

Preoperative Glucose-to-Albumin Ratio and Postoperative Acute Kidney Injury in Patients Admitted to the Cardiac Surgery Recovery Unit: Association Analyses and Interpretable Machine Learning Based on the MIMIC-IV Database

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Abstract

Background

Acute kidney injury (AKI) is a frequent and serious complication after cardiac surgery. The glucose-to-albumin ratio (GAR) is an emerging composite biomarker, but its association with postoperative AKI in the cardiac surgery recovery unit (CSRU) remains unclear.

Methods

Adult CSRU patients were extracted from the Medical Information Mart for Intensive Care IV (MIMIC-IV, version 3.1). AKI was defined and staged according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria using both serum creatinine and urine output. Multivariable logistic regression, restricted cubic splines, propensity score matching, subgroup interaction tests and causal mediation analyses were used to characterize the GAR–AKI association. Ten machine learning algorithms were trained on 15 candidate predictors including GAR, and model performance was assessed by the area under the receiver operating characteristic curve (AUC), calibration curves, decision curve analysis and SHapley Additive exPlanations (SHAP).

Results

Of 4,418 patients, 3,524 (79.8%) developed AKI. Median GAR increased stepwise with AKI severity (non-AKI 26.92; stage 1, 27.78; stage 2, 29.36; stage 3, 31.94; P for trend < 0.001). In the fully adjusted model, the third and fourth GAR quartiles were associated with higher odds of AKI (OR 1.608, 95% CI 1.292–2.004; OR 1.465, 95% CI 1.181–1.821, respectively). Restricted cubic spline analysis indicated an approximately linear dose-response relationship (P for nonlinear = 0.444). The association remained robust after propensity score adjustment and matching. Significant interactions were observed for body mass index, hypertension and diabetes. Mediation analysis suggested that hypoalbuminemia, comorbidity burden and illness severity partially mediated the association. The logistic regression model achieved the best discrimination in the validation set (AUC = 0.942), with good calibration and clinical net benefit. SHAP analysis confirmed GAR as an independent contributor.

Conclusions

Elevated preoperative GAR is independently associated with postoperative AKI and its severity in CSRU patients. As an inexpensive, routinely available composite biomarker, GAR may facilitate early AKI risk stratification, and interpretable machine learning models incorporating GAR show excellent predictive performance pending external validation.

1. Introduction

Cardiac surgery remains a cornerstone in the management of a wide spectrum of cardiovascular diseases, including coronary artery disease, valvular heart disease, congenital heart defects and aortic pathologies, with coronary artery bypass grafting (CABG) and valve procedures being the most commonly performed operations[1, 2]. Despite continuous advances in surgical techniques and perioperative care, postoperative acute kidney injury (AKI) remains one of the most frequent and clinically consequential complications, with a reported incidence as high as 30–40% after cardiac surgery[3] and substantial global morbidity and mortality[10]. Among patients admitted to the cardiac surgery recovery unit (CSRU), more than half develop some stage of AKI[4], which is closely associated with prolonged mechanical ventilation and hospital stay, increased healthcare expenditure, higher readmission rates, and elevated short- and long-term mortality[5–8]. Contemporary cohorts applying stringent KDIGO criteria across critically ill populations have reported similarly high AKI incidence and associated morbidity[9]. These observations underscore the importance of early identification and risk stratification of patients at high risk of postoperative AKI.

Serum albumin accounts for more than half of total plasma protein and is a key indicator of nutritional reserve, plasma oncotic pressure and systemic physiological integrity[11]. Hypoalbuminemia has been linked to postoperative infection, impaired wound healing, multiple organ dysfunction and an increased risk of AKI in observational studies[12, 15]. Conversely, fluctuations in blood glucose reflect metabolic stress and the acute systemic response to surgical insult; stress hyperglycaemia may aggravate kidney injury through oxidative stress, inflammatory activation and endothelial dysfunction[13, 14]. Because these two routinely measured laboratory parameters capture complementary pathophysiological dimensions, their combination may provide a more informative risk signal than either parameter alone.

The glucose-to-albumin ratio (GAR) is a composite biomarker that integrates glycaemic status with nutritional and inflammatory reserve. GAR has demonstrated prognostic value in non-alcoholic fatty liver disease, acute pancreatitis, sepsis and intracerebral haemorrhage[16–19]. However, the association between GAR and postoperative AKI in cardiac surgery patients has not been systematically investigated. In parallel, machine learning (ML) approaches have increasingly been applied to AKI prediction in critically ill populations[20–22]; however, AKI represents a heterogeneous syndrome, and recent advances in sub-phenotyping suggest that biomarker performance may vary across distinct pathophysiological clusters[23]. Consequently, few existing models have incorporated composite metabolic-nutritional biomarkers together with transparent, interpretable methodology that can be readily translated to bedside risk stratification.

Using the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, the present study aimed to: (1) characterize the distribution of preoperative GAR across AKI severity strata and its dose-response relationship with postoperative AKI; (2) evaluate whether GAR is independently associated with postoperative AKI after stepwise adjustment for demographic, clinical and laboratory confounders; (3) verify the robustness of the association through propensity score-based sensitivity analyses; (4) explore

effect modification in clinically relevant subgroups and potential mediating pathways; and (5) develop and internally validate interpretable ML prediction models incorporating GAR for postoperative AKI.

2. Methods

2.1. Data source and ethical statement

This retrospective cohort study was based on the MIMIC-IV database (version 3.1), a large, publicly available, de-identified critical care database comprising more than 94,000 intensive care unit (ICU) admissions and over 200,000 emergency department encounters at the Beth Israel Deaconess Medical Center (Boston, MA, USA) between 2008 and 2022[24]. The database provides high-resolution physiological waveforms validated by algorithms and nursing staff, laboratory results, and standardized diagnostic codes (ICD-9/ICD-10). All protected health information was de-identified in accordance with the Health Insurance Portability and Accountability Act (HIPAA); the institutional review boards of the Massachusetts Institute of Technology and the Beth Israel Deaconess Medical Center approved the use of the database for research, and the requirement for individual informed consent was waived. The author completed the required Collaborative Institutional Training Initiative (CITI) programme and signed the data use agreement. This report adheres to the STROBE statement for observational studies[25] and to the TRIPOD statement for the prediction modelling component[26].

2.2. Study population

Adult patients (aged 18 years or older) admitted to the CSRU with an ICU stay longer than 24 hours were eligible. For patients with multiple ICU admissions, only the first ICU stay of the first hospitalization was analysed. Patients were excluded if they were not admitted to the CSRU, had missing serum glucose or albumin measurements, lacked urine output or serum creatinine records, or had pre-existing renal failure. The participant selection process is shown in Fig. 1.

2.3. Exposure, outcome and covariates

The exposure was the preoperative GAR, calculated as serum glucose (mg/dL) divided by serum albumin (g/dL), using the last available measurement before surgery. The outcome was postoperative AKI occurring during the CSRU stay, defined and staged according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria using both serum creatinine and urine output[27]. Baseline serum creatinine was defined as the lowest creatinine value within the preceding 7 days; severe AKI was defined as KDIGO stage 2 or 3.

Covariates included demographics (age, sex, ethnicity, body weight, height, body mass index [BMI], smoking and alcohol use), vital signs (heart rate, systolic and diastolic blood pressure, peripheral oxygen saturation and respiratory rate), the last preoperative laboratory parameters (serum sodium, potassium, chloride, haemoglobin, blood urea nitrogen [BUN], creatinine, platelet count, white blood cell count and international normalized ratio [INR]), illness severity scores at ICU admission (Sequential Organ Failure

Assessment [SOFA], Charlson Comorbidity Index [CCI], Acute Physiology Score III [APSIII] and Glasgow Coma Scale [GCS]), comorbidities (acute myocardial infarction, congestive heart failure, hypertension, cerebrovascular disease, chronic pulmonary disease, liver disease, pre-existing AKI diagnosis, chronic kidney disease [CKD], diabetes, malignancy, hyperlipidaemia and sepsis), and interventions (preoperative benzodiazepine and beta-blocker use, renal replacement therapy [RRT] and postoperative extracorporeal membrane oxygenation [ECMO]).

2.4. Statistical analysis of the GAR-AKI association

Normally distributed continuous variables are presented as mean +/- standard deviation, non-normally distributed variables as median (interquartile range), and categorical variables as counts (percentages). Between-group comparisons used the unpaired t-test, the Mann-Whitney U test or the chi-square test, as appropriate. Variables with more than 20% missing data were excluded from the analysis. Multivariable logistic regression models were constructed to estimate odds ratios (ORs) with 95% confidence intervals (CIs) for the association between GAR quartiles and postoperative AKI: model 1 was unadjusted; model 2 was adjusted for age, ethnicity, smoking, alcohol use, hypertension, cerebrovascular disease, chronic pulmonary disease and liver disease; and model 3 was additionally adjusted for sepsis, SOFA score and GCS score. Restricted cubic spline (RCS) analysis was used to explore potential non-linearity[28]. Robustness was assessed through three strategies: conventional multivariable adjustment, propensity score (PS) adjustment, and 1:1 nearest-neighbour propensity score matching (PSM) with covariate balance evaluated by standardized mean differences[29]. Subgroup analyses with formal interaction tests (likelihood ratio tests) were performed across prespecified strata. Causal mediation analysis was conducted using the R mediation package to quantify the average causal mediation effect (ACME) and the proportion mediated by candidate intermediate variables[30]. All analyses were performed with R software (R Foundation for Statistical Computing, Vienna, Austria), and a two-sided P value < 0.05 was considered statistically significant.

2.5. Machine learning model development and internal validation

Fifteen candidate predictors were entered into the ML pipeline: GAR, age, sex, BMI, APSIII score, SOFA score, GCS score, congestive heart failure, hypertension, diabetes, cerebrovascular disease, chronic pulmonary disease, liver disease, CKD and sepsis. The cohort was randomly divided into a training set (70%) and an internal validation set (30%) with stratified sampling to preserve the outcome ratio. Ten classification algorithms were developed: logistic regression, least absolute shrinkage and selection operator (LASSO) logistic regression, random forest, kernel support vector machine, k-nearest neighbours, partial least squares, gradient boosting, neural network, naive Bayes and discriminant analysis. Hyperparameters were optimized by grid search with 10-fold cross-validation within the training set. Model discrimination was primarily evaluated by the area under the receiver operating characteristic curve (AUC); accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), F1 score and Youden's index were also calculated. Calibration was assessed with calibration plots for the best-performing model, and clinical utility was evaluated by decision curve analysis (DCA)

[31]. SHapley Additive exPlanations (SHAP) were used to interpret the optimal model at the global and individual levels[32]. The modelling workflow is reported in accordance with the TRIPOD statement[26, 33].

3. Results

3.1. Baseline characteristics

A total of 4,418 CSRU patients met the inclusion criteria, of whom 3,524 (79.8%) developed postoperative AKI and 894 (20.2%) did not (Fig. 1). Compared with non-AKI patients, those who developed AKI were older, had higher preoperative glucose, lower preoperative albumin and consequently higher GAR, and presented with greater body weight, BMI, BUN, creatinine, INR and illness severity scores (SOFA, CCI and APSIII), together with lower haemoglobin, platelet count, serum sodium and chloride (all $P < 0.05$; Supplementary Table 1). The prevalence of hypertension, cerebrovascular disease, chronic pulmonary disease, liver disease, CKD, diabetes, congestive heart failure and sepsis was also significantly higher in the AKI group, indicating a heavier baseline disease burden and poorer perioperative renal reserve. In-hospital mortality was significantly higher among patients with AKI.

When patients were stratified by GAR quartiles (Q1-Q4), the incidence of AKI rose from 74.8% in Q1 to 77.1%, 83.8% and 83.4% in Q2-Q4 ($P < 0.001$), and the mean AKI stage score increased accordingly (Supplementary Table 2). Higher GAR strata were also characterized by older age, more metabolic comorbidities, higher severity scores and greater in-hospital mortality, suggesting that GAR captures both metabolic-nutritional derangement and the overall perioperative risk burden.

3.2. Distribution of GAR across AKI severity

Median GAR increased stepwise with AKI severity: 26.92 (interquartile range [IQR] 23.33–33.73) in non-AKI patients, 27.78 (IQR 23.72–34.62) in stage 1, 29.36 (IQR 24.43–37.13) in stage 2 and 31.94 (IQR 26.38–43.87) in stage 3 (P for trend < 0.001 ; Fig. 2). This graded increase indicates a positive dose-response relationship between preoperative GAR and both the occurrence and severity of postoperative AKI.

3.3. Association between GAR and postoperative AKI

Using GAR Q1 as the reference, Q2 was not significantly associated with AKI in any model. In contrast, Q3 and Q4 were consistently associated with increased AKI risk (Table 1). In the unadjusted model, the ORs were 1.745 (95% CI 1.416–2.155) for Q3 and 1.688 (95% CI 1.372–2.082) for Q4. After adjustment for demographic factors, lifestyle factors and comorbidities (model 2), the ORs were 1.727 and 1.586, respectively. In the fully adjusted model additionally accounting for sepsis, SOFA and GCS scores (model 3), Q3 and Q4 remained associated with 60.8% and 46.5% higher odds of AKI (OR 1.608, 95% CI 1.292–2.004, $P < 0.001$; OR 1.465, 95% CI 1.181–1.821, $P < 0.001$, respectively).

Table 1

Logistic regression analysis of the association between GAR quartiles and postoperative AKI.

GAR quartile	Model 1, OR (95% CI)	P value	Model 2, OR (95% CI)	P value	Model 3, OR (95% CI)	P value
Q1	Reference		Reference		Reference	
Q2	1.133 (0.932–1.377)	0.212	1.068 (0.874–1.304)	0.521	1.066 (0.870–1.306)	0.537
Q3	1.745 (1.416–2.155)	< 0.001	1.727 (1.394–2.146)	< 0.001	1.608 (1.292–2.004)	< 0.001
Q4	1.688 (1.372–2.082)	< 0.001	1.586 (1.283–1.965)	< 0.001	1.465 (1.181–1.821)	< 0.001

3.4. Dose-response relationship assessed by restricted cubic splines

RCS analysis confirmed a significant overall association between GAR and postoperative AKI (P for overall < 0.001; Fig. 3). The fitted curve rose continuously with increasing GAR, with a steeper increment at higher GAR levels. The non-linearity test was not significant (P for nonlinear = 0.444), indicating that the dose-response relationship was approximately linear rather than threshold-shaped, consistent with the quartile-based logistic regression results.

3.5. Sensitivity analyses

The association remained robust across all sensitivity analysis strategies (Table 2). In the multivariable-adjusted model, propensity score-adjusted model and propensity score-matched cohort, the ORs for Q3 were 1.633, 1.598 and 1.486 (95% CI 1.106–2.001), and those for Q4 were 1.528, 1.459 and 1.415 (95% CI 1.058–1.896), respectively; Q2 remained non-significant in all models. Regarding the GAR components, higher preoperative glucose was associated with increased AKI risk (OR 1.004 per unit in all models), whereas higher preoperative albumin was consistently protective (ORs 0.407, 0.421 and 0.483 across the three models). These findings indicate that the GAR-AKI association is not driven by baseline imbalances and that GAR integrates the opposing contributions of its two components.

Table 2

Sensitivity analyses of the association between GAR and postoperative AKI using multivariable adjustment, propensity score adjustment and propensity score matching.

Variable	Multivariable-adjusted, OR (95% CI)	P value	PS-adjusted, OR (95% CI)	P value	PS-matched, OR (95% CI)	P value
GAR Q1	Reference		Reference		Reference	
GAR Q2	1.023 (0.784–1.335)	0.868	1.096 (0.826–1.456)	0.525	1.062 (0.795–1.420)	0.683
GAR Q3	1.633 (1.251–2.134)	< 0.001	1.598 (1.199–2.134)	0.001	1.486 (1.106–2.001)	0.009
GAR Q4	1.528 (1.174–1.991)	0.002	1.459 (1.098–1.941)	0.009	1.415 (1.058–1.896)	0.020
Preoperative glucose	1.004 (1.001–1.006)	0.001	1.004 (1.002–1.006)	0.001	1.004 (1.002–1.006)	0.001
Preoperative albumin	0.407 (0.324–0.508)	< 0.001	0.421 (0.326–0.540)	< 0.001	0.483 (0.372–0.623)	< 0.001

3.6. Subgroup analyses

Overall, each one-unit increment in GAR was associated with a 2% increase in the odds of AKI (OR 1.02, 95% CI 1.02–1.03; $P < 0.001$; Fig. 4). This positive association was consistent across most prespecified subgroups, including strata defined by age, sex, ethnicity, cerebrovascular disease, chronic pulmonary disease, malignancy, sepsis, preoperative medication use and RRT status, with no significant interactions. Significant effect modification was observed for BMI (P for interaction = 0.013), hypertension ($P = 0.021$) and diabetes ($P = 0.023$): the GAR-AKI association was stronger in normal-weight and overweight patients, in patients without hypertension, and in patients without diabetes, whereas it was attenuated and non-significant in obese patients.

3.7. Mediation analyses

Causal mediation analysis was performed to explore potential intermediate pathways linking GAR to postoperative AKI (Supplementary Table 3; Supplementary Figs. 1 and 2). Among the GAR components, albumin showed the largest positive mediation (ACME 0.0021; proportion mediated 41.84%), whereas glucose exhibited a negative mediation proportion (-268.32%), suggesting a suppression pattern in which the risk signal of GAR cannot be attributed to hyperglycaemia alone but rather reflects the combined metabolic-nutritional imbalance. Significant positive mediation was also observed for BMI (16.87%), haemoglobin (19.24%), body weight (12.97%), BUN (14.38%), creatinine (14.65%) and chloride

(11.26%). Illness severity and comorbidity burden mediated a substantial proportion of the association, led by the Charlson Comorbidity Index (42.58%), RRT requirement (45.93%), pre-existing AKI diagnosis (22.14%), APSIII (19.42%), diabetes (13.87%), congestive heart failure (13.67%), CKD (12.21%), sepsis (7.84%) and SOFA score (7.24%). In all models, the direct effect of GAR on AKI remained statistically significant, indicating that the association is only partly explained by these intermediate pathways.

Table 3
Performance of the ten machine learning models in the training and internal validation sets.

Model	Sensitivity	Specificity	Accuracy	PPV	NPV	F1	Youden's index
Logistic regression	0.733	0.893	0.834	0.800	0.851	0.765	0.626
LASSO	0.736	0.902	0.841	0.815	0.854	0.774	0.639
Random forest	0.731	0.899	0.837	0.809	0.851	0.768	0.630
Support vector machine	0.750	0.899	0.844	0.813	0.860	0.780	0.649
k-nearest neighbours	0.669	0.894	0.811	0.788	0.822	0.724	0.564
Partial least squares	0.647	0.902	0.808	0.795	0.814	0.714	0.550
Gradient boosting	0.722	0.898	0.833	0.805	0.847	0.761	0.620
Neural network	0.736	0.876	0.825	0.777	0.850	0.756	0.613
Naive Bayes	0.711	0.870	0.811	0.762	0.837	0.736	0.581
Discriminant analysis	0.711	0.912	0.838	0.826	0.844	0.764	0.623
Model	Sensitivity	Specificity	Accuracy	PPV	NPV	F1	Youden's index
Logistic regression	0.779	0.925	0.876	0.838	0.893	0.807	0.703
LASSO	0.786	0.928	0.881	0.846	0.896	0.815	0.714
Random forest	0.807	0.921	0.883	0.837	0.905	0.822	0.728
Support vector machine	0.757	0.907	0.857	0.803	0.882	0.779	0.664
k-nearest neighbours	0.686	0.914	0.838	0.800	0.853	0.738	0.600
Partial least squares	0.636	0.903	0.814	0.767	0.832	0.695	0.539
Gradient boosting	0.764	0.925	0.871	0.836	0.887	0.799	0.689
Neural network	0.743	0.921	0.862	0.825	0.877	0.782	0.664
Naive Bayes	0.679	0.900	0.826	0.772	0.848	0.722	0.578

Model	Sensitivity	Specificity	Accuracy	PPV	NPV	F1	Youden's index
Discriminant analysis	0.757	0.928	0.871	0.841	0.884	0.797	0.685

3.8. Development and internal validation of machine learning models

Ten ML models were trained to predict postoperative AKI using 15 candidate predictors including GAR. In the training set, AUCs ranged from 0.855 (k-nearest neighbours) to 0.899 (LASSO and discriminant analysis); in the validation set, AUCs ranged from 0.889 (partial least squares) to 0.942 (logistic regression) (Table 3; Fig. 5; Figure 6). The logistic regression model achieved the best overall discrimination in the validation set (AUC 0.942), with accuracy 0.876, sensitivity 0.779, specificity 0.925, PPV 0.838, NPV 0.893, F1 score 0.807 and Youden's index 0.703, followed closely by LASSO (AUC 0.941), discriminant analysis and random forest (both AUC 0.939). Calibration curves of the logistic model showed good agreement between predicted and observed probabilities in both the training and validation sets (Supplementary Fig. 3), and DCA demonstrated a favourable net benefit across a wide range of threshold probabilities compared with treat-all and treat-none strategies (Fig. 7).

3.9. Model interpretation with SHAP

SHAP analysis of the optimal model ranked APSIII as the most influential predictor (mean |SHAP| 0.137), followed by BMI (0.072), CKD (0.065), GCS score (0.054), congestive heart failure (0.054), SOFA score (0.051), age (0.037) and GAR (0.026) (Fig. 8A). The beeswarm plot (Fig. 8B) showed that higher GAR values contributed positively to the predicted AKI risk, supporting the direction of the association identified in the regression analyses. Individual-level explanations using waterfall and force plots illustrate how each feature shifted a given patient's prediction from the base value to the final risk estimate (Supplementary Fig. 4), which may facilitate bedside interpretation.

4. Discussion

In this large retrospective cohort of 4,418 CSRU patients from the MIMIC-IV database, elevated preoperative GAR was independently associated with postoperative AKI and increased in a stepwise manner with AKI severity. For the practicing intensivist, these findings suggest that preoperative GAR can be readily calculated from routine laboratory tests and used to identify patients who may benefit from intensified hemodynamic monitoring and kidney-protective bundles in the CSRU. The association was approximately linear, remained robust after multivariable adjustment, propensity score adjustment and propensity score matching, and was modified by BMI, hypertension and diabetes status. Mediation analyses suggested that hypoalbuminemia, comorbidity burden, pre-existing kidney disease and overall illness severity partially explained the association. Furthermore, an interpretable ML model incorporating

GAR achieved excellent discrimination (validation AUC 0.942) with good calibration and clinical utility, and SHAP analysis confirmed GAR as an independent contributor to AKI prediction.

The incidence of AKI in our cohort (79.8%) is higher than the commonly cited 30–40% after cardiac surgery[3]. This discrepancy is expected because we applied the full KDIGO definition incorporating both serum creatinine and urine output criteria, and urine output-based detection substantially increases the apparent incidence of AKI; a similar epidemiological pattern has been reported in cardiac intensive care populations, where more than half of patients develop at least stage 1 AKI[4, 34]. Consistent with previous studies, AKI in our cohort was associated with higher in-hospital mortality and a heavier comorbidity burden[5–8].

Our findings extend the growing literature on GAR as a prognostic biomarker. Previous studies linked GAR to outcomes in non-alcoholic fatty liver disease, acute pancreatitis, sepsis and intracerebral haemorrhage[16–19], but evidence in the cardiac surgical setting was lacking. The biological plausibility of the association is supported by the two components of the ratio. Hyperglycaemia promotes renal injury through oxidative stress, mitochondrial dysfunction, pro-inflammatory signalling and endothelial damage[13, 14], whereas hypoalbuminemia compromises plasma oncotic pressure, antioxidant and anti-inflammatory capacity and reflects malnutrition, all of which increase susceptibility to AKI[11, 12, 15]. By dividing glucose by albumin, GAR simultaneously captures metabolic stress and depleted physiological reserve; the protective direction of albumin and the harmful direction of glucose observed in our sensitivity analyses corroborate this interpretation.

The mediation analyses provide additional mechanistic insight. Albumin mediated 41.84% of the GAR-AKI association, whereas glucose showed a marked negative (suppression) mediation proportion, reinforcing that GAR is not a simple surrogate of glycaemia but an integrated metabolic-nutritional signal. The large mediation proportions of the Charlson Comorbidity Index (42.58%), RRT requirement (45.93%), pre-existing AKI diagnosis (22.14%) and APSIII (19.42%) indicate that GAR partly reflects accumulated chronic disease burden and acute illness severity. Nevertheless, the direct effect of GAR remained significant in every mediation model, suggesting an independent contribution beyond these pathways. The attenuation of the association in obese, hypertensive and diabetic subgroups may reflect a metabolic ceiling effect, whereby chronic metabolic derangement in these populations diminishes the incremental information carried by GAR, although residual confounding and effect-measure modification cannot be excluded.

From a prediction perspective, it is noteworthy that the logistic regression model outperformed more complex algorithms in internal validation, in line with evidence that regularized and linear models can match or exceed flexible ML methods for low-dimensional structured clinical data[33]. The high specificity (0.925) of the model supports its use for ruling in high-risk patients who may benefit from intensified monitoring and kidney-protective bundles, such as those evaluated in biomarker-guided prevention trials[35]. SHAP analysis confirmed clinical face validity: acute physiology scores, BMI and CKD were the dominant predictors, while GAR contributed independently and in the expected direction.

Decision curve analysis further suggested potential clinical net benefit across plausible risk thresholds[31]. Because GAR is computed from two inexpensive, universally available preoperative measurements, it could be readily embedded into preoperative assessment workflows to complement established severity scores.

Several strengths of this study deserve mention: the large, well-characterized cohort; the use of the complete KDIGO criteria combining creatinine and urine output; the multi-strategy robustness verification; formal interaction and mediation analyses; and a transparent ML workflow reported according to TRIPOD with SHAP-based interpretability[26, 32]. However, several limitations should be acknowledged. First, this was a single-centre retrospective observational study, and causal inference is inherently limited despite propensity score methods; residual confounding by unmeasured factors (e.g., cardiopulmonary bypass time, intraoperative hypotension, nephrotoxic agents and contrast exposure) is likely. Second, validation was internal only; external, multicentre prospective validation is required before clinical deployment, particularly because validation-set performance exceeded training-set performance, suggesting favourable case-mix in the validation split rather than true generalizability. Third, GAR was assessed at a single preoperative time point, and its perioperative trajectory may carry additional prognostic information. Fourth, the estimated baseline creatinine may misclassify AKI in patients with undocumented premorbid kidney function. Finally, mediation estimates rely on strong, untestable no-unmeasured-confounding assumptions and should be interpreted as exploratory.

Future studies should validate these findings in prospective multicentre cohorts, evaluate dynamic perioperative GAR trajectories, investigate whether GAR-guided preventive strategies (such as KDIGO care bundles in high-risk patients) improve renal outcomes, and test incremental predictive value of GAR over established risk scores with measures of reclassification.

5. Conclusions

Elevated preoperative glucose-to-albumin ratio is independently associated with postoperative AKI and its severity in patients admitted to the cardiac surgery recovery unit, following an approximately linear dose-response pattern that is robust to multiple sensitivity analyses. The association is partly mediated by hypoalbuminemia, comorbidity burden, pre-existing kidney disease and illness severity, and is modified by BMI, hypertension and diabetes. Interpretable machine learning models incorporating GAR achieved excellent discrimination, calibration and clinical utility in internal validation. For intensivists, preoperative GAR assessment offers a simple, inexpensive means to complement established severity scores and guide perioperative AKI prevention strategies after cardiac surgery, pending external prospective validation.

Abbreviations

AKI
acute kidney injury

APSIII
Acute Physiology Score III
BMI
body mass index
BUN
blood urea nitrogen
CABG
coronary artery bypass grafting
CCI
Charlson Comorbidity Index
CKD
chronic kidney disease
CSRU
cardiac surgery recovery unit
DCA
decision curve analysis
ECMO
extracorporeal membrane oxygenation
GAR
glucose-to-albumin ratio
GCS
Glasgow Coma Scale
HIPAA
Health Insurance Portability and Accountability Act
ICU
intensive care unit
INR
international normalized ratio
KDIGO
Kidney Disease:Improving Global Outcomes
LASSO
least absolute shrinkage and selection operator
ML
machine learning
MIMIC-IV
Medical Information Mart for Intensive Care IV
NPV
negative predictive value
OR
odds ratio

PPV
positive predictive value
PS
propensity score
PSM
propensity score matching
RCS
restricted cubic splines
RRT
renal replacement therapy
SHAP
SHapley Additive exPlanations
SOFA
Sequential Organ Failure Assessment
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
TRIPOD
Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis

Declarations

Ethics approval and consent to participate

This retrospective cohort study was conducted in accordance with the Declaration of Helsinki and the ethical standards of the institutional research committee. This study was based on the MIMIC-IV database (version 3.1), a publicly available, de-identified critical care database. All protected health information was de-identified in accordance with the Health Insurance Portability and Accountability Act (HIPAA). The institutional review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center approved the use of the database for research, and the requirement for individual informed consent was waived. Because the data were de-identified, the requirement for individual patient consent was waived by the IRB. The author completed the required Collaborative Institutional Training Initiative (CITI) programme and signed the data use agreement. This was a retrospective observational study using publicly available data; trial registration was not required.

Consent for publication

Not applicable.

Availability of data and materials

The MIMIC-IV database (version 3.1) is publicly available to qualified researchers via PhysioNet (<https://physionet.org/>) upon completion of the required training and data use agreement. The analysis

code is available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Conceptualization: Conceptualization: Wang Pingping, Ren Haibo, Zhang Qiong; Data curation: Wang Pingping; Formal analysis: Wang Pingping; Funding acquisition: none; Investigation: Wang Pingping, Ren Haibo; Methodology: Wang Pingping; Project administration: Ren Haibo; Resources: Ren Haibo; Software: Wang Pingping; Supervision: Ren Haibo; Validation: Wang Pingping, Zhang Qiong; Visualization: Wang Pingping, Zhang Qiong; Writing – original draft: Wang Pingping; Writing – review & editing: Ren Haibo. All authors read and approved the final manuscript.

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Use of generative AI

The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

Code availability

The R code for statistical analyses, machine learning pipeline, and SHAP interpretation is available from the corresponding author upon reasonable request.

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Figures

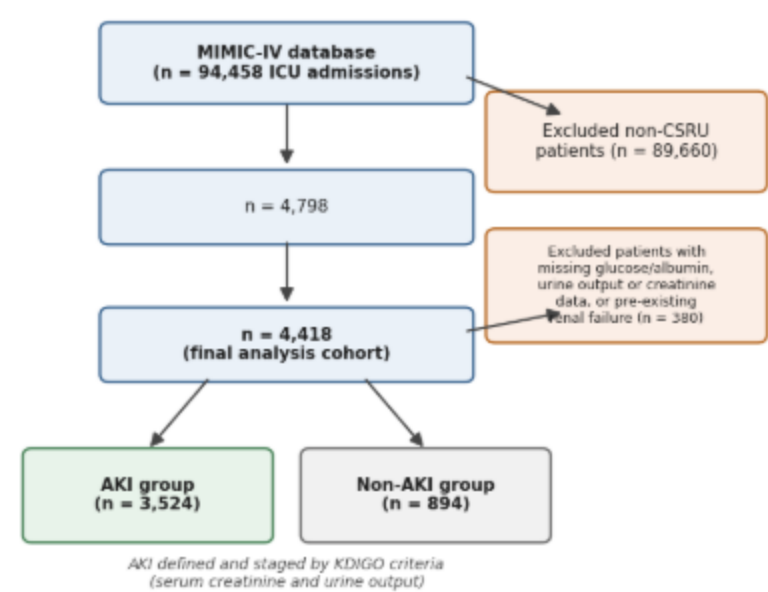


Figure 1

Flow chart of participant selection from the MIMIC-IV database. CSRU, cardiac surgery recovery unit; AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes.

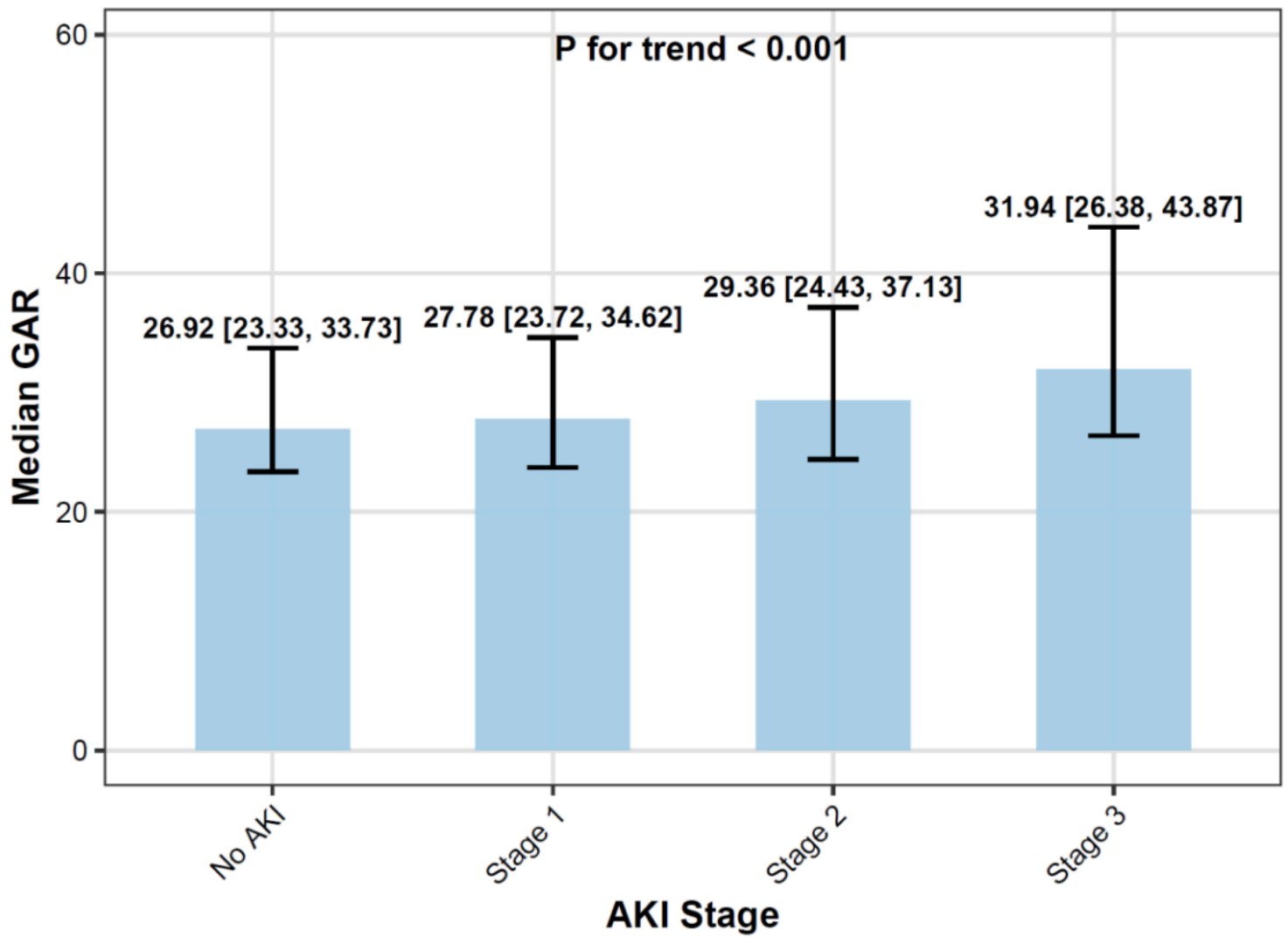


Figure 2

Distribution of preoperative GAR across AKI severity strata. Bars show medians with interquartile ranges; the P value for trend was obtained from the Jonckheere-Terpstra trend test.

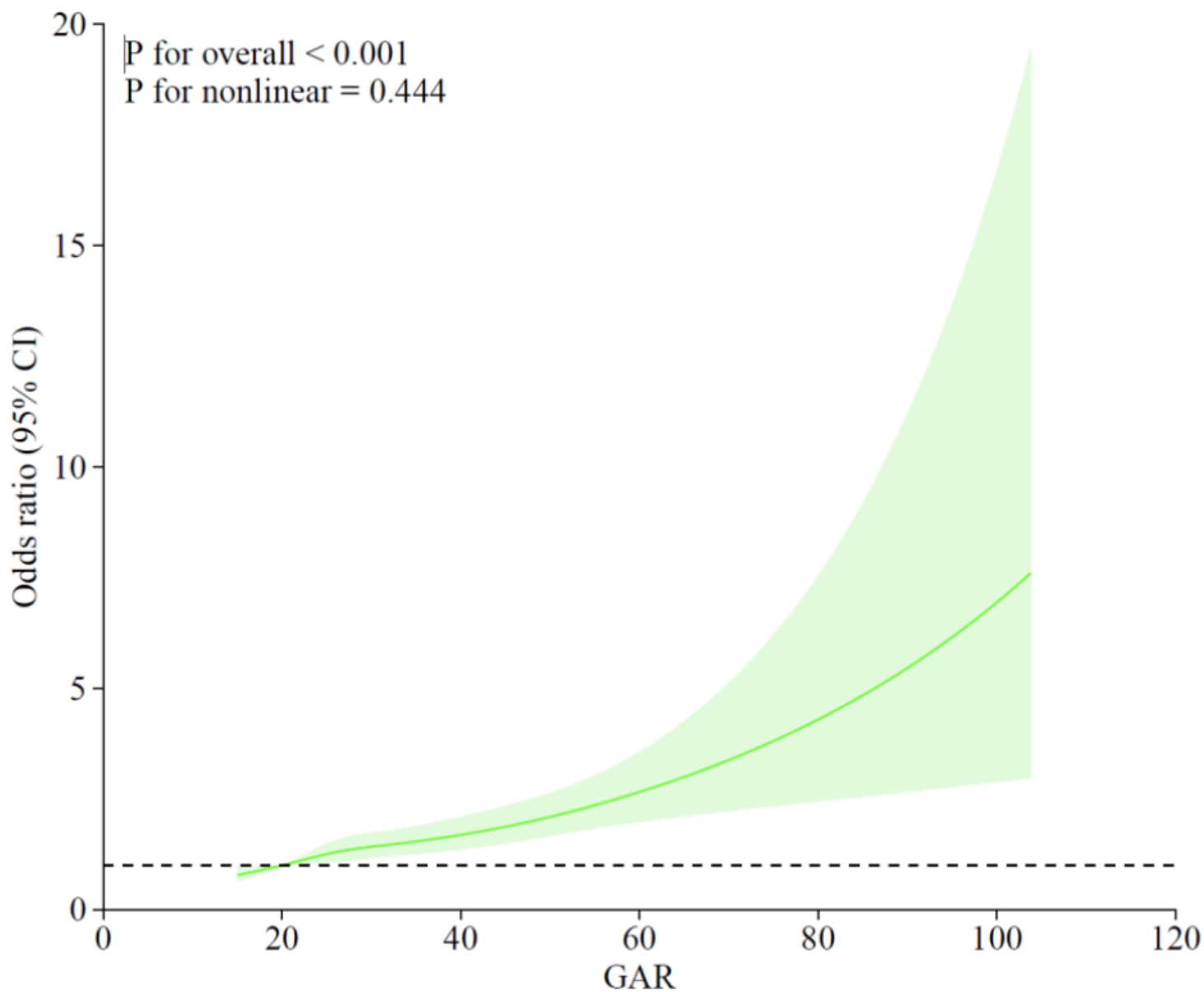


Figure 3

Restricted cubic spline analysis of the association between preoperative GAR and postoperative AKI. The solid line represents the estimated odds ratio and the shaded area the 95% confidence interval; the dashed line indicates an odds ratio of 1.

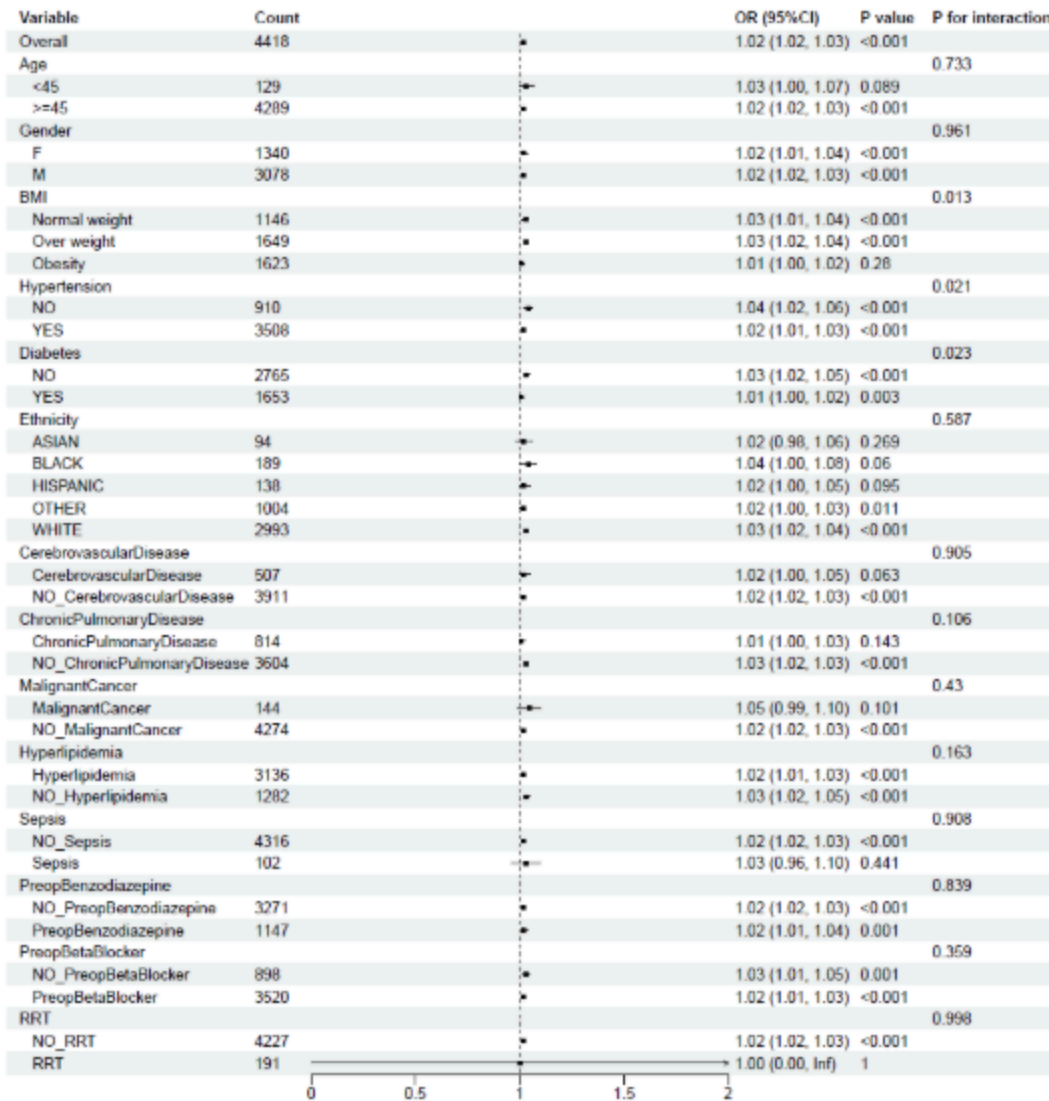


Figure 4

Subgroup analyses of the association between GAR (per unit increment) and postoperative AKI. Squares denote odds ratios and horizontal lines 95% confidence intervals; P values for interaction were obtained from likelihood ratio tests.

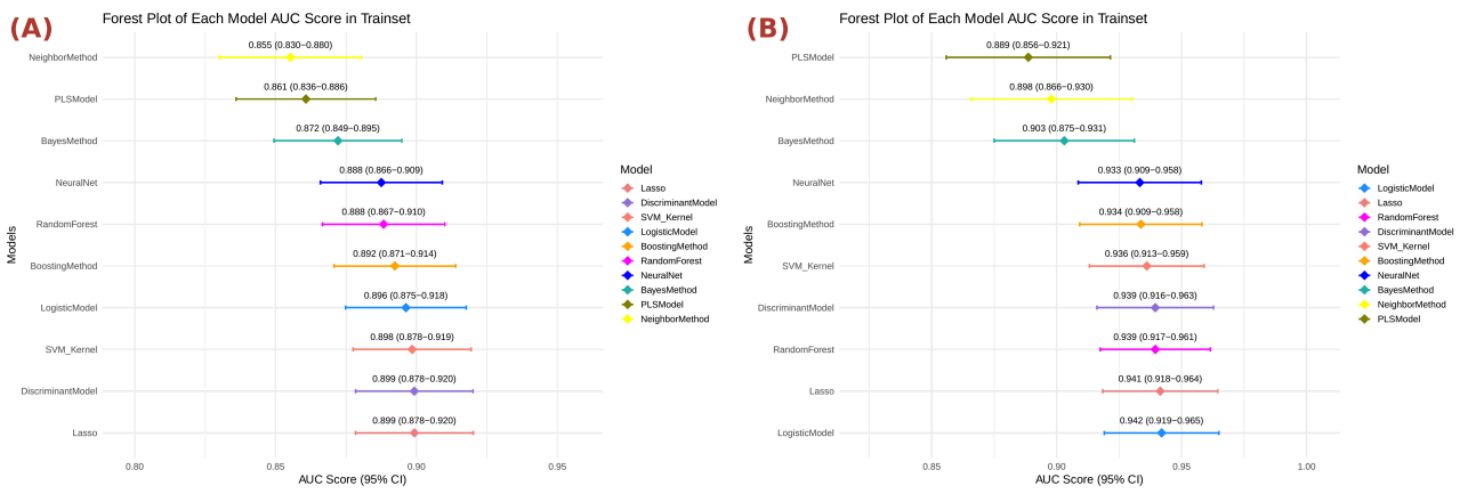


Figure 5

Forest plots of the area under the receiver operating characteristic curve (AUC) with 95% confidence intervals for the ten machine learning models in the training set (A) and the internal validation set (B).

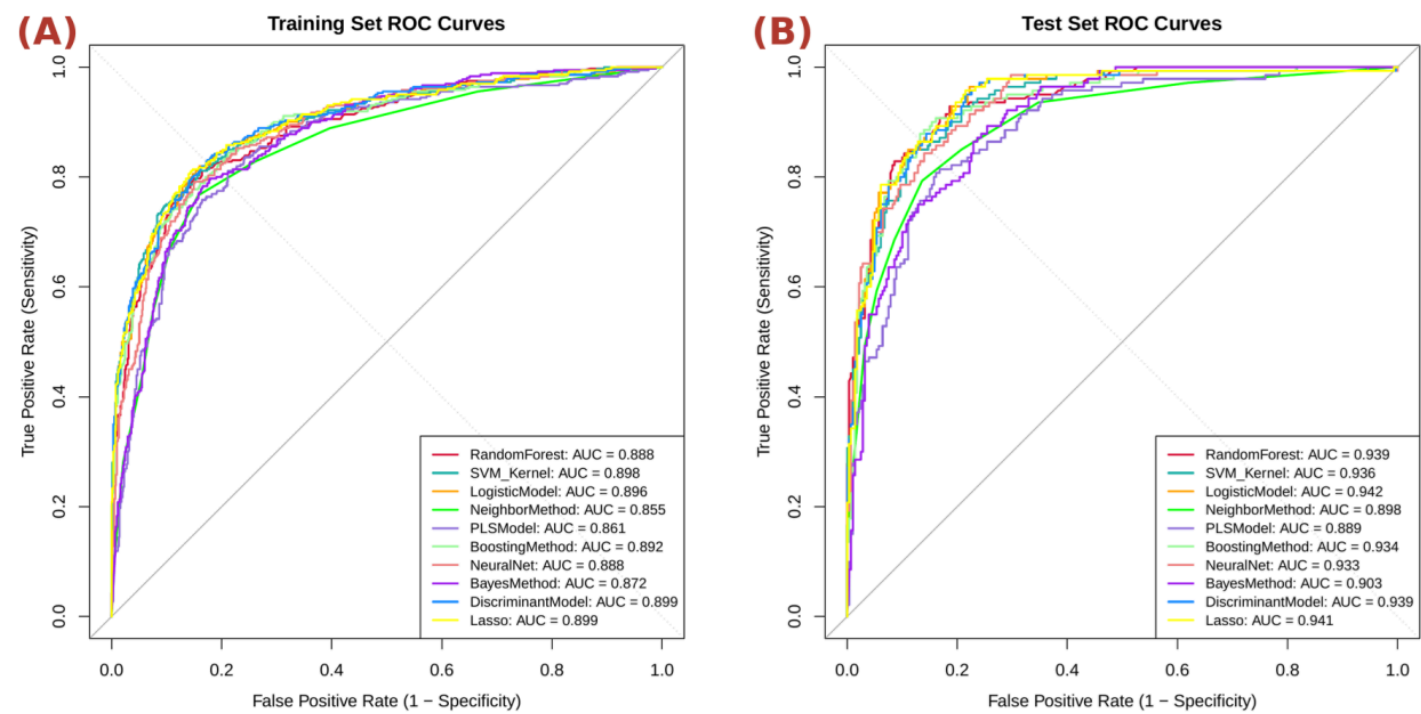


Figure 6

.Receiver operating characteristic curves of the ten machine learning models in the training set (A) and the internal validation set (B). SVM, support vector machine; PLS, partial least squares.

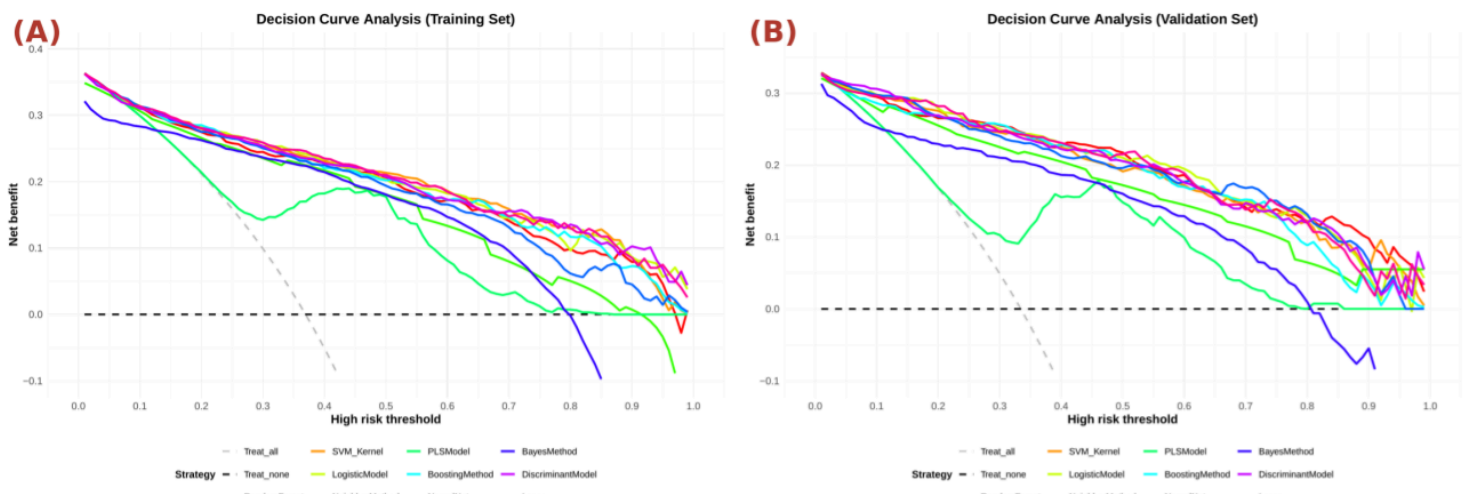


Figure 7

Decision curve analysis of the ten machine learning models in the training set (A) and the internal validation set (B). The curves show the net benefit across threshold probabilities compared with treat-all and treat-none strategies.

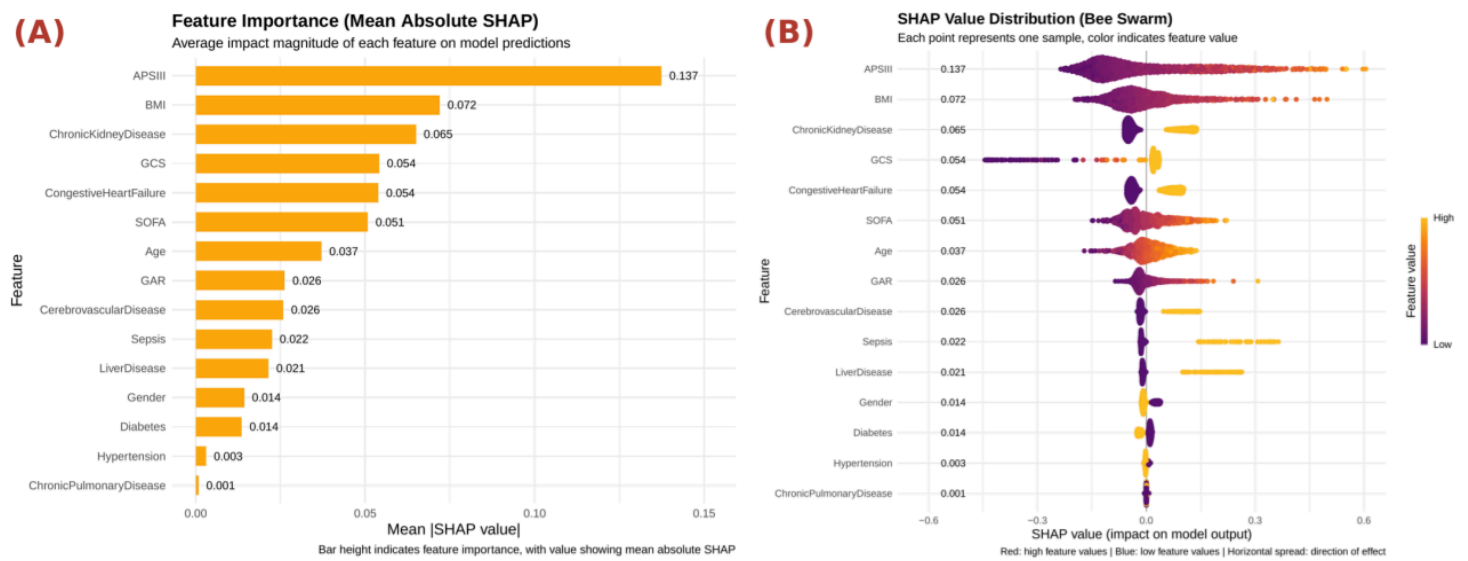


Figure 8

Global model interpretation with SHAP. (A) Feature importance ranked by mean absolute SHAP values. (B) Beeswarm plot of SHAP value distributions; each point represents one patient, with colour indicating the feature value (yellow, high; purple, low) and the horizontal position indicating the impact on the predicted risk.