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**RESEARCH
ARTICLE**

**TRANSLATIONAL AND
CLINICAL RESEARCH**

As and Engin: mABG/eAG predicts post-CABG pneumonia

The predictive role of modified stress hyperglycemia rate in predicting early pneumonia after isolated coronary bypass surgery in patients with diabetes mellitus

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ABSTRACT

Postoperative pneumonia (PP) is one of the most serious complications following coronary artery bypass graft (CABG) surgery. The recently developed admission blood glucose (ABG)/estimated average glucose (eAG) ratio has been identified as a prognostic marker in cardiovascular diseases. This study aimed to investigate the predictive role of the modified ABG/eAG (mABG/eAG) ratio in the development of pneumonia during the early postoperative period in diabetic patients undergoing CABG surgery. In this single-center study, diabetic patients who underwent isolated coronary bypass surgery at the Training and Research Hospital between January 1 2018 and January 1 2023 were included. Patients who did not develop PP were assigned to the control group, while those who developed PP were assigned to the PP group. A total of 549 patients were included in the study, 478 patients in the control group (median age = 58 years [range 35-81]) and 71 patients in the PP group (median age = 63 years [37-86]). In the multivariate analysis, the use of packed blood products (Odds ratio [OR] = 1.685, 95% confidence interval [CI] 1.453 - 1.892; $P = 0.027$), mABG/eAG ratio (OR = 1.659, 95% CI 1.190 - 2.397; $P = 0.019$), and re-intubation (OR = 1.829, 95% CI 1.656 - 1.945; $P = 0.034$) were identified as independent predictors for the development of PP. Our findings demonstrate that the mABG/eAG ratio is an independent predictor of PP in diabetic patients undergoing CABG surgery. Based on our results, high-risk patients can be identified by calculating the mABG/eAG ratio.

Keywords: Coronary artery bypass graft; postoperative term; pneumonia; risk factor.

INTRODUCTION

Coronary artery bypass graft (CABG) surgery is a procedure performed with high success rates today; however, serious complications that can occur following these operations remain significant concerns [1]. Postoperative pneumonia (PP) is among the most severe complications [2]. This condition is associated with prolonged hospital stays and an increased risk of morbidity and mortality. According to the literature, the rate of postoperative pneumonia ranges from 5% to 21%, with mortality rates varying between 6.2% and 28% in these cases [3-5]. Various inflammatory parameters obtained from routine blood tests in cardiovascular surgery have been the subject of research for their prognostic value. These parameters have played a role both in the diagnostic approach and as prognostic markers [6, 7]. Hyperglycemia is one of the stress-related factors that requires close monitoring during and after major surgical procedures, particularly in cardiac surgery. Numerous publications have reported that hyperglycemia is associated with a high risk of morbidity and mortality in these cases [8-14]. Beyond hyperglycemia, the recently developed admission blood glucose (ABG)/estimated average glucose (eAG) ratio has emerged as a prognostic marker in cardiovascular diseases [15, 16]. One study demonstrated a relationship between the ABG/eAG ratio and the development of pneumonia in stroke patients [17]. Another study investigating the predictive power of this ratio found that the ABG/eAG ratio was associated with mortality and poor outcomes in patients with COVID-19 [18].

In the current study, we aimed to investigate the predictive role of the modified ABG/eAG (mABG/eAG) ratio, created by modifying blood glucose data, in the development of pneumonia during the early postoperative period following CABG surgery in diabetic patients.

MATERIALS AND METHODS

This study was designed as a single-center investigation, including diabetic patients who underwent isolated coronary bypass surgery with cardiopulmonary bypass (CPB) at the Bursa

Yüksek İhtisas Training and Research Hospital between January 1 2018 and January 1 2023. Patients who underwent re-operations, emergency cases, those requiring additional cardiac interventions other than isolated coronary bypass surgery, those with a known history of lung disease, those with chronic renal failure, a history of previous pneumonia, and non-diabetic patients were all excluded from the study. After applying the exclusion criteria, a total of 549 consecutive patients were included. The demographic characteristics of all patients, preoperative blood values, operative data, and blood glucose measurements during surgery were recorded. Patients who did not develop PP were assigned to the control group, while those who developed PP were assigned to the PP group.

Operative management

All procedures were performed with median sternotomy and under cardiopulmonary bypass. Pedicled left internal thoracic arteries and saphenous vein grafts were harvested in all patients. Radial artery or right internal thoracic artery grafts were not used in patients included in the study. Aorto-venous two-stage cannulation was performed to accomplish CPB after heparinization. To achieve cardiac arrest, a cross-clamp was put on the ascending aorta, and cold antegrade cardioplegia with high potassium was administered (PLEGISOL® | Pfizer). Blood cardioplegia was administered every 15 to 20 minutes to maintain cardiac arrest. CPB was established with a roller pump equipped with a membrane oxygenator and arterial line filter (Maquet, Getinge Group, Germany). The pump's flow rates were 2-2.4 L/min/m². Also, moderate hypothermia (32°C) was utilized. Arterial blood gas was evaluated every 20 to 30 minutes; immediately before removing the cross-clamp, 500 milliliters of hot blood cardioplegia were administered. The patients were transferred to the cardiovascular intensive care unit when the surgery was completed. Intra-aortic balloon pump support was provided to patients with low cardiac output, visibly deteriorating cardiac function, and resistant cardiac arrhythmias. All patients received the usual postoperative care. Patients were evaluated hourly

for eligibility for extubation. The provision of hemodynamic stabilization (without severe cardiac rhythm problems, without the need for high-dose vasoactive inotropic support; urine output >0.5 mL/kg/hours) was followed by extubation as soon as it was practicable.

Calculation of m-ABG/eAG

Blood parameters were obtained from the blood samples taken from the peripheral venous structures of all patients during their hospitalization. ABG/eAG value, also known as the stress hyperglycemia ratio, is calculated by the ratio of the patient's hyperglycemia response to stress to the estimated glucose value [19]. In our study, we established the ABG value as the average of blood glucose values in all analyses (blood glucose levels due to surgical stress), starting from the blood gas analysis of the patients before anesthesia induction in the operating room, to the first blood gas analysis after transfer to the intensive care unit at the end of the operation. After this modification, the mABG/eAG value was obtained with the following formula:

m-ABG = Blood glucose levels (Before induction of anaesthesia + after induction + during the surgery + on admission to intensive care unit) (mg/dl) / n

The n represents the number of tests for blood glucose analysis in the perioperative period (This number ranged from 6 to 10 in our study group.)

eAG = (28.7 x glycosylated hemoglobin %) - 46.7

Diagnosis of postoperative pneumonia

In patients with clinically suspected pneumonia, newly detected infiltration on chest X-ray or an increase in the current infiltration degree were considered. In addition, pneumonia was diagnosed with the presence of at least two of the following criteria [20]: 1) Fever (>38.5°C) or hypothermia (<36.0°C); 2) Presence of purulent tracheobronchial secretion or increase in the amount of secretion present; and 3) Leukocytosis (12,000/ μ L) or leukopenia (4,000/ μ L).

Also, C reactive protein and procalcitonin values were used to support the diagnosis.

Ethical statement

This study was approved with its protocol by the Bursa Yuksek Ihtisas Training and Research Hospital Clinical Research Ethics Committee, dated March 22, 2023, and numbered 2011-KAEK-25 2023/03-14.

Statistical analysis

In this study, the SPSS 21.0 (IBM Statistical Package for the Social Sciences Statistic Inc. version 21.0, Chicago, IL, USA) program was performed to analyze the data. The Kolmogorov-Smirnov test and Shapiro-Wilk test were utilized for normality distribution analysis. While Student's t-test was applied for the data presenting normal distribution, the Mann-Whitney U test was applied for data that did not conform to normal distribution. This data was presented as mean \pm sd or as median (minimum-maximum), respectively. Categorical variables were presented as frequency and percentage, and the Chi-Square test was used for analysis. Multivariate binary logistic regression analysis was performed to analyze postoperative pneumonia predictors. A p-value being less than 0.05 was accepted as statistically significant. In predicting in-hospital pneumonia development, receiver operating characteristics (ROC) curve analysis was performed for mABG/eAG value and the area under the curve (AUC) was calculated. Youden's J statistic was used to find the best cut-off value of mABG/eAG.

RESULTS

A total of 549 patients were included in the study. The diagnosis of pneumonia was made on a mean of 3.4+ 2.6 days after the operation. Those who did not develop postoperative pneumonia were included in the Control Group [N = 478, median age = 58 (35- 81) years], and those who did were included in the PP Group [n = 71, median age = 63 (37- 86) years]. The median age value of the patients was statistically significantly higher in the PP Group ($P < 0.001$). While the female gender ratio was 32.6% (N = 156) in Group 1, it was 36.6% (N = 26) in the PP Group ($P=0.506$). There were no statistically significant differences between the two groups in terms

of body mass index (BMI), presence of hypertension (HT), smoking, hyperlipidemia (HL), and left ventricular ejection fraction (EF) (Table 1). The preoperative blood values of the patients are shown in Table 1.

Perioperative features of the patients are presented in Table 2. Used packed blood products, use of intra-aortic balloon pump (IABP) rates, m-ABG, m-ABG/eAG value, extubation times, re-intubation and postoperative atrial fibrillation (PoAF) rates were statistically significantly higher in the PP Group ($P < 0.001$, $P = 0.002$, $P = 0.019$, $P < 0.001$, $P = 0.012$, $P = 0.029$, and $P = 0.017$, respectively). Also, the mortality rate was higher in the PP Group (1.8% vs 7%, $P = 0.010$).

Logistic regression analysis was performed to reveal the factors affecting postoperative pneumonia development (Table 3). In univariate analysis, development of postoperative pneumonia was found to be significantly associated with age > 70 (odds ratio [OR]: 1.347, 95% confidence interval [CI]: 1.190-1.740, $P = 0.007$), COPD (OR: 1.114, 95% CI: 1.018- 1.668, $P = 0.022$), used packed blood products (OR: 0.775, 95% CI: 0.535-0.889, $P < 0.001$), use of IABP (OR: 0.855, 95% CI: 0.537-0.971, $P = 0.006$), m-ABG (OR: 1.648, 95% CI: 1.452-1.856, $P = 0.023$), m-ABG/eAG (OR: 2.361, 95% CI: 1.796-4.650, $P < 0.001$), extubation time (OR: 1.812, 95% CI: 1.715-1.994, $P = 0.019$), and re-intubation (OR: 1.530, 95% CI: 1.250-2.194, $P = 0.021$). In the multivariate analysis, packed blood products used (OR: 1.685, 95% CI: 1.453-1.892, $P = 0.027$), m-ABG/eAG (OR: 1.659, 95% CI: 1.190-2.397, $P = 0.019$) and re-intubation (OR: 1.829, 95% CI: 1.656- 1.945, $P = 0.034$) were determined as independent predictors for development of postoperative pneumonia.

For predicting postoperative pneumonia, the cutoff level in the ROC curve analysis was 1.23 for m-ABG/eAG (AUC 0.750, 95 % CI 0.691–0.810, $P < 0.001$, 75.7% sensitivity and 69.1% specificity) (Figure 1).

DISCUSSION

Today, with the developing technology in cardiac surgery, postoperative mortality has decreased considerably. However, the incidence of postoperative pneumonia is still high and has been reported to be up to 21% [21, 22]. In addition, some studies have investigated the presence of various predictive factors for the risk of postoperative pneumonia [23]. In this current study, we demonstrated that mABG/eAG value is an independent predictor, in addition to known risk factors such as re-intubation and excess blood product use, in predicting the risk of pneumonia after isolated CABG operations.

The incidence of coronary artery disease increases with diabetes mellitus, and these patients need CABG more frequently [24]. It has been revealed that hyperglycemia existing before surgery increases various postoperative complications, and high HbA1c value, which is an important indicator of long-term blood sugar control, negatively affects the results after CABG in diabetic patients [25, 26].

In recent years, the stress hyperglycemia ratio (ABG to eAG value) obtained from the eAG value calculated by the blood glucose value and HbA1c value at the time of admission has been widely investigated in predicting the prognosis of cardiovascular diseases. In a recent study, in diabetic patients with ST-segment elevation myocardial infarction, ABG/eAG value was found to be significantly associated with the amount of intracoronary thrombus. In this study, the authors found that the predictive power of ABG/eAG value was higher than the blood glucose level at the time of admission [27]. In another study, in non-surgical DM patients with heart failure, ABG/eAG value at hospital admissions was shown to be associated with acute renal damage and major systemic infections [28]. In a recent study published in mid-2023, a significant relationship was revealed between high ABG/eAG value and coronary artery disease complexity, in patients with acute coronary syndrome with DM [29].

In another study evaluating the ABG/eAG, the importance of ABG/eAG value in predicting the risk of pneumonia after type A acute aortic dissection operation, which is a cardiovascular emergency, was investigated. In this study, which included 124 patients retrospectively, in addition to prolonged ventilation time, ABG/eAG value was shown as an independent predictor in forecasting postoperative pneumonia [30]. In a multicenter and retrospective study, in which 1631 diabetic patients were included, the relationship between ABG/eAG value and worse outcomes, was shown in patients presenting with a pneumonia clinic [31]. Also, in a retrospective study, 395 patients hospitalized for COVID-19 were examined. Here, ABG/eAG value calculated from admission blood values was shown to be associated with worse outcomes and in-hospital mortality [18].

Unlike this literature information, in our study, we obtained the ABG value from the average of the perioperative blood glucose values that occur due to the operational stress of the patients. We recorded this value as the modified ABG (mABG) value. We showed the mABG/eAG value we calculated together with this value as an independent predictor of the risk of pneumonia, after isolated CABG operation. When we examine the literature, the ABG/eAG value is calculated with the blood glucose value obtained when the patient is exposed to acute stress [27-31]. Our patient group consisted of insulin-dependent diabetic patients who were hospitalized and prepared for elective CABG surgery. We calculated the average of the patient's blood glucose values during the surgery, depending on their response to the surgical stress. Therefore, unlike the literature, we used mABG value instead of ABG value in our study.

In addition, we found re-intubation and increased blood product use as independent predictors of pneumonia risk. The risk of nosocomial pneumonia due to repeated intubation increases. In a study conducted by Perrotti et al., it was revealed that the frequency of pneumonia increased in patients who underwent re-intubation after elective cardiac surgery [32]. During blood product storage, various immunosuppressive substances are transferred from white blood cells

to red blood cells. This immune-modulation state also increases the risk of postoperative infection [33]. In a study by Topal and Eren, increased blood transfusion was shown as an independent predictor in predicting the risk of pneumonia after cardiac surgeries [34].

Our study has several limitations. Our study was designed as a single-center and retrospective study, which were limitations. It was also a limited study among patients undergoing isolated coronary bypass surgery and the relatively small number of patients is another constraint of the study. In conclusion, blood glucose levels may be affected by many factors in CABG operations performed with CPB. In addition, prolonged ventilation and various morbidities in the postoperative period may lead to an increase in blood glucose levels. This is an important limitation of our study. Multicenter prospective studies are needed in which continuous blood glucose monitoring is performed throughout the perioperative period.

CONCLUSION

This study has provided a new perspective by modifying the ABG/eAG value which has recently been used more often to predict disease development. We showed that our modification of mABG/eAG value is an independent predictor of the development of pneumonia, in diabetic patients undergoing coronary bypass surgery. Additionally, when we combined this value with the amount of blood product use, we obtained a stronger predictive value. In line with our results, high-risk patients can be identified by calculating the mABG/eAG value.

Data availability

The data supporting this article will be made available upon reasonable request to the corresponding author.

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TABLES AND FIGURES WITH LEGENDS

TABLE 1. Preoperative features and preoperative laboratory variables of the patients

Variables	Control group (n = 478)	PP group (n = 71)	P value
Age, years	58 (35 - 81)	63 (37 - 86)	<0.001
Female gender, n (%)	156 (32.6)	26 (36.6)	0.506
BMI, kg/m ²	27.3 (21.9 - 43)	27.7 (22.1 - 41)	0.335
Hypertension, n (%)	325 (68)	49 (69)	0.863
COPD, n (%)	79 (16.5)	20 (28.2)	0.017
Smoking, n (%)	98 (20.5)	19 (26.8)	0.230
Hyperlipidemia, n (%)	194 (40.6)	35 (49.3)	0.165
OAD use with insulin, n (%)	189 (39.5)	30 (42.2)	0.663
Ejection fraction, %	50 (25 - 65)	50 (30 - 65)	0.447
White blood cell, 10 ³ /μL	8.8 (4.6 - 11.2)	9.1 (4.1 - 10.7)	0.654
Hemoglobin, mg/dL	13.1 (11 - 16.2)	12.9 (11.4 - 15.7)	0.076
Platelet, 10 ³ /μL	244.8 (137 - 440.9)	251.8 (148 - 390)	0.515
ABG, mg/dL	196 (180 - 390)	200 (176 - 420)	0.121‡
HbA1c, %	7.1 (6.9 - 11.1)	7.2 (6.7 - 10.8)	0.439‡
eAG, mg/dL	159 (149.4 - 269.8)	165 (146 - 255.9)	0.081
Creatinine, mg/dL	1 (0.8 - 1.88)	0.9 (0.7 - 1.91)	0.418
BUN, mg/dL	12 (10 - 34)	14 (8 - 32)	0.196

Albumin, g/dL	4.1 (3.8- 5.3)	4.2 (3.6- 5.2)	0.289
CRP, mg/L	5.7 (0.7- 9)	5.5 (0.6- 11)	0.321

Numerical variables were presented as median (minimum-maximum). BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; BUN: Blood urea nitrogen; CRP: C reactive protein; ABG: Admission blood glucose; HbA1c: Glycated haemoglobin; eAG: Estimated average glucose; OAD: Oral antidiabetic drug.

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TABLE 2. Operative and postoperative features of the patients

Variables	Control group	PP group	P value
	(n = 478)	(n = 71)	
Total perfusion time	92 (55 - 195)	98 (60 - 200)	0.116
Cross-clamp time	54 (25 - 135)	56 (28 - 166)	0.218
CABG number, n (%)	3 (1- 6)	3 (1- 6)	0.675
Packed blood products (units)	4 (3 - 9)	7 (4 - 12)	<0.001
Use of IABP, n (%)	39 (8.2)	14 (19.7)	0.002
Inotropic support, n (%)	101 (21.1)	20 (28.2)	0.182
^a Number of BG measurements	7.2 ± 1.9	7.3 ± 1.8	0.769
mABG	185 (108 - 396)	198 (96 - 342)	0.019
mABG/eAG	1.12 (0.69 - 2.38)	1.34 (0.71- 2.44)	<0.001
Extubation time, hours	6 (4 - 12)	8 (4 - 24)	0.012
Re-intubation, n (%)	6 (1.3)	4 (5.6)	0.029
PoAF, n (%)	95 (19.9)	23 (32.4)	0.017
Mortality, n (%)	9 (1.8)	5 (7)	0.010

^aData was presented as mean ± SD, other numerical variables were presented as median (minimum-maximum). CABG: Coronary artery bypass graft; IABP: Intra-aortic balloon pump;

mABG: Modified admission blood glucose; eAG: Estimated average glucose; PoAF: Postoperative atrial fibrillation; BG: Blood glucose.

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TABLE 3. Logistic regression analysis to identify factors affecting development of postoperative pneumonia

Variables	Univariate analysis			Multivariate analysis		
	<i>P</i>	Exp(B) odds ratio	95% C.I. lower-upper	<i>P</i>	Exp(B) odds ratio	95% C.I. lower-upper
Age > 70 years	0.007	1.347	1.190 - 1.740	0.076	1.685	0.944 - 1.984
COPD	0.022	1.114	1.018 - 1.668	0.218	1.139	0.845 - 1.730
Packed blood products	< 0.001	0.775	0.535 - 0.889	0.027	1.685	1.453 - 1.892
Use of IABP	0.006	0.855	0.537 - 0.971	0.138	1.176	0.989 - 1.296
mABG	0.023	1.648	1.452 - 1.856	--	--	--
mABG/eAG	< 0.001	2.361	1.796 - 4.650	0.019	1.659	1.190 - 2.397
Extubation time, hours	0.019	1.812	1.715 - 1.994	0.285	1.190	0.796 - 1.370
Re-intubation	0.021	1.530	1.250 - 2.194	0.034	1.829	1.656 - 1.945

COPD: Chronic obstructive pulmonary disease; IABP: Intra-aortic balloon pump; mABG: Modified admission blood glucose; eAG: Estimated average glucose.

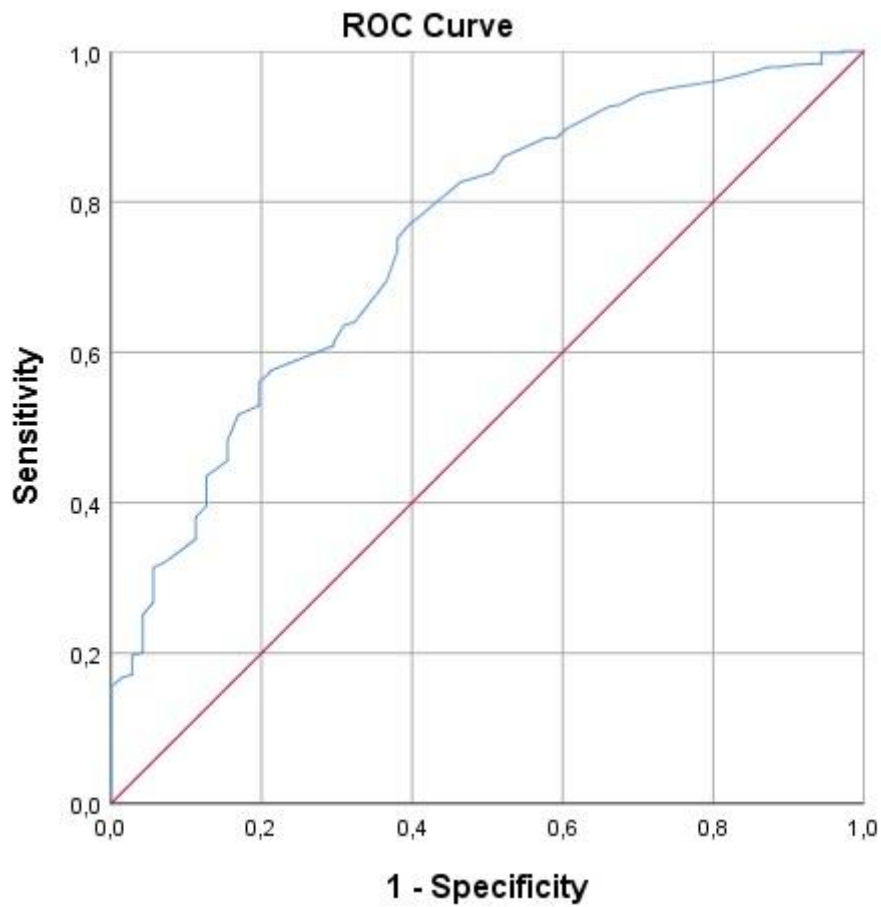


FIGURE 1. Data figure of the area under the curve (AUC), confidence interval (CI), and cut-off values in receiver-operating characteristic (ROC) curve analysis for mABG/eAG value, to predict postoperative in-hospital pneumonia development (cut off = 1.23; AUC = 0.750, 95% CI 0.691 - 0.810; $P < 0.001$, with 75.7% sensitivity and 69.1% specificity).