VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2024, Vol. 31, No. 4, 573–582
DOI: 10.5603/CJ.a2023.0041

ISSN 1897–5593
eISSN 1898–018X

The role of stress hyperglycemia and hyperlactatemia in non-diabetic patients with myocardial infarction treated with percutaneous coronary intervention

Michał Terlecki, Maryla Kocowska-Trytko, Christopher Pavlinec, Aleksandra Ostrowska, Paweł Lis, Adam Bednarski, Wiktoria Wojciechowska, Katarzyna Stolarz-Skrzypek, Marek Rajzer

First Department of Cardiology, Interventional Electrocardiology and Arterial Hypertension, Jagiellonian University Medical College, Institute of Cardiology, Krakow, Poland

Abstract

Background: *Stress hyperglycemia and lactates have been used separately as markers of a severe clinical condition and poor outcomes in patients with myocardial infarction (MI). However, the interplay between glucose and lactate metabolism in patients with MI have not been sufficiently studied. The aim in the present study was to examine the relationship of glycemia on admission (AG) and lactate levels and their impact on the outcome in non-diabetic MI patients treated with percutaneous coronary intervention (PCI).*

Methods: *A total of 405 consecutive, non-diabetic, MI patients were enrolled in this retrospective, observational, single-center study. Clinical characteristic including glucose and lactate levels on admission and at 30-day mortality were assessed.*

Results: *Patients with stress hyperglycemia (AG ≥ 7.8 mmol/L, n = 103) had higher GRACE score (median [interquartile range]: 143.4 [115.4–178.9] vs. 129.4 [105.7–154.5], p = 0.002) than normoglycemic patients (AG level < 7.8 mmol/L, n = 302). A positive correlation of AG with lactate level (R = 0.520, p < 0.001) was observed. The coexistence of both hyperglycemia and hyperlactatemia (lactate level ≥ 2.0 mmol/L) was associated with lower survival rate in the Kaplan-Meier estimates (p < 0.001). In multivariable analysis both hyperglycemia and hyperlactatemia were related to a higher risk of death at 30-day follow-up (hazard ratio [HR] 3.21, 95%, confidence interval [CI] 1.04–9.93; p = 0.043 and HR 7.08; 95% CI 1.44–34.93; p = 0.016, respectively).*

Conclusions: *There is a relationship between hyperglycemia and hyperlactatemia in non-diabetic MI patients treated with PCI and both markers are independent predictors of 30-day mortality. Moreover the coexistence of hyperglycemia and hyperlactatemia decreases survival much more than each factor separately then should be evaluated simultaneously.* (Cardiol J 2024; 31, 4: 573–582)

Keywords: hyperglycemia, lactates, myocardial infarction

Address for correspondence: Marek Rajzer, MD, PhD, First Department of Cardiology, Interventional Electrocardiology and Arterial Hypertension, Jagiellonian University Medical College, ul. Jakubowskiego 2, 30–688 Kraków, Poland, tel: +48 12 400 21 50, e-mail: marek.rajzer@uj.edu.pl

Received: 26.01.2023 Accepted: 12.05.2023 Early publication date: 20.06.2023

Introduction

Stress hyperglycemia, defined as a transient elevation of blood-glucose concentrations in the acute phase of the disease, e.g., in sepsis, brain trauma or stroke, is a well-known marker of a poor outcome among critically-ill patients [1–7]. The occurrence and level of stress hyperglycemia reflects the range of a body-stress reaction during the acute phase of a severe disease [8]. The above-mentioned observations were an inspiration to conduct interventional studies on the influence of strict glycemic control and intensive hypoglycemic therapy on the outcome of critically-ill patients. Disappointingly, in many studies including NICE-SUGAR [9], it has not been proven that interventions aimed at lowering glucose levels led to a reduction in the mortality of intensive-care-unit patients. These findings have some clinical implications — stress hyperglycemia cannot be considered as a common parameter which improves a patient's state when it is well-controlled. It should be considered as a marker of the disease severity and there is likely an additional pathomechanism related to stress hyperglycemia.

There are several studies confirming that stress hyperglycemia is observed in patients with myocardial infarction (MI), and it is proven to be a marker of a worse prognosis in this group of patients [10–14]. Some researchers underline that among patients with MI, hyperglycemia at admission is a marker of a worse outcome irrespective of diabetic status and it may even be more pronounced in patients without diabetes [3, 10, 13, 15].

Hyperlactatemia is another prognostic marker among critically-ill patients [16, 17], with multiorgan trauma [18], sepsis [17, 19] or in patients with acute cardiac conditions including MI [20]. Previous studies have shown that in MI patients, the higher the blood lactate level, the higher the risk of in-hospital death at 30-day follow up [21–23].

There are some pathophysiological premises indicating that abnormal glucose accumulation could be at least in part due to the elevated lactates levels because excess lactates observed in critically-ill patients may be eliminated by oxidation to pyruvate or may be transformed into glucose by gluconeogenesis or into glucagon via the Cori cycle [24]. It is possible that stress hyperglycemia and hyperlactatemia may be dependent on each other as indicators of the same phenomenon. However, there are very few studies evaluating the association of stress hyperglycemia with hyperlactatemia and how early lactate and glucose levels correlate with the outcome in critically-ill patients [25–29]. According to available research, this relationship has not yet been explored in patients with MI. Thus, it was decided to conduct the current study to examine the interplay between lactatemia and stress hyperglycemia in non-diabetic MI patients treated with percutaneous coronary intervention (PCI). It was hypothesized that in critically-ill patients with MI, both parameters coexist and are closely correlated. Moreover, it may be possible that hyperlactatemia may also impact the relationship between stress hyperglycemia and a worse prognosis among patients with MI.

Methods

Medical records of consecutive non-diabetic patients who were admitted to a PCI-capable Cardiology Department at University Hospital, Krakow, Poland were retrospectively analyzed between January 1, 2016, and December 31, 2019, with MI treated with PCI and standard medical therapy according to the European Society of Cardiology (ESC) guidelines [30, 31]. To avoid the influence of diabetes and hypoglycemic treatment on the results obtained, patients with diabetes (with a prior history or *de novo*) were excluded from this study (Fig. 1). Blood samples were obtained directly on admission in each patient and basic laboratory results including serum lactate level and glucose level were measured.

Myocardial infarction is a heterogeneous disease with various clinical presentations (including both relatively stable but also unstable, life-threatening conditions such as pulmonary edema or cardiogenic shock) and different electrocardiographic manifestations (ST segment elevation MI [STEMI] or non-ST segment elevation MI [NSTEMI]), thus, it was decided to include both STEMI and NSTEMI patients. The diagnosis of MI was based on the criteria set forth by the most current ESC guidelines [30, 31]. Lactate levels and glucose levels were measured using an ABL90 FLEX analyzer (Radiometer, Copenhagen, Denmark) from blood samples obtained directly after admission to hospital (within a few minutes). Stress hyperglycemia was defined as serum glucose levels on admission ≥ 7.8 mmol/L and hyperlactatemia as serum lactate level on admission ≥ 2.0 mmol/L. The same blood sample was used to obtain other biochemical parameters: i.e.: high sensitive troponin I (hsTnI) and creatinine. Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula [32]. Heart

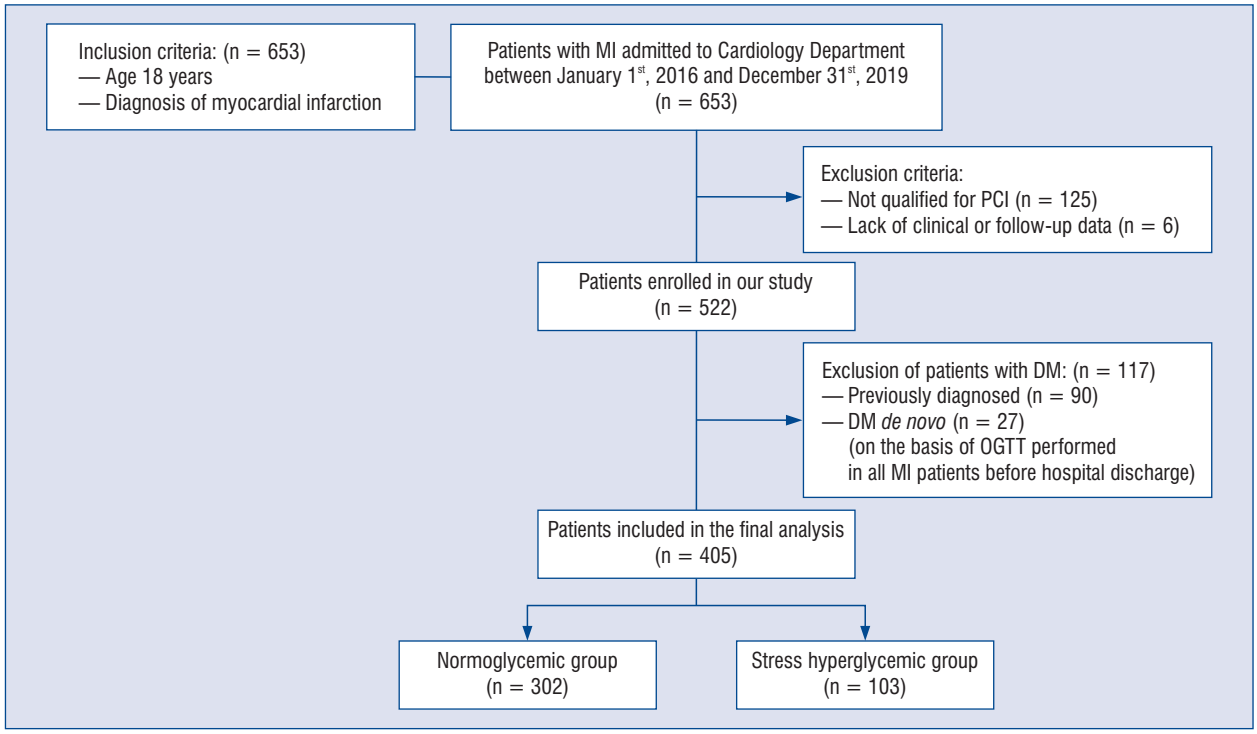


Figure 1. Flow chart of patient inclusion; DM — diabetes mellitus; MI — myocardial infarction, OGTT — oral glucose tolerance test; PCI — percutaneous coronary intervention

rate, arterial blood pressure, Killip class and Global Registry of Acute Coronary Events (GRACE) risk scores were assessed in all patients on admission [33]. Thrombolysis In Myocardial Infarction (TIMI) coronary flow grade score was evaluated before and after PCI [34]. After the analysis of serial creatinine measurements during their hospital stay, the occurrence of renal function worsening was assessed and defined as lowering of glomerular filtration rate by at least 30% compared to admission values. Based on data obtained from the Universal Electronic System for Registration of the Population in Poland, the occurrence of death from all causes at 30 days from the admission to the hospital was evaluated for all study participants.

Statistical analysis

Categorical variables were presented as numbers and percentages. Continuous variables were expressed as means and standard deviation (SD) or medians and interquartile range (IQR). Normality was assessed by the Shapiro–Wilk test. Equality of variances was assessed using Levene's test. The study's population was divided into two groups according to their glucose levels on admission (normoglycemia group: < 7.8 mmol/L, hyperglycemia group: ≥ 7.8 mmol/L). Differences between groups were compared using the Student or Welch t-test depending on the equality of variances for normally distributed variables. The Mann-Whitney U-test was used for non-normally distributed continuous variables. Ordinal variables were compared using the Cochran–Armitage test for trend. Categorical variables were compared by the Pearson χ^2 test or by the Monte Carlo simulation for the Fisher test if 20% of cells had an expected count of less than 5. The Spearman Rank correlation coefficient was calculated to measure the monotonic trend between two variables. Multivariable logistic regression was used for searching possible covariates of the likelihood of hyperlactatemia (lactates level on admission ≥ 2.0 mmol/L). Then odds ratios (OR) and corresponding 95% confidence intervals (95% CI) were calculated for possible covariates influencing the occurrence of hyperlactatemia. To analyze event-free survival in the groups according to their glucose and lactate levels, Kaplan-Meier curves were generated. The log-rank statistic was used to test for the differences in outcomes between the groups. Additionally, univariable and multivariable Cox proportional hazard analyses were performed to identify independent predictors of mortality. The variables used in the univariable analyses were selected as potential risk factors based

on their clinical relevance for death at a 30-day follow-up period. The variables selected for the final multivariable model had to be clinically significant and associated with an increased risk of 30-day mortality during the univariable analyses (p-value < 0.05). The variables entered into the Cox regression model were demographic and clinical variables including sex, body mass index, STEMI, MI in their history, arterial hypertension, smoking, left ventricular ejection fraction (LVEF), hyperglycemia (glucose on admission ≥7.8 mmol/L), hyperlactatemia (lactates on admission ≥ 2.0 mmol/L), post-procedural TIMI flow grade 0–2, time from pain to hospital admission and GRACE score [35]. Due to the fact that some variables (age, cardiac arrest before admission, eGFR on admission, Killip class, heart rate on admission, systolic blood pressure on admission, the presence of ST segment deviation on electrocardiogram on admission and abnormal results of cardiac hsTnI on admission) were used to calculate the GRACE scores, only GRACE score was included in the final multivariable analysis (instead of the above-mentioned variables). The results are presented as hazard ratios (HR) with 95% CI. The proportional hazards model assumptions were checked using Schoenfeld test and graphical diagnostics. Statistical analyses were performed with JMP®, Version 14.2.0 (SAS Institute INC., Cary, NC, USA) and using R, Version 3.4.1 (R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, 2017, https://www.r-project.org/).

Results

The present study group consisted of 405 patients (72.8% males), with MI. The mean (SD) age was 65.70 (12.21) years. There were 183 (45.2%) STEMI and 222 (54.8%) NSTEMI patients. Arterial hypertension (70.4%) was the predominant coexisting disease. There were 44 (10.9%) patients with Killip class 3 or 4. Cardiac arrest before admission occurred in 20 (4.9%) subjects. Median (IQR) time from pain to hospital admission was 663,0 (182.0––792.0) min. Median (IQR) GRACE score was 131.8 (107.8–160.9), median (IQR) LVEF 48.0% (38.0–55.0). Left main coronary artery (LMCA) was an infarct related artery in 13 (3.2%) patients and 177 (43.7%) subjects had multi-vessel disease. In 19 (4.7%) patients TIMI 0 persisted after PCI and the 30-day mortality rate was 5.4% (n = 22).

There were 302 patients with a glucose level < 7.8 mmol/L (normoglycemia group), and 103 patients with ≥ 7.8 mmol/L (hyperglycemia group). Patients with higher glucose levels were older, were more frequently non-smokers and in more severe general clinical conditions (lower blood pressure, higher Killip class, higher GRACE score and more frequently had out-of-hospital cardiac arrest before admission). Higher lactate levels (reference range < 2.0 mmol/L) were noticed in patients with higher glucose levels on admission (Table 1).

The location of the culprit-related artery in angiography was similar in both groups with the only exception: LMCA was the more frequent culprit-related artery in patients with hyperglycemia when compared to the normoglycemia group. Occurrence of TIMI 0–2 after PCI was similar in both groups while a worsening of kidney function and the need for mechanical ventilation occurred more often in the hyperglycemia group than in the normoglycemia group. Lower frequency rate of beta-blocker and higher catecholamines use was observed in hyperglycemic group in comparison to normoglycemic group. Patients with higher glucose levels (hyperglycemia group) had a significantly higher 30-day mortality rate (Table 2).

Significant correlations between GRACE scores, glucose levels and lactate levels at admission were observed and there was a significant positive correlation with glucose and lactate levels as seen in Figure 2.

In a multivariable logistic regression model (including Killip class, STEMI, GRACE score, age, LVEF, out of hospital cardiac arrest and hyperglycemia), it was determined that the severity of the clinical state on admission (assessed by Killip class) and hyperglycemia observed on admission were significantly associated, after adjustment, with hyperlactatemia (lactates ≥ 2 mmol/L) (Fig. 3). In comparison to the survivors, the patients who died prior to the 30-day follow-up period had significantly higher admission glucose levels (median [IQR], 9.7 [7.5–13.0] vs. 6.6 [5.8–7.6] mmol/L, p < 0.001) and admission lactates (median [IQR], 4.4 [2.1–8.6] vs. 1.5 [1.1–2.0], p < 0.001) (Fig. 4).

The Kaplan-Meier estimate showed that patients with coexisting stress hyperglycemia and hyperlactatemia had the lowest survival rate in comparison to patients with either normal lactate levels (both normoglycemic and hyperglycemic groups) or hyperlactatemia with normoglycemia (Fig. 5).

The Cox proportional hazards model was constructed to evaluate the contribution of the studied parameters — glucose and lactate levels

Table 1. Baseline characteristics according to glycemic status on admission

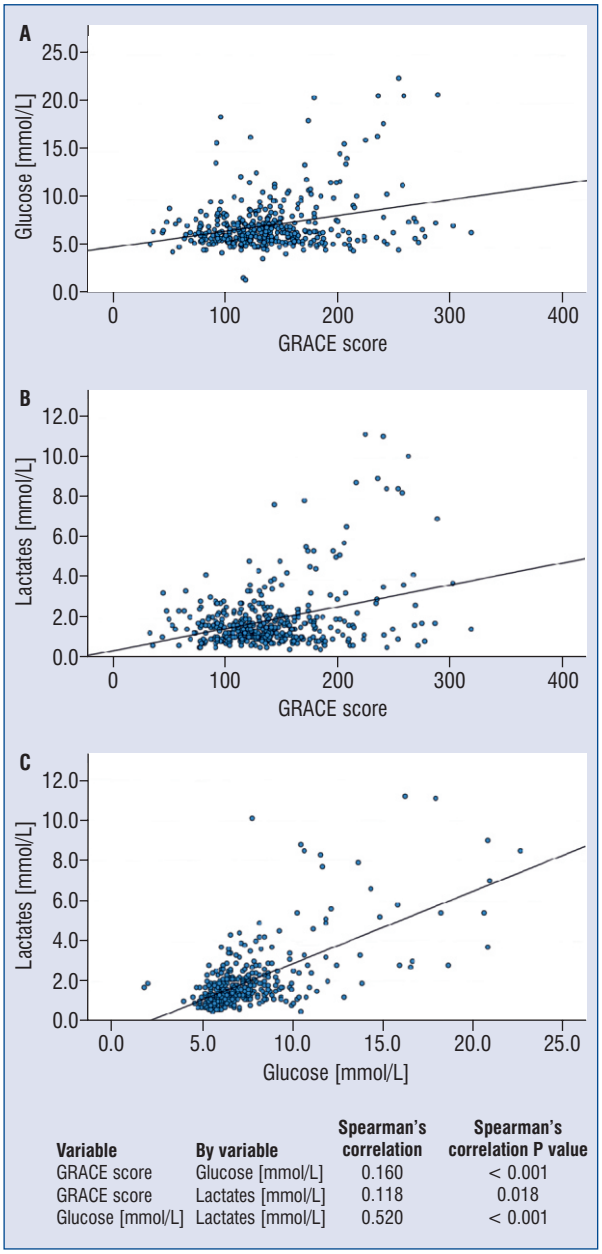
	Normoglycemia (glucose < 7.8 mmol/L), n = 302 (74.6%)	Hyperglycemia (glucose ≥ 7.8 mmol/L), n = 103 (25.4%)	P
Age [years]	64.8 (11.9)	68.5 (12.6)	0.007
Male	232 (76.8%)	63 (61.2%)	0.002
BMI [kg/m^2]*	27.5 (4.3)	27.7 (4.9)	0.68
STEMI	134 (44.4%)	49 (47.6%)	0.33
Cardiac arrest before admission	5 (1.7%)	15 (14.6%)	< 0.001
MI in the history	65 (21.5%)	22 (21.4%)	0.55
Arterial hypertension	206 (68.2%)	79 (76.7%)	0.07
Smoking	119 (39.4%)	26 (25.2%)	0.006
Atrial fibrillation	29 (9.6%)	19 (18.4%)	0.049
LVEF [%]**	45.9 (12.2)	43.0 (13.3)	0.06
Heart rate [min^{-1}]	80.0 (16.8%)	79.7 (18.8%)	0.86
Systolic BP [mmHg]	143.0 (127.0–160.0)	139 (119.0–152.0)	0.003
Diastolic BP [mmHg]	80.0 (71.3–90.0)	78.0 (64.5–90.0)	0.001
Glucose [mmol/L]	6.2 (5.6–6.8)	9.3 (8.4–11.6)	< 0.001
Troponin I hs [umol/L]	9296.14 (9247.56)	8393.59 (9271.13)	0.63
eGFR [mL/min/1.73 m^2]	94.6 (33.8)	86.5 (34.1)	0.04
Lactates [mmol/L]	1.4 (1.0–1.8)	2.3 (1.5–3.7)	< 0.001
Killip 3 or 4	19 (6.3%)	25 (24.3%)	< 0.001
GRACE score [points]	129.4 (105.7–154.5)	143.4 (115.4–178.9)	0.002
Time from pain to hospital admission [min]	360 (145–713)	255 (131–410)	0.477

Continous data are presented as mean (standard deviation) or median (interquartile range) unless indicated otherwise; *Data available for 247 patients with normoglycemia and 76 with hyperglycemia; **Data available for 298 patients with normoglycemia and 103 with hyperglycemia; BMI — body mass index; BP — blood pressure; eGFR — estimated glomerular filtration rate; GRACE — Global Registry of Acute Coronary Events; LVEF — left ventricular ejection fraction; MI — myocardial infarction; STEMI — ST-segment elevation myocardial infarction

Table 2. Angiography results, in-hospital drug therapy and patient outcome according to glycemic status on admission

	Normoglycemia (glucose < 7.8 mmol/L), n = 302 (74.6%)	Hyperglycemia (glucose ≥ 7.8 mmol/L), n = 103 (25.4%)	P
LMCA as IRA	6 (2.0%)	7 (6.8%)	0.03
LAD as IRA	109 (36.1%)	43 (41.7%)	0.18
Cx as IRA	71 (23.5%)	23 (22.3%)	0.46
RCA as IRA	102 (33.8%)	32 (31.1%)	0.35
Multivessel disease	129 (42.7%)	48 (46.6%)	0.28
Post-procedural TIMI flow grade 0–2	24 (7.9%)	17 (16.5%)	0.013
ACEI/ARB	269 (89.1%)	89 (87.3%)	0.47
Beta-blockers	267 (88.4%)	78 (76.5%)	0.002
Statins	284 (94.0%)	91 (89.2%)	0.10
MRA	57 (18.9%)	31 (30.4%)	0.02
Calcium blockers	49 (16.2%)	14 (13.7%)	0.52
Glycoprotein IIb/IIIa inhibitors	36 (11.9%)	15 (14.7%)	0.49
Catecholamines	22 (7.3%)	35 (34.3%)	< 0.001
Worsening of kidney function	44 (14.6%)	27 (26.2%)	0.007
Mechanical ventilation	7 (2.3%)	22 (21.4%)	< 0.001
Death from any cause within 30 days since admission	7 (2.3%)	15 (14.6%)	< 0.001

ACEI — angiotensin-converting enzyme inhibitors; ARB — angiotensin receptor blockers; Cx — left circumflex artery; IRA — infarct related artery, LAD — left anterior descending artery; LMCA — left main coronary artery; MRA — mineralocorticoid receptor antagonists; RCA — right coronary artery; TIMI — thrombolysis in myocardial infarction



Variable	By variable	Spearman's correlation	Spearman's correlation P value
GRACE score	Glucose [mmol/L]	0.160	< 0.001
GRACE score	Lactates [mmol/L]	0.118	0.018
Glucose [mmol/L]	Lactates [mmol/L]	0.520	< 0.001

Figure 2. A–C. The correlation between glucose, lactate and Global Registry of Acute Coronary Events (GRACE) score

— on the prognosis measured at 30-day mortality. In multivariable analysis both hyperglycemia and hyperlactatemia next to GRACE score were independently associated with an increased risk of death in 30-day follow up (Table 3).

Discussion

In the current study, it was confirmed that in non-diabetic MI patients treated with PCI, stress hyperglycemia at admission is a marker of worse clinical outcome. Moreover, it was found that increased glucose levels were positively correlated to lactate levels. It was also confirmed that the severity of the patient's state at admission and higher glucose levels are associated with a higher probability of the occurrence of hyperlactatemia. The coexistence of both hyperglycemia and hyperlactatemia is associated with lower survival rate at 30-day follow-up and in multivariable analysis, both hyperglycemia and hyperlactatemia remained independent predictors of higher mortality.

Despite the pathophysiological rationale indicating that hyperglycemia may be directly linked to lactate metabolism, only a few papers evaluated the simultaneous relationship of hyperglycemia and hyperlactatemia in critically-ill patients [25–29] and according to available research, there are no studies assessing this phenomenon in patients with MI treated with PCI. Stress hyperglycemia is associated with hyperlactatemia in critically-ill patients including patients with MI via several mechanisms. It appears that in patients with MI with varying degrees of circulatory compromise, an increased blood lactate concentration is related to its increased production [18]. Classically, increased lactate production is explained by dysoxia at the tissue level, which leads to anaerobic glycolysis and consequent lactate production [18]. On the other hand, there are indications that lactate formation can also manifest even in the absence of dysoxia, such as after catecholamine release in response to a stressful stimulus (in this case — MI) or other factors (ex.: triggered in a similar mechanism by an inflammatory response cascade) stimulating Na^+/K^+ adenosine triphosphatase activity, which in turn, augments glycogenolysis [18, 36]. The increased hepatic glycogenolysis and gluconeogenesis observed during MI (which represents a degree of hypermetabolic stress for the body), impaired insulin secretion by pancreatic cells, increased insulin resistance and reduced glucose consumption in the periphery are mechanisms that attenuate glucose-lactate cycling and lead to an increased lactate production resulting in hyperlactatemia. Subsequently, accumulated lactates can be cleared by oxidation to pyruvate or transformed into glucose by gluconeogenesis or into glycogen via the Cori cycle [24]. Hyperlactatemia appears to inhibit glucose uptake by muscle cells and decrease activity of the GLUT-4 transporters, resulting in hyperglycemia [37]. Hyperlactatemia has also been shown to increase insulin resistance directly [38]. Revelly et al. [18] conducted a study in which they evaluated the relationship of lactate

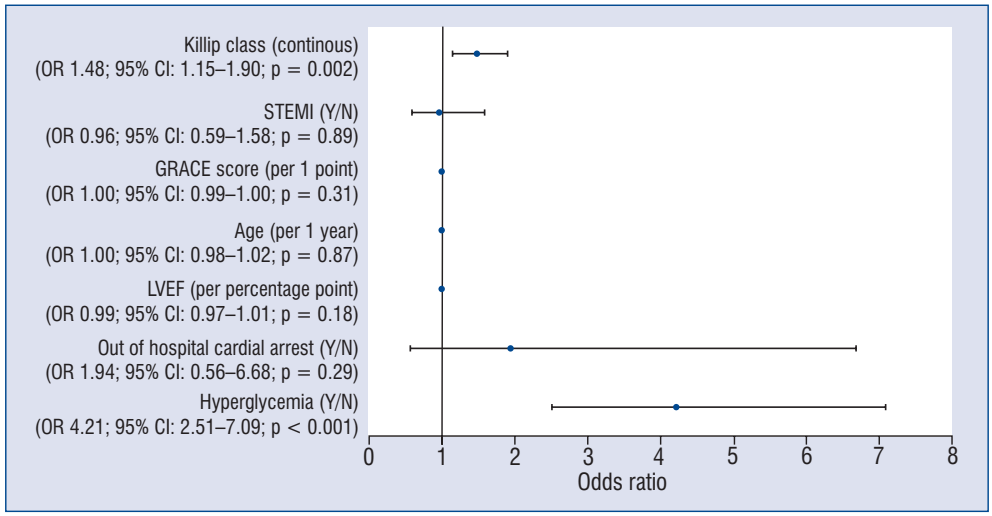


Figure 3. Multivariable logistic regressions demonstrating the adjusted odds ratio for diagnosis of hyperlactatemia (lactates levels ≥ 2.0 mmol/L); GRACE — Global Registry of Acute Coronary Events; LVEF — left ventricular ejection fraction; OR — odds ratio; STEMI — ST segment-elevation myocardial infarction; N — no; Y — yes

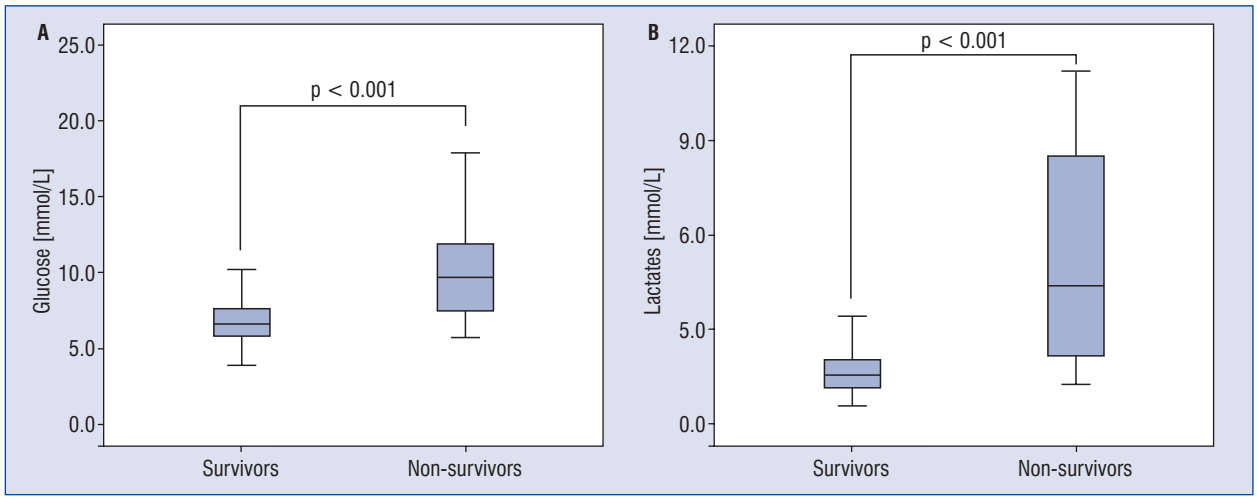


Figure 4. Glucose (**A**), lactate (**B**) levels in the comparison between survivors and non-survivors at a 30-day follow-up. Boxes represent the median and the 25–75th percentile

and glucose levels in cardiogenic shock by infusing radiolabeled lactate and glucose into critically-ill adults and healthy volunteers. They showed that increased production of lactate was concomitant to markedly increased glucose turnover, which they considered the main cause that contributed to the hyperlactatemia in this group of patients [18]. This investigation was experimental in which 7 patients in cardiogenic shock were included. In the present observational study in which 26 (6.4%) patients had Killip 4, it was confirmed that a severe clinical condition and increasing glycemic levels are factors that increase the likelihood of hyperlactatemia.

Based on the present results, it was confirmed that the coexistence of both hyperglycemia and hyperlactatemia is associated with lower survival rate at a 30-day follow-up and in multivariable analysis, both hyperglycemia and hyperlactatemia remained independent predictors of higher mortality. Observations herein, are consistent with prior literature [28, 39]. It is believed, based on the results, that such a correlation is further evidence that glycemia and lactate share a common metabolic pathway as a function of carbohydrate metabolism and can be explained by the fact that during an increased stress response, such as MI, hyperglycemia reflects not

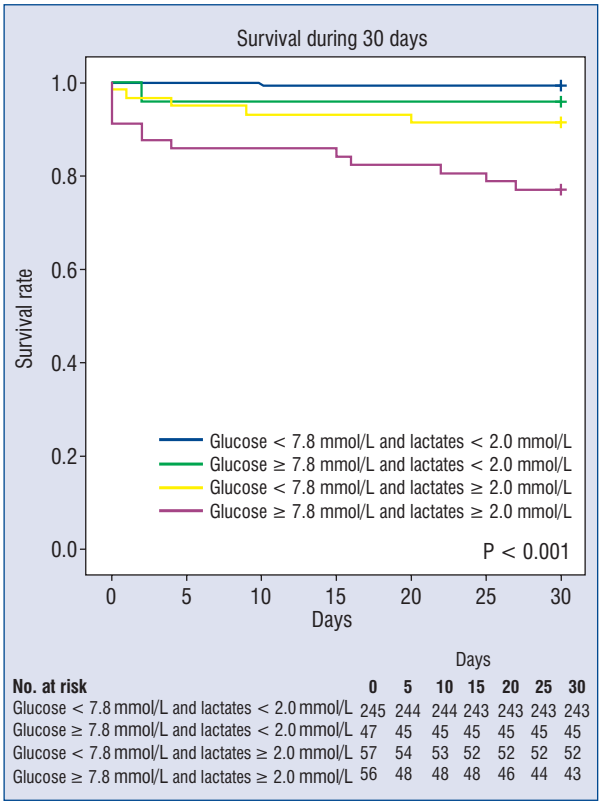


Figure 5. The Kaplan-Meier curve displaying proportional survival rate in 30 day follow-up stratified by glucose and lactate levels on admission

only an increased adrenergic response via altered gluconeogenesis but also by increased lactate production. It should be noted once again that most previous investigations had only analyzed hyperglycemia and hyperlactatemia separately, without considering both parameters simultaneously.

The conclusions of the current study further explains the reasons for the failure of the NICE sugar trial [9]. Stress hyperglycemia cannot be considered as a simple parameter which can reduce mortality risk when it is being tightly controlled in a critically-ill patient. It is postulated herein, that interventions directed to the prevention of an excessive increase in lactate levels are of crucial importance in this population. In the case of MI patients, this includes effective revascularization without unnecessary delay, a more prompt introduction of medications to optimize cardiac output or improvement of oxygen delivery to tissues (catecholamines, diuretics, or fluid supplementation, oxygen therapy, correction of hemoglobin level, etc.).

The results of the present study have some clinical implications. Among patients with MI, there is a whole range of clinical situations when risk stratification is not straightforward, e.g.: especially in patients with NSTEMI, electrocardiography has

Table 3. Univariable and multivariable Cox regression model assessing the risk of death at a 30-day follow-up

Variable	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P
Male sex	0.99 (0.39–2.54)	0.99		
STEMI	5.64 (1.91–16.66)	< 0.001	3.70 (1.00–13.72)	0.05
MI in the history	0.81 (0.28–2.40)	0.71		
Arterial hypertension	0.89 (0.36–2.19)	0.81		
Smoking	0.39 (0.13–1.16)	0.08		
Time from pain to hospital admission (per 10 min)	0.98 (0.96–1.01)	0.23		
LVEF (per 1%)	2.84 (1.05–7.69)	0.03	0.97 (0.93–1.01)	0.10
Hyperglycemia (glucose on admission ≥ 7.8 mmol/L)	6.62 (2.70–16.25)	< 0.001	3.21 (1.04–9.93)	0.043
Troponin I hs (per 50 umol/L)	0.99 (0.99–1.00)	0.37		
Hyperlactatemia (lactates on admission ≥ 2.0 mmol/L)	15.47 (4.58–52.27)	< 0.001	7.08 (1.44–34.93)	0.016
Post-procedural TIMI flow grade 0–2	10.17 (4.40–23.48)	< 0.001	2.26 (0.70–7.24)	0.17
GRACE score (per 1 point)	1.03 (1.02–1.03)	< 0.001	1.02 (1.005–1.03)	0.003

CI — confidence interval; GRACE — Global Registry of Acute Coronary Events; HR — hazard ratio; LVEF — left ventricular ejection fraction; MI — myocardial infarction; TIMI — Thrombolysis in Myocardial Infarction; STEMI — ST-segment elevation myocardial infarction

insufficient sensitivity and specificity [40, 41] and risk scales e.g.: GRACE are time-consuming. In these situations, laboratory markers can be utilized to allow for a more prompt and streamlined approach to triage patients with suspected MI and to screen those with a higher risk of mortality. Due to the increased availability of point of care analyzers which have been tested and confirmed to be reliable in multiple previous investigations [42–44], the screening for glucose and lactate levels at admission should be encouraged and is an "easy-to-obtain" method to aid in risk stratification. As demonstrated in this investigation, even seemingly stable patients at admission may quickly deteriorate if hyperglycemia and hyperlactatemia are found, meaning these blood tests could serve as markers of organ hypoprivation and indicate a need for more decisive intervention.

Limitations of the study

There are several limitations in this study. Firstly, this study was a single-center observational, retrospective study. This data collection method is prone to misclassification and selection bias. Additionally, it cannot be excluded that, at least theoretically, other confounding factors could exist, which would modify the association between glucose and lactates and would impact on their relationship with increased mortality risk. However, the correlations cited and the common metabolic pathways shared by glucose and lactate metabolism are so significant that the possible influence of other factors on the results obtained seem to be insignificant. Additionally, the present analysis was conducted before the severe acute respiratory syndrome coronavirus 2 infection era, thus, the potential relationship between stress hyperglycemia, lactates and the outcome among patients with MI affected by COVID-19 was not assessed.

Conclusions

There is a relationship between hyperglycemia and hyperlactatemia in non-diabetic MI patients treated with PCI and both markers are independent predictors of 30-day mortality. Moreover the coexistence of hyperglycemia and hyperlactatemia decreases survival much more than each factor separately then should be evaluated simultaneously.

Conflict of interest: None declared.

References

1. Godinjak A, Iglica A, Burekovic A, et al. Hyperglycemia in critically ill patients: management and prognosis. Med Arch. 2015; 69(3): 157–160, doi: 10.5455/medarh.2015.69.157-160, indexed in Pubmed: 26261382.
2. Falciglia M, Freyberg RW, Almenoff PL, et al. Hyperglycemia-related mortality in critically ill patients varies with admission diagnosis. Crit Care Med. 2009; 37(12): 3001–3009, doi: 10.1097/CCM.0b013e3181b083f7, indexed in Pubmed: 19661802.
3. Umpierrez GE, Isaacs SD, Bazargan N, et al. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. J Clin Endocrinol Metab. 2002; 87(3): 978–982, doi: 10.1210/jcem.87.3.8341, indexed in Pubmed: 11889147.
4. Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. Mayo Clin Proc. 2003; 78(12): 1471–1478, doi: 10.4065/78.12.1471, indexed in Pubmed: 14661676.
5. Whitcomb BW, Pradhan EK, Pittas AG, et al. Impact of admission hyperglycemia on hospital mortality in various intensive care unit populations. Crit Care Med. 2005; 33(12): 2772–2777, doi: 10.1097/01.ccm.0000189741.44071.25, indexed in Pubmed: 16352959.
6. Laird AM, Miller PR, Kilgo PD, et al. Relationship of early hyperglycemia to mortality in trauma patients. J Trauma. 2004; 56(5): 1058–1062, doi: 10.1097/01.ta.0000123267.39011.9f, indexed in Pubmed: 15179246.
7. Rovlias A, Kotsou S. The influence of hyperglycemia on neurological outcome in patients with severe head injury. Neurosurgery. 2000; 46(2): 335–42; discussion 342, doi: 10.1097/00006123-200002000-00015, indexed in Pubmed: 10690722.
8. Little RA, Frayn KN, Randall PE, et al. Plasma catecholamines in the acute phase of the response to myocardial infarction. Arch Emerg Med. 1986; 3(1): 20–27, doi: 10.1136/emj.3.1.20, indexed in Pubmed: 3524599.
9. Finfer S, Chittock DR, Su SYS, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009; 360(13): 1283–1297, doi: 10.1056/NEJMoa0810625, indexed in Pubmed: 19318384.
10. Capes SE, Hunt D, Malmberg K, et al. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet. 2000; 355(9206): 773–778, doi: 10.1016/S0140-6736(99)08415-9, indexed in Pubmed: 10711923.
11. Sanjuán R, Núñez J, Blasco ML, et al. Prognostic implications of stress hyperglycemia in acute ST elevation myocardial infarction. Prospective observational study. Rev Esp Cardiol. 2011; 64(3): 201–207, doi: 10.1016/j.recesp.2010.08.002, indexed in Pubmed: 21330037.
12. Angeli F, Verdecchia P, Karthikeyan G, et al. New-onset hyperglycemia and acute coronary syndrome: a systematic overview and meta-analysis. Curr Diabetes Rev. 2010; 6(2): 102–110, doi: 10.2174/157339910790909413, indexed in Pubmed: 20034367.
13. Dziewierz A, Giszterowicz D, Siudak Z, et al. Admission glucose level and in-hospital outcomes in diabetic and non-diabetic patients with acute myocardial infarction. Clin Res Cardiol. 2010; 99(11): 715–721, doi: 10.1007/s00392-010-0175-1, indexed in Pubmed: 20458486.

14. Sala J, Masiá R, González de Molina FJ, et al. Short-term mortality of myocardial infarction patients with diabetes or hyperglycaemia during admission. J Epidemiol Community Health. 2002; 56(9): 707–712, doi: 10.1136/jech.56.9.707, indexed in Pubmed: 12177090.
15. Gasior M, Stasik-Pres G, Pres D, et al. Relationship between blood glucose on admission and prognosis in patients with acute myocardial infarction treated with percutaneous coronary intervention. Kardiol Pol. 2007; 65(9): 1031–1039, indexed in Pubmed: 17975750.
16. Jansen TC, van Bommel J, Bakker J. Blood lactate monitoring in critically ill patients: a systematic health technology assessment. Crit Care Med. 2009; 37(10): 2827–2839, doi: 10.1097/CCM.0b013e3181a98899, indexed in Pubmed: 19707124.
17. Shapiro NI, Howell MD, Talmor D, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med. 2005; 45(5): 524–528, doi: 10.1016/j.annemergmed.2004.12.006, indexed in Pubmed: 15855951.
18. Revelly JP, Tappy L, Martinez A, et al. Lactate and glucose metabolism in severe sepsis and cardiogenic shock. Crit Care Med. 2005; 33(10): 2235–2240, doi: 10.1097/01.ccm.0000181525.99295.8f, indexed in Pubmed: 16215376.
19. Howell MD, Donnino M, Clardy P, et al. Occult hypoperfusion and mortality in patients with suspected infection. Intensive Care Med. 2007; 33(11): 1892–1899, doi: 10.1007/s00134-007-0680-5, indexed in Pubmed: 17618418.
20. Attanà P, Lazzeri C, Picariello C, et al. Lactate and lactate clearance in acute cardiac care patients. Eur Heart J Acute Cardiovasc Care. 2012; 1(2): 115–121, doi: 10.1177/2048872612451168, indexed in Pubmed: 24062898.
21. Frydland M, Møller JE, Wiberg S, et al. Lactate is a prognostic factor in patients admitted with suspected st-elevation myocardial infarction. Shock. 2019; 51(3): 321–327, doi: 10.1097/SHK.0000000000001191, indexed in Pubmed: 30286032.
22. Lazzeri C, Valente S, Chiostri M, et al. Lactate in the acute phase of ST-elevation myocardial infarction treated with mechanical revascularization: a single-center experience. Am J Emerg Med. 2012; 30(1): 92–96, doi: 10.1016/j.ajem.2010.10.008, indexed in Pubmed: 21109381.
23. Vermeulen RP, Hoekstra M, Nijsten MWn, et al. Clinical correlates of arterial lactate levels in patients with ST-segment elevation myocardial infarction at admission: a descriptive study. Crit Care. 2010; 14(5): R164, doi: 10.1186/cc9253, indexed in Pubmed: 20825687.
24. Barth E, Albuszies G, Baumgart K, et al. Glucose metabolism and catecholamines. Crit Care Med. 2007; 35(9 Suppl): S508–S518, doi: 10.1097/01.CCM.0000278047.06965.20, indexed in Pubmed: 17713401.
25. Kaukonen KM, Bailey M, Egi M, et al. Stress hyperlactatemia modifies the relationship between stress hyperglycemia and outcome: a retrospective observational study. Crit Care Med. 2014; 42(6): 1379–1385, doi: 10.1097/CCM.0000000000000214, indexed in Pubmed: 24561567.
26. Freire Jorge P, Wieringa N, de Felice E, et al. The association of early combined lactate and glucose levels with subsequent renal and liver dysfunction and hospital mortality in critically ill patients. Crit Care. 2017; 21(1): 218, doi: 10.1186/s13054-017-1785-z, indexed in Pubmed: 28826408.
27. Chen X, Bi J, Zhang J, et al. The impact of serum glucose on the predictive value of serum lactate for hospital mortality in critically ill surgical patients. Dis Markers. 2019; 2019: 1578502, doi: 10.1155/2019/1578502, indexed in Pubmed: 31885730.
28. Green JP, Berger T, Garg N, et al. Hyperlactatemia affects the association of hyperglycemia with mortality in nondiabetic adults with sepsis. Acad Emerg Med. 2012; 19(11): 1268–1275, doi: 10.1111/acem.12015, indexed in Pubmed: 23167858.
29. Sotello D, Yang S, Nugent K. Glucose and lactate levels at admission as predictors of in-hospital mortality. Cureus. 2019; 11(10): e6027, doi: 10.7759/cureus.6027, indexed in Pubmed: 31824794.
30. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018; 39(2): 119–177, doi: 10.1093/eurheartj/ehx393, indexed in Pubmed: 28886621.
31. Collet JP, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021; 42: 1289–1367, doi: 10.1093/eurheartj/ehaa575, indexed in Pubmed: 32860058.
32. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006; 145: 247–254, doi: 10.7326/0003-4819-145-4-200608150-00004, indexed in Pubmed: 16908915.
33. Fox KAA, Dabbous OH, Goldberg RJ, et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). BMJ. 2006; 333(7578): 1091, doi: 10.1136/bmj.38985.646481.55, indexed in Pubmed: 17032691.
34. Chesebro JH, Knatterud G, Roberts R, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation. 1987; 76(1): 142–154, doi: 10.1161/01.cir.76.1.142, indexed in Pubmed: 3109764.
35. Hosmer D, Lamesow S. Applied survival analysis: regression modeling of time-to-event data. John Wiley & Sons, New York, NY 1999.
36. Levy B. Lactate and shock state: the metabolic view. Curr Opin Crit Care. 2006; 12(4): 315–321, doi: 10.1097/01.ccx.0000235208.77450.15, indexed in Pubmed: 16810041.
37. Lombardi AM, Fabris R, Bassetto F, et al. Hyperlactatemia reduces muscle glucose uptake and GLUT-4 mRNA while increasing (E1alpha)PDH gene expression in rat. Am J Physiol. 1999; 276(5): E922–E929, doi: 10.1152/ajpendo.1999.276.5.E922, indexed in Pubmed: 10329987.
38. Choi CS, Kim YB, Lee FN, et al. Lactate induces insulin resistance in skeletal muscle by suppressing glycolysis and impairing insulin signaling. Am J Physiol Endocrinol Metab. 2002; 283(2): E233–E240, doi: 10.1152/ajpendo.00557.2001, indexed in Pubmed: 12110527.
39. Richards JE, Scalea TM, Mazzeffi MA, et al. Does lactate affect the association of early hyperglycemia and multiple organ failure in severely injured blunt trauma patients? Anesth Analg. 2018; 126(3): 904–910, doi: 10.1213/ANE.0000000000002626, indexed in Pubmed: 29283920.
40. Aslanger EK, Yıldırımtürk Ö, Şimşek B, et al. DIagnostic accuracy oF electrocardiogram for acute coronary OCClUsion resuLTing in myocardial infarction (DIFOCCULT Study). Int J Cardiol Heart Vasc. 2020; 30: 100603, doi: 10.1016/j.ijcha.2020.100603, indexed in Pubmed: 32775606.
41. Schmitt C, Lehmann G, Schmieder S, et al. Diagnosis of acute myocardial infarction in angiographically documented occluded infarct vessel : limitations of ST-segment elevation in standard and extended ECG leads. Chest. 2001; 120(5): 1540–1546, doi: 10.1378/chest.120.5.1540, indexed in Pubmed: 11713132.
42. Mazlan ZM, Ismail AHM, Ali S, et al. Efficacy and safety of the point-of-care procalcitonin test for determining the antibiotic treatment duration in patients with ventilator-associated pneumonia in the intensive care unit: a randomised controlled trial. Anaesthesiol Intensive Ther. 2021; 53(3): 207–214, doi: 10.5114/ait.2021.104300, indexed in Pubmed: 34006044.
43. Steinfelder-Visscher J, Weerwind PW, Teerenstra S, et al. Reliability of point-of-care hematocrit, blood gas, electrolyte, lactate and glucose measurement during cardiopulmonary bypass. Perfusion. 2006; 21(1): 33–37, doi: 10.1191/0267659106pf846oa, indexed in Pubmed: 16485697.
44. Rossi AF, Khan DM, Hannan R, et al. Goal-directed medical therapy and point-of-care testing improve outcomes after congenital heart surgery. Intensive Care Med. 2005; 31(1): 98–104, doi: 10.1007/s00134-004-2504-1, indexed in Pubmed: 15650863.