A comparison between the measurements of arterial lactate and mixed venous oxygen saturation for the evaluation of tissue perfusion after coronary artery bypass grafting

Koroner arter baypas greftleme sonrası doku perfüzyonunun değerlendirilmesinde arteriyel laktat ile miks venöz oksijen satürasyonu ölçümlerinin karşılaştırılması

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ABSTRACT

Background: This study aims to analyze the possible correlation between the blood lactate levels and mixed venous oxygen saturation after coronary artery bypass grafting.

Methods: The study included a total of 147 adult patients (104 males, 43 females; mean age 59±11 years; range 36 to 87 years) who underwent elective coronary artery bypass grafting with extracorporeal circulation between November 2011 and December 2012. Arterial blood gas, mixed venous gas, and hemodynamic variables were recorded at postoperative 30, 60, 120 and 240 min, and 24 hours. The patients were classified based on the use of inotropic agents: group 1 included 53 patients who received inotropic support and group 2 included 94 patients who did not. Both groups were assessed with respect to the correlation between the arterial lactate level and mixed venous oxygen saturation, and for other hemodynamic variables.

Results: Early postoperative mortality did not occur. In group 1, a significant correlation was found between the arterial lactate level (1.6±0.1 mmol/L) and mixed venous oxygen saturation (7.4±0.0%) at 240 min postoperatively. In both groups and at any time points, the levels of arterial blood gas lactate and blood glucose consistently showed a significant correlation.

Conclusion: Although blood lactate levels provide invaluable information on the adequacy of tissue perfusion, changes in lactate levels do not correlate with mixed venous oxygen saturation, addressing the need for evaluating hemodynamic changes together with lactate levels.

Keywords: Arterial lactate; mixed venous oxygen saturation; tissue perfusion.

ÖZ

Amaç: Bu çalışmada koroner arter baypas greftleme sonrasında kan laktat düzeyleri ve miks venöz oksijen satürasyonu arasındaki muhtemel ilişki incelendi.

Çalışma planı: Çalışmaya Kasım 2011 - Aralık 2012 tarihleri arasında ekstrakorporeal dolaşım ile elektif koroner arter baypas greftleme yapılan toplam 147 erişkin hasta (104 erkek, 43 kadın; ort. yaş 59±11 yıl; dağılım 36-87 yıl) alındı. Ameliyat sonrası 30, 60, 120. ve 240. dakikalarda ve 24. saatte ölçülen arteriyel kan gazı, miks venöz gaz ve hemodinamik parametreler kaydedildi. Hastalar inotropic ajan kullanımına göre sınıflandırıldı: grup 1'e inotropic destek verilen 53 hasta ve grup 2'ye destek verilmeyen 94 hasta alındı. Her iki grup da arteriyel laktat düzeyi ve miks venöz oksijen satürasyonu arasındaki ilişki ve diğer hemodinamik değişkenler açısından değerlendirildi.

Bulgular: Ameliyat sonrası erken dönemde mortalite görülmedi. Grup 1'de arteriyel laktat düzeyi (1.6±0.1 mmol/L) ve miks venöz oksijen satürasyonu (%7.4±0.0) arasında ameliyat sonrasında 240. dakikada anlamlı bir ilişki bulundu. Her iki grupta ve her zaman noktasında, arteriyel kan gazı laktat ve kan glukoz düzeyleri istikrarlı bir şekilde anlamlı bir ilişki gösterdi.

Sonuç: Kan laktat düzeyleri doku perfüzyonunun yeterliliğine ilişkin değerli bilgiler vermesine karşın, laktat düzeylerinde görülen değişiklikler miks venöz oksijen satürasyonu ile ilişkili değildir; bu da, laktat düzeyleri ile birlikte hemodinamik değişikliklerin de değerlendirilmesine gereksinim olduğunu göstermektedir.

Anahtar sözcükler: Arteriyel laktat; miks venöz oksijen satürasyonu; doku perfüzyonu.

Hemodynamic monitoring and arterial blood gas analysis are routine analyses as indirect indicators of tissue perfusion in patients admitted to cardiovascular intensive care units. Arterial blood gas analysis includes partial pressures of oxygen and carbon dioxide (PaO_2, $PaCO_2$), oxygen saturation (SaO_2), pH, blood electrolytes, and lactate levels. In particular, changes in the blood lactate level serve as a useful indicator of the degree of tissue perfusion. However, apart from ischemic causes, non-ischemic causes may also result in changes in blood lactate levels, as seen in hepatic dysfunction.[1] Another contradictory factor for the interpretation of ischemia-induced changes in blood lactate levels is the delayed release of lactate to the circulation from ischemic areas (wash-out).[2]

Another recent method of tissue perfusion analysis is monitoring of mixed venous oxygen saturation ($S_{mv}O_2$).[3] However, the need for pulmonary artery catheter insertion represents a major drawback for its routine use due to both procedure-related complications and its high cost.[2]

In this study, we aimed to investigate the possible correlation between the blood lactate levels and $S_{mv}O_2$ measurement after coronary artery bypass grafting (CABG).

PATIENTS AND METHODS

The study included a total of 147 adult patients (103 males, 44 females; mean age 59±11 years; range 36 to 87 years) who underwent elective CABG with extracorporeal circulation. Patients with any known systemic disease apart from hypertension and diabetes mellitus were excluded. All patients were followed up by the same surgical and anesthesia team. The study protocol was approved by the institutional Ethics Board of Acıbadem University (ATADEK 2011/236) and a written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Blood samples were collected from all the patients for the arterial blood gas and mixed venous gas measurements on admission to the intensive care unit (T_0), before intubation (T_1), at 30, 60, 120 and 240 min after intubation (T_2, T_3, T_4, T_5), and before transfer to the ward (T_6). A possible correlation between the lactate level in arterial blood gas and $S_{mv}O_2$ was analyzed and other hemodynamic variables were evaluated. During data analysis, no significant correlation was found between the arterial lactate level and $S_{mv}O_2$, which further necessitated the classification of the patients according to the use of inotropic agents: group 1 included 53 patients who received inotropic support

and group 2 included 94 patients who did not. In terms of randomization, this type classification enabled us to compensate the patients variety according to their cardiac output ranges and necessity of inotropic support to maintain adequate perfusion pressure right after cardiopulmonary bypass (CPB). The two groups were compared with respect to the correlation between the arterial lactate level and $S_{mv}O_2$, and for other hemodynamic variables.

All patients were given 0.5 mg of alprazolam (Xanax) orally the night before surgery. Thirty minutes before the operation, midazolam (125 mg/kg) was administered. In the operating room, a 16-gauge cannula was placed for venous access and physiological saline administration was initiated at a rate of 100 mL/hour. Arterial blood pressure monitoring was performed by two-channel echocardiography (ECG) (DII, V5), pulse oximetry, and invasive artery cannulation using an 18-gauge arterial cannula. Pulmonary artery pressure monitoring and $S_{mv}O_2$ evaluation were performed by a pulmonary artery catheter placed in the right internal jugular vein under local anesthesia. Induction of anesthesia was obtained using 50 mg/kg of midazolam and 2 mg of pancuronium followed by 25-35 µg/kg of fentanyl and a total of 0.1 mg/kg of pancuronium. Extracorporeal circulation was maintained with a hematocrit level of 23-30%. The mean arterial blood pressure was 50 to 80 mmHg with a pump flow rate of at least 2 $L/min/m^2$. The adequacy of tissue perfusion during ECC was assessed using venous-to-arterial carbon dioxide partial pressure difference (Pv-aCO_2), lactate level, and base deficit in arterial blood gas, and diuresis. All operations were performed under moderate hypothermia (32 °C).

Warming of the patients was started with a heating blanket placed over the patient in the intensive care unit. Upon achieving a rectal temperature of 37 °C, the heating blanket was removed. The patients with uncontrolled shivering were given intramuscular/intravenous meperidine 0.4 mg/kg. Mechanical ventilation was initiated in the mode of synchronized intermittent mandatory ventilation plus pressure support with the following settings: respiratory rate 12/min, tidal volume 8 mL/kg, fraction of inspired oxygen 50%, positive end-expiratory pressure 0-5 cm H_2O, pressure support 10 cm H_2O, and trigger sensitivity -2 cm H_2O. With the beginning of spontaneous respiration, respiratory rate was decreased to 8/min and, then, to 4/min. Upon the patient's respiratory effort and tidal volume, pressure support was gradually decreased to 4 cm H_2O. The patients who met the following criteria were extubated: re-gained consciousnes, hemodynamical stability, no

Table 1. Demographic and operational data of the patients

	n	%	Mean±SD
Age (years)			59±11
Gender			
Male	104		
Female	43		
Body mass index (kg/m²)			1.860±0.030
Diabetes mellitus	39	27.1	
Hypertension	74	50.4	
The mean EuroSCORE			4.8±3.1
Duration of bypass (min)			65.7±22.3
Cross-clamp time (min)			41.4±19.8
Ejection fraction (%)			47.4±13.3
The duration of intubation (hr)			6.2±4.1

drainage, $PaCO_2$ <48 mmHg, pH>7.30, and the ratio of PaO_2 to fraction of inspired oxygen >250. Following extubation, necessary adjustments were made at 30, 60, and 120 min depending on the results of arterial blood gas analysis.

Statistical analysis

Statistical analysis was performed using the GraphPad Prism Software, version 5.0 (GraphPad Software Inc., San Diego, CA, USA). Data were expressed in mean±standard deviation. Normally distributed $S_{mv}O_2$ and lactate values were compared using the Pearson's correlation test. A *p* value of <0.05 was considered statistically significant.

RESULTS

The demographic characteristics and operational data of the patients are shown in Table 1. Hemodynamic and arterial blood gas variables are shown in Table 2. As aforementioned, overall analysis of 147 patients showed no significant correlation between the arterial lactate levels and $S_{mv}O_2$ measured at each of the specified time points.

The mean logistic EuroSCORE was 4.8±3.1. Hemodynamic and arterial blood gas variables of the two groups are shown in Tables 3 and 4. In group 1, a significant correlation was found between the arterial lactate level and $S_{mv}O_2$ at T_5 (240 min after intubation) (Figure 1) (Pearson r=0.98; p<0.0001). In addition, group 1 showed a significant correlation between the levels of arterial blood gas bicarbonate and arterial lactate at T_5 (Figure 2) (Pearson r=0.328; p<0.05).

In both groups and at any time points, the levels of arterial blood gas lactate and blood glucose consistently showed a significant correlation, which was most prominent at T_2 (30 min after intubation) in group 2 (Figure 3) (Pearson r=0.456; p<0.0001).

DISCUSSION

Lactic acid is an organic hydroxy compound with the formula CH3CHOH-COOH and chemical name as alpha-hydroxypropanoic acid.[4] In hyperlactatemia, intracellular lactate concentration decreases due to failure of pyruvate, an end-product of anaerobic metabolism, to enter mitochondria, resulting in high blood lactate concentrations.[4,5]

Table 2. Hemodynamic and blood gas parameters of the patients

	T_0	T_1	T_2	T_3	T_4	T_5	T_6
Cardiac index	1.9±0.1	2.5±0.1	2.6±0.1	2.6±0.1	2.6±0.1	2.5±0.1	2.6±0.1
Cardiac output	3.7±0.1	4.7±0.1	4.9±0.1	4.9±0.1	5.3±0.5	4.8±0.1	5.2±0.1
Arterial lactate (mmol/L)	1.5±0.1	1.8±0.1	1.8±0.1	1.7±0.1	1.6±0.1	1.5±0.1	1.4±0.1
Mixed venous lactate (mmol/L)	1.5±0.1	1.7±0.1	1.7±0.1	1.6±0.1	1.6±0.1	1.5±0.1	1.4±0.0
$S_{mv}O_2$ (%)	60±0.7	61±0.8	63±0.8	62±0.9	61±0.9	60±0.8	56±1.0
pH	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.6±0.0
PCO_2 (mmHg)	33±0.4	35±0.5	38±0.5	38±0.6	39±0.5	38±0.4	35±0.5
PO_2 (mmHg)	32±0.4	34±0.8	36±0.6	35±0.6	35±0.6	34±0.9	30±0.7
HCO_3 (mmol/L)	22±0.2	22±0.2	21±0.2	21±0.2	22±0.2	22±0.2	23±0.2
Cardiac index (mmol/L)	2.0±0.1	2.6±0.1	2.7±0.1	2.6±0.1	2.6±0.1	2.6±0.1	2.8±0.1
Hematocrit (%)	36±0.5	33±0.5	33±0.5	33±0.6	32±0.5	31±0.5	30±0.6
MAP (mmHg)	84±1	85±1	84±1	82±2	82±1	82±2	80±2
SVR (dyne*sec)/cm⁵)	1873±68	1477±51	1359±45	1353±55	1374±45	1344±43	1190±43
PVR (dyne*sec/cm⁵)	229±15	172±14	125±6	125±8	128±7	126±6	145±13
Drainage (mL)	126±12	333±24	358±25	337±30	397±26	436±26	619±39
Glucose (mg/dL)	165±4	157±3	158±3	155±3	153±2	152±2	148±3

$S_{mv}O_2$: Mixed venous oxygen saturation; MAP: Mean arterial pressure; SVR: Systemic vascular resistance; PVR: Pulmonary vascular resistance.

Table 3. Hemodynamic and blood gas parameters of the patients in group 1

	T_0	T_1	T_2	T_3	T_4	T_5	T_6
Arterial lactate (mmol/L)	1.7±0.1	1.9±0.1	1.9±0.1	1.7±0.1	1.7±0.1	1.6±0.1	1.4±0.1
Mixed venous lactate (mmol/L)	1.7±0.1	1.9±0.1	1.9±0.1	1.7±0.1	1.6±0.1	1.5±0.1	1.2±0.1
$S_{mv}O_2$ (%)	34±0.7	36±0.7	37±0.7	39±1.2	38±0.7	38±0.7	36±0.8
pH	7.3±0.1	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0
PCO_2 (mmHg)	31±0.7	32±0.7	35±0.8	34±0.8	33±0.9	33±2.0	28±1.0
PO_2 (mmHg)	22±0.3	22±0.2	22±0.3	21±0.4	22±0.3	22±0.3	23±0.4
HCO_3 (mmol/L)	57±1.4	58±1.4	60±1.4	60±1.5	57±1.3	55±1.2	52±1.3
Cardiac index (mmol/L)	2.1±0.1	2.6±0.1	2.7±0.1	2.6±0.2	2.6±0.1	2.6±0.1	2.8±0.2
Hematocrit (%)	33±0.7	30±0.7	30±0.7	31±0.9	30±0.7	29±0.6	28±0.9
MAP (mmHg)	80±2	82±1	80±1	77±3	77±2	77±2	78±3
SVR (dyne*sec)/cm^5	1664±95	1382±65	1260±70	1284±88	1319±68	1297±62	1239±88
PVR (dyne*sec/cm^5)	217±13	176±13	137±10	141±15	141±12	138±10	130±13
Drainage (mL)	131±18	395±46	421±49	437±71	460±49	505±50	691±85
Glucose (mg/dL)	173±7	160±4	162±4	161±6,0	155±4	152±4	151±4

$S_{mv}O_2$: Mixed venous oxygen saturation; MAP: Mean arterial pressure; SVR: Systemic vascular resistance; PVR: Pulmonary vascular resistance.

Lactic acidosis, which is a common cause of metabolic acidosis characterized by a high anion gap, occurs when plasma lactate concentration exceeds 4 to 5 mmol/L (normal range: 0.5 to 1.5 mmol/L).[5] Lactic acidosis may be caused by hypoxia resulting from hypovolemia, hemorrhage, left ventricular failure, or respiratory failure;[1] however, other causes which are unrelated to hypoxia such as malignancies, drugs, and metabolic diseases.[4] can also lead to lactic acidosis.[4] Therefore, it would not be reasonable to consider hyperlactatemia to be a direct indication of impaired tissue perfusion.

Lactate is considered to be the gold standard of the tissue perfusion indicators.[6] Micro-circulation fails in non-pulsatile flow and during hypothermia; however,

re-distribution occurs.[6] Although tissue hypoxia exists, blood lactate levels may stay within normal range similar to other tissue perfusion variables.[6] However, in case of improved regional perfusion, the level of blood lactate also increases.[3] For the timely diagnosis of poor tissue perfusion, all of the indirect tissue perfusion variables should be closely monitored and evaluated, as they work in conjunction with each other.[3]

Routine postoperative evaluation of tissue perfusion presents a significant challenge following open cardiac surgery in patients in whom cardiac pressure-volume relationship has been worsened and, thus, become difficult to assess due to several causes such as impaired left ventricular function, presence of degenerative

Table 4. Hemodynamic and blood gas parameters of the patients in group 2

	T_0	T_1	T_2	T_3	T_4	T_5	T_6
Arterial lactate (mmol/L)	1.4±0.1	1.7±0.1	1.7±0.1	1.6±0.1	1.6±0.1	1.5±0.1	1.3±0.1
Mixed venous lactate (mmol/L)	1.4±0.1	1.6±0.1	1.6±0.1	1.6±0.1	1.5±0.1	1.5±0.1	1.2±0.1
$S_{mv}O_2$ (%)	33±0.5	35±0.7	39±0.6	38±0.6	39±0.7	38±0.5	36±0.6
pH	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.4±0.0	7.7±0.3
PCO_2 (mmHg)	32±0.5	35±1.3	36±0.7	36±0.8	36±0.7	34±0.7	30±0.9
PO_2 (mmHg)	22±0.2	22±0.2	21±0.2	21±0.2	21±0.2	22±0.2	23±0.3
HCO_3 (mmol/L)	61±0.9	63±1.0	65±0.9	64±1.2	64±1.0	62±1.0	57±1.4
Cardiac index (mmol/L)	1.9±0.1	2.5±0.1	2.7±0.1	2.6±0.1	2.7±0.1	2.6±0.1	2.7±0.1
Hematocrit (%)	38±0.5	35±0.6	34±0.6	34±0.7	33±0.6	32±0.7	31±0.7
MAP (mmHg)	86±2	86±1	87±1	84±2	85±1	85±2	81±1
SVR (dyne*sec)/cm^5	2013±91	1544±74	1421±59	1398±70	1414±61	1376±59	1165±48
PVR (dyne*sec/cm^5)	236±22	170±23	118±8	115±8	118±9	118±7	153±20
Drainage (mL)	122±16	295±26	321±2	288±2	356±29	392±28	583±41
Glucose (mg/dL)	160±4	155±3	155±3	153±3	152±3	148±3	147±3

$S_{mv}O_2$: Mixed venous oxygen saturation; MAP: Mean arterial pressure; SVR: Systemic vascular resistance; PVR: Pulmonary vascular resistance.
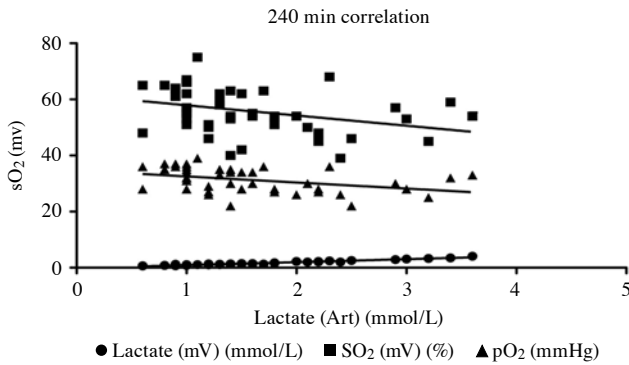
Figure 1. The correlation between the arterial blood lactate level and mixed venous oxygen saturation at 240 min (T_5) in group 1 (patients receiving inotropic support).

valve pathologies, sternotomy-induced impaired thorax integrity, and positive pressure ventilation. Although the main goal of monitoring standard hemodynamic variables and arterial blood gas analysis is to obtain indirect information about the adequacy of tissue perfusion, almost none of the monitoring variables, most of which are invasively obtained, provides a clear idea about impairment in tissue perfusion occurring in the early postoperative period. In cardiac surgery patients, due to some compensatory mechanisms, significant changes may not be observed in pre-load (e.g. central venous pressure and pulmonary artery pressure) and afterload (e.g. cardiac output and arterial blood pressure) determinants, although impairment in tissue perfusion and organ damage have already begun.[7] Similarly, $S_{mv}O_2$ monitoring may fail to detect impaired tissue hypoperfusion at an early stage due to compensatory mechanisms.[8,9]

Mixed venous oxygen saturation is commonly used to assess the balance of total body oxygen delivery to oxygen demand of patient whom CPB used. Despite
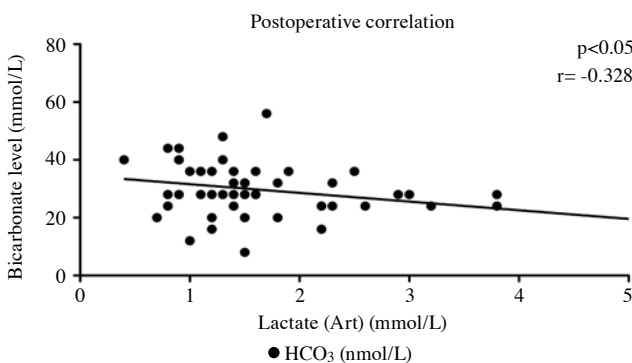
the general acceptance of this fact, major postoperative end-organ complications potentially secondary to undetected regional ischemia during bypass.[3]

During CPB practice, changes in the re-distribution of blood flow along with any associated negative outcomes has led clinicians to prefer to work with the highest blood flow, MAP and hematocrit values during CPB. In addition, with hypothermia, the total body O_2 consumption (VO_2) decreases more than the O_2 supply and an increase in the SvO_2 is observed, particularly in the hypothermic period of CPB. This situation decreases the reliability of SvO_2.[3]

On the other hand, macro-circulation may remain normal in some patients with impaired micro-circulation and intracellular hypoperfusion, often deceptive clinicians.[2,10-14] Likewise, impaired micro-circulation in the early postoperative period due to a variety of causes may restrict the passage of intracellular lactate to blood, giving a rise to normal blood lactate measurements, despite significant intracellular hypoperfusion. In our study, this phenomenon may account for the lack of a significant correlation between the lactate level and $S_{mv}O_2$ in the early period. In the following stages at which micro-circulation improved and the transport of lactate between the cells and blood was restored, a significant correlation was observed between the lactate level and $S_{mv}O_2$ at T_5 (240 min after intubation).

Ranucci et al.[15] reported that hyperlactatemia was more frequent after CABG requiring prolonged ECC and in patients taking inotropic agents and that it was independently associated with insufficient oxygen delivery and almost always associated with hyperglycemia. In our study, in both groups, the levels of arterial blood gas lactate and blood glucose consistently showed significant correlations
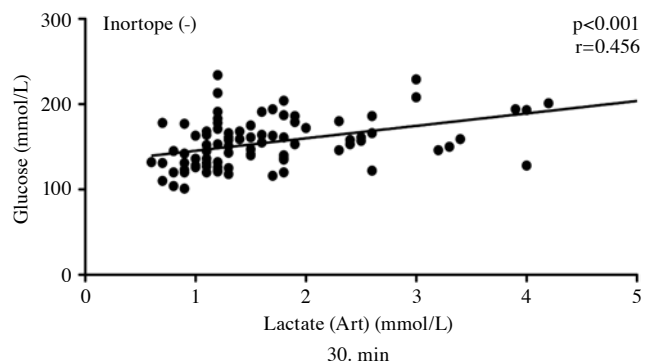

Figure 2. The correlation between the arterial blood lactate level and arterial blood gas bicarbonate at (T_0) postoperatively in group 1.

Figure 3. The correlation between the arterial blood lactate level and blood glucose at (T_2) 30 min in group 2 (patients without inotropic support).

at any time points. These correlations were more noticeable in patients who did not use inotropic agents (group 2), which further led us to compare the two groups. Then, it was found that group 2 patients had a significantly higher incidence of diabetes mellitus and significantly higher HbA1c levels (Table 1). Our findings on the correlation between blood glucose and lactate levels support the findings of Ranucci et al.[15] However, in group 2 patients exhibiting a stronger correlation, this correlation raises the possibility that even hyperglycemia alone can cause hyperlactatemia in patients who do not need inotropic support (those with sufficient cardiac output and postoperative hemodynamic stability). Thus, taking into consideration the frequencies and the effects of diabetes mellitus and blood glucose levels on blood lactate levels, it can be postulated that monitoring hyperlactatemia alone may not be adequate in the assessment of tissue perfusion following open heart surgery.

Using a Swan-ganz catheter routinely is challenging for low income countries, particularly. The study design is another limitation of the study in terms of randomization beside the classification of the groups. Single-subject designs in special manner are methodological limitations itself. As we try to conclude with an overall comment on this issue for daily practice, the subject is needed to be assessed with larger and high number groups in multi-center studies.

In conclusion, it is well-known that patients undergoing open heart surgery may develop impaired pressure-volume balance and microcirculation resulting from various causes. Changes in the volume-pressure balance reduce the value of hemodynamic variables in the evaluation of tissue perfusion. Therefore, simply monitoring lactate levels in arterial blood gases for the evaluation of tissue hypoperfusion does not seem to be a reliable follow-up variable due to adverse effects of open heart surgery on micro-circulation; rather, it may be used in combination with another method such as $S_{mv}O_2$, which is not affected by changes in micro-circulation and volume-pressure balance.

Based on our study results, despite its high cost and complication rates, we recommend using pulmonary artery catheter for all kind open cardiac surgery to monitor highly invaluable variables as routinely being done for artery blood gas analysis.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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