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The relationship between inotropic support therapy and central partial pressure of venous-arterial carbon dioxide after cardiopulmonary bypass

Kardiyopulmoner baypas sonrasında inotropik destek tedavisi ve santral parsiyel venö-arteriyel karbondioksit basıncı arasındaki ilişki

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ABSTRACT

Background: This study aims to investigate the effects of partial pressure of venous-arterial carbon dioxide changes in the early period after cardiopulmonary bypass in patients who did or did not receive inotropic support therapy and the effect of these changes on tissue perfusion.

Methods: A total of 100 consecutive patients (70 males, 30 females; mean age 61.8±2.3 years; range, 20 to 75 years) who underwent open heart surgery were divided into two groups as those who did not receive any inotropic agent (group 1, n=50) and those who received at least one inotropic agent (group 2, n=50) during the early postoperative period. Heart rate, blood oxygen saturation level, mean arterial pressure, central venous pressure and urine volume, lactate and base excess levels were recorded during the postoperative first 24 hours. At the same timeframe, partial pressure of venous-arterial carbon dioxide level was calculated from central venous and peripheral blood samples.

Results: In both groups, partial pressure of venous-arterial carbon dioxide were significantly higher in the postoperative fourth hour compared with basal values. This significant difference continued for the postoperative first 24 hours. Partial pressure of venous-arterial carbon dioxide in group 2 was significantly higher at the 12th-hour measurement (p=0.002). Lactate levels at zeroth and eighth hours were significantly higher in group 2 (p=0.012 and p=0.017, respectively). Fourth-hour urine excretion volumes were significantly lower in group 1 (p=0.010). Mean arterial pressure at zeroth, 12th and 20th hours was significantly higher in group 2 (p=0.001, p=0.016, and p=0.027, respectively). At the eighth-hour measurement, a positive weak relationship was detected between partial pressure of venous-arterial carbon dioxide and lactate levels (r=0.253 and p=0.033).

Conclusion: This study demonstrated that partial pressure of venous-arterial carbon dioxide increased in the first few hours and remained to be high for 24 hours after cardiopulmonary bypass independently of the use of inotropic support. However, in the postoperative period, even after lactate and base excess levels return to baseline values, partial pressure of venous-arterial carbon dioxide may continue to remain at high values, which may indicate impaired perfusion in some tissues.

Keywords: Cardiopulmonary bypass, tissue perfusion, venous-arterial carbon dioxide pressure.

ÖZ

Amaç: Bu çalışmada kardiyopulmoner baypas sonrası erken dönemde inotropik destek tedavisi alan veya almayan hastalarda parsiyel venö-arteriyel karbondioksit basıncı değişikliklerinin etkileri ve bu değişikliklerin doku perfüzyonu üzerindeki etkisi araştırıldı.

Çalışma planı: Açık kalp cerrahisi geçiren toplam 100 hasta (70 erkek, 30 kadın; ort. yaş 61.8±2.3 yıl; dağılım, 20-75 yıl) ameliyat sonrası erken dönemde herhangi bir inotropik ajan almayanlar (grup 1, n=50) ve en az bir inotropik ajan alanlar (grup 2, n=50) olmak üzere iki gruba ayrıldı. Ameliyat sonrası ilk 24 saatte kalp atım hızı, kan oksijen satürasyonu düzeyi, ortalama arteriyel basınç, santral venöz basınç ve idrar hacmi, laktat ve baz açığı düzeyleri kaydedildi. Aynı zaman diliminde, parsiyel venö-arteriyel karbondioksit basıncı düzeyi santral venöz ve periferik kan örneklerinden hesaplandı.

Bulgular: Her iki grupta parsiyel venö-arteriyel karbondioksit basıncı ameliyat sonrası dördüncü saatte bazal değerlere göre anlamlı olarak daha yüksek idi. Bu anlamlı farklılık ameliyat sonrası ilk 24 saat boyunca devam etti. Grup 2'de parsiyel venö-arteriyel karbondioksit basıncı 12. saat ölçümünde anlamlı olarak daha yüksek idi (p=0.002). Grup 2'de laktat düzeyleri sıfırıncı ve sekizinci saatte anlamlı olarak daha yüksek idi (sırasıyla, p=0.012 ve p=0.017). Grup 1'de idrar atılım hacimleri dördüncü saatte anlamlı olarak daha düşük idi (p=0.010). Grup 2'de ortalama arteriyel basınç sıfırıncı, 12. ve 20. saatte anlamlı olarak daha yüksek idi (sırasıyla, p=0.001, p=0.016 ve p=0.027). Sekizinci saat ölçümünde, parsiyel venö-arteriyel karbondioksit basıncı ve laktat düzeyleri arasında pozitif zayıf bir ilişki saptandı (r=0.253 ve p=0.033).

Sonuç: Bu çalışma, kardiyopulmoner baypas sonrasında parsiyel venö-arteriyel karbondioksit basıncının inotropik destek kullanımından bağımsız olarak ilk birkaç saat yükseldiğini ve 24 saat yüksek kalmaya devam ettiğini gösterdi. Ancak ameliyat sonrası dönemde laktat ve baz açığı düzeylerinin normale dönmesinden sonra bile parsiyel venö-arteriyel karbondioksit basınç yüksek değerlerde kalmaya devam edebilir ve bu durum bazı dokularda bozulmuş perfüzyona işaret edebilir.

Anahtar sözcükler: Kardiyopulmoner baypas, doku perfüzyonu, venö-arteriyel karbondioksit basıncı.

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Deterioration in cardiac performance, decreased cardiac output, and need for inotropic support are frequent conditions after open heart surgery. Hypoperfusion, which can lead to multiple organ failure in open heart surgery patients, is a preventable cause of morbidity and mortality.[1] Previous studies have shown that central venous oxygen saturation measured from the superior vena cava ($ScvO_2$) can be an indirect indicator of mixed venous oxygen saturation (SvO_2) and cardiac output, and hence it has indicated the tissue perfusion under certain conditions.[2-4] Low perfusion pressure, even in the absence of hypoxia, leads to increased carbon dioxide in the peripheral tissues and venous hypercarbia by incorporation of the carbon dioxide into the circulation. This leads to increased difference between the partial pressure of carbon dioxide ($ScvCO_2$) measured in venous blood and partial pressure of venous-arterial carbon dioxide (ΔPCO_2).[5] Partial pressure of venous-arterial carbon dioxide may be considered to be a good indicator of the adequacy of blood flow to remove total CO_2 produced by peripheral tissues. Previous studies reported that a ΔPCO_2 value higher than 6 mmHg in patients with high-risk surgery or in patients with sepsis might identify adequately untreated patients.[2,6,7] In this study, we aimed to investigate the effects of ΔPCO_2 changes in the early period after cardiopulmonary bypass (CPB) in patients who did or did not receive inotropic support therapy and the effect of these changes on tissue perfusion.

PATIENTS AND METHODS

This study was conducted at Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital between January 2013 and September 2013. A total of 100 consecutive patients (70 males, 30 females; mean age 61.8±2.3 years; range, 20 to 75 years) who underwent elective open heart surgery were divided into two groups as those who did not receive any inotropic agent (group 1, n=50) and those who received at least one inotropic agent and/or vasopressor support to maintain the mean arterial pressure (MAP) above 65 mmHg (group 2, n=50) during the early postoperative period. Patients with preoperative low cardiac ejection fraction (<40%), history of cerebrovascular disease, chronic renal insufficiency, chronic obstructive pulmonary disease, peripheral arterial occlusive disease, postoperative intra-aortic balloon pump need or those reoperated at first six hours after primary surgery were excluded. The study protocol was approved by the Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (approval number 28001928-051.99). A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

On arrival to the operating room, a peripheral intravenous catheter was inserted. A 20-gauge cannula was inserted in the contralateral radial artery for invasive arterial blood pressure measuring. Other monitoring included five-lead electrocardiography and pulse oximetry. The induction of anesthesia was established with 2 mg/kg propofol, 15 µg/kg fentanyl, 0.5 mg/kg rocuronium intravenously with 100% oxygen inhalation. Anesthesia was maintained with 50% air and 5-6% desflurane in oxygen with positive pressure ventilation in a circle system. End-tidal CO_2 was maintained between 30 and 35 mmHg. An esophageal temperature probe and a urine catheter were also placed. After induction of anesthesia, a central venous catheter was inserted in the right internal jugular vein.

After the sternotomy incision, 300 U/kg heparin was administered to provide an activated coagulation time >400 sec. Membrane oxygenators (Medtronic, Inc., Minneapolis, USA) were primed with 1,000-1,500 mL of Ringer's solution. A non-pulsatile pump flow was set at with 2.2-2.4 L/min/m^2 to maintain MAP between 50 and 70 mmHg. Mild hypothermia with a core temperature of 33°C was provided during CPB. Intermittent antegrade cardioplegia was used for myocardial protection. Protamine sulfate was used to antagonize the heparin.

Postoperative care in the intensive care unit (ICU) was provided according to the institutional standard of care. After surgery, patients were transferred to the ICU for full monitoring, where they were monitored with electrocardiography, MAP, pulse oximetry, central venous pressure (CVP) and were mechanically ventilated with synchronized intermittent-mandatory ventilation plus pressure support mode with fraction of inspired oxygen of 0.6, respiratory rate of 10-14, and a positive end-expiratory pressure of 5-8. Low cardiac output was considered in those who met the following criteria before discharge from the first hospitalization in ICU immediately after surgery: need for inotropic support with vasoactive drugs (dopamine 4 µg/kg/min at least for 12 h and/or dobutamine and/or norepinephrine) to maintain systolic blood pressure above 90 mmHg or need for mechanical circulatory support with intra-aortic balloon pump to maintain systolic blood above 90 mmHg and signs of impairment of body perfusion, hypothermia, hypotension, oliguria/anuria, lowered level of consciousness or a combination of these signs.[8,9]

Table 1. Patients' characteristics and perioperative data

	Inotrope (-) (n=50)			Inotrope (+) (n=50)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			61.4±2.1			62.1±1.9	0.654
Gender							
Female	18	36.0		12	24.0		0.145
Male	32	64.0		38	76.0		0.231
Body mass index (kg/m^2)			28.6±5.2			27.9±4.7	0.478
Cross-clamping time (min)			51±18			77±34	0.001*
Cardiopulmonary bypass time (min)			85±35			117±44	0.001*
Intensive care unit stay (day)			1.5±0.9			4±1.5	0.003*
Hospital stay (day)			4.9±0.9			7.2±1.4	0.001*
Inotropic agents doses							
Dopamine (µg/kg/min)			-			10.8±2.5	-
Dobutamine (µg/kg/min)			-			6.4±5.2	-
Norepinephrine (µg/kg/min)			-			0.7±0.4	-

SD: Standard deviation; * $p<0.05$.

The dose was determined according to the patient's body weight. Doses of dopamine or dobutamine were increased or decreased by 2 µg/kg/min and doses of norepinephrine by 0.02 µg/kg/min to maintain the target MAP (>65 mmHg).[10]

Extubation criteria for the patients were adequate neurologic response, sufficient muscle strength, hemodynamic stability without high dose inotropic/vasoactive support, and an arterial PO_2>60 mmHg with an inspired oxygen fraction ≤40%. Criteria for discharge from the ICU were that patients must be awake, cooperative, and hemodynamically stable (without inotropes), while having an acceptable respiratory pattern, blood gas analysis (arterial PO_2 >70 mmHg, PCO_2 <50 mmHg), and visual analog scale score ≤5.

End of surgery was accepted as a zero-hour point, and, during the postoperative first 24 hours, heart rate, blood oxygen saturation level, MAP, CVP and urine volume, lactate, glucose, and base excess levels in arterial blood gas were recorded in every four hours. At the same timeframe, P(v-a) CO_2=(ΔpCO_2) level was calculated from central venous and peripheral blood samples.

Statistical analysis

Statistical analysis was performed with Number Cruncher Statistical System 2007 & Power Analysis and Sample Size 2008 Statistical Software (NCSS, Kaysville, UT, USA). Student's t-test was used for comparison of parametric variables and Mann-Whitney U was used for nonparametric variables. Qualitative variables were compared with Yates continuity correction test (Yates corrected chi-square).

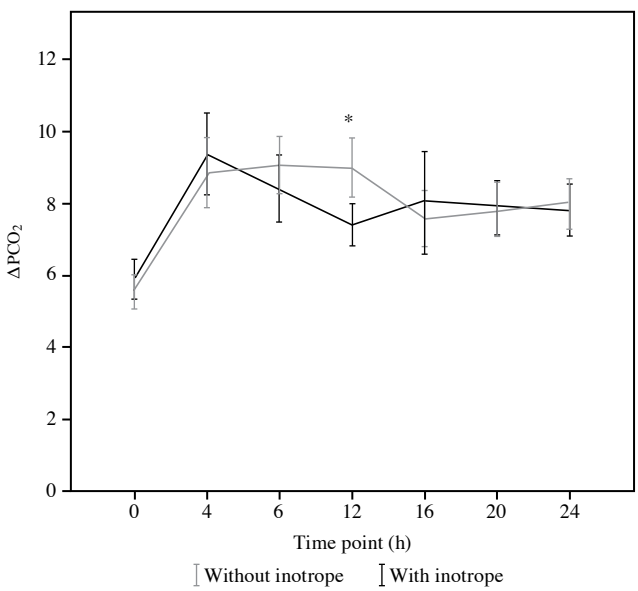

Figure 1. Comparison of partial pressure of venous-arterial carbon dioxide levels by groups.
ΔpCO_2: Partial pressure of venous-arterial carbon dioxide.

Table 2. Comparisons for different time points

	Inotrope (-) n=50)		Inotrope (+) n=50)		
	Mean±SD	Median	Mean±SD	Median	*p*
Lactate					
0th-hour	2.1±0.8	2.15	3.9±1.6	2.50	0.012*
4th-hour	2.3±1.5	1.95	3.0±2.6	2.20	0.099
8th-hour	1.9±0.8	1.85	3.9±2.7	2.35	0.017*
12th-hour	2.2±0.9	2.15	2.9±2.7	2.30	0.288
16th-hour	2.0±1.2	1.65	2.4±2.3	1.80	0.339
20th-hour	1.8±0.8	1.60	2.4±2.2	1.60	0.303
24th-hour	2.0±0.8	1.90	2.4±2.2	1.80	0.537
Urine excretion					
0th-hour	218.3±158.1	150	209.8±139.3	150	0.868
4th-hour	147.4±97.4	150	196.0±114.1	150	0.010*
8th-hour	148.0±84.5	125	211.0±239.9	150	0.219
12th-hour	151.0±102.3	150	155.2±78.8	150	0.446
16th-hour	138.1±72.2	100	159.6±87.8	150	0.142
20th-hour	135.6±77.9	150	165.4±103.5	150	0.098
24th-hour	129.5±58.4	100	145.0±50.8	150	0.060
Base excess					
0th-hour	-2.9±2.5	-2.60	-4.5±3.0	-4.51	0.002*
4th-hour	-1.8±3.4	-1.65	-2.6±3.6	-2.30	0.452
8th-hour	-1.6±2.5	-1.75	-2.3±3.3	-1.65	0.312
12th-hour	-1.9±2.9	-1.90	-2.2±3.1	-1.80	0.664
16th-hour	-1.1±2.5	-1.55	-2.2±3.0	-1.80	0.167
20th-hour	-0.9±2.4	-0.95	-1.8±2.8	-1.65	0.130
24th-hour	-0.9±2.5	-1.00	-1.8±2.9	-1.70	0.152
Central venous pressure					
0th-hour	10.1±3.5		9.2±3.1		0.184
4th-hour	9.3±3.6		8.5±3.3		0.262
8th-hour	9.2±2.9		8.5±3.2		0.297
12th-hour	9.4±2.8		8.5±3.4		0.157
16th-hour	9.3±2.9		8.5±3.3		0.254
20th-hour	9.4±2.8		8.7±3.4		0.307
24th-hour	9.3±2.5		8.5±3.0		0.153
Glucose level					
0th-hour	147±37		157±45		0.240
4th-hour	167±42		166±41		0.866
8th-hour	187±51		177±45		0.293
12th-hour	177±41		170±40		0.425
16th-hour	176±43		161±36		0.062
20th-hour	174±42		160±31		0.061
24th-hour	164±48		161±31		0.689

Table 2. Continued

	Inotrope (-) n=50)		Inotrope (+) n=50)		
	Mean±SD	Median	Mean±SD	Median	*p*
Mean arterial pressure					
0th-hour	75.2±5.5		64.6±6.7		0.001*
4th-hour	72.8±2.6		69.2±6.3		0.066
8th-hour	77.6±4		73.8±5.9		0.118
12th-hour	72.1±3.5		60.8±5.3		0.016*
16th-hour	74.9±2.6		71.4±5.5		0.091
20th-hour	75.4±4.2		63.7±7.1		0.027*
24th-hour	71.8±6.8		69.9±9.5		0.616
Heart rate					
0th-hour	85±14		101±17		0.001*
4th-hour	95±14		102±16		0.017*
8th-hour	95±16		100±16		0.144
12th-hour	94±14		98±16		0.240
16th-hour	93±13		98±12		0.100
20th-hour	93±13		96±12		0.177
24th-hour	95±12		98±12		0.370

SD: Standard deviation; * p<0.05.

The relationship between parameters was determined with Pearson's correlation analysis and Spearman's correlation analysis. A *p* value of <0.05 was considered to indicate statistical significance.

RESULTS

There were no significant differences between study groups in terms of gender, age, or body mass index. Cross-clamping time, CBP time, ICU stay and hospital stay were significantly longer in group 2 (p=0.001, p=0.001, p=0.003, and p=0.001, respectively) (Table 1).

The mean ΔPCO_2 were 5.9±1.9 in group 1 and 5.5±1.6 in group 2 during admission to ICU (baseline) (p=0.330). Partial pressure of venous-arterial carbon dioxide levels increased significantly in both groups at the postoperative fourth hour and this rate remained for 24 hours postoperatively. Fourth-, eighth-, 16th-, and 24th-hour ΔPCO_2 value measurements were similar in both groups. Partial pressure of venous-arterial carbon dioxide level in group 2 was significantly higher at the 12th-hour measurement (p=0.002) (Figure 1).

Lactate levels at zeroth- and at eighth-hours were significantly higher in group 2 (p=0.012 and p=0.017, respectively), but no difference was detected in fourth-, 12th-, 16th-, 20th-, or 24th-hours. Fourth-hour urine excretion volumes were significantly lower in group 1 (p=0.010). There were no statistical differences in terms of urine excretion in other time points. Although a statistical difference was found in terms of BE levels in zeroth hour (p=0.002), no statistical difference was found in other time points. Heart rate measurements showed statistically significant difference at zeroth- and fourth-hours (p=0.001 and p=0.017, respectively) in favor of group 2. There were no significant differences in terms of heart rate at eighth-, 12th-, 16th-, 20th-, or 24th-hours. Mean arterial pressure at zeroth-, 12th-, and 20th-hours were significantly higher in group 2 (p=0.001, p=0.016, and p=0.027, respectively). No statistical difference was detected in terms of central venous pressure values or glucose levels in any time point (Table 2).

There was no statistically significant relationship between ΔPCO_2 and lactate levels at the zeroth-, fourth-, 12th-, 16th-, 20th-, or 24th-hour measurements. Meanwhile, in eighth-hour measurement, a positive weak relationship was detected (r=0.253, p=0.033). No significant relationship was found between ΔPCO_2, urine excretion, BE, MAP, and CVP (Table 3).

Table 3. Relationship between partial pressure of venous-arterial carbon dioxide and other parameters

	0^{th}-hour	4^{th}-hour	8^{th}-hour	12^{th}-hour	16^{th}-hour	20^{th}-hour	24^{th}-hour
Urine excretion							
r	-0.103	-0.054	0.027	-0.189	-0.025	-0.214	-0.108
p	0.308	0.594	0.786	0.060	0.805	0.033*	0.284
Lactate							
r	-0.155	0.133	0.253	0.121	0.141	0.075	0.105
p	0.123	0.187	0.011*	0.230	0.163	0.456	0.298
BE							
r	-0.007	-0.125	-0.099	-0.039	0.011	-0.029	0.008
p	0.943	0.217	0.329	0.702	0.914	0.777	0.940
MAP							
r	0.071	-0.002	-0.137	-0.119	0.143	0.195	0.170
p	0.481	0.983	0.173	0.238	0.156	0.052	0.091
CVP							
r	-0.191	0.054	0.096	0.151	-0.032	-0.055	0.047
p	0.058	0.594	0.342	0.132	0.749	0.588	0.642

BE: Base excess; MAP: Mean arterial pressure; CVP: Central venous pressure; * $p<0.05$.

DISCUSSION

The current study demonstrated that ΔPCO_2 increased in the first few hours and remained to be high for 24 hours in the postoperative period after CPB independently of the use of inotropic support. However, in the postoperative period, even after lactate and BE levels returned to baseline values, ΔPCO_2 may continue to remain at high values, which may indicate impaired perfusion in some tissues.

Monitoring tissue perfusion is among the main aims after cardiac surgery in postoperative care units. Increase of ΔPCO_2 in response to alterations in systemic and pulmonary blood flow in cardiac and CPB surgery patients was shown in previous studies.[11,12] Toraman et al.[13] reported that during the hypothermic period of CBP, the increase in ΔPCO_2 was not inversely associated with insufficient blood flow and there was a significant correlation between ΔPCO_2 and tissue perfusion parameters. Moreover, Takami and Masumoto[11] showed that increased ΔPCO_2 was associated with decreased cardiac index, SvO_2, arterial bicarbonate (HCO3), and high lactate levels and elevation of ΔPCO_2 related to surgical invasiveness and CPB and cross-clamping time. In the current study, the highest level of ΔPCO_2 after CPB in both inotropic agent administered and non-administered groups was reached at postoperative fourth hour and the high levels of ΔPCO_2 remained for the first 24 hours postoperatively. The increase of ΔPCO_2 was not different between the two groups until the 12^{th} hour, whereas at 12^{th}-hour measurement, ΔPCO_2 was higher in inotropic agent administered group. Similar to the previous studies,[11] the lactate and BE levels were higher, MAP was lower, CBP and cross-clamping time were longer in inotropic agent administered group in the postoperative period. Utoh et al.[14] reported that ΔPCO_2 was correlated with cardiac index, oxygen delivery, minimum rectal temperature, and duration of CPB while increased ΔPCO_2 decreased to within normal ranges at 12 hours postoperatively. In our study, except for the postoperative 12^{th} hour, similar ΔPCO_2 values in both inotropic agent administered and non-administered groups may be an indication that ΔPCO_2 is unrelated to inotropic support.

It was shown that SvO_2 was superior than MAP and heart rate in cardiac surgery patients as a hemodynamic measurement.[15] However, the clinically predictable threshold of SvO_2 has been differently presented. Pölönen et al.[16] showed that $ScvO_2$ values higher than 70% and lactate values lower than 2 mmol improved treatment targets in the early postoperative period. Meanwhile, the negative predictive value of high initial $ScvO_2$ levels in septic patients was also stated in other studies.[15,16] The reliability of the $ScvO_2$ in association

with tissue perfusion markers such as lactate and ΔPCO_2 was also shown in previous studies.[17-19] Although ΔPCO_2 is not an excellent marker for tissue hypoxia, it may show that venous blood flow is not sufficient to remove carbon dioxide produced in peripheral tissues.[17] Habicher et al.[18] stated that although oxygen delivery and consumption balance might be assumed as normal with $ScvO_2$ level and cardiac index interpretation, this fact was insufficient to show the hypoperfused regions of the body.

Several studies have reported different results regarding lactate changes and its association with ΔPCO_2 after CPB. Habicher et al.[18] reported that the high level of ΔPCO_2 was related to hyperlactatemia and this relationship was associated with splanchnic perfusion alteration after CPB. They also found a high complication rate and long length of ICU stay. However, Okten et al.[20] reported that although blood lactate levels provided information on the adequacy of tissue perfusion, changes in lactate levels did not correlate with mixed venous oxygen saturation. Furthermore, Guinot et al.[21] stated that ΔPCO_2 was associated weakly with arterial lactate. Although serum lactate levels have been used as a marker of global tissue hypoxia in circulatory shock, hyperlactatemia after cardiac surgery may occur depending on other mechanisms such as stress response to surgery and the use of beta-adrenergics.[22,23] Therefore, early after CPB, hyperlactatemia may reflect intraoperative factors rather than anaerobic metabolism, which may not be reliable for evaluating the adequacy of tissue oxygenation. Gasparovic et al.[23] reported that pulmonary lactate levels rise significantly after CPB and may contribute significantly to circulating lactate levels up to six hours postoperatively. In addition, Naik et al.[24] reported that serum lactate levels increased from the onset of CPB to peak and remained high up to six hours in the ICU and returned to normal by 24 hours. In a study on infants and neonates undergoing cardiac surgery, Rhodes et al.[25] reported that ΔPCO_2 continued to increase within the first 24 hours after admission to ICU compared with admission levels, while patients remaining on inotropes at 24 hours showed a trend toward higher 24-hour ΔPCO_2 compared with patients who were weaned off inotropes. Changes in ΔPCO_2 over time could be related to high CO_2 production or changes in each factor determining the relationship between partial CO_2 pressure and CO_2 content. Cardiopulmonary bypass may increase CO_2 tissue production as a result of increased metabolic needs, redistribution of blood flow to peripheral tissues, and changes in hepatosplanchnic perfusion; which may result in increased ΔPCO_2.[18] In addition, extubation and rewarming in cardiac surgical patients may contribute to increased ΔPCO_2. Extubation is associated with redistribution of systemic blood flow from peripheral tissues to respiratory muscles.[26] Hypothermia during surgery and rewarming in the ICU may affect both CO_2 production and the relationship between CO_2 content and partial CO_2 pressure.[27] In the current study, lactate level was found significantly increased at eighth-hour measurement in inotropic agent administered group, which had a tendency to decrease afterward. On the other hand, the decreased lactate, MAP, and ΔPCO_2 levels at 12th-hour measurement approved impaired perfusion. However, lactate level was not assessed after the 24th-hour period in the current study.

Futier et al.[19] suggested that measurement of $ScvO_2$ complementary to ΔPCO_2 might be applied for assessment of intravascular volume sufficiency and hypoperfusion in target treatment for high-risk surgery. Moreover, it was stated that if ΔPCO_2 was measured to be higher than 6 mmHg, care to keep adequate fluid levels and increased cardiac output should be given in sepsis patients.[28] Studies in the literature stating the simplicity, usefulness, and accessibility of ΔPCO_2 measurement to follow the tissue perfusion after cardiac surgery are limited and, to our knowledge, have not investigated the inotropic agents in these groups.[11,12]

The current study does, however, have several limitations. Firstly, PCO_2 was measured from central venous blood instead of mixed venous blood which could lead to under-estimation of CO_2 exchanges. However, previous studies demonstrated good correlation between central ΔPCO_2 and mixed ΔPCO_2.[19] Secondly, the study population was a cohort of relatively older patients. Therefore, our findings may not be generalizable to other populations. Finally, in the current study, ΔPCO_2 within the first 24 hours after cardiac surgery were evaluated while changes in ΔPCO_2 after the first 24 hours of surgery are unclear and merit further investigation.

In conclusion, although there is an increase in partial pressure of venous-arterial carbon dioxide in the postoperative period after cardiopulmonary bypass, partial pressure of venous-arterial carbon dioxide is insufficient to guide inotropic support therapy when evaluated alone. Even if indirect parameters of tissue perfusion return to baseline values, partial pressure of venous-arterial carbon dioxide can continue to remain high for the first 24 hours postoperatively. Further prospective studies are needed to confirm the results.

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