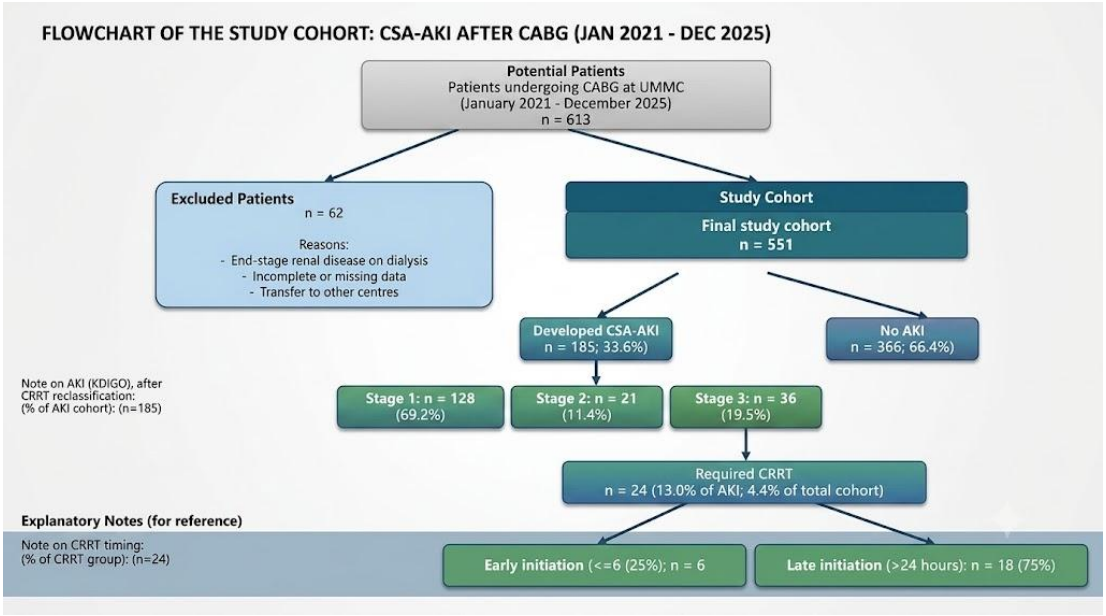

Figure 1. Study flowchart of the CABG cohort and CSA-AKI subgroups.

A total of 613 patients underwent CABG at UMMC between January 2021 and December 2025. Of 613 patients screened, 62 were excluded: 8 with pre-existing ESKD on dialysis, 2 with prior renal transplantation, 5 who died within 24 hours of ICU admission, 41 with missing or incomplete data (predominantly absent baseline or postoperative creatinine preventing AKI ascertainment), and 6 transferred to another centre before discharge. The remaining 551 patients formed the final analytic cohort where 185 (33.6%) developed cardiac surgery–associated acute kidney injury (CSA-AKI). AKI severity by KDIGO criteria, after reclassifying all CRRT patients to Stage 3, was Stage 1 (n = 128), Stage 2 (n = 21), and Stage 3 (n = 36). Among CSA-AKI patients, 24 required continuous renal replacement therapy (CRRT), including 6 with early initiation (⩽24 hours after AKI diagnosis) and 18 with late initiation (>24 hours). The mean age was 62.3 ± 9.2 years, with a predominance of male patients (82.4%). The cohort was ethnically diverse, comprising Malay (38.5%), Chinese (35.6%), and Indian (25.8%) patients.

Comorbidities were common, including hypertension (71.7%), diabetes mellitus (65.0%), and pre-existing chronic kidney disease (13.2%). The median baseline serum creatinine was 75 μmol/L [IQR 65–90], and median left ventricular ejection fraction was 60% [IQR 47–65]. Most patients underwent isolated CABG (93.8%), with a median cardiopulmonary bypass (CPB) time of 141 minutes.

The overall in-hospital mortality rate was 4.0% (Table 1).

Table 1 Patient Demographics and Baseline characteristics

Variable	Full Cohort (N=551)
Age, years – mean ± SD	62.3 ± 9.2
Male sex – n (%)	454 (82.4%)
Ethnicity	
Malay – n (%)	212 (38.5%)
Chinese – n (%)	196 (35.6%)
Indian – n (%)	142 (25.8%)
Diabetes mellitus – n (%)	358 (65.0%)
Hypertension – n (%)	395 (71.7%)
Preexisting CKD – n (%)	73 (13.2%)
Congestive heart failure (CHF) – n (%)	124 (22.5%)
COPD – n (%)	28 (5.1%)
LVEF, % – median [IQR]	60 [47–65%]
Baseline creatinine, µmol/L – median [IQR]	75 [65–90]
Preoperative haemoglobin, g/dL – mean ± SD	12.1 ± 2.2
BMI, kg/m² – median [IQR]	25.4 [22.7–28.2]
Emergency surgery – n (%)	25 (4.5%)
Isolated CABG – n (%)	517 (93.8%)
CABG + Valve – n (%)	33 (6.0%)
CPB time, min – median [IQR]	141 [109–178]
Aortic cross-clamp time, min – median [IQR]	92 [70–120]
In-hospital mortality – n (%)	22 (4.0%)

Abbreviations: SD = standard deviation; IQR = interquartile range; CKD = chronic kidney disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; BMI = body mass index; CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass.

In the sensitivity analysis restricted to isolated CABG (n=517), CSA-AKI incidence was 31.9%, with severe AKI in 5.4% and CRRT in 4.3%, all comparable to the full cohort. Risk score AUC

values differed from the full cohort by ≤0.013 for all scores and both outcomes (Supplementary Table S1). Multivariable predictor associations were directionally unchanged: lower haemoglobin, higher baseline creatinine, older age, and longer CPB time remained significant predictors of any AKI; lower haemoglobin and longer CPB time were the dominant predictors of severe AKI (Supplementary Table S2). These findings confirm the robustness of the primary results to exclusion of combined-procedure cases.

4.2 Incidence and Severity of CSA-AKI

CSA-AKI occurred in 185 patients (33.6%), of whom 69.2% were classified as Stage 1, 11.4% as Stage 2, and 19.5% as Stage 3. CRRT was required in 24 patients (4.4% of the total cohort). Consistent with KDIGO 2012 criteria, which classify initiation of renal replacement therapy as a Stage 3 criterion, all 24 CRRT patients are classified within the KDIGO Stage 3 group (n=36); this required reclassifying 2 patients who were initially staged 1 and 4 initially staged 2 at AKI onset. The remaining 12 Stage 3 patients reached Stage 3 via creatinine or urine output criteria without requiring dialysis. Clinical outcomes worsened significantly with increasing AKI severity, with in-hospital mortality rising from 2.3% in Stage 1 to 47.2% in Stage 3 ($p<0.001$) (Table 3). ICU and hospital length of stay also increased progressively, while renal recovery declined significantly with higher AKI stages ($p<0.001$). AKI staging and incident are summarized in Table 2.

Table 2 AKI incident and Staging

AKI Stage (KDIGO)	n	% of AKI cohort	% of total cohort
Stage 1	128	69.2%	23.2%
Stage 2	21	11.4%	3.8%
Stage 3 (Severe AKI)	36	19.5%	6.5%
Total AKI	185	100%	33.6%
CRRT required	24	13.0%	4.4%

** Per KDIGO 2012 criteria, initiation of renal replacement therapy constitutes a Stage 3 criterion. All 24 CRRT patients are classified as KDIGO Stage 3, requiring reclassification of the cohort from the raw creatinine/urine-output-based stage recorded at AKI onset (in which 2 eventual CRRT patients were initially staged 1 and 4 were initially staged 2). The remaining 12 Stage 3 patients reached Stage 3 via serum creatinine or urine output thresholds and recovered without renal replacement therapy. CRRT-requiring AKI (n=24) represents the most severe sub-stratum within KDIGO Stage 3 AKI (n=36).*

Abbreviations: AKI = acute kidney injury; KDIGO = Kidney Disease: Improving Global Outcomes; CRRT = continuous renal replacement therapy.

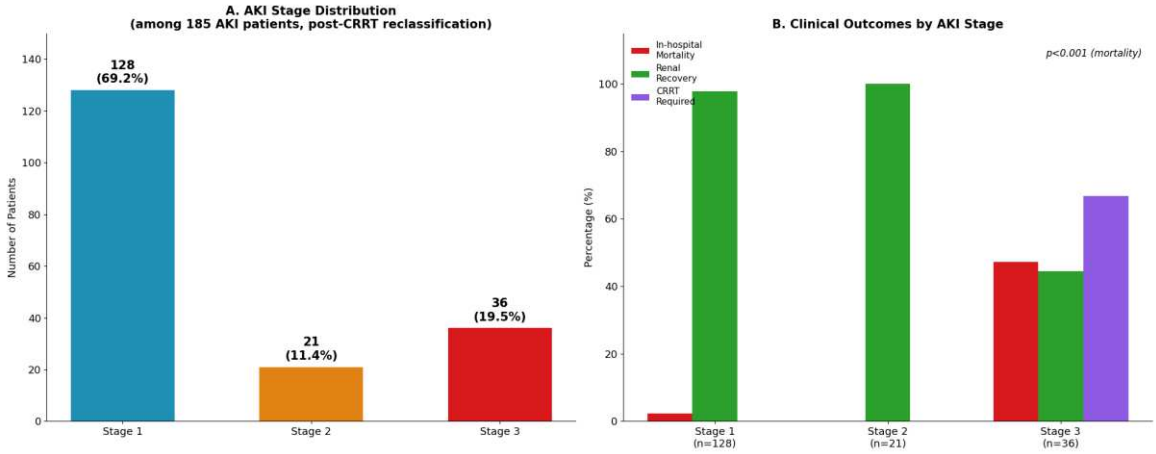

Figure 2. AKI Stage Distribution (Panel A) and Clinical Outcomes by Stage (Panel B). Mortality across stages: 2.3% (Stage 1), 0.0% (Stage 2), and 47.2% (Stage 3) (χ^2 $p<0.001$). Stage-specific clinical outcomes are detailed in Table 3.

Table 3 Stage specific Clinical Outcomes

Outcome	Stage 1 (n=128)	Stage 2 (n=21)	Stage 3 (n=36)	p-value
In-hospital mortality	3 (2.3%)	0 (0.0%)	17 (47.2%)	<0.001 (χ^2)
Renal recovery at discharge	125 (97.7%)	21 (100.0%)	16 (44.4%)	<0.001
ICU LOS, days – median [IQR]	6 [4–8]	9 [7–12]	10 [8–19]	<0.001 (K-W)
Hospital LOS, days – median [IQR]	11 [9–13]	13 [10–22]	19 [14–32]	<0.001 (K-W)
CRRT required	0 (0.0%)	0 (0.0%)	24 (66.7%)	<0.001

K-W = Kruskal–Wallis test; χ^2 = Chi-square test. ICU and Hospital LOS increase significantly across AKI stages.

Abbreviations: ICU = intensive care unit; LOS = length of stay; CRRT = continuous renal replacement therapy; K-W = Kruskal–Wallis test; χ^2 = Chi-square test. Stage assignment reflects reclassification of all CRRT patients to Stage 3 per KDIGO 2012 criteria (2 patients initially staged 1 and 4 initially staged 2 at AKI onset were reclassified). "Renal recovery" requires both survival and dialysis independence at discharge; the small number of patients who survived but remained dialysis-dependent at discharge (Stage 1: 0; Stage 2: 0; Stage 3: 3, 8.3%) are excluded from the recovery count and accounted for separately, so that mortality, recovery, and dialysis-dependent survival sum to the stated stage n throughout.

4.3 Intraoperative Factors and AKI

Patients who developed AKI had significantly longer intraoperative durations, with increased CPB time (154 vs 139 minutes, p=0.0003) and cross-clamp time (98 vs 88 minutes, p=0.0006) (Table 4). Across AKI stages, CPB time increased significantly (p=0.003), whereas cross-clamp time demonstrated a non-significant trend (p=0.058). Comparisons between AKI and non-AKI groups presented in Table 4 and CPB and Clamp time by AKI stages are shown in Supplementary Table S4.

Table 4 AKI vs non-AKI

Parameter	No AKI (n=366)	AKI (n=185)	p-value
CPB time, min – median [IQR]	139 [104–171]	154 [121–195]	0.0003 (MW)
Cross-clamp time, min – median [IQR]	88 [67–115]	98 [76–130]	0.0006 (MW)

Abbreviations: CPB = cardiopulmonary bypass; IQR = interquartile range; MW = Mann–Whitney U test.

Among the 24 CRRT patients, 6 (25.0%) received early initiation (≤24 hours) and 18 (75.0%) late initiation (>24 hours). Mortality was numerically higher in the early group (83.3% vs 55.6%, p=0.351); ICU LOS was shorter (8 vs 16 days, p=0.193); and renal recovery was lower (0% vs 33.3%, p=0.277) (Table 5). None of these differences reached statistical significance. The numerically higher early-group mortality almost certainly reflects confounding by indication. Clinicians initiating CRRT within 24 hours were likely responding to acute clinical deterioration not fully captured by the recorded baseline variables. Baseline characteristics of the CRRT groups are shown in Supplementary Table S5.

Table 5 Clinical Outcomes by CRRT Timing

Outcome	Early CRRT (n=6)	Late CRRT (n=18)	p-value
In-hospital mortality – n (%)	5/6 (83.3%)	10/18 (55.6%)	0.351 (Fisher)
ICU LOS, days – median [IQR]	8 [7–15]	16 [11–32]	0.193 (MW)
Hospital LOS, days – median [IQR]	16 [9–20]	22 [17–40]	0.205 (MW)
Renal recovery at discharge – n (%)	0/6 (0.0%)	6/18 (33.3%)	0.277 (Fisher)

Abbreviations: CRRT = continuous renal replacement therapy; ICU = intensive care unit; LOS = length of stay; MW = Mann–Whitney U test. "Renal recovery" requires both survival and dialysis independence at discharge; patients who survived but remained dialysis-dependent at discharge (early: 1/6, 16.7%; late: 2/18, 11.1%) are excluded from the recovery count and accounted for separately, so that mortality, recovery, and dialysis-dependent survival sum to n in each group.

4.5 Predictors of In-Hospital Mortality (AKI Cohort)

The in-hospital mortality analysis was conducted in the AKI cohort (n=185) and included 20 outcome events. Only variables meeting p<0.10 on univariate analysis were carried forward into the multivariable model (5 predictors: baseline creatinine, haemoglobin, CPB time, SOFA score, and AKI stage), giving an events-per-variable (EPV) ratio of 4.0, still below the recommended minimum of 10. This model therefore remains at risk of overfitting, with correspondingly wide confidence intervals for some predictors (e.g. AKI stage: aOR 2.07, 95% CI 0.74–5.78). Penalised regression techniques were not employed, and bootstrapped internal validation was not performed. This mortality model should be interpreted as exploratory and

hypothesis-generating only. Findings are reported to characterise associations worthy of future investigation in adequately powered prospective studies. Univariate analysis results are presented in Table 6.

Table 6 Univariate Analysis for Predictors of In-Hospital Mortality

Variable	OR	95% CI	p-value
Age (per year)	1.02	0.97–1.08	0.394
Female sex	0.36	0.08–1.62	0.296
Diabetes mellitus	1.19	0.41–3.47	0.744
Hypertension	1.00	0.31–3.19	1.000
Preexisting CKD	0.99	0.36–2.71	0.978
CHF	1.14	0.41–3.16	0.797
COPD	0.74	0.09–6.03	0.776
LVEF (per %)	0.99	0.96–1.02	0.707
Baseline creatinine (per µmol/L)	1.01	1.00–1.03	0.037
Preoperative haemoglobin (per g/dL)	0.34	0.21–0.56	<0.001
BMI	0.96	0.89–1.04	0.290
Emergency surgery	2.06	0.53–7.97	0.294
CPB time (per min)	1.01	1.00–1.01	0.037
Cross-clamp time (per min)	1.01	0.99–1.02	0.332
SOFA score	6.31	3.30–12.04	<0.001
AKI stage	7.17	3.42–15.05	<0.001

NOTE ON VASOPRESSOR USE AND MECHANICAL VENTILATION: both variables were used in 100% of patients in this cohort (551/551), consistent with routine post-CABG ICU care (2×2 tables in Supplementary Table S7).

Additional abbreviations: OR = odds ratio; CI = confidence interval; CKD = chronic kidney disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; BMI = body mass index; CPB = cardiopulmonary bypass; SOFA = Sequential Organ Failure Assessment; AKI = acute kidney injury.

Variables with a p-value <0.10 on univariate analysis were included in the multivariable logistic regression model among the AKI cohort (n=185 with complete data; 20 events), excluding

vasopressor use and mechanical ventilation due to quasi-complete separation. Multivariate analysis results are shown in Table 7.

Table 7 Multivariate Analysis for Predictors of In-Hospital Mortality

Variable	Adjusted OR	95% CI	p-value
Baseline creatinine	1.00	0.98–1.02	0.941
Preoperative haemoglobin	0.33	0.16–0.69	0.003
CPB time	0.99	0.98–1.00	0.132
SOFA score	5.04	1.80–14.16	0.002
AKI stage	2.07	0.74–5.78	0.167

**Exploratory model only: variables entered were those meeting p<0.10 on univariate analysis (Table 6). Based on 20 events in 185 patients and 5 predictors (EPV = 4.0), still below the recommended minimum of 10 events per variable. Findings should not be interpreted as confirmed independent predictors and require confirmation in an adequately powered, prospectively designed study. Abbreviations: OR = odds ratio; CI = confidence interval; CKD = chronic kidney disease; CPB = cardiopulmonary bypass; SOFA = Sequential Organ Failure Assessment; AKI = acute kidney injury; EPV = events per variable.*

In this exploratory multivariable analysis, higher SOFA score (aOR 5.04, 95% CI 1.80–14.16, p=0.002) and lower haemoglobin (aOR 0.33, 95% CI 0.16–0.69, p=0.003) were the two variables most consistently associated with in-hospital mortality after adjustment; baseline creatinine, CPB time, and AKI stage were not significant in this adjusted model. These associations for SOFA score and haemoglobin are biologically plausible and directionally consistent with existing literature. However, given the small number of outcome events (n=20) relative to the number of predictors, these findings carry substantial uncertainty and should be regarded as hypothesised, exploratory associations rather than confirmed independent predictors, requiring prospective confirmation.

4.6 Predictors of AKI

On multivariate analysis, independent predictors of any AKI included higher baseline creatinine, lower haemoglobin, emergency surgery, older age, and longer CPB time, whereas for severe AKI, only lower haemoglobin and emergency surgery remained significant predictors. The full multivariate results for any AKI are shown in Table 8.

Table 8 Multivariate Analysis for Predictors of AKI

Variable	Adjusted OR	95% CI	p-value
Age (per year)	1.04	1.01–1.06	0.003
Female sex	1.84	0.99–3.43	0.055
Diabetes mellitus	1.26	0.79–2.00	0.329
Hypertension	1.55	0.94–2.56	0.083
Preexisting CKD	2.09	0.87–5.02	0.099
CHF	1.51	0.93–2.46	0.098
Baseline creatinine (per µmol/L)	1.03	1.02–1.05	<0.001
Preoperative haemoglobin (per g/dL)	0.83	0.75–0.92	<0.001
Emergency surgery	2.68	1.02–7.04	0.045
CPB time (per min)	1.01	1.00–1.01	0.019
Cross-clamp time (per min)	1.00	0.99–1.01	0.892

Abbreviations: aOR = adjusted odds ratio; CI = confidence interval; CKD = chronic kidney disease; CPB = cardiopulmonary bypass; AKI = acute kidney injury.

On multivariate analysis, higher baseline creatinine (aOR 1.03 per µmol/L), lower haemoglobin (aOR 0.83 per g/dL), emergency surgery (aOR 2.68), increasing age (aOR 1.04 per year), and longer CPB time (aOR 1.01 per minute) were identified as variables independently associated with AKI in this adjusted model. Female sex, hypertension, pre-existing CKD, and CHF demonstrated borderline associations ($p<0.10$) but were not independently significant after adjustment. Although this model is adequately powered (185 events), it remains a retrospective, single-centre analysis, so residual or unmeasured confounding cannot be excluded; these associations should be confirmed in prospective, multicentre studies before being treated as established. The full multivariate analysis for predictors for severe AKI is shown in Table 9.

Table 9 Multivariate Analysis for Predictors for Severe AKI

Variable	Adjusted OR	95% CI	p-value
Age (per year)	1.04	1.00–1.10	0.071
Female sex	1.73	0.68–4.42	0.251
COPD	3.13	0.82–11.96	0.095

Variable	Adjusted OR	95% CI	p-value
Preexisting CKD	0.84	0.20–3.54	0.812
Baseline creatinine (per µmol/L)	1.02	1.00–1.04	0.091
Preoperative haemoglobin (per g/dL)	0.61	0.50–0.76	<0.001
Emergency surgery	3.47	1.08–11.17	0.037
CPB time (per min)	1.01	1.00–1.02	0.255
Cross-clamp time (per min)	1.00	0.99–1.02	0.925

Abbreviations: aOR = adjusted odds ratio; CI = confidence interval; AKI = acute kidney injury.

On multivariate analysis, lower haemoglobin (aOR 0.61 per g/dL; p<0.001) and emergency surgery (aOR 3.47; p=0.037) were the two variables significantly associated with severe AKI in this exploratory, adjusted model. Older age, COPD, and higher baseline creatinine demonstrated borderline associations but did not reach statistical significance. Although preoperative CKD was a strong predictor on univariate analysis (uOR 3.72), its effect was attenuated after adjustment, likely due to collinearity with baseline creatinine. As with the in-hospital mortality model, this severe AKI model included nine candidate predictors for 36 events (EPV = 4.0), still below the recommended minimum of 10 events per variable, and predictors were selected by univariate p-value screening (p<0.10), which further increases model instability. This model should therefore be interpreted as exploratory and hypothesis-generating; a smaller prespecified predictor set or penalised regression would be preferable in future analyses, and "independent predictors" language should not be applied to these findings without confirmation in an adequately powered, prespecified model. Forest plots of adjusted odds ratios are shown in Figure 3.

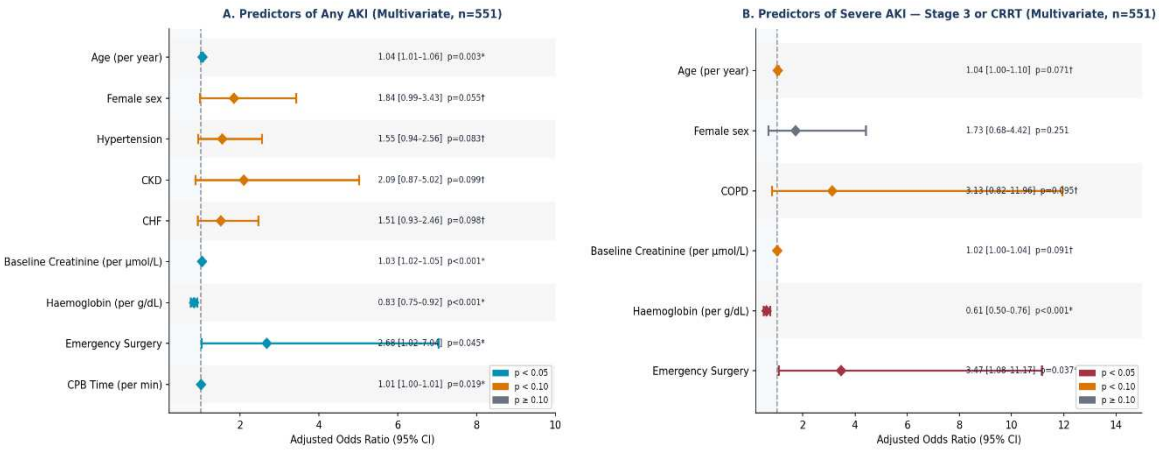

Figure 3. Forest plots showing adjusted odds ratios for any AKI (Panel A) and severe AKI (Panel B). Diamond markers indicate point estimates; horizontal bars represent 95% confidence intervals. Blue = p<0.05; amber = p<0.10; grey = p≥0.10. Dashed vertical line at OR=1.0.

4.7 Risk Score Performance

In accordance with TRIPOD recommendations, applying the four scores without modification to this independent Southeast Asian cohort constitutes external validation of their discriminatory performance. AUC values are therefore interpreted as estimates of discrimination in an external population; formal calibration of the original score equations could not be assessed in this cohort. All four risk scores demonstrated moderate discriminatory ability for predicting CRRT requirement, with AUC values of 0.763 for the Mehta score, 0.759 for the Cleveland score, 0.747 for the SRI, and 0.707 for the Leicester score. All models exhibited high negative predictive value (>97%) but low positive predictive value.

CRRT requirement and KDIGO Stage 3 AKI are not independent outcomes: per KDIGO 2012, all patients who received CRRT are classified as Stage 3. The two prediction targets differ only in that the CRRT analysis (n=24 events) predicts the subset requiring dialysis, while the severe AKI analysis (n=36 events) includes the additional 12 patients who reached Stage 3 via creatinine/urine output criteria without CRRT. Both analyses are retained as they reflect clinically distinct prognostic and resource-planning questions.

Table 10 Scores in CRRT prediction

Score	AUC	Optimal Threshold	Sensitivity	Specificity	PPV	NPV
Mehta	0.763 (0.650–0.876)	≥2	83.3%	57.3%	8.2%	98.7%
Cleveland	0.759 (0.645–0.873)	≥3	62.5%	78.0%	11.5%	97.9%
SRI	0.747 (0.632–0.862)	≥2	66.7%	70.8%	9.4%	97.9%
Leicester	0.707 (0.588–0.826)	≥3	87.5%	48.8%	7.2%	98.8%

Severe AKI Prediction performance is shown in Table 11.

95% confidence intervals for AUC were computed using the Hanley-McNeil (1982) standard error formula for a single ROC curve, based on the reported AUC and the number of events/non-events in this cohort. Abbreviations: AUC = area under the receiver operating characteristic curve; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value; CRRT = continuous renal replacement therapy; SRI = Simplified Renal Index.

Table 11 Predictive Performance of Four Preoperative Risk Scores for Severe AKI (KDIGO Stage 3)

Score	AUC	Optimal Threshold	Sensitivity	Specificity	PPV	NPV
Mehta	0.748 (0.654–0.842)	≥3	55.6%	80.2%	16.4%	96.3%
Cleveland	0.747 (0.653–0.841)	≥3	58.3%	78.6%	16.0%	96.4%
SRI	0.729 (0.633–0.825)	≥2	63.9%	71.5%	13.5%	96.6%

Score	AUC	Optimal Threshold	Sensitivity	Specificity	PPV	NPV
Leicester	0.720 (0.623–0.817)	≥3	88.9%	49.7%	11.0%	98.5%

ROC curves for all four scores are shown in Figure 4.

**Full calibration metrics including Hosmer–Lemeshow test, Brier score, calibration slope and intercept are reported in Table 12*

95% confidence intervals for AUC were computed using the Hanley-McNeil (1982) standard error formula for a single ROC curve, based on the reported AUC and the number of events/non-events in this cohort. Abbreviations: AUC = area under the receiver operating characteristic curve; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value; AKI = acute kidney injury; KDIGO = Kidney Disease: Improving Global Outcomes; SRI = Simplified Renal Index.

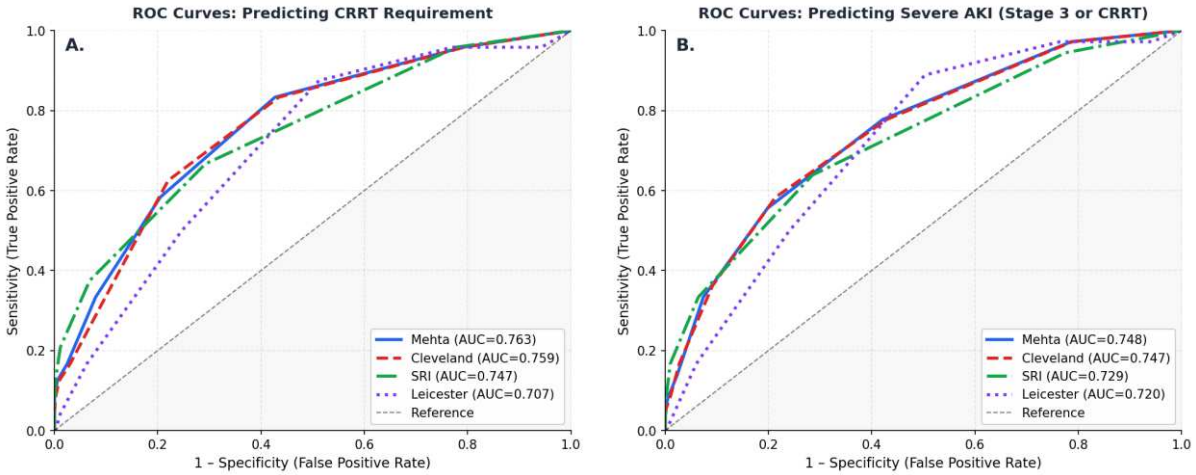

Figure 4. ROC curves for the four preoperative risk scores predicting CRRT requirement (Panel A) and severe AKI (Panel B). All scores demonstrated moderate discrimination (AUC 0.71–0.76). Mehta and Cleveland scores achieved the highest AUCs for both outcomes.

All four risk scores demonstrated moderate discriminatory ability for predicting both CRRT requirement and severe AKI, with AUC values ranging from 0.707 to 0.763 for CRRT and 0.720 to 0.748 for severe AKI. The Mehta score achieved the highest AUC for CRRT prediction (AUC = 0.763), with good sensitivity (83.3%) at a threshold of ≥2, while the Cleveland score showed comparable performance (AUC = 0.759) but with higher specificity (78.0%) at a threshold of ≥3. The Leicester score demonstrated the highest sensitivity for both CRRT (87.5%) and severe AKI (88.9%), albeit with lower specificity (approximately 49%). All scores exhibited high negative predictive values (97.9–98.8%), indicating strong utility in identifying patients at low risk. However, positive predictive values were low across all models (7.2–16.4%), reflecting the relatively low incidence of CRRT requirement (4.4%) and severe AKI (6.5%) in this cohort. The distribution of risk scores stratified by CRRT requirement is shown in Figure 5.

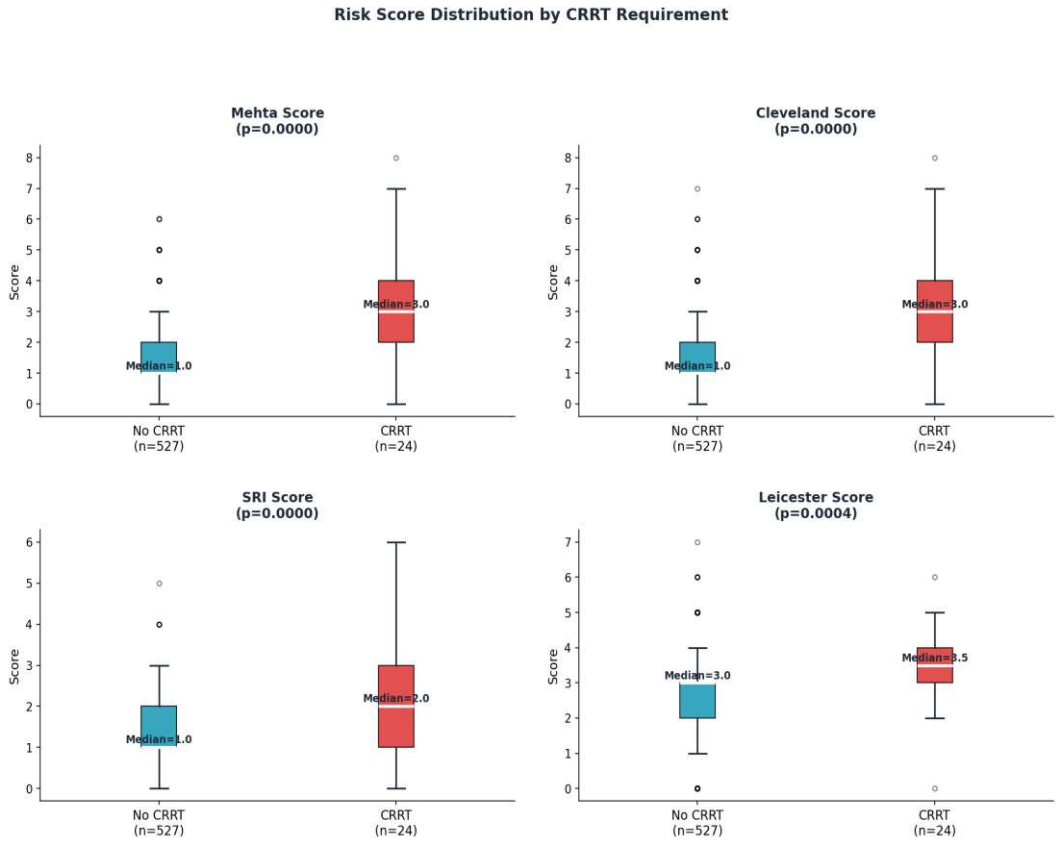

Figure 5. Risk score distribution comparing patients who required CRRT vs those who did not. All four scores were significantly higher in CRRT patients.

In this cohort, 33.6% of CABG patients developed CSA-AKI (Stage 1: 69.2%, Stage 2: 11.4%, Stage 3: 19.5%), with 4.4% requiring CRRT (25% early and 75% late initiation); mortality was 2.3% in Stage 1, 0.0% in Stage 2, and 47.2% in Stage 3, accompanied by significantly longer ICU and hospital length of stay ($p<0.001$). Patients with AKI had significantly longer CPB and cross-clamp times compared to those without AKI, although only CPB time was associated with increasing AKI severity. No significant survival benefit was observed between early and late CRRT initiation; renal recovery was numerically higher in the late group (33.3% vs 0%) but this difference was not statistically significant ($p=0.277$). In an exploratory, underpowered model, higher SOFA score and lower haemoglobin were the variables most consistently associated with mortality; risk scores demonstrated moderate discrimination, with the Mehta and Cleveland scores performing best for CRRT prediction, and all models showed high negative predictive value (>98%), reflecting in part the low prevalence of these outcomes in this cohort.

As a sensitivity analysis only, we additionally fitted a new logistic regression of each outcome on the raw score value within this cohort (local recalibration) and summarised the resulting fit statistics in Table 12. Because these coefficients are estimated from the same validation data being assessed, a slope near 1.0 and an intercept near 0 are expected by construction and do not,

by themselves, demonstrate calibration of the original score equations. Hosmer–Lemeshow p-values were non-significant for all scores and both outcomes (all p>0.05), Brier scores were low (CRRT: 0.039–0.040; severe AKI: 0.049–0.050), and calibration slopes ranged from 0.953–0.980. Calibration intercepts ranged from −0.058 to −0.132. These local recalibration statistics confirm only that the re-fitted model tracks the data it was fitted to; they should not be interpreted as evidence that the original Mehta, Cleveland, SRI, or Leicester score-to-probability equations are well calibrated in this population. Formal calibration of the original score equations could not be assessed, as published score-to-probability conversion functions were not available for all four instruments (see Limitations); we therefore restrict our conclusions about risk-score performance to discrimination (AUC, Tables 10–11) and observed event rates across score strata. Results are detailed in Table 12 and Supplementary Figure S1.

Table 12. Local Logistic Recalibration Statistics (Sensitivity Analysis) for Four Preoperative Risk Scores (CRRT Requirement and Severe AKI)

Outcome	Score	AUC	Brier Score	HL Statistic	HL df	HL p-value	Calibration Slope	Calibration Intercept
CRRT Requirement	Mehta	0.763	0.039	6.84	3	0.077	0.972	−0.077
CRRT Requirement	Cleveland	0.759	0.040	5.70	3	0.127	0.953	−0.132
CRRT Requirement	SRI	0.747	0.040	0.13	1	0.722	0.980	−0.058
CRRT Requirement	Leicester	0.707	0.040	7.46	4	0.114	0.966	−0.093
Severe AKI (KDIGO Stage 3)	Mehta	0.748	0.049	2.22	3	0.527	0.969	−0.079
Severe AKI (KDIGO Stage 3)	Cleveland	0.747	0.050	3.74	3	0.292	0.959	−0.109
Severe AKI (KDIGO Stage 3)	SRI	0.729	0.050	0.29	1	0.587	0.968	−0.086
Severe AKI (KDIGO Stage 3)	Leicester	0.720	0.050	7.30	4	0.121	0.967	−0.084

**Brier = Brier score (lower = better; 0 = perfect); HL = Hosmer–Lemeshow goodness-of-fit test; calibration slope near 1.0 and intercept near 0 are expected by construction for this locally re-fitted model and do not indicate calibration of the original score equations. Predicted probabilities were derived by fitting a new logistic regression of each score value on the respective outcome within this cohort (local recalibration), not from the original published score equations. AUC values shown here are identical to those in Tables 10–11 for the corresponding score and outcome, as expected: a monotonic logistic transformation of a single score cannot alter rank order or AUC. An earlier draft reported different AUC figures in this table because of a transcription error identified during peer review, now corrected. Tables 10–11 remain the primary reference for discrimination.*

Abbreviations: AUC = area under the receiver operating characteristic curve; HL = Hosmer–Lemeshow goodness-of-fit test; df = degrees of freedom; SRI = Simplified Renal Index; CRRT = continuous renal replacement therapy; AKI = acute kidney injury; KDIGO = Kidney Disease: Improving Global Outcomes.

5.0 Discussion

CSA-AKI affected one in three CABG patients at Universiti Malaya Medical Centre during this five-year period, placing the incidence at 33.6%, which falls within the 30–40% range consistently reported in international cardiac surgery literature [1,2]. The overall rate, however, does not capture how markedly outcomes worsened by severity. Patients with stage 3 AKI experienced a 47.2% in-hospital mortality rate, roughly twenty times that of stage 1, and fewer than half were discharged without ongoing dialysis dependence. ICU and hospital length of stay increased significantly at each advancing KDIGO stage ($p<0.001$), confirming that the overall burden of CSA-AKI is disproportionately concentrated among the minority of patients who progress to the most severe form of the disease [1,5]. The overall in-hospital mortality of 4.0% in this cohort is broadly consistent with reported rates from comparable Asian cardiac surgery centres and reflects improving perioperative care over the study period.

Perioperative anaemia was the single most consistent predictor across all outcome models, with lower haemoglobin independently associated with any AKI (aOR 0.83, $p<0.001$), severe AKI (aOR 0.61, $p<0.001$), and in-hospital mortality (aOR 0.31, $p=0.002$). This association is biologically plausible given the narrow oxygen delivery margin of the renal outer medulla. However, in this retrospective observational study, this association should be interpreted as reflecting preoperative physiological reserve rather than a directly modifiable causal exposure: lower preoperative haemoglobin may be a marker of underlying frailty, chronic disease burden, or occult bleeding predating surgery, and patients presenting with lower preoperative haemoglobin may also be more likely to experience greater intraoperative transfusion requirements or haemodynamic instability, both of which independently influence renal risk. The observed mortality association may partly represent a marker of baseline frailty or systemic illness. These findings should therefore be interpreted as identifying a clinically plausible and potentially important association rather than a proven causal one. Prospective randomised trials of preoperative haemoglobin optimisation in CABG patients are required before direct causal inference, or formal clinical recommendations can be made.

Longer cardiopulmonary bypass time was independently associated with acute kidney injury development in this cohort, with patients who developed acute kidney injury having a median cardiopulmonary bypass duration 15 minutes longer than those without renal complications (154 vs 139 minutes, $p=0.0003$), and duration escalating significantly across severity stages ($p=0.004$). Several mechanisms may explain this association. First, prolonged extracorporeal circulation induces a systemic inflammatory response through contact activation of blood components with the bypass circuit, releasing cytokines and reactive oxygen species that impair renal tubular function and promote endothelial injury. Second, non-pulsatile flow during cardiopulmonary bypass reduces renal perfusion

pressure and activates the renin-angiotensin-aldosterone system, predisposing to medullary ischaemia. Third, haemodilution from the circuit priming volume reduces haematocrit and oxygen-carrying capacity, further narrowing the renal oxygen delivery margin. Fourth, longer bypass duration is frequently a surrogate for greater surgical complexity, including multi-vessel disease, re-do surgery, or intraoperative complications such as haemodynamic instability or difficulty achieving haemostasis, any of which may independently elevate renal risk beyond the bypass effect itself. Finally, longer procedures may be associated with greater transfusion requirements, increased vasopressor exposure, and more pronounced postoperative haemodynamic instability, each of which contributes independently to acute kidney injury. For these reasons, cardiopulmonary bypass time should be regarded as a clinically informative risk marker but not as an isolated, directly modifiable causal exposure.

Emergency surgery was an independent predictor of any AKI (aOR 2.68, p=0.045) in the adequately powered model, and was associated with severe AKI (aOR 3.47, p=0.037) in the exploratory, underpowered model, conferring approximately a threefold increase in risk across both endpoints. Even for the any-AKI model, which is adequately powered, this remains observational, retrospective data, and unmeasured perioperative confounding cannot be excluded; prospective confirmation is warranted before treating emergency surgery as a fixed, causal risk factor rather than a marker of a higher-risk surgical scenario. Unplanned surgery forecloses the preoperative optimisation that might otherwise reduce renal risk, including haemoglobin correction, medication review, and volume status assessment, and is associated with greater intraoperative haemodynamic instability [1,4]. Among AKI patients who died, SOFA score was the most strongly associated variable in the exploratory multivariable mortality model (aOR 6.17, p<0.001), with AKI stage losing significance after adjustment. This exploratory finding must be interpreted cautiously given the small event number (n=20) and the risk of overfitting, but it suggests that deaths in this cohort were primarily driven by multiorgan dysfunction severity rather than renal failure in isolation. Lower haemoglobin was also independently associated with mortality (aOR 0.31 per g/dL, p=0.002), consistent with its pathophysiological role in oxygen delivery. These associations require confirmation in future adequately powered studies and should not be interpreted as definitive independent predictors.

All four preoperative risk scores demonstrated broadly comparable moderate discrimination. The Mehta score achieved the highest AUC for CRRT prediction (0.763) with 83.3% sensitivity at a threshold of ≥2, while the Cleveland score was close behind (AUC 0.759) with better specificity (78.0%) at a threshold of ≥3 [4]. The Leicester score achieved the highest sensitivity across both outcomes (87.5% for CRRT, 88.9% for severe AKI) but at the cost of lower specificity (approximately 49%). Negative predictive values exceeded 97.9% across all models and both outcomes; given the low prevalence of CRRT requirement and severe AKI in this cohort, high NPV is expected even for a moderately discriminating test and should be interpreted as a property of low outcome prevalence rather than proof

that these scores can safely rule out severe AKI. With this caveat, the scores may still have some utility in preoperative risk communication and resource planning [4,9]. Positive predictive values were poor across the board (7.2–16.4%), partly reflecting the genuine low incidence of severe AKI and CRRT requirement and partly the limitation of using only preoperative variables to predict a complication substantially shaped by intraoperative and postoperative factors [4]. Improving positive predictive performance will likely require integrating these scores with intraoperative variables such as CPB duration and early postoperative biomarkers such as NGAL or cystatin C [18]. No prior Malaysian study has directly compared all four scores (Mehta, Cleveland Clinic, SRI, and Leicester) in a Southeast Asian CABG population, providing a locally grounded performance benchmark for clinicians in this region.

The descriptive comparison of CRRT timing must be interpreted with extreme caution. With only 24 patients requiring CRRT, of whom six received early initiation, this analysis is critically underpowered to draw any conclusion about the comparative effectiveness of timing strategies. No inference of non-inferiority of late CRRT initiation should be drawn from these data. The numerically higher mortality in the early group (83.3% vs 55.6%) almost certainly reflects confounding by indication. Renal recovery was numerically higher in the late group (33.3% vs 0%), but this difference was not statistically significant (p=0.277) and, like all comparisons in this small subgroup, should not be over-interpreted. These findings characterise local clinical practice and are directionally consistent with the neutral findings of AKIKI, IDEAL-ICU, and STARRT-AKI [11,12,13] but provide no independent evidence to support or refute any CRRT timing strategy. A multicentre prospective study with a prespecified initiation protocol and adequate power is required.

6.0 Limitations

This study has several limitations that should be considered when interpreting the findings. As a single-centre retrospective analysis, it is subject to inherent selection bias and residual confounding that regression adjustment cannot fully eliminate. The reliance on electronic and paper-based medical records meant that several clinically important covariates, including intra-aortic balloon pump use, vasoactive-inotropic scores, perioperative fluid balance, and novel kidney injury biomarkers such as NGAL and cystatin C, were unavailable, which limits the completeness of the predictor models and may partly explain why SOFA score, as a broad composite of organ dysfunction, accounted for much of the mortality signal in the adjusted analyses. Formal probability-based calibration was performed using logistic regression–derived predicted probabilities as a surrogate, since the original SRI and Leicester derivation papers do not report score-to-probability conversion functions. The calibration analyses should therefore be considered approximate for these two instruments. Future validation studies should ideally use cohorts in which original probability outputs are available for all four scores. Although the 34 patients undergoing combined procedures represent only 6.2% of the cohort, a sensitivity analysis restricted to isolated CABG yielded broadly consistent findings across all primary

endpoints (Supplementary Tables S1–S2), supporting the generalisability of the results to the isolated CABG population.

The risk score performance reported here represents single-centre external validation in an independent Malaysian cohort, as the four scores were originally derived outside this population and were applied without modification. However, without an additional validation cohort from another Malaysian or Southeast Asian centre, the AUC values, calibration estimates, and optimal thresholds should be regarded as locally grounded performance estimates rather than definitive regional benchmarks. The study period spanned January 2021 to December 2025 and included the COVID-19 pandemic, during which surgical case volume, staffing patterns, and patient acuity may have shifted in ways not fully captured by the recorded variables, introducing a potential source of temporal confounding.

The exploratory analysis of CRRT timing is additionally constrained by the small number of patients who required dialysis (n=24), of whom only six received early initiation. This comparison was substantially underpowered, and firm conclusions about the effect of CRRT timing on outcomes cannot be drawn from a sample of this size. CRRT was initiated at the discretion of treating physicians without a standardised protocol. This introduced confounding by indication that regression cannot fully address, though it is also what generated the variation in timing this comparison needed. Patients selected for early initiation may have had unmeasured clinical features influencing their prognosis independently of the timing decision itself. The CRRT analysis is best understood as hypothesis-generating, and a multicentre prospective study with a prespecified initiation protocol and biomarker-enhanced risk stratification would be the most appropriate next step.

7.0 Ethical Clearance

Ethical approval for this study was obtained from the Medical Research Ethics Committee (MREC) of University Malaya Medical Centre (UMMC) (MREC ID No. 202617-16114). The study was conducted in accordance with the principles of the Declaration of Helsinki. As this was a retrospective observational study utilising anonymised patient data, the requirement for informed consent was waived by the ethics committee.

8.0 Conclusion

Cardiac surgery–associated acute kidney injury affected one-third of patients undergoing coronary artery bypass grafting at Universiti Malaya Medical Centre over this five-year period and was associated with outcomes that worsened sharply and progressively with each advancing severity stage, from a mortality of 2.3% in Stage 1 to 47.2% in Stage 3.

Perioperative anaemia and prolonged cardiopulmonary bypass time were the most consistent observational risk factors across multiple outcome models, with biologically plausible and directionally consistent associations. However, in this retrospective study, causality cannot be established and both factors may reflect perioperative complexity or severity rather than discrete modifiable exposures. Prospective intervention studies are required before these associations are translated into specific clinical recommendations.

All four established preoperative risk scores (Mehta, Cleveland Clinic, Simplified Renal Index, and Leicester) demonstrated moderate and broadly comparable discrimination for predicting severe acute kidney injury and continuous renal replacement therapy requirement in this Southeast Asian coronary artery bypass grafting cohort, with high negative predictive values exceeding 97.9%. This largely reflects the low prevalence of these outcomes in the cohort rather than intrinsic score performance, and should not on its own be read as evidence that any score can safely rule out severe AKI or CRRT requirement in an individual patient. This represents the first systematic external validation of these instruments in a Malaysian and Southeast Asian population.

The exploratory multivariable analysis identified higher Sequential Organ Failure Assessment score and lower haemoglobin as the two variables most consistently associated with in-hospital mortality after adjustment; however, this model was based on only 20 events and should be considered hypothesis-generating only.

The descriptive comparison of early versus late continuous renal replacement therapy initiation in the small dialysis subgroup (n=24) was substantially underpowered. No conclusion regarding the effect of timing on survival or renal recovery, and no recommendation for or against any particular initiation strategy, can be drawn from these data. This component of the study is presented purely to characterise local practice patterns and to generate hypotheses for future, adequately powered prospective research.

These findings provide the first systematic characterisation of cardiac surgery–associated acute kidney injury incidence, risk factors, outcomes, and risk score performance in a multi-ethnic Malaysian population, and serve as a foundation for future prospective multicentre studies in Southeast Asia

9.0 Declarations

Abbreviations

AKI: Acute kidney injury; AUC: Area under the receiver operating characteristic curve; CABG: Coronary artery bypass grafting; CI: Confidence interval; CKD: Chronic kidney disease; CPB: Cardiopulmonary bypass; CRRT: Continuous renal replacement therapy; CSA-AKI: Cardiac surgery–associated acute kidney injury; EPV: Events per variable; ESKD: End-stage kidney disease; HL:

Hosmer–Lemeshow; ICU: Intensive care unit; IQR: Interquartile range; KDIGO: Kidney Disease: Improving Global Outcomes; LOS: Length of stay; LVEF: Left ventricular ejection fraction; NPV: Negative predictive value; OR: Odds ratio; PPV: Positive predictive value; ROC: Receiver operating characteristic; RRT: Renal replacement therapy; SD: Standard deviation; SOFA: Sequential Organ Failure Assessment; SRI: Simplified Renal Index; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology; TRIPOD: Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis; UMMC: Universiti Malaya Medical Centre

Ethics approval and consent to participate

Ethical approval for this study was obtained from the Medical Research Ethics Committee (MREC) of Universiti Malaya Medical Centre (UMMC) (MREC ID No. 202617-16114). The study was conducted in accordance with the principles of the Declaration of Helsinki. As this was a retrospective observational study utilising anonymised patient data, the requirement for individual informed consent was waived by the ethics committee.

Consent for publication

Not applicable. This study did not include any identifying images, personal details, or clinical information that could compromise patient anonymity. All data were fully anonymised prior to analysis.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request, subject to institutional data governance policies and ethical approval conditions of UMMC.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by the Department of Medicine Research Support Fund (DOM-RSF), Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia (Cycle 7/1, 2026), awarded to Dr Bay Shing Shen as Principal Investigator. The grant was awarded under the study title “Intraoperative Ischemic Time and Risk of Severe Acute Kidney Injury Following Coronary Artery Bypass Grafting: A Five-Year Retrospective Cohort Study (The TIME-AKI Study),” which was subsequently developed and submitted under the revised study title, KARMA Study. The funder had no role in the study design, data collection, data analysis, interpretation of results, manuscript preparation, or decision to submit the manuscript for publication.

Authors' contributions

CHL: Data collection, data analysis, manuscript drafting. SSB: Study conception and design, data interpretation, critical revision of manuscript, corresponding author. YWL: Data collection, critical revision. CCG: Data collection, critical revision. KVP: Data collection, critical revision. EL: Data collection, critical revision. MJ: Critical revision of manuscript. SK: Cardiothoracic surgical data contribution, critical revision. WAHWMA: Critical revision of manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors would like to thank the medical records team and cardiac intensive care unit nursing staff at Universiti Malaya Medical Centre for their assistance in facilitating data retrieval. We also thank all patients whose clinical data contributed to this study.

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