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Prediction of low cardiac output syndrome in patients following non-isolated coronary artery bypass grafting surgery using machine learning

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Abstract

Aim: Low cardiac output syndrome (LCOS) may be improvable; hence, timely detection and intervention are essential. However, no model has been established for the prediction of LCOS onset post non-isolated coronary artery bypass grafting (CABG) surgery. Therefore, this study aimed to develop a machine-learning-based model to predict LCOS after non-isolated CABG.

Methods: A total of 378 patients who underwent non-isolated CABG at Nanjing First Hospital, China, were retrospectively assessed. Five algorithms [L2 regularized logistic regression (LR), random forest (RF) classifier, extreme gradient boosting (XGB), light gradient boosting machine (LGBM), and support vector machine (SVM)] were employed. Model performance and clinical utility were evaluated using area under the curve (AUC), 10-fold cross-validation, and decision curve analysis (DCA). SHapley Additive exPlanations (SHAP) were used to assess the model's interpretability. A web calculator was developed.

Results: XGB showed superior performance and calibration (AUC: 0.933, 95% CI: 0.903–0.962; Brier score of 0.107), with excellent specificity (0.865), accuracy (0.860), and precision (0.753). In testing, XGB maintained excellent discrimination (AUC: 0.868, 95% CI: 0.799–0.936), best specificity (0.785), accuracy (0.781), and precision (0.614). DCA confirmed clinical usefulness. SHAP analysis identified the ejection fraction, left ventricular end-systolic diameter, and lactate levels as the most influential predictors. The web calculator is accessible via https://lcos-cabg-xgb-model.streamlit.app/

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Conclusions: The developed web-based XGB model effectively predicts LCOS after non-isolated CABG, aiding early risk stratification and detection.

Keywords

low cardiac output syndrome, cardiac surgery, non-isolated coronary artery bypass grafting surgery, machine learning, postoperative risk prediction

Introduction

Low cardiac output syndrome (LCOS) is a common complication after surgery that is characterized by decreased cardiac output and may result in organ impairment and even death [1]. As a severe complication following coronary artery bypass grafting (CABG), LCOS is associated with a 3% to 45% mortality rate, extended hospitalization, increased respiratory support, and increased healthcare expenses [2]. Also, the complexity of non-isolated CABG procedures suggests that the risk of LCOS may vary. Importantly, LCOS may be reversible; hence, early identification and timely therapeutic intervention are key to improving prognosis [3].

Efforts to enhance the early identification of postoperative complications in patients undergoing cardiac surgery have led to the development of various conventional risk prediction models. These conventional models, such as the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgeons (STS) risk models, are primarily based on logistic regression (LR) [4, 5]. Despite their widespread use, these models assume linear relationships between risk factors and outcomes, often oversimplifying the complex, nonlinear interactions inherent in postoperative complications like LCOS. This oversimplification can result in inaccurate risk-averse practices and impaired decision-making [4, 6]. Notably, EuroSCORE and STS risk models tend to perform poorly in high-risk groups, often overestimating postoperative complications in complex cardiac surgeries [5, 7]. These limitations emphasize the need for more advanced predictive tools.

Machine learning (ML) has emerged as a promising alternative for clinical risk prediction. ML is capable of automatically learning complex interactions and nonlinear relationships from data in clinical risk prediction [8, 9]. ML models enable precise, localized predictions by learning from multiple sources of data and maintaining robustness against data noise [10]. This enables more in-depth analysis of the underlying mechanisms behind various clinical complications. For example, Hong et al. [11] reported superior prediction and calibration of ML models compared to LR, with the support vector machine (SVM) model showing better specificity (83.5% vs. 81.8%), accuracy (80.6% vs. 80.0%), and Brier score (0.107 vs. 0.133) for predicting LCOS after valve surgery. Similarly, a previous study reported that random forest (RF) and extreme gradient boosting (XGB) models outperformed traditional LR models in predicting LCOS post-cardiac surgery [3].

Given the complexity of CABG surgeries, ML is particularly valuable for predicting postoperative LCOS [11, 12]. Non-isolated CABG, often involving multiple comorbidities and heterogeneous postoperative courses, presents greater clinical uncertainty than isolated CABG [13]. This complexity renders ML's ability to analyze high-dimensional data and detect subtle, non-linear risk patterns especially advantageous. By incorporating diverse preoperative and intraoperative variables, ML models can provide more precise risk stratification than traditional LR-based approaches, thereby facilitating tailored clinical decision-making for LCOS prediction in non-isolated CABG patients.

Although previous studies have established models to predict various clinical outcomes and mortality in CABG patients, to the best of our knowledge, no model specifically predicts LCOS following non-isolated CABG, a subgroup that presents greater complexity and higher clinical uncertainty. While some studies have employed ML to predict postoperative complications, including LCOS after cardiac and valve surgeries [3, 11, 14], their findings may not be directly transferable to this clinically distinct subgroup with notable complexities, without further study.

Therefore, this study aimed to develop a web-based model to predict LCOS post non-isolated CABG surgery using ML, with the goal of improving early detection and intervention for better clinical outcomes.

Materials and methods

Ethical approval

Our study adhered to the Declaration of Helsinki and postoperative ethical standards. The ethics committee of the Nanjing First Hospital approved this study (Grant No. KY20220518-KS-01) and waived the need for informed consent.

Study population

We retrospectively collected data from 419 adult patients who had undergone non-isolated CABG surgery in the intensive care unit (ICU) of Nanjing First Hospital from April 2019 to February 2022, from electronic medical records (EMR) and physiological monitors. All patients included in this study underwent CABG for documented coronary artery disease. Concurrently, some patients underwent additional cardiac procedures due to coexisting cardiac pathologies (such as valvular disease, aortic pathology, or congenital anomalies) as shown in Table 1. Patients were excluded under the following conditions: (i) if they underwent isolated CABG (CABG only) without any concomitant procedure; (ii) if they had LCOS within 1 hour; and (iii) if they died or were discharged during or within 48 hours after surgery. Patients who had LCOS within 1 hour were excluded to avoid confounding by transient hemodynamic instability associated with anesthesia emergence, rewarming, or immediate post-bypass circulatory adjustment, which often resolves spontaneously without therapeutic intervention [3]. The study included 378 patients, which was in accordance with the sample size requirements of the binary outcome prediction model [15].

Table 1. Demographics and clinical characteristics of patients based on baseline characteristics and laboratory values.

Variables	Total (n = 378)	Non-LCOS (n = 257)	LCOS (n = 121)	p-value
Baseline characteristics				
Age, median (IQR)	68.00 (62.00, 73.00)	68.00 (62.00, 73.00)	69.00 (61.00, 74.00)	0.364
Sex = 1 (%)	265 (70.1)	173 (67.3)	92 (76.0)	0.108
BMI, mean (SD)	24.00 (3.24)	24.28 (3.19)	23.41 (3.28)	0.015
Optime, median (IQR)	5.25 (4.50, 6.00)	5.25 (4.42, 6.00)	5.25 (4.67, 6.08)	0.355
Cpbtime, median (IQR)	139.00 (107.00, 168.00)	135.00 (107.00, 167.00)	145.00 (115.00, 172.00)	0.112
Actime, median (IQR)	97.50 (76.00, 121.00)	96.00 (76.00, 120.00)	103.00 (76.00, 126.00)	0.369
Laboratory indicators				
Lac, median (IQR)	2.00 (1.30, 3.40)	1.80 (1.10, 2.90)	3.00 (1.60, 5.00)	<0.001
Total bilirubin, median (IQR)	11.00 (8.10, 15.07)	10.70 (7.90, 14.10)	12.40 (8.70, 17.10)	0.006
Indirect bilirubin, median (IQR)	7.80 (5.60, 11.07)	7.70 (5.50, 10.40)	8.80 (6.00, 11.60)	0.038
Direct bilirubin, median (IQR)	3.00 (2.20, 4.40)	2.80 (2.10, 4.00)	3.40 (2.50, 5.40)	<0.001
Total protein (mean, SD)	65.03 (6.05)	65.50 (5.74)	64.05 (6.59)	0.03
AMT, median (IQR)	22.52 (18.00, 28.01)	22.00 (18.00, 28.00)	23.75 (19.00, 28.94)	0.263
AAT, median (IQR)	19.75 (14.00, 30.00)	19.00 (14.00, 30.00)	20.00 (15.00, 31.00)	0.518
Preop_max_Cr, median (IQR)	80.80 (68.00, 94.63)	78.60 (67.30, 93.30)	85.50 (71.00, 104.00)	0.013
Globulin, median (IQR)	26.11 (23.30, 29.00)	26.10 (23.20, 29.00)	26.30 (23.30, 28.90)	0.914
Urea, median (IQR)	6.60 (5.30, 8.15)	6.30 (5.15, 7.90)	7.06 (5.90, 8.90)	0.003
Hemoglobin, median (IQR)	127.74 (119.23, 138.00)	128.00 (120.00, 138.00)	127.00 (118.54, 138.00)	0.553
WBC, median (IQR)	6.43 (5.46, 7.40)	6.35 (5.43, 7.32)	6.74 (5.48, 7.87)	0.067
PLT, median (IQR)	180.80 (143.25, 216.00)	181.00 (145.00, 215.00)	180.00 (138.00, 219.00)	0.779
Lymphocyte, mean (SD)	24.57 (8.19)	25.38 (7.91)	22.86 (8.55)	0.005
Neutrophil, median (IQR)	63.35 (57.62, 69.80)	63.10 (57.00, 68.80)	64.80 (59.60, 73.90)	0.025
LDL, median (IQR)	2.19 (1.81, 2.73)	2.24 (1.82, 2.77)	2.14 (1.78, 2.61)	0.256
TSH, median (IQR)	2.32 (1.60, 3.43)	2.36 (1.66, 3.43)	2.26 (1.42, 3.25)	0.191

Table 1. Demographics and clinical characteristics of patients based on baseline characteristics and laboratory values. (*continued*)

Variables	Total (n = 378)	Non-LCOS (n = 257)	LCOS (n = 121)	p-value
Thyroxine, median (IQR)	97.16 (87.92, 107.06)	98.31 (88.14, 107.52)	95.28 (87.39, 104.77)	0.228
Triiodothyronine, median (IQR)	1.27 (1.11, 1.42)	1.31 (1.12, 1.44)	1.20 (1.03, 1.37)	0.002
Concomitant procedures				
AVS = 1 (%)	136 (36.0)	100 (38.9)	36 (29.8)	0.106
MVS = 1 (%)	189 (50.0)	119 (46.3)	70 (57.9)	0.047
TVS = 1 (%)	121 (32.0)	78 (30.4)	43 (35.5)	0.373
AS = 1 (%)	45 (11.9)	33 (12.8)	12 (9.9)	0.517
CHS = 1 (%)	9 (2.4)	7 (2.7)	2 (1.7)	0.783
Other = 1 (%)	91 (24.1)	51 (19.8)	40 (33.1)	0.007

Males and patients with LCOS are represented as numbers (%), and other variables are represented as median (IQR). IQR: interquartile range; BMI: body mass index; SD: standard deviation; Optime: operating time; Cpbtime: cardiopulmonary bypass time; actime: aortic clamping time; Lac: lactate; AMT: aminomethyltransferase; AAT: alpha-1 antitrypsin; preop_max_Cr: preoperative maximum creatinine; WBC: white blood cell; PLT: platelet; LDL: low-density lipoprotein; TSH: thyroid-stimulating hormone; AVS: aortic valve surgery; MVS: mitral valve surgery; TVS: tricuspid valve surgery; AS: aortic surgery; CHS: congenital heart disease surgery.

Outcome

The outcome was the occurrence of LCOS between 1 h and 48 h postoperatively. With reference to Hong et al. [3], we set three LCOS-defining criteria as follows: (i) a cardiac index (CI) reduced to < 2.2 L/min/m^2; (ii) systolic blood pressure > 90 mmHg with signs of tissue hypoperfusion, including oliguria (urine output < 1 mL/kg·h), and/or elevated lactate (Lac) level (> 3.0 mmol/L) persisting for > 10 minutes; (iii) the requirement of mechanical circulatory support or the simultaneous administration of two or more inotropic agents (such as dopamine, dobutamine, milrinone, or levosimendan) for ≥ 12 hours to maintain hemodynamics after optimizing preload. This composite approach reflects the heterogeneous clinical presentation of LCOS and enhances sensitivity in capturing cases that may not satisfy all criteria simultaneously. Isolated reliance on any single criterion, such as CI only, may lead to missing patients with clinically significant hypoperfusion despite preserved CI, or those requiring prolonged inotropic support without documented low CI [1]. LCOS was not diagnosed in patients who received vasoconstrictive drugs to increase peripheral vascular resistance while maintaining normal cardiac output. LCOS was diagnosed if the patient met ≥ 1 of the criteria. CI and Lac measurements were routinely obtained for all patients as part of standardized postoperative monitoring. CI was measured using invasive hemodynamic monitoring, which is routinely applied in non-isolated CABG cases. Lac was measured for all patients immediately upon ICU admission.

Potential predictors

Based on previous studies [3, 11], we selected and extracted potential predictors of LCOS from the EMR database. Demographic data were collected for age, sex, weight (kg), height (m), and body mass index (BMI, kg/m^2). Echocardiographic parameters [16] collected using color Doppler ultrasound at the patient's bedside before surgery included measurements of the aortic diameter (AoD), left atrial diameter (LAD), left ventricular end-systolic diameter (LVDs), left ventricular posterior wall thickness (LVPW), ejection fraction (EF), and fractional shortening (FS). Preoperative laboratory indicators included white blood cell (WBC), Alpha-1 Antitrypsin (AAT), thyroid-stimulating hormone (TSH), low-density lipoprotein (LDL), thyroxine (T4), Lac, indirect bilirubin, direct bilirubin, total bilirubin, lymphocyte, aminomethyltransferase (AMT), urea, globulin, Triiodothyronine (T3), hemoglobin, platelet (PLT), neutrophil, total protein, and maximum preoperative creatinine (preop_max_cr). Patient's operation time (optime), the utilization of cardiopulmonary bypass (CPB) time (cpbtime), and aortic cross-clamping time (actime) were additionally recorded.

To better characterize the hemodynamic status, we calculated the time, area under the curve (AUC), and time-weighted AUC (TWA) below the thresholds for mean arterial pressure (MAP) (< 65, < 60, < 55, and < 50 mmHg) and above the thresholds for central venous pressure (CVP) (> 12, > 16, and > 20 mmHg) using the time-series data automatically recorded by the intraoperative monitor.

The first value of Lac was recorded within 30 minutes postoperatively, between discharge from non-isolated CABG surgery in the operating theatre and admission to the ICU.

The outcome was the development of LCOS > 1 hour after surgery. There were no uniform clinical criteria to define LCOS. Thus, we referred to and applied the definition set in the study by Hong et al. [3].

Data pre-processing

In this dataset, variables with missing values > 15 % were excluded. The missing values were imputed using the K-Nearest Neighbors (KNN) method. The dataset was divided into training and test sets in a 7:3 ratio to prevent overfitting. To eliminate the dimensional influence of different features and improve the model accuracy and training speed, the segmented data were normalized. The training set was used for feature selection, fitting the model, and adjusting the hyperparameters, while the test set was used for internal validation to assess the model's ability to generalize unknown data.

Feature selection

In the training set, univariate regression analysis was initially performed on 53 candidate predictors, and all variables with $p < 0.1$ were further included in the least absolute shrinkage and selection operator (LASSO) regression. LASSO introduces the L1 paradigm penalty as a regularization term based on the traditional linear regression model, which can compress the coefficients of unimportant variables to 0, thereby enabling automatic feature selection [17]. We assessed multicollinearity among the selected variables using the variance inflation factor (VIF) < 5. Features showing high collinearity (VIF > 5) were excluded to ensure model stability [18].

Model construction and evaluation

To build the best prediction model, we selected five algorithms—including L2 regularized LR (LR with L2), RF classifier (RFC), XGB, light gradient boosting machine (LGBM), and SVM—to develop predictive models based on the training set. In the training set, a grid search method with ten-fold cross-validation was used to find the best hyperparameters for each model (Table S1).

In the test set, the AUC quantified the discriminative ability of the model. Sensitivity, specificity, precision, and accuracy of the model were calculated by determining the optimal threshold based on the maximum Youden index. Moreover, the area under the precision-recall curve (AUPRC) was calculated to evaluate model performance amidst unbalanced data. Sensitivity analysis was conducted to assess the potential risk of data leakage between the LCOS definition and the predictor sets, particularly regarding the model's predictive performance's potential over-reliance on early Lac indicators involved in the diagnosis of LCOS. Using the same hyperparameters as the prediction model, a model was constructed without incorporating postoperative Lac characteristics. Furthermore, we calculated the area under the receiver operating characteristic curve (AUROC) and other evaluation indicators for both models on independent test sets and compared the differences in AUROC between the two models using the DeLong test, 95% CI was also reported. We also considered precision and recall. Positive predictive value (PPV) was used to assess the accuracy of the model in predicting the occurrence of low cardiac output in patients. Recall was used to assess the performance of the model in identifying the actual occurrence of low cardiac output. A lower Brier score indicates a more accurate probabilistic prediction by the model. Calibration curves were used to evaluate the concordance between the predicted probability of the model and the actual observed occurrence. The decision curve analysis (DCA) was carried out to evaluate the clinical utility of the predictive models [19]. We are convinced that the optimal model results from rigorous evaluation. In addition, an interactive web calculator was built with Streamlit (https://lcos-cabg-xgb-model.streamlit.app/).

Model interpretation

We used Shapley Additive exPlanations (SHAP) [20] to compute the SHAP value for each feature in the prediction model. The SHAP summary bar chart illustrates the significant impact of each feature on predicting LCOS, providing insight into the model's predictions.

Statistical analysis

Upon assessment by the Shapiro-Wilk test, continuous variables that were normally distributed were analyzed using Student's *t*-test, with results presented as the median [interquartile range (IQR)]. Non-normally distributed continuous variables were tested using the Mann-Whitney *U*-test and expressed as the median (IQR). Categorical variables were tested using the *chi*-square test or Fisher's exact test and expressed as a percentage. To analyse the differences in the data distributions and their significance, we compared the data balance between the LCOS and non-LCOS groups as well as between the training and test sets. The R programming language (version 4.3.2) was used for data visualization and statistical analysis, while Python (version 3.8.10) was used for ML operations. *p*-values were considered statistically significant when they were less than 0.05. All *p*-values were two-tailed.

Results

Study population

378 patients were included in this study (Figure 1). 121 (32.0%) of the included patients developed LCOS, out of which 11 had CABG only, 23 developed LCOS within 1 hour after surgery, and 7 died or were discharged within 48 hours after surgery. The study population comprised 69.3% males, with the overall population's median age being 68.00 (IQR, 62.00–73.25).

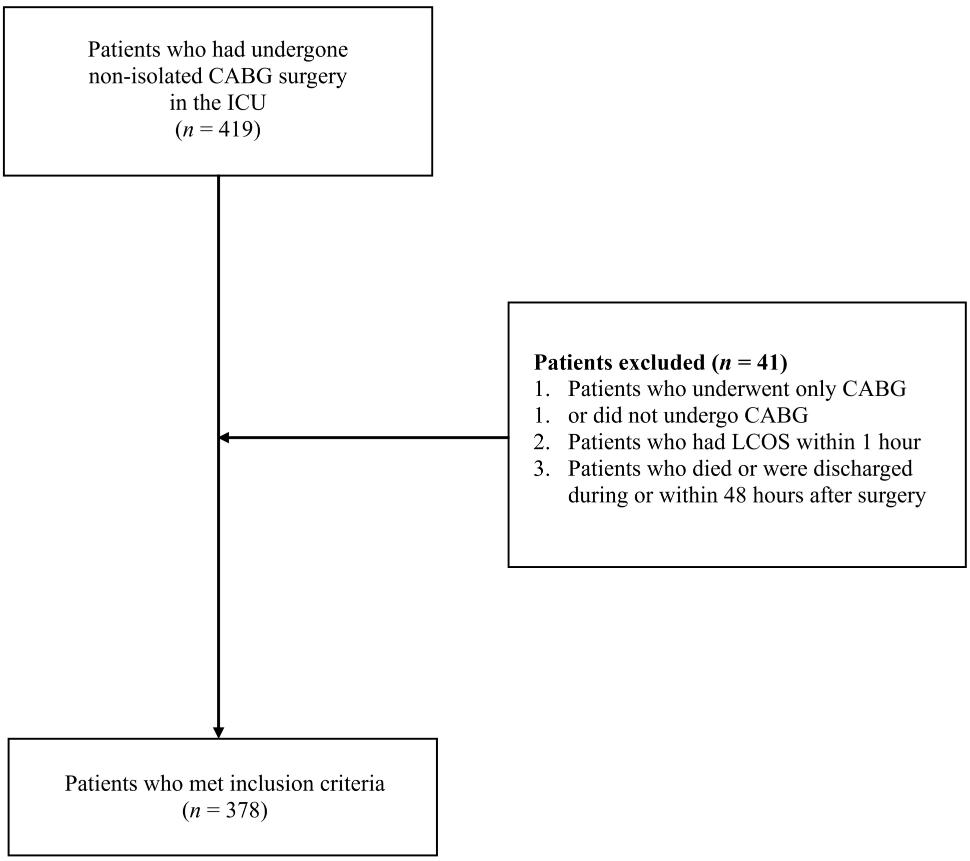

Figure 1. The schematic chart for inclusion and exclusion of patients in this study. CABG: coronary artery bypass grafting; ICU: intensive care unit; LCOS: low cardiac output syndrome.

Baseline characteristics

Table 1 and Table S2 show the baseline data for LCOS and non-LCOS cohorts. It was observed that sex, age, AAT, AoD, optime, cpbtime, actime, and time-weighted AUC (TWA-MAP, with thresholds set at 65, 60, 55, and 50; as well as TWA-CVP, with thresholds set at 16 mmHg and 20 mmHg) did not significantly differ between patients with and without LCOS ($p > 0.05$).

Feature selection

The study's feature selection employed the LASSO regression incorporated with all variables. The model's resultant output highlighted 9 key variables: preop_max_cr (1 mg/dL = 88.4 μmol/L), direct bilirubin (1 mg/dL = 17.1 μmol/L), lymphocyte, T3, EF, LVDs, MAP_55_time, BMI, and Lac (1 mmol/L = 9.0 mg/dL). All correlations between the output features and predictive output of the study's model were further evaluated using SHAP, with the outcome shown in Figure 2A. The interactive web-based calculator can be accessed via https://lcos-cabg-xgb-model.streamlit.app/.

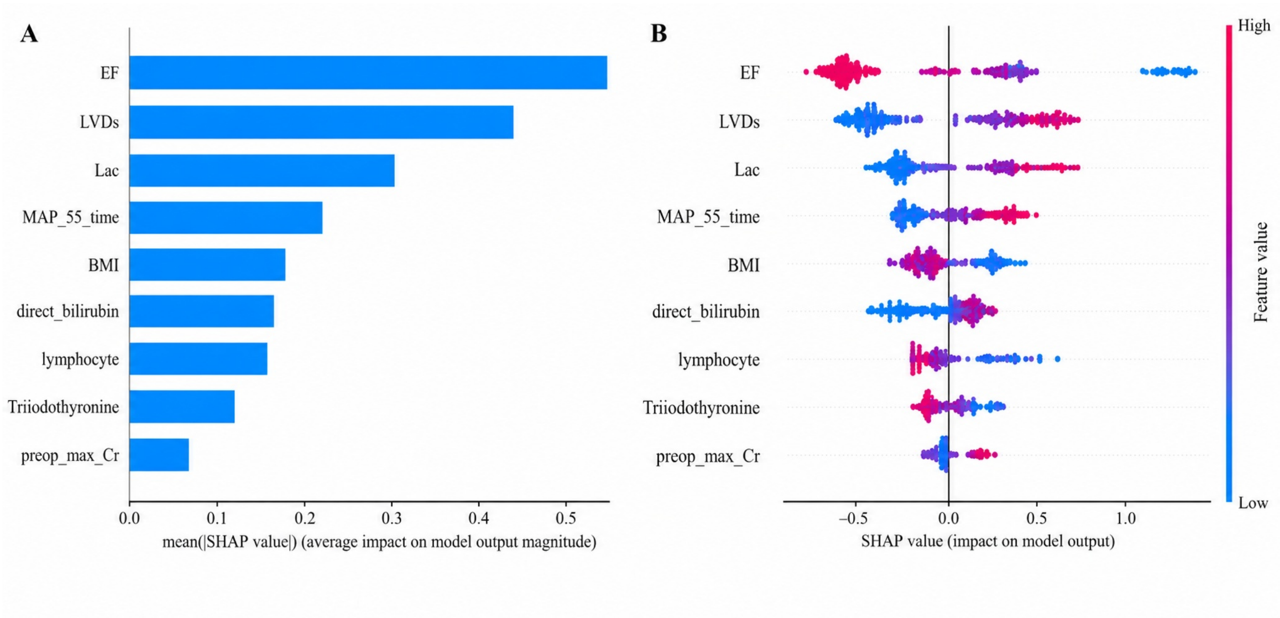

Figure 2. Visualized interpretation of the developed prediction model based on SHapley Additive exPlanations (SHAP) values. (**A**) The SHAP summary bar chart presents a visualized ranking of the features in order of their impact on the model's predictive output. (**B**) SHAP value distributions of the various features included in the model are represented by beeswarm plots. This visualized chart combines feature importance and feature impact to provide an overview of the distribution of SHAP values for each feature, with a higher SHAP value depicted by a redder sample swarm and a bluer sample swarm indicating a lower SHAP value. Positive correlation with the incidence of LCOS is inferred from a greater tilt of the red sample swarm to the right side of the vertical axis, and negative correlation with the incidence of LCOS is inferred from a greater tilt of the red sample swarm to the left side. EF: ejection fraction; LVDs: left ventricular end-systolic diameter; Lac: lactate; BMI: body mass index; SHAP: SHapley Additive exPlanations.

Model performance

Training set

Using AUC and Brier score, the ability of the 5 constructed models (LR, RFC, SVM, XGB, and LGBM) to predict LCOS was assessed. With AUC > 0.7, all models presented an acceptable performance in predicting LCOS post non-isolated CABG surgery [16]. The XGB algorithm-based model exhibited excellent AUC [0.933 (CI 0.903–0.962)] and best calibration capability (achieving the lowest Brier score of 0.107) among the five algorithms in the training model (Table 2). The XGB model further demonstrated the highest accuracy (0.860), specificity (0.865), and precision (0.753) in predicting LCOS (Table 2). Additionally, the discriminative performance of the five algorithms showed no significant difference ($p > 0.05$).

Testing set

Among the testing cohort, LR, XGB, and SVM exhibited better calibration capability, albeit relatively low, with Brier scores of 0.137, 0.138, and 0.137, respectively (Table 3). Overall, XGB demonstrated better stability and excellent discrimination [AUC: 0.868 (0.799–0.936)], with the best specificity (0.797), accuracy (0.781), and precision (0.619) as shown in Table 3. Also, the decision curve showed that the ML models, including XGB, maintained higher net benefit, reflecting robust performance across all threshold probabilities (Figure S1). XGB was ultimately chosen for the construction of the final prediction model. Upon observation of the discriminative performance of the model in the testing cohort, as shown in

Table 2. Prediction and calibration performance of the five algorithms in the training cohort of the model.

Algorithm	AUC (95% CI)	Sensitivity	Specificity	Accuracy	Precision	Brier score
LR	0.854 (0.808–0.900)	0.826	0.73	0.761	0.597	0.145
XGB	0.933 (0.903–0.962)	0.849	0.865	0.86	0.753	0.107
RFC	0.918 (0.884–0.952)	0.872	0.831	0.845	0.714	0.131
SVM	0.850 (0.803–0.898)	0.767	0.798	0.788	0.647	0.146
LGBM	0.936 (0.907–0.964)	0.942	0.764	0.822	0.659	0.12

AUC: area under the curve; CI: confidence interval; LR: logistic regression; XGB: extreme gradient boosting; RFC: random forest classifier; SVM: support vector machine; LGBM: light gradient boosting machine.

Figure 3, no statistically significant difference was revealed. The calibration curve and Brier score of the models in the testing cohorts are demonstrated in Figure 4.

Table 3. Prediction and calibration performance of the five algorithms in the testing cohort of the model.

Algorithm	AUC (95% CI)	Sensitivity	Specificity	Accuracy	Precision	Brier score
LR	0.867 (0.797–0.937)	0.914	0.696	0.763	0.571	0.137
XGB	0.868 (0.799–0.936)	0.743	0.797	0.781	0.619	0.138
RFC	0.865 (0.798–0.933)	0.829	0.759	0.781	0.604	0.15
SVM	0.880 (0.815–0.945)	0.829	0.797	0.807	0.644	0.137
LGBM	0.855 (0.781–0.930)	0.829	0.658	0.711	0.518	0.148

AUC: area under the curve; CI: confidence interval; LR: logistic regression; XGB: extreme gradient boosting; RFC: random forest classifier; SVM: support vector machine; LGBM: light gradient boosting machine.

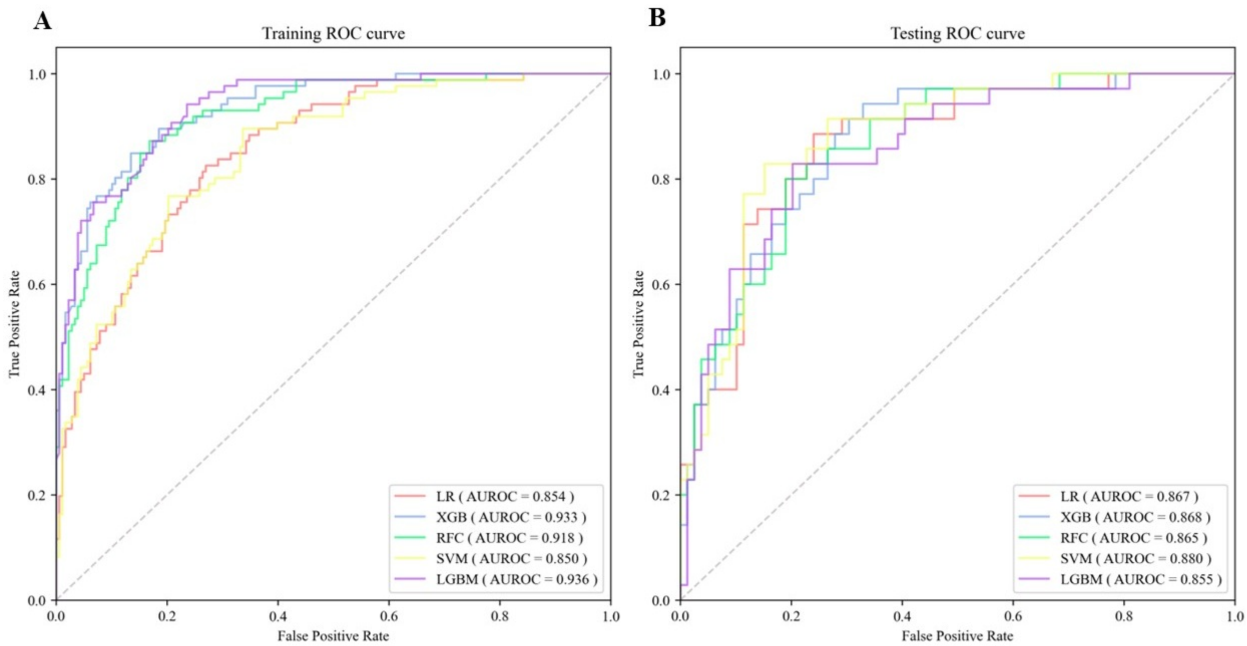

Figure 3. The receiver operating characteristic (ROC) curve for testing the cohort of the machine learning model for predicting low cardiac output syndrome. LR: logistic regression; XGB: extreme gradient boosting; RFC: random forest classifier; SVM: support vector machine; LGBM: light gradient boosting machine.

Sensitivity analysis

Although the AUC of the model without Lac (0.842) showed a marginal difference from the AUC of the Lac-incorporated model (0.868), which was observed to be very close, with significant overlap in CI noted, the observed difference was not statistically significant. This therefore suggests that the model's predictive ability does not significantly decrease with the exclusion of variables such as Lac from the postoperative data, thus highlighting the robustness of the model. Inferentially, the risk of data leakage is relatively low (Table S3 and Table S4).

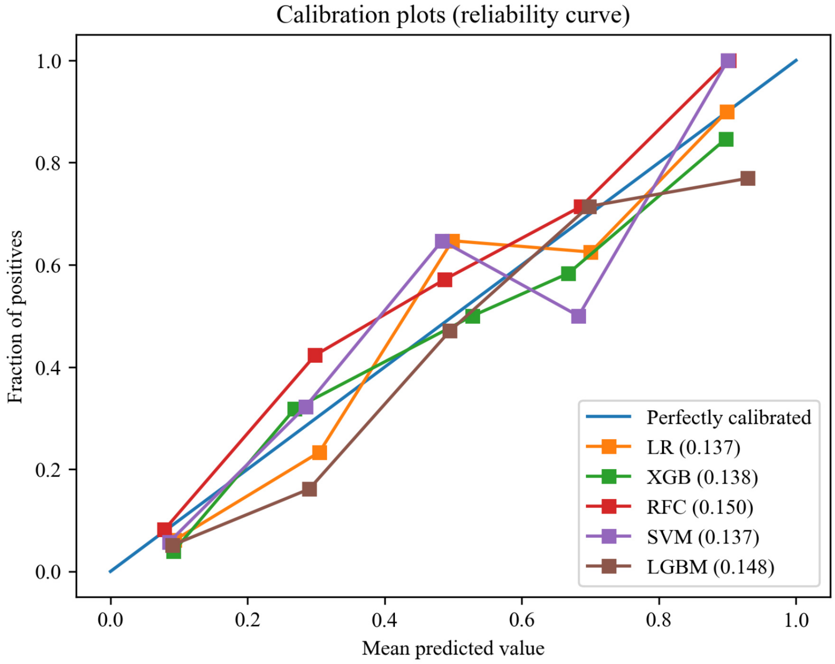

Figure 4. The calibration curve for the area under the curve of the testing cohort. LR: logistic regression; XGB: extreme gradient boosting; RFC: random forest classifier; SVM: support vector machine; LGBM: light gradient boosting machine.

Model interpretation

The predictive outcome of the chosen model, XGB, was subjected to the SHAP algorithm for further visualized interpretation. Figure 2A summarily presents a visualized ranking of the features in order of their impact on the model's predictive output. The three most influential features on the model's predictive output were EF, LVDs, and Lac (Figure 2A). SHAP value distributions of the various features included in the model are represented by beeswarm plots (Figure 2B). This visualized chart combines feature importance and feature impact to provide an overview of the distribution of SHAP values for each feature. A higher SHAP value was depicted by the redder sample swarm and consequently implied an increased likelihood of developing LCOS. The red colour correlates with the increased likelihood of developing LCOS. This implies an inverse association between EF and low cardiac output, while suggesting a direct relationship between low cardiac output and both Lac and LVDs (Figure 2B).

Discussion

There is continuous interest in developing models for predicting LCOS after cardiac surgery, with ML-based models exhibiting superior risk prediction accuracy in comparison with LR approaches [3, 11, 12]. Using the XGB algorithm, we developed an ML-based model for predicting LCOS after a non-isolated CABG. The model demonstrated excellent specificity, accuracy, and clinical utility. Aiding early risk stratification and prompt intervention, it may help reduce the length of hospitalisation and healthcare expenditure [21].

This study's definition of LCOS, in accordance with a previous study by Hong et al. [3], employed a combination of hemodynamic, perfusion, and therapeutic criteria, ensuring more comprehensiveness than definitions solely reliant on CI [1] or inotropic requirement [22]. We prioritized clinical sensitivity over specificity by ensuring inclusion when ≥ 1 of the criteria for the definition was met. This aligned with the clinically practical objective of early risk identification. Our study further ensured that persistent LCOS requiring intervention was distinct from transient perioperative instability by excluding patients who developed LCOS within the first postoperative hour [1, 3]

We assessed five algorithms (LR, RFC, SVM, XGB, and LGBM) to develop the predictive model. All models showed acceptable predictive performance (AUC > 0.7); nonetheless, XGB outperformed. The highest net clinical benefit of XGB across threshold probabilities emphasizes its reliability in identifying high-risk patients and optimizing interventions such as inotropic support or hemodynamic monitoring. Our model's superior performance is consistent with findings from a previous study by Hong et al. [3], with the model's superiority over the conventional LR model further validating our study's innovative contribution.

A notable drawback of ML-based models in clinical practice is their limited explainability resulting from their inherent opaque nature, which contrasts with conventional LR models. To address this, we applied SHAP to shed light on the impact of each of the incorporated features in the model's predictive output. Nine variables, including EF, LVDs, Lac, MAP_55_time, BMI, direct bilirubin, lymphocyte, T3, and preop_max_cr, independently influenced the model's LCOS risk prediction output.

EF emerged as our model's most important independent predictor. EF is widely used in the assessment of cardiac contractility and left ventricular systolic function, with reduced EF suggesting weak cardiac muscles. As demonstrated by our study, poor preoperative EF has consistently been associated with increased risk of LCOS, particularly following CABG [22, 23]. The significance of EF is further highlighted by its role as a key cardiogenic shock indicator, with preoperative cardiogenic shock increasing LCOS risk by more than 8-fold [24, 25].

LVDs were the second most influential independent variable. Increased LVDs (> 40 mm) are independently associated with a higher risk of postoperative chronic left ventricular dysfunction and subsequent LCOS, especially when co-presented with decreased EF [23]. This is consistent with our study's outcome.

Furthermore, in agreement with our study, earlier studies have demonstrated postoperative Lac value as a significant marker for predicting LCOS after cardiac surgery, with elevated arterial Lac level being a valuable tool in assessing tissue oxygenation status and LCOS risk [26].

Transient intraoperative hypotension (MAP < 55 mmHg for brief periods up to 65 mmHg) has also been linked to increased risk of postoperative complications, including myocardial infarction and LCOS [27], even with brief episodes of MAP > 55 mmHg [28]. Although MAP_55_Time was associated with modest influence on our model's predictive output, it valuably offers real-time guidance on optimal blood pressure targets and timely interventions, thereby helping prevent or mitigate prolonged hypotension and consequent LCOS during non-isolated CABG.

In further agreement with our study, low BMI (< 20 kg/m^2), more common among older patients, is reportedly associated with severe impairment of left ventricular ejection and subsequent increased risk of LCOS [22].

Other variables like direct bilirubin and lymphocyte were also mildly influential, with elevated bilirubin and decreased lymphocyte levels demonstrating mild associations with increased risk of LCOS. Hyperbilirubinemia, a common post-cardiac surgery complication [11], is reportedly linked to intraoperative complications like hemolysis and blood transfusions during CPB [29], suggesting susceptibility to hemodynamic instability, decreased cardiac function, and, in effect, LCOS. This thus validates bilirubin's influence on our model's predictive output.

In addition, a decline in preoperative lymphocytes may suggest compromised heart function or underlying systemic conditions [30, 31], thereby supporting our study's highlight of lymphocytes as an independent predictor of LCOS after non-isolated CABG.

The inclusion of variables like T3 and TSH was particularly with reference to previously reported association between non-thyroidal illness syndrome and postoperative cardiac dysfunction [31], with T3 shown to present direct inotropic effects on myocardium [32]. T3, a preoperative laboratory indicator, demonstrated a mild influence in the study's model, with a decrease in SHAP value linked to higher LCOS risk. Notably, the study's outcome demonstrated a significant difference in T3 levels between LCOS and non-LCOS cohorts, while TSH levels were comparable. This dissociation likely reflects non-thyroidal illness syndrome, a condition that is commonly characterized by impaired peripheral conversion of T4 to T3, with sustained hypothalamic-pituitary feedback [3]. Essentially, T3's direct influence on myocardial function [4] renders it a more sensitive predictor of postoperative cardiac dysfunction than TSH, thereby supporting its inclusion in our model. Also, while T3 is not routinely measured in all CABG patients [33], its inclusion in our model is supported by its physiological significance in cardiac function and reported association with perioperative and postoperative complications such as hemodynamic instability and decreased cardiac output [34]. Additionally, its inclusion in developing our model reflects the study's comprehensive approach to risk prediction, utilizing ML to identify subtle yet physiologically influential predictors.

Moreover, our study's selection of various features relating to CABG and LCOS was generally carried out following an extensive review of previous studies [1, 2, 5, 6]. Notably, NT-proBNP and troponin are relevant cardiac biomarkers [35]. Nonetheless, preoperative values of these biomarkers were not obtained routinely in all patients undergoing non-isolated CABG over the period of the study's dataset, thereby accounting for excessively high missing values (> 40%) beyond this study's exclusion threshold (≤ 15%), and hence the need to exclude from selection. This observed limitation reflects variations in preoperative examination practices across real-world clinical settings. Overall, variables including echocardiographic parameters such as EF and LVDs, and routine laboratory predictors such as creatinine and bilirubin were consistently collected. Essentially, the subsequent identification of the 9 predictors from this study's available candidate variables by our LASSO regression was further justified physiologically by the respective explanatory outcome of our SHAP analysis.

Clinical utility

To enhance the usefulness of the model in real-world clinical settings, a user-friendly, interactive web-based tool (https://lcos-cabg-xgb-model.streamlit.app/) was developed for early postoperative risk stratification, specifically during the immediate postoperative period upon ICU admission after non-isolated CABG. The web-based calculator requires clinicians to input the nine key predictors, including preop_max_cr, direct bilirubin, lymphocyte, T3, EF, LVDs, MAP_55_time, BMI, and Lac, to generate a personalized predicted risk of LCOS, which is presented both numerically and graphically. The developed model incorporates readily available clinical and laboratory variables for early LCOS risk stratification and hence enhances its application in routine care. Furthermore, the transparency offered by the visual interpretability of feature contributions enhances clinicians' understanding and clinical acceptance, facilitating informed decision-making.

Strengths and limitations

Our current study was characterized by several strengths. Firstly, we developed an ML-based model specifically for predicting LCOS after non-isolated CABG surgery. Secondly, the user-friendly design of the web-based calculator renders the model readily accessible for clinicians, using variables easily accessible from hospital EMR. Thirdly, unlike conventional statistical scoring models, our model employed advanced ML algorithms to significantly reduce the risk of bias in the substantial dataset, thereby improving prediction accuracy. Finally, the dataset was characterized by a large and broader spectrum of variables, including multi-period variables such as laboratory testing, hemodynamic monitoring, and demographic information, which provided improved risk classification [36].

Despite the strengths noted, the study was also marked by limitations. As a single-center retrospective study with a relatively modest sample size, the generalizability of the findings may be limited by the custom demographic characteristics of the study population and variability in institutional practices. For instance, myocardial protection interventions such as cardioplegia type and temperature management, inotrope and vasopressor protocols including timing, agent selection, and thresholds for initiation, and hemodynamic monitoring practices such as routine use of pulmonary artery catheters, cardiac output measurement frequency, can be significantly variable across cardiac surgical centers, thus highlighting the need for external validation. In effect, the incidence of LCOS and the predictor data obtained from patients may be influenced by these noted differences across centers, likely altering the discrimination and calibration of the model when externally applied. Notably, this study was marked by limitations in providing a fully comprehensive presentation of all patient characteristics due to the inherent complexity of cardiac surgical practice, thereby resulting in a certain degree of clinical heterogeneity of our study population. In addition, the potential introduction of heterogeneity within the LCOS cohort may result from the multiple diagnostic criteria employed by the study. Another limitation observed was that the model's calibration in extremely high-risk patients required cautious interpretation, and as such, further evaluation through multicenter studies with external validation in larger cohorts is recommended. Another inherent limitation associated with our study is the possible overestimation of the model's discriminatory performance due to the dual role of Lac as both a predictor and a component of the outcome definition. Moreover, overfitting generally remains a concern in any predictive modeling study, particularly in studies where sample size is relatively modest and associated with numerous candidate predictive variables [15]. Although we employed regularization strategies as demonstrated in Figure S2 and Table S5, it is important to note that the model may still be associated with some degree of noise custom to our dataset, emphasizing the need for external validation in a larger, independent cohort to assure robustness and generalizability during application in a real-world clinical setting. Finally, prospective studies may be further explored to further assess the model's predictive performance and practical effect on the prevention and management of LCOS after non-isolated CABG.

Conclusions

The study developed ML-based models for early prediction of LCOS following non-isolated CABG surgery, with the XGB model showing the best performance. The model's output was based on nine specific predictors, with EF, LVDs, and Lac levels emerging as the most clinically significant, demonstrating good explainability. It thus enhances clinical acceptance, aids risk stratification, and ultimately enhances early detection of LCOS risk. Nonetheless, prospective external validation via a multicenter study in a larger cohort is recommended to enhance its reassurance in clinical application.

Abbreviations

AAT: alpha-1 antitrypsin

AoD: aortic diameter

AUC: area under the curve

AUROC: area under the receiver operating characteristic curve

BMI: body mass index

CABG: coronary artery bypass grafting

CI: cardiac index

CPB: cardiopulmonary bypass

CVP: central venous pressure

DCA: decision curve analysis

EF: ejection fraction

EMR: electronic medical records

EuroSCORE: European System for Cardiac Operative Risk Evaluation

ICU: intensive care unit

IQR: interquartile range

Lac: lactate

LASSO: least absolute shrinkage and selection operator

LCOS: low cardiac output syndrome

LGBM: light gradient boosting machine

LR: logistic regression

LVDs: left ventricular end-systolic diameter

MAP: mean arterial pressure

ML: machine learning

RF: random forest

RFC: random forest classifier

SHAP: SHapley Additive exPlanations

STS: Society of Thoracic Surgeons

SVM: support vector machine

TSH: thyroid-stimulating hormone

TWA: time-weighted area under the curve

VIF: variance inflation factor

XGB: extreme gradient boosting

Supplementary materials

The supplementary figures and tables for this article are available at: https://www.explorationpub.com/uploads/Article/file/1012111_sup_1.pdf.

Declarations

Author contributions

EDKF and JW: Conceptualization, Data curation, Formal analysis, Methodology, Software, Writing—original draft. SHS: Writing—original draft. TF: Conceptualization, Data curation, Formal analysis, Methodology, Software. ZGK, DKN, ESN, and EJI: Writing—review & editing. WY, LH, and JZ: Writing—review & editing, Supervision, Funding acquisition. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Ethical approval

Our study adhered to the Declaration of Helsinki and postoperative ethical standards. The ethics committee of the Nanjing First Hospital approved this study (Grant No. KY20220518-KS-01).

Consent to participate

As a retrospective study, the need for written informed consent of participants was waived by the ethics committee of the Nanjing First Hospital. Our study did not border on confidential information as pertains to patients.

Consent to publication

As a retrospective study, the need for written informed consent of participants was waived by the ethics committee of the Nanjing First Hospital. Our study did not border on confidential information as pertains to patients.

Availability of data and materials

The data supporting this study's findings are available from the corresponding author, [Jianjun Zou], upon reasonable request.

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