INTRODUCTION

Delirium, which is defined as an acute confessional condition whose characteristics include impaired mental state, is correlated with significant economic costs, high incidence of falls and fall-related accidents, self-removal of medical equipment, long-term hospitalizations, and even increased fatality rates.\(^1,2\) The incidence of postoperative delirium (POD) in heart surgery patients ranges from 50 to 70 percent. According to many prospective studies\(^3-^5\), POD is correlated with significant short-term repercussions, such as longer...
stays in the intensive care unit (ICU) and the hospital, as well as higher post-surgical morbidity and death. Furthermore, POD has an influence on long-term cognitive and functional deterioration, resulting in an increased demand for health care resources and expenses.

Even though the exact mechanism behind the development of POD is not known at this time, neuroinflammation generated by the surgery-induced systemic inflammatory process has been suggested to participate in this condition. While an elevated level of C-reactive protein and interleukin-6 (IL-6) has also been shown to be correlated with POD, whereas one cohort research found no correlation between the level of plasma IL-6 and delirium in elderly hospitalized patients. Consequently, the relationship between plasma markers of inflammation and POD is still unclear. POD might possibly be predicted using biomarkers associated with inflammation. It has been shown that the aberrant elevation in inflammation blood cell variables, including the neutrophil count, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio, functions as a basic indicator of inflammatory response; all of these parameters have been evaluated for their potential in POD. However, the predictive value of inflammatory biomarkers in POD has not been investigated independently and remains unknown.

Hemogram derived inflammatory markers have been reported to be associated with outcome in ICU population. These include platelet-to-lymphocyte count ratio, neutrophil-to-lymphocyte count ratio, and mean platelet volume. Therefore, another hemogram derived marker, monocyte-to-lymphocyte ratio (MLR), could be associated with worse outcome in ICU patients after cardiac surgery. The MLR is a newly developed and integrative inflammatory biomarker that is based on monocyte and lymphocyte counts. The increased MLR was initially used to assess the diabetic kidney injury, liver steatosis, irritable bowel syndrome, cancer, and Covid-19 infection. MLR is currently believed to better represent the inflammatory state of patients. The function of MLR and POD, on the other hand, remains controversial. We hypothesized that individuals with POD who had greater levels of inflammation, as evaluated by MLR, are at an elevated risk of developing POD. To investigate if MLR levels have a role in predicting POD, the present research examined the relationship between POD and MLR levels while controlling for a broad variety of possible confounders.

2 | METHODS

2.1 | Source of data and sample

We conducted a single-center retrospective cohort study; we collected all relevant data from Medical Information Mart for Intensive Care-III (MIMIC-III Version 1.4) database. MIMIC-III database is an open and freely available database developed by the Massachusetts Institute of Technology (MIT) computational Physiology Laboratory. The database records clinical medical information on patients admitted to the ICU at Beth Israel Deacon Medical Center from 2001 to 2012. The recorded information in the database included basic information, vital signs, supplementary tests, medication status, and diagnosis. The institutional Review Board of MIT and Beth Israel Deacon Medical Center granted approval to this database. The database is available to researchers who obtain a certificate after completing an online course on protecting Human Study Subjects, organized by the National Institutes of Health. Informed consent of the patients was exempted because the current study was a clinical database-related study.

2.2 | Selection criteria

Among the more than 50,000 different patients in the database, the subjects included in this study had to meet the following criteria: (1) The current procedural terminology (CPT) was utilized to identify patients undergoing cardiac surgery; ideally, the CPT number ought to fall between 33,010 and 37,799, and (2) age ≥ 16 years. Exclusion criteria of this study were as follows: (1) younger than 16 years of age; (2) monocytes and lymphocyte count data were lost on the first day of admission to ICU; (3) data were missing by more than 20%; (4) intubated patients; and (5) patients had a hematologic neoplasm diagnosis.

2.3 | Evaluation of MLR

The blood count was recorded, which included the absolute numbers of lymphocytes and monocytes. In addition, MLR was defined as MLR = M/L.

2.4 | Assessment of outcome

Delirium within a hospitalization was defined by International Classification of Diseases-ninth (ICD-9) code. ICD-9-CM diagnostic code “2930,” “2931,” “29281,” “29011,” “2903,” “29041,” “2910,” “2939,” “78009,” “29381,” “29382,” “29383,” “29384,” “29389,” “29012,” “29013,” “29043,” “29211,” “29212,” “2922,” “78002,” “2902,” “29042,” “2908,” “2909,” “2920,” “29282,” “3483,” “34831,” “34832,” and “78097.”

2.5 | Baseline variables

Data were extracted by structured query language PostgreSQL 9.6. Demographic variables such as age, gender, race, and complications included hypertension, arrhythmia, heart valve disease, congestive heart failure, pulmonary circulation disorders, peripheral vascular disease, diabetes were acquired. All vital signs, results of blood gas (anions gap, lactate, and bicarbonate concentrations), lab findings, mechanical breathing time, and perioperative transfusion data were obtained. The sequential organ failure assessment (SOFA) score and
s simplified acute physiology score II (SAPS II) were all computed while being admitted to the ICU.

2.6 | Statistical Analysis

To verify normality, the Kolmogorov–Smirnov test and the Shapiro–Wilk test were performed. For normally distributed data, continuous variables are expressed as means ± standard deviations, whereas non-normal distributed data are expressed as median ± interquartile range. Numeric values (%) are used to express categorical variables. Statistical comparisons were carried out utilizing the Mann–Whitney U-test in the case of continuous data whereas the two-tailed t-test or Fisher exact test were utilized in the case of categorical data. To evaluate the relationship between MLR and all outcomes, a univariate logistic regression analysis was performed. Subsequently, a multivariate logistic regression analysis was carried out for the purpose of calibrating the subsequent important covariates. The odds ratio (OR) was calculated with a 95 percent confidence interval (CI) to represent the effect. We also made adjustments for the factors that were correlated with the dominant and secondary outcomes. In addition, multivariate analysis was used to control for the corresponding confounding factors; in model I, the confounding factors, including age, gender, and race were adjusted, while in model II, confounding factors, including age, sex, race, diastolic blood pressure, heart rate, respiratory rate, temperature, SpO2, heart failure anion gap, platelet, serum chloride. Were adjusted. Furthermore, subgroup analyses were conducted in order to corroborate the validity of our results.

STATA (version: 15.0) (STATA Corp LLC) was employed to conduct the statistical analyses. Statistical significance was considered to have been attained when \( p < 0.05 \).

3 | RESULTS

3.1 | Patient characteristics

A total of 3868 patients with cardiac surgery were retrospectively enrolled, including 2171 males and 1697 females, with a mean age of \( 63.9 \pm 16.2 \) years. According to the absence or presence of POD, the patients were classified into POD and non-POD groups; data for a sum of 562 patients in the POD cohort and 3306 in the non-POD cohort were analyzed. The patient baseline information is shown in Table 1. The patients in the POD group had significantly higher SOFA scores, SAPS II scores, Elixhauser comorbidity index scores, and MLR as compared to those in the POD group. Vital signs, including mean heart rate, respiration rate, temperature, SBP, DBP, and MAP were higher in the POD group, Laboratory indicators were used for the assessment of organ functions for both groups of patients. The results demonstrated that there was no significant difference between the two groups. Patients in the Pod group had higher rates of drug and alcohol addiction. We further compared three groups based on MLR, and the patient baseline information shown in Table 2. As opposed to the patients in the low MLR group, those in the high MLR group are dominantly female, the white race, elevated CHF rate, arrhythmia, delirium, hypertension, kidney failure disease, greater platelet, and WBC counts, elevated heart rate, PT, APTT, anion gap, BUN, creatinine, lactate, and respiratory rate, reduced levels of SP02, chloride, bicarbonate, MAP, hemoglobin, and elevated SOFA scores, SAPS II scores, Elixhauser comorbidity index scores.

3.2 | Relationship between MLR and POD

Following adjustments for the potential confounding variables, we developed distinct models for the purpose of evaluating the independent impacts of MLR on the POD. As shown in Table 3, the OR and 95% CI values and the univariate analysis suggested that high MLR (As a continuous variable) is associated with a 21% higher risk of POD (OR: \( 1.12; 95\% \text{ CI, } 1.02–1.43, p = 0.0259 \)), After adjustments for other confounding factors, gender, age, race, temperature, SBP, DBP, MAP, respiratory rate, SOFA, peripheral vascular disease, AG, psychoses, drug, and alcohol addiction, the results showed that high MLR (As a continuous variable) independently served as a risk factor to predict POD (OR: \( 1.21; 95\% \text{ CI: } 1.01–1.44; p = 0.0378 \)).

When MLR was assessed as tertiles, we found that patients in high MLR (MLR ≥51) also had significantly higher risks of POD (OR 1.45, 95% CI 1.15–1.82, \( p = 0.0014 \)) as opposed to patients in the low group (MLR <26) in the univariate model, After adjustments for other confounding factors, gender, age, race, temperature, SBP, DBP, MAP, respiratory rate, SOFA, peripheral vascular disease, AG, psychoses, drug, and alcohol addiction, the results showed that high MLR (MLR ≥51) independently served as a risk factor to predict POD (OR: \( 1.55; 95\% \text{ CI } 1.15–1.82, p = 0.0014 \)).

When MLR was assessed as quintile, we found that patients in high MLR (MLR ≥73) also had significantly higher risks of POD (OR 1.57, 95% CI 1.17–2.11, \( p = 0.0027 \)) than patients in the low group (MLR <26) in the univariate model, After adjustments for other confounding factors, gender, age, race, temperature, SBP, DBP, MAP, respiratory rate, SOFA, peripheral vascular disease, AG, psychoses, drug and alcohol addiction, the results showed that high MLR (MLR ≥73) independently served as a risk factor to predict POD (OR: \( 1.51; 95\% \text{ CI } 1.10–2.07; p = 0.0115 \)).

3.3 | subgroup analysis

The results of subgroup analysis are shown in Table 4. There were no differences in MLR for patients with POD in pre-specified subgroups.

4 | DISCUSSION

As far as we know, this study is the first to demonstrate the strong correlation between MLR and POD. We observed that patients
| Characteristics         | Non-POD     | POD         | p value |
|-------------------------|-------------|-------------|---------|
| N                       | 3306        | 562         |         |
| Age, years              | 64.0±16.1   | 64.1±17.0   | 0.833   |
| Gender, n (%)           |             |             |         |
| Female                  | 1456 (44.0) | 241 (42.9)  | 0.609   |
| Male                    | 1850 (56.0) | 321 (57.1)  |         |
| Ethnicity, n (%)        |             |             |         |
| White                   | 2361 (71.4) | 411 (73.1)  | 0.695   |
| Black                   | 345 (10.4)  | 54 (9.6)    |         |
| Other                   | 600 (18.1)  | 97 (17.3)   |         |
| Vital signs              |             |             |         |
| Heart rate, beats/min   | 89.2±16.7   | 91.3±17.5   | 0.004   |
| SBP, mmHg               | 114.8±16.1  | 118.1±17.8  | <0.001  |
| DBP, mmHg               | 59.4±10.5   | 61.9±11.3   | <0.001  |
| MAP, mmHg               | 76.2±10.8   | 78.2±12.0   | <0.001  |
| RR, times/min           | 19.9±4.4    | 20.6±4.8    | 0.003   |
| Temperature, °C         | 36.8±0.7    | 36.9±0.8    | 0.010   |
| SpO2, %                 | 97.2±2.4    | 97.1±2.3    | 0.636   |
| Comorbidities, n (%)    |             |             |         |
| CS                      | 174 (5.3)   | 21 (3.7)    | 0.126   |
| CHF                     | 1089 (32.9) | 199 (35.4)  | 0.251   |
| Cardiac arrhythmias     | 1105 (33.4) | 201 (35.8)  | 0.278   |
| PCD                     | 309 (9.3)   | 56 (10.0)   | 0.643   |
| Valvular disease        | 466 (14.1)  | 77 (13.7)   | 0.803   |
| PVD                     | 375 (11.3)  | 86 (15.3)   | 0.007   |
| Hypertension            | 1872 (56.6) | 335 (59.6)  | 0.186   |
| Diabetes                | 740 (22.4)  | 112 (19.9)  | 0.194   |
| Renal failure           | 680 (20.6)  | 133 (23.7)  | 0.096   |
| Drug abuse              | 113 (3.4)   | 51 (9.1)    | <0.001  |
| Alcohol abuse           | 256 (7.7)   | 87 (15.5)   | <0.001  |
| Laboratory parameters   |             |             |         |
| MLR (%)                 | 60±100      | 60±90       | <0.001  |
| Anion gap, mmol/L       | 16.9±5.5    | 17.4±5.5    | 0.028   |
| Albumin, mg/dl          | 3.1±0.7     | 3.1±0.7     | 0.636   |
| Bilirubin, mg/dl        | 2.5±5.4     | 2.0±4.3     | 0.115   |
| Creatinine, mg/dl       | 2.0±2.0     | 2.1±2.6     | 0.098   |
| Chloride, mmol/L        | 108.1±7.1   | 108.1±7.4   | 0.981   |
| Maximum glucose, mg/dl  | 192.2±103.8 | 190.9±102.1 | 0.793   |
| Mean glucose, mg/dl     | 143.3±44.7  | 144.4±47.7  | 0.577   |
| WBC, 10^9/L             | 13.6±11.1   | 13.1±7.7    | 0.285   |
| Monocyte, %             | 4.3±3.5     | 4.5±3.5     | 0.020   |
| Hematocrit, %           | 35.5±6.1    | 35.5±6.4    | 0.958   |
| Hemoglobin, g/dl        | 11.8±2.1    | 11.8±2.2    | 0.825   |
| Band neutrophils, %     | 11.0±11.2   | 11.0±11.9   | 0.969   |
| Lactate, mmol/L         | 3.4±2.8     | 3.1±2.6     | 0.043   |
| Bicarbonate, mmol/L     | 24.6±5.0    | 24.8±5.0    | 0.234   |
All of which contribute to secondary brain injury, manifesting as citotoxic compounds, oxidative stress, and mitochondrial illnesses, by POD delivers a chain of occurrences, such as the secretion of inflammation in individuals suffering from depression. 34 It is common biomarker for both systematic inflammatory responses and neuroinflammation. It has been shown that the MLR may function as a full blood count examination, they are simple to use and affordable to obtain. It has been shown that one of the early cell types to react when these potential lethal signals are received. Following injury, microglia become stimulated, experience structural changes, and release cytokines in just a few minutes. Various investigations have demonstrated that the mobilization and stimulation of monocytes may enhance the inflammatory response and exert a function comparable to that of microglia, elevating the expression of pro-inflammatory factors as well as chemokines. We believe that our results will pave the way for a new line of study, including the examination of blood cell counts and inflammation metrics in POD patients in the future. Obviously, inflammatory ratios are low-cost and readily available measures of inflammation, and they may be obtained by a standard blood test. Furthermore, research has revealed that inflammatory ratios are significantly correlated with other recognized inflammatory indicators, including oxidative stress, and several pro-inflammatory cytokines. Notably, these measures appear to be less impacted by exercise, catecholamine secretion, and other confounding variables compared to single leukocyte measurements or other regularly used indicators of inflammation.

There were some positive aspects to our research. Above all, the continual sampling of patients eliminates the possibility of selection bias. Secondly, the target-independent factors are divided into three or five groups, which minimized the likelihood of error in data analysis and increases the robustness of the conclusions in the present research. Thirdly, repeated imputations were performed to analyze the incomplete data and ensure that the findings obtained from the whole data set and the numerous imputed datasets were congruent with one another.

### TABLE 1 (Continued)

| Characteristics | Non-POD | POD | p value |
|-----------------|---------|-----|---------|
| Sodium, mmol/L  | 140.5±5.2 | 140.8±5.4 | 0.045   |
| Potassium, mmol/L| 4.9±1.0 | 4.8±1.0 | 0.254   |
| APTT, second    | 49.0±33.3 | 45.3±29.8 | 0.017   |
| PT, second      | 18.6±11.4 | 19.0±14.5 | 0.487   |
| INR             | 1.8±1.7 | 1.8±1.7 | 0.027   |
| BUN, mg/dl      | 35.1±27.5 | 37.3±29.5 | 0.085   |

**Scoring system**

| Scoring system | Non-POD | POD | p value |
|----------------|---------|-----|---------|
| ECI            | 18.6±14.0 | 21.7±15.6 | <0.001 |
| SOFA           | 6.2±3.8  | 6.5±3.6 | 0.024   |
| SAPSII         | 42.4±14.8 | 43.9±14.6 | 0.027   |

**Hospital LOS (days)**

| Hospital LOS, days | Non-POD | POD | p value |
|--------------------|---------|-----|---------|
| 15.2±13.8         | 22.0±17.9 | <0.001 |

Abbreviations: APTT, activated partial thromboplastin time; BUN, blood urea nitrogen; CHF, congestive heart failure; CS, cardiac shock; DBP, diastolic blood pressure; ECI, Elixhauser comorbidity index; INR, international normalized ratio; LOS, length of stay; MBP, mean blood pressure; PCD, pulmonary circulation disease; PT, prothrombin time; PVD, peripheral vascular disease; RR, respiration rate; SAPSII, simplified acute physiology score II; SBP, systolic blood pressure; SOFA, sequential organ failure assessment; SpO2, pulse oximetry-derived oxygen saturation; WBC, white blood cell. Bold values represent p<0.05.
| Characteristics               | Monocyte-to-lymphocyte ratio(%) |
|-------------------------------|---------------------------------|
|                               | <27    | 27-53 | 53    | p value |
| N                             | 1288   | 1288  | 1292  |         |
| Admission age, years          | 63.3 ± 16.2 | 64.1 ± 16.2 | 64.5 ± 16.3 | 0.159  |
| Gender, n (%)                 |        |       |       |         |
| 0                             | 589 (45.7) | 583 (45.3) | 525 (40.6) | 0.016  |
| 1                             | 699 (54.3) | 705 (54.7) | 767 (59.4) |         |
| Ethnicity, n (%)              |        |       |       |         |
| 0                             | 866 (67.2) | 937 (72.7) | 969 (75.0) | <0.001  |
| 1                             | 166 (12.9) | 144 (11.2) | 89 (6.9) |         |
| 2                             | 256 (19.9) | 207 (16.1) | 234 (18.1) |         |
| Vital signs                   |        |       |       |         |
| Heart rate, beats/min         | 87.9 ± 16.2 | 88.3 ± 16.3 | 92.2 ± 17.6 | <0.001  |
| SBP, mmHg                     | 115.8 ± 15.8 | 116.7 ± 16.9 | 113.4 ± 16.4 | <0.001  |
| DBP, mmHg                     | 59.9 ± 10.2 | 60.5 ± 11.1 | 58.9 ± 10.6 | <0.001  |
| MBP, mmHg                     | 77.0 ± 10.7 | 77.2 ± 11.4 | 75.3 ± 10.8 | <0.001  |
| RR, times/min                 | 19.4 ± 4.4 | 20.1 ± 4.3 | 20.6 ± 4.6 | <0.001  |
| Temperature, °C               | 36.8 ± 0.7 | 36.9 ± 0.7 | 36.9 ± 0.7 | 0.252  |
| SpO2, %                       | 97.4 ± 2.5 | 97.1 ± 2.4 | 97.0 ± 2.3 | <0.001  |
| Comorbidities, n (%)          |        |       |       |         |
| Delirium                      | 150 (11.6) | 206 (16.0) | 206 (15.9) | 0.002  |
| CS                            | 50 (3.9) | 65 (5.0) | 80 (6.2) | 0.027  |
| CHF                           | 375 (29.1) | 466 (36.2) | 447 (34.6) | <0.001  |
| Cardiac arrhythmias           | 399 (31.0) | 438 (34.0) | 469 (36.3) | 0.016  |
| PCD                           | 116 (9.0) | 133 (10.3) | 116 (9.0) | 0.409  |
| Valvular disease              | 183 (14.2) | 186 (14.4) | 174 (13.5) | 0.759  |
| PVD                           | 166 (12.9) | 161 (12.5) | 134 (10.4) | 0.105  |
| Hypertension                  | 775 (60.2) | 733 (56.9) | 699 (54.1) | 0.008  |
| Diabetes                      | 295 (22.9) | 272 (21.1) | 285 (22.1) | 0.550  |
| Renal failure                 | 231 (17.9) | 286 (22.2) | 296 (22.9) | 0.004  |
| Drug abuse                    | 53 (4.1) | 62 (4.8) | 49 (3.8) | 0.421  |
| Alcohol abuse                 | 85 (6.6) | 132 (10.2) | 126 (9.8) | 0.002  |
| Laboratory parameters         |        |       |       |         |
| MLR                           | 0.2 ± 0.1 | 0.4 ± 0.1 | 1.3 ± 1.4 | <0.001  |
| Anion gap, mmol/L             | 15.8 ± 5.4 | 17.1 ± 5.5 | 17.9 ± 5.6 | <0.001  |
| Albumin, mg/dl                | 3.2 ± 0.7 | 3.1 ± 0.7 | 3.0 ± 0.7 | <0.001  |
| Bilirubin, mg/dl              | 1.6 ± 3.5 | 2.3 ± 5.4 | 3.0 ± 6.1 | <0.001  |
| Creatinine, mg/dl             | 1.7 ± 2.1 | 2.1 ± 2.2 | 2.2 ± 2.1 | <0.001  |
| Chloride, mmol/L              | 109.6 ± 6.5 | 107.6 ± 6.9 | 107.2 ± 7.6 | <0.001  |
| Maximum glucose, mg/dl        | 196.9 ± 106.6 | 187.3 ± 102.7 | 191.9 ± 101.1 | 0.063  |
| Mean glucose, mg/dl           | 141.1 ± 44.6 | 143.6 ± 44.7 | 145.7 ± 46.2 | 0.035  |
| WBC, 10³/L                    | 11.4 ± 7.4 | 12.6 ± 6.7 | 16.4 ± 15.1 | <0.001  |
| Monocyte, %                   | 2.9 ± 1.7 | 4.1 ± 2.1 | 5.9 ± 5.0 | <0.001  |
| Hematocrit, %                 | 36.2 ± 5.9 | 35.2 ± 6.1 | 35.2 ± 6.4 | <0.001  |
| Hemoglobin, g/dl              | 12.0 ± 2.1 | 11.7 ± 2.1 | 11.6 ± 2.2 | <0.001  |
| Band neutrophils, %           | 12.3 ± 13.5 | 10.4 ± 10.2 | 10.8 ± 10.8 | 0.091  |
Our research, on the other hand, has several drawbacks: (1) Causality cannot be established because of the retrospective observational study design. Prospective studies are needed to solve this. (2) The information was obtained from a single blood test. Serial testing might be more beneficial than a single test performed upon admission. (3) With respect to clinical practice, obtaining MLR is very
### TABLE 4 Subgroup analysis of MLR and POD

| Characteristic       | N    | 27       | 27–53   | 53       | p for interaction |
|----------------------|------|----------|---------|----------|------------------|
| **Monocyte-to-lymphocyte ratio (%)**                                                                                          |
| **Age, years**       |      |          |         |          |                  |
| <65.4                | 1900 | 1.0      | 1.64 (1.18, 2.29) | 1.69 (1.21, 2.36) | 0.833 |
| ≥65.4                | 1910 | 1.0      | 1.21 (0.88, 1.66) | 1.25 (0.91, 1.70) |
| **Gender, n (%)**    |      |          |         |          |                  |
| Female               | 1676 | 1.0      | 1.45 (1.04, 2.02) | 1.22 (0.86, 1.74) | 0.499 |
| Male                 | 2134 | 1.0      | 1.37 (1.00, 1.87) | 1.62 (1.20, 2.18) |
| **Ethnicity, n (%)** |      |          |         |          |                  |
| White                | 2726 | 1.0      | 1.48 (1.13, 1.95) | 1.42 (1.08, 1.86) | 0.493 |
| Black                | 396  | 1.0      | 1.31 (0.68, 2.51) | 1.12 (0.52, 2.42) |
| Other                | 688  | 1.0      | 1.13 (0.64, 1.99) | 1.73 (1.04, 2.89) |
| **Neutrophils, %**   |      |          |         |          |                  |
| <82.5                | 1910 | 1.0      | 1.69 (1.25, 2.28) | 1.52 (1.09, 2.11) | 0.104 |
| ≥82.5                | 1900 | 1.0      | 1.11 (0.77, 1.59) | 1.28 (0.90, 1.81) |
| **Lymphocytes, %**   |      |          |         |          |                  |
| <9.6                 | 1872 | 1.0      | 1.01 (0.66, 1.54) | 0.96 (0.64, 1.43) | 0.087 |
| ≥9.6                 | 1938 | 1.0      | 1.52 (1.14, 2.01) | 2.14 (1.45, 3.16) |
| **WBC, 10^9/L**      |      |          |         |          |                  |
| <11.7                | 1909 | 1.0      | 1.48 (1.10, 2.00) | 1.81 (1.32, 2.49) | 0.876 |
| ≥11.7                | 1901 | 1.0      | 1.31 (0.92, 1.87) | 1.24 (0.88, 1.74) |
| **SOFA**             |      |          |         |          |                  |
| <6                   | 1869 | 1.0      | 1.70 (1.22, 2.38) | 1.68 (1.19, 2.38) | 0.124 |
| ≥6                   | 1941 | 1.0      | 1.17 (0.85, 1.60) | 1.23 (0.91, 1.66) |
| **SAPSII**           |      |          |         |          |                  |
| <41                  | 1885 | 1.0      | 1.86 (1.35, 2.58) | 1.53 (1.08, 2.18) | 0.051 |
| ≥41                  | 1925 | 1.0      | 1.03 (0.75, 1.42) | 1.24 (0.91, 1.67) |
| **Heart rate, beats/min** |    |          |         |          |                  |
| <88.3                | 1902 | 1.0      | 1.19 (0.86, 1.65) | 1.44 (1.03, 2.00) | 0.900 |
| ≥88.3                | 1898 | 1.0      | 1.61 (1.16, 2.22) | 1.43 (1.04, 1.96) |
| **SBP, mmHg**        |      |          |         |          |                  |
| <112.1               | 1892 | 1.0      | 1.56 (1.09, 2.23) | 1.66 (1.18, 2.34) | 0.375 |
| ≥112.1               | 1903 | 1.0      | 1.27 (0.95, 1.72) | 1.34 (0.99, 1.82) |
| **DBP, mmHg**        |      |          |         |          |                  |
| <58.8                | 1887 | 1.0      | 1.40 (1.00, 1.97) | 1.24 (0.89, 1.74) | 0.749 |
| ≥58.8                | 1907 | 1.0      | 1.36 (1.00, 1.86) | 1.67 (1.23, 2.28) |
| **MBP, mmHg**        |      |          |         |          |                  |
| <74.95               | 1890 | 1.0      | 1.59 (1.13, 2.25) | 1.41 (1.00, 1.98) | 0.129 |
| ≥74.95               | 1910 | 1.0      | 1.25 (0.92, 1.70) | 1.56 (1.15, 2.11) |
| **Temperature, °C**  |      |          |         |          |                  |
| <36.8                | 1825 | 1.0      | 1.54 (1.08, 2.19) | 1.96 (1.39, 2.75) | 0.030 |
| ≥36.8                | 1825 | 1.0      | 1.34 (0.98, 1.85) | 1.14 (0.83, 1.59) |
| **RR, times/min**    |      |          |         |          |                  |
| <19.2                | 1910 | 1.0      | 1.50 (1.09, 2.07) | 1.52 (1.09, 2.11) | 0.504 |
| ≥19.2                | 1890 | 1.0      | 1.25 (0.90, 1.73) | 1.32 (0.96, 1.81) |
| Characteristic       | N    | 27    | 27–53 | 53    | p for interaction |
|---------------------|------|-------|-------|-------|------------------|
| Monocyte- to- lymphocyte ratio (%) |      |       |       |       |                  |
| <97.5               | 1889 | 1.0   | 1.40  | 1.01, 1.94 | 1.32 (0.95, 1.83) | 0.148 |
| ≥97.5               | 1909 | 1.0   | 1.35  | 0.97, 1.86 | 1.58 (1.15, 2.17) |       |
| Mean glucose, mg/dl |      |       |       |       |                  |
| <133.7              | 1910 | 1.0   | 1.53  | 1.10, 2.12 | 1.35 (0.98, 1.85) | 0.668 |
| ≥133.7              | 1890 | 1.0   | 1.19  | 0.85, 1.66 | 1.35 (0.98, 1.85) |       |
| Monocyte, %         |      |       |       |       |                  |
| <3.6                | 1884 | 1.0   | 1.30  | 0.92, 1.82 | 1.30 (0.92, 1.82) | 0.692 |
| ≥3.6                | 1926 | 1.0   | 1.58  | (1.15, 2.17) | 1.58 (1.16, 2.16) |       |
| Anion gap, mmol/L   |      |       |       |       |                  |
| <16                 | 1739 | 1.0   | 1.95  | 1.37, 2.76 | 1.95 (1.37, 2.76) | 0.051 |
| ≥16                 | 2052 | 1.0   | 1.12  | 0.82, 1.53 | 1.12 (0.82, 1.53) |       |
| Albumin, mg/dl      |      |       |       |       |                  |
| <3.1                | 1068 | 1.0   | 1.50  | 0.96, 2.34 | 1.50 (0.96, 2.34) | 0.489 |
| ≥3.1                | 1085 | 1.0   | 1.20  | 0.80, 1.47 | 1.20 (0.80, 1.47) |       |
| Bilirubin, mg/dl    |      |       |       |       |                  |
| <0.8                | 1280 | 1.0   | 1.22  | 0.83, 1.79 | 1.22 (0.84, 1.78) | 0.701 |
| ≥0.8                | 1329 | 1.0   | 1.22  | 0.84, 1.78 | 1.22 (0.84, 1.78) |       |
| Creatinine, mg/dl   |      |       |       |       |                  |
| <1.2                | 1711 | 1.0   | 1.96  | 1.37, 2.80 | 1.96 (1.37, 2.80) | 0.036 |
| ≥1.2                | 2096 | 1.0   | 1.11  | 0.83, 1.50 | 1.11 (0.83, 1.50) |       |
| Chloride, mmol/L    |      |       |       |       |                  |
| <108                | 1748 | 1.0   | 1.25  | 0.88, 1.79 | 1.25 (0.88, 1.79) | 0.015 |
| ≥108                | 2060 | 1.0   | 1.66  | 1.23, 2.24 | 1.66 (1.23, 2.24) |       |
| Maximum glucose, mg/dl |  |       |       |       |                  |
| <166                | 1899 | 1.0   | 1.32  | 0.95, 1.82 | 1.32 (0.95, 1.82) | 0.221 |
| ≥166                | 1909 | 1.0   | 1.58  | 1.16, 2.16 | 1.58 (1.16, 2.16) |       |
| Hematocrit, %       |      |       |       |       |                  |
| <35                 | 1886 | 1.0   | 1.42  | 1.03, 1.96 | 1.26 (0.91, 1.74) | 0.132 |
| ≥35                 | 1922 | 1.0   | 1.34  | 0.96, 1.85 | 1.34 (0.96, 1.85) |       |
| Hemoglobin, g/dl    |      |       |       |       |                  |
| <11.6               | 1863 | 1.0   | 1.28  | 0.92, 1.77 | 1.28 (0.92, 1.77) | 0.423 |
| ≥11.6               | 1943 | 1.0   | 1.62  | 1.18, 2.22 | 1.62 (1.18, 2.22) |       |
| Lactate, mmol/L     |      |       |       |       |                  |
| <2.5                | 1605 | 1.0   | 1.56  | 1.12, 2.19 | 1.56 (1.12, 2.19) | 0.977 |
| ≥2.5                | 1601 | 1.0   | 1.34  | 0.94, 1.90 | 1.34 (0.94, 1.90) |       |
| Potassium, mmol/L   |      |       |       |       |                  |
| <4.6                | 1720 | 1.0   | 1.35  | 0.96, 1.90 | 1.35 (0.96, 1.90) | 0.572 |
| ≥4.6                | 2088 | 1.0   | 1.52  | 1.12, 2.06 | 1.52 (1.12, 2.06) |       |
| APTT, second        |      |       |       |       |                  |
| <35.7               | 1847 | 1.0   | 1.40  | 1.02, 1.93 | 1.40 (1.02, 1.93) | 0.936 |
| ≥35.7               | 1857 | 1.0   | 1.48  | 1.06, 2.07 | 1.48 (1.06, 2.07) |       |
| INR                 |      |       |       |       |                  |
| <1.4                | 1685 | 1.0   | 1.29  | 0.92, 1.80 | 1.29 (0.92, 1.80) | 0.508 |
| ≥1.4                | 2021 | 1.0   | 1.63  | 1.18, 2.25 | 1.63 (1.18, 2.25) |       |
| Characteristic                  | N    | 27   | 27–53 | 53   | p for interaction |
|--------------------------------|------|------|--------|------|------------------|
| PT, second                     |      |      |        |      |                  |
| <15.4                          | 1822 | 1.0  | 1.24 (0.91, 1.68) | 1.16 (0.84, 1.61) | 0.724 |
| ≥15.4                          | 1884 | 1.0  | 1.62 (1.14, 2.31) | 1.83 (1.31, 2.56) |      |
| Sodium, mmol/L                 |      |      |        |      |                  |
| <140                           | 1547 | 1.0  | 1.46 (0.99, 2.14) | 1.37 (0.94, 1.99) | 0.422 |
| ≥140                           | 2261 | 1.0  | 1.38 (1.04, 1.83) | 1.54 (1.16, 2.06) |      |
| BUN, mg/dl                     |      |      |        |      |                  |
| <26                            | 1855 | 1.0  | 1.87 (1.35, 2.58) | 1.88 (1.34, 2.65) | 0.153 |
| ≥26                            | 1953 | 1.0  | 1.03 (0.74, 1.42) | 1.09 (0.80, 1.49) |      |
| Bicarbonate, mmol/L            |      |      |        |      |                  |
| <25                            | 1884 | 1.0  | 1.31 (0.93, 1.85) | 1.46 (1.05, 2.02) | 0.622 |
| ≥25                            | 1921 | 1.0  | 1.49 (1.10, 2.02) | 1.47 (1.07, 2.02) |      |
| Band neutrophils, %            |      |      |        |      |                  |
| <7                             | 514  | 1.0  | 1.20 (0.61, 2.39) | 1.41 (0.77, 2.57) | 0.183 |
| ≥7                             | 603  | 1.0  | 1.51 (0.80, 2.86) | 0.97 (0.53, 1.77) |      |
| CS                             |      |      |        |      |                  |
| No                             | 3615 | 1.0  | 1.41 (1.12, 1.77) | 1.46 (1.16, 1.85) | 0.976 |
| Yes                            | 195  | 1.0  | 1.58 (0.45, 5.58) | 1.41 (0.41, 4.84) |      |
| CHF                            |      |      |        |      |                  |
| No                             | 2545 | 1.0  | 1.45 (1.09, 1.91) | 1.44 (1.09, 1.91) | 0.890 |
| Yes                            | 1265 | 1.0  | 1.31 (0.88, 1.94) | 1.43 (0.96, 2.11) |      |
| Cardiac arrhythmias            |      |      |        |      |                  |
| No                             | 2527 | 1.0  | 1.40 (1.06, 1.85) | 1.34 (1.01, 1.77) | 0.419 |
| Yes                            | 1283 | 1.0  | 1.42 (0.95, 2.11) | 1.65 (1.12, 2.43) |      |
| PCD                            |      |      |        |      |                  |
| No                             | 3448 | 1.0  | 1.38 (1.09, 1.76) | 1.40 (1.10, 1.78) | 0.711 |
| Yes                            | 362  | 1.0  | 1.65 (0.78, 3.51) | 1.99 (0.93, 4.25) |      |
| Valvular disease               |      |      |        |      |                  |
| No                             | 3273 | 1.0  | 1.37 (1.07, 1.75) | 1.49 (1.16, 1.90) | 0.450 |
| Yes                            | 537  | 1.0  | 1.66 (0.92, 3.00) | 1.22 (0.65, 2.28) |      |
| PVD                            |      |      |        |      |                  |
| No                             | 3354 | 1.0  | 1.43 (1.11, 1.84) | 1.52 (1.19, 1.94) | 0.849 |
| Yes                            | 456  | 1.0  | 1.30 (0.74, 2.28) | 1.18 (0.65, 2.14) |      |
| Hypertension                   |      |      |        |      |                  |
| No                             | 1638 | 1.0  | 1.30 (0.91, 1.86) | 1.23 (0.86, 1.77) | 0.604 |
| Yes                            | 2172 | 1.0  | 1.49 (1.11, 2.00) | 1.64 (1.22, 2.20) |      |
| Diabetes                       |      |      |        |      |                  |
| No                             | 2969 | 1.0  | 1.38 (1.07, 1.77) | 1.35 (1.04, 1.74) | 0.528 |
| Yes                            | 841  | 1.0  | 1.52 (0.90, 2.58) | 1.92 (1.16, 3.18) |      |
| Renal failure                  |      |      |        |      |                  |
| No                             | 3016 | 1.0  | 1.46 (1.12, 1.90) | 1.60 (1.24, 2.07) | 0.247 |
| Yes                            | 794  | 1.0  | 1.19 (0.74, 1.90) | 0.99 (0.61, 1.59) |      |
simple; nonetheless, the absence of M and L in the database remains prevalent, resulting in selection bias.

5 | CONCLUSION

In conclusion, we offered the first proof that MLR is correlated with an elevated chance of developing POD. MLR might be an accessible and reliable marker that can be used to predict POD in ICU patients in cardiac surgery. This finding should be confirmed in prospective studies.

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CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

All the data used to support this study are available from the corresponding author (E-mail: kapalu1979@sina.com) upon request.

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SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

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