JARSS 2020;28(4):261-6
doi: 10.5222/jarss.2020.80299

Özgün Araştırma / *Original Article*

Does Central Venous Lactate Measurement Replace Arterial Lactate Measurement in Cardiac Surgery?

Kardiyak Cerrahide Santral Venöz Laktat Ölçümü Arteryel Laktat Ölçümünün Yerini Tutabilir mi?

Büşra Tezcan
İbrahim Mungan
Alev Şaylan
Derya Ademoğlu
Sema Sarı
Çilem Bayındır Dicle
Bahadır Aytekin
Ayşegül Özgök
Hija Yazıcıoğlu

ABSTRACT

Objective: *Lactate levels, which provide valuable information about the adequacy of tissue perfusion, are usually measured by blood gas analyzers simultaneously with blood gases. Although arterial blood is the "gold standard" for measurement of lactate, the interchangeable use of arterial and venous lactate measurements can avoid increased costs and iatrogenic anemia resulting from frequent blood sampling when evaluation of venous blood gas samples are preferred. In this study; we aimed to examine the correlation and agreement between the arterial lactate (AL) and central venous lactate (CVL) values in patients undergoing on-pump cardiac surgery.*
Method: *Adult patients who had both arterial and central venous blood gas sampling simultaneously in three stages (T1: after anesthesia induction, T2: during cross- clamping, T3: during skin closure) of operation as part of anesthetic management were eligible for inclusion in this retrospective study. CVL and AL concentrations were estimated during blood gas analysis at stages T1, T2 and T3. Spearman Rho and Bland-Altman Tests were used to assess correlation and agreement between AL and CVL measurements, respectively.*
Results: *Totally 366 pairs of blood samples were obtained from 122 eligible patients. The 95% limits of agreement were -0.07 to -0.00 at T1; 0.30 to -0.10 at T2 and -0.16 to -0.03 at T3. The 95% CIs were detected 0.86 to 0.93 (r=0.90 and p<0.0001) at T1;0.95 to 0.97 at T2 (r=0.96 and p<0.0001) and 0.92 to 0.96 (r=0.94 and p<0.0001) at T3.*
Conclusion: *Although sampling from arterial lactate can be considered as the "gold standard" for lactate measurement, sampling from central venous blood is an acceptable alternative for lactate measurement in on-pump cardiac surgery patients.*

Keywords: *Arterial lactate, venous lactate, cardiac surgery, correlation, agreement*

ÖZ

Amaç: *Doku perfüzyonunun yeterliliği için önemli bilgi veren laktat düzeyleri, genellikle kan gazlarıyla birlikte kan gazı cihazları tarafından ölçülür. Her ne kadar arteriyel kan, laktat ölçümü için "altın standart" olsa da, arteryel ve venöz laktat ölçümlerinin birbirinin yerine kullanılabilmesi, venöz kan gazı değerlendirmesinin tercih edildiği durumlarda, sık kan örneklemesinin neden olabileceği artmış maliyet ve iatrojenik anemiye engel olabilir. Bu çalışmada amacımız; on-pump kardiyak cerrahide arteryel (AL) ve santral venöz laktat (CVL) değerleri arasındaki korelasyon ve uyumu incelemektir.*
Yöntem: *Anestezik yönetim dahilinde, T1: anestezi indüksiyonu sonrası, T2: kros klemp sırasında ve T3: cilt kapatılırken olmak üzere üç aşamada eşzamanlı olarak arteryel ve venöz kan örnekleri olan yetişkin hastalar, bu retrospektif gözlemsel çalışmaya dahil edildi. CVL ve AL konsantrasyonları, T1, T2 ve T3 aşamalarındaki kan gazı analizinden elde edildi. Spearman Rho and Bland-Altman Testleri, AL ve CVL arasındaki sırasıyla korelasyon ve uyumu değerlendirmek için kullanıldı.*
Bulgular: *Toplamda 122 uygun hastadan 366 çift kan örneği elde edildi. 95% güven aralıkları sırasıyla; T1'de -0.07 ve -0.00, T2'de 0.30 ve -0.10 ve T3'de -0.16 ve -0.03'tü. 95% CI ise T1'de 0.86 ve 0.93 (r=0.90 ve p<0.0001); T2'de 0.95 ve 0.97 (r=0.96 ve p<0.0001) ve T3'de 0.92 to 0.96 (r=0.94 and p<.0001) olarak saptandı.*
Sonuç: *Her ne kadar laktat ölçümünün arteryel kandan örneklenmesi "altın standart" olarak kabul edilse de, on-pump kalp cerrahisi hastalarında santral venöz kandan örnekleme de kabul edilebilir bir alternatif olabilir.*

Anahtar kelimeler: *Arteryel laktat, venöz laktat, kardiyak cerrahi, korelasyon, uyum*

Received/Geliş: 11 April 2020
Accepted/Kabul: 09 August 2020
Publication date: 27 October 2020

Cite as: Tezcan B, Mungan İ, Şaylan A, et al. Does central venous lactate measurement replace arterial lactate measurement in cardiac surgery?. JARSS 2020;28(4):261-6.

Büşra Tezcan
Ankara Şehir Hastanesi,
Yoğun Bakım Kliniği,
Ankara - Türkiye
busraytezcan@yahoo.com
ORCID: 0000-0001-8914-0234

İ. Mungan 0000-0003-0002-3643
D. Ademoğlu 0000-0002-4493-4353
Ç. Bayındır Dicle 0000-0003-3554-9450
Ankara Şehir Hastanesi,
Yoğun Bakım Kliniği,
Ankara, Türkiye

A. Şaylan 0000-0002-3261-1004
Dışkapı Yıldırım Beyazıt
Eğitim ve Araştırma Hastanesi,
Anesteziyoloji ve Reanimasyon Kliniği,
Ankara, Türkiye

S. Sarı 0000-0002-1977-8547
Niğde Üniversitesi
Eğitim ve Araştırma Hastanesi,
Genel Yoğun Bakım Kliniği,
Niğde, Türkiye

B. Aytekin 0000-0003-4275-0072
Ankara Şehir Hastanesi,
Kardiyovasküler Cerrahi Kliniği,
Ankara, Türkiye

A. Özgök 0000-0002-0105-3388
H. Yazıcıoğlu 0000-0002-5407-5783
Ankara Şehir Hastanesi,
Anesteziyoloji ve Reanimasyon Kliniği,
Ankara, Türkiye

INTRODUCTION

Lactate is the metabolic end product of anaerobic glycolysis and consequently measurements of blood lactate levels provide important information on the adequacy of tissue perfusion [1]. Especially trend of lactate levels has been used to detect global tissue hypoxia, most notably in the assessment and monitoring of critically ill and trauma patients [2]. In the setting of cardiac surgery, extracorporeal circulation also increases blood lactate levels by inducing tissue hypoperfusion and impairing the balance between tissue O_2 demand and supply [3]. Therefore especially serial lactate measurements may also be valuable in cardiac surgery for detecting tissue oxygenation problems, predicting complications and applying preventive strategies [4,5].

Arterial blood is the "gold standard" for measurement of lactate, because it represents mixed venous blood which also can be considered to represent the sum of all sources of tissue lactate production [2]. The blood gas analyzers simultaneously measure lactate and blood gases usually in the same arterial blood sample. On the other hand, venous blood gas sampling is increasingly replacing arterial one in international practice in the last years [1]. Therefore if one choses to measure blood gases by venous blood sampling during cardiac anesthesia at any time point, the validity of using venous blood in lieu of arterial blood for lactate measurement gains importance, especially to avoid increased costs and iatrogenic anemia resulting from frequent blood sampling. On the other hand; although invasive arterial line insertion seems essential especially for continuous arterial pressure monitoring during cardiac surgery today, noninvasive continuous arterial pressure monitoring devices are under development and may replace invasive arterial monitoring in selected cases in the future [6,7]. Therefore central venous line insertion may be adequate for blood gas and lactate evaluation with noninvasive continuous arterial pressure monitoring devices.

Some published reports suggest that venous and arterial lactate measurements can be used interchangeably in pediatric, critically ill and emergency department patients [8-11]. The aim of our present retrospective study was to evaluate if central venous blood is an acceptable alternative sample for lactate measurement in on-pump cardiac surgery patients.

MATERIAL and METHODS

We performed this retrospective study at an education and research hospital. This was a study performed with cardiovascular surgery operating room patients over the course of one year between January 2018 and December 2018 inclusive. Institutional ethical approval was obtained. A computer search for all on-pump valvular heart and coronary artery bypass grafting (CABG) patients was conducted. Adult patients who had both arterial and central venous blood gas sampling simultaneously in three steps (T1: after anesthesia induction, T2: during cross- clamping, at 30-32°C, T3: during skin closure) of operation as part of anesthetic management were eligible for inclusion in the study. Obtaining both arterial and central venous samples for blood gas analysis was the routine procedure of an anesthesiology team in our hospital, during this time period. Acute surgical patients, patients aged <18 or >75 years with any hepatic disease, ASA physical status III-IV, those using inotropic or cardiac mechanical support, and whose surgery was anticipated to last more than >5 hours were excluded from the study.

All surgeries were performed under general anaesthesia with cardiopulmonary bypass (CPB) by the same team of anesthesiologists. Patients' radial or brachial artery was cannulated for blood sampling and invasive blood pressure monitorization was performed before anesthesia induction. Anesthesia was induced with midazolam, propofol, fentanyl and rocuronium and maintained with sevoflurane, midazolam, rocuronium and fentanyl. The internal jugular vein was also cannulated for blood sampling, central venous pressure monitorization, intravenous infusions and injections after anaesthesia induction and endotracheal intubation. Arterial and central venous blood gas samples were simultaneously obtained from patients' radial or brachial arteries and internal jugular veins, respectively at three steps (T1: after anesthesia induction, T2:during cross- clamping at 30-32°C, T3: during skin closure). There were no fluid administration between venous and arterial blood sampling. Central venous and arterial lactate concentrations estimated during blood gas analysis at

T1, T2 and T3 and were recorded. Samples were drawn into self-prepared heparinized syringes and analyzed on a Radiometer ABL800 FLEX (Radiometer, Copenhagen, Denmark) which is a point- of- care blood gas analyzer requiring 1.5 mL of whole blood.

Statistical analysis

Statistical analyses were done by Statistical Package for Social Sciences 20.0 and MedCalcver 16.4.3 software programmes. The continuous variables were displayed as mean and standard deviation. After the initial statistical analysis with the Kolmogorov-Smirnov test; since the data did not exhibit a normal distribution, non- parametric tests were chosen. The correlation between arterial lactate (AL) and central venous lactate (CVL) levels was assessed through Spearman rank correlation coefficient. Also data were graphically displayed on Bland-Altman plots. Mean difference with 95% limits of agreement were calculated and graphically represented using bias plots. All statistical analyses were 2 tailed and $p<0.05$ was required to determine statistical significance.

RESULTS

A total of 122 eligible patients were included. The mean age was 59.1±9.9 years. There were 89 (73%) male, 33 female (27%) patients. The operations performed were CABG (n=99) and valve surgery (n=23). The mean operation duration was 258.1±43.1 min, CPB was 93.8±24.6 min and the aortic cross-clamp time was 64.7±22.2 min. Totally 366 pairs (arterial and central venous pairs) of blood samples were obtained from 122 patients who met the inclusion criteria. Patient characteristics and operative variables are summarized in Table I. Mean AL and CVL values, the differences, 95% limits of agreement, coefficient of repeatability, 95% CI and Spearman

Table I. Patient characteristics and operative variables

Gender; Male/Female (n)	89/33
Age (years)	59.1±9.9
Type of operation (CABG/Valve surgery)	99/23
Body surface area (m²)	1.83±0.4
Comorbidities	
HT (n)	57
DM (n)	12
Other (n)	28
Operation duration (min)	258.1±43.1
CPB duration (min)	93.8±24.6
Cross clamp duration (min)	64.7±22.2
Postoperative complications	
Major adverse cardiac events (n)	5 (4%)
Respiratory complications (n)	3 (2%)
Surgical revision (n)	2 (1.6%)
Mortality (n)	3 (2%)

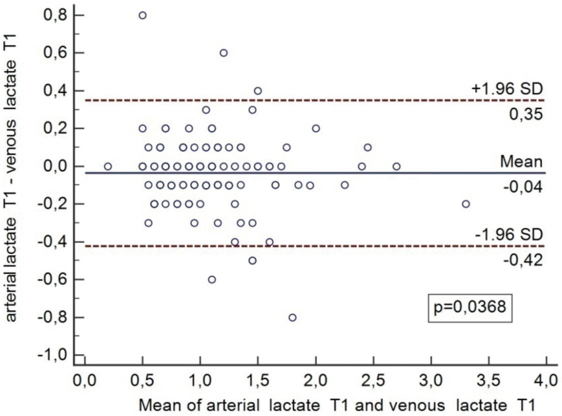

Figure 1. Bland-Altman plot of arterial and central venous lactate at T_1 (after anesthesia induction)

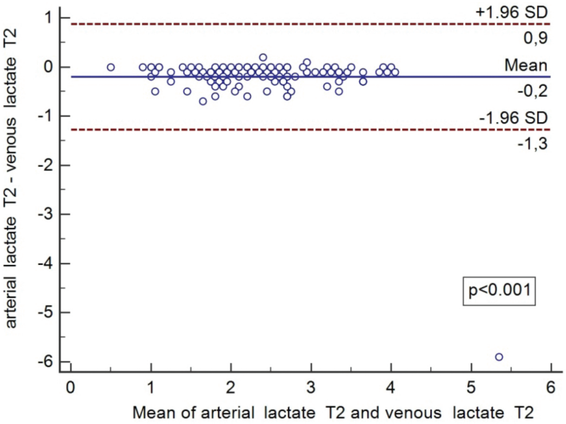

Figure 2. Bland-Altman plot of arterial and central venous lactate at T_2 (during cross clamp)

Table II. Lactate values (mmol L^{-1}) measured after anesthesia induction (T1), during cross clamp (T2) and during skin closure (T3); correlation, limits of agreement and coefficient of repeatability between arterial and venous lactate measurements at these three time points

Sampling times	AL (mean± std dev.)	VL (mean±std dev.)	Difference	95% limits of agreement	Coefficient of Repeatability	Spearman rank correlation coefficient(r)	95% CI	p*
T1	1.06±0.48	1.10±0.5	0.04±0.2	-0.07 to -0.00	0.39	0.902	0.863 to 0.931	p<0.001
T2	2.27±0.77	2.47±0.93	0.20±0.54	0.30 to -0.10	1.14	0.963	0.947 to 0.974	p<0.001
T3	2.34±1.18	2.43±1.21	0.09±0.37	-0.16 to -0.03	0.73	0.943	0.919 to 0.960	p<0.001

rank correlation coefficients are given in Table II. 95% limits of agreements were -0.07 to -0.00 at T1; 0.30 to -0.10 at T2 and -0.16 to -0.03 at T3. The 95% CIs were 0.86 to 0.93 (r=0.90 and p<0.0001) at T1; 0.95 to 0.97 at T2 (r=0.96 and p<0.0001) and 0.92 to 0.96 (r=0.94 and p<0.0001) at T3. The Bland-Altman plots are presented in Figure 1-3. Agreement between arterial and venous samples was good at all sampling times with narrow 95% limits of agreement. Strong correlations were found between CVL and AL at all time points.

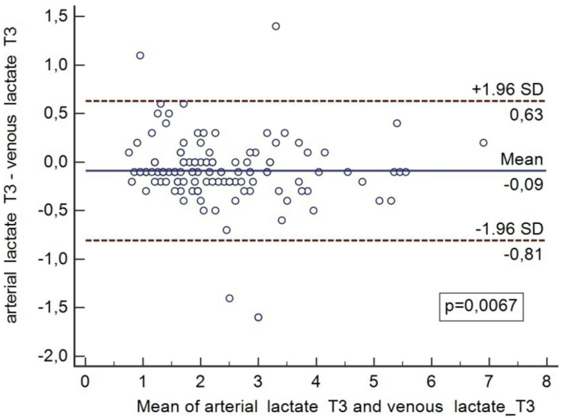

Figure 3. Bland-Altman plot of arterial and central venous lactate at T_3 (during the skin closure)

DISCUSSION

The aim of this study was to examine the correlation and agreement between the AL and CVL in patients undergoing CABG. The study findings showed a good agreement and correlation between lactate concentrations in central venous and arterial blood samples.

Lactate levels are useful markers of hypoperfusion and even in those patients considered hemodynamically stable, and the mortality rates are significantly higher in patients with hyperlactatemia [12]. Elevation of arterial lactate levels can be useful for detecting occult tissue hypoperfusion before clinical signs of organ dysfunction become manifest [12,13]. During cardiac surgery; peaks in lactate levels can be observed during or soon after the initiation of CPB. Cardiac surgery patients who have intraoperative hyperlactatemia have higher postoperative mortality rates than those with a normal lactate profile [14]. As a result lactate measurements are valuable especially in on-pump cardiac surgery.

The blood samples obtained using central venous catheters reflects only the blood lactate levels in the vessels of the upper part of the body. Since mixed venous blood is the mixture of superior vena cava and inferior vena cava blood; it can be accepted as a summary of the last blood sample in contact with the tissues at the microcirculatory level and representative of the the sum of whole body's lactate production. But mixed venous blood samples can only be obtained by pulmonary artery catheterization, which is a costly and risky practice [15]. Besides of this, arterial blood samples were used in the early studies about clinical utility of lactate and so, reference range of lactate was first established using arterial blood samples [16,17]. Therefore arterial lactate is accepted as the gold standard for lactate measurement based on the consideration that arterial blood is the derivative of mixed venous blood.

Considering the lactate concentration gradient from superior vena cava to a peripheral artery with the streaming of blood, the relationship between lactate levels at different points of this stream are investigated in specific patient populations by researchers. The agreement between arterial lactate and mixed venous lactate levels was first reported by Murdoch et al. [8] in 1994. But some authors have reported that lactate levels in mixed venous blood is not exactly equal to arterial lactate levels because of lactate production by the lungs during ARDS or acute lung injury [18,19]. Benjelid et al. [19] reported that following CPB the lungs release lactate into the systemic circulation. De Backer et al. [18] demonstrated that lung lactate production occurs in patients with acute lung injury.

Several authors reported a good correlation between arterial and central or mixed venous blood lactate concentrations with varying agreements, among critically ill patients [8,11,16,20]. Weil et al. [16] reported that the lactate concentrations in both central venous and pulmonary artery blood samples obtained from critically ill patients are the same as their arterial lactate concentrations. Reminiac et al. [11] concludes that CVL concentration is similar to AL concentration in critically ill patients with circulatory and/or respiratory failure and many critically ill patients can be managed without systematic arterial cannulation after further prospective and comperative studies.

To our knowledge, our study is the first to estimate the correlation and level of agreement between arterial and central venous blood measurement of lactate during cardiac surgery. The studies about the agreement and correlation between arterial and venous lactate values generally aims to decrease the need for arterial cannulation or puncture, in situations which venous blood gas measurements also can replace or are even preferred to arterial blood gas measurements. Although insertion of an arterial line seems essential for intermittent arterial blood gas sampling and continuous invasive arterial pressure monitoring in cardiac surgery; the agreement between arterial and central venous blood lactate concentrations may decrease frequency of blood sampling. During cardiac surgery, in clinical situations which central venous blood gases are preffered for evaluation, based on the fact that the blood gas analyzers simultaneously measure lactate and blood gases in the same blood sample, there will be no need to obtain arterial blood sample for lactate measurement. On the other hand there is a trend towards more noninvasive monitoring techniques and continuous noninvasive blood pressure monitoring systems are under development for even high risk surgeries [6,7]. Central venous blood gas sampling and continuous noninvasive blood pressure monitoring systems may reduce the need of arterial line insertion in the selected patients of cardiac surgery in the future.

The agreement and correlation between AL and CVL after anesthesia induction are maintained at a good level during the CPB. The blood is drained from the right side of the heart and returns to the systemic circulation through the aorta in CPB which does not affect the relationship between the AL and CVL. In fact, the best correlation was obtained during CPB, probably with the exclusion of lung circulation, because lactate production from the lung may become clinically evident in disease states [21]. But the difference between the AL and CVL during CPB was the highest at all time points, indicating an increased release of lactate from the upper part of the body. The AL measured at the end of the operation is the highest lactate value, probably because of the increased release of lactate from the whole body which is a result of anaerobic metabolism shift during the surgery and CPB period. As a result CVL and AL agree sufficiently well, at three different stages of on-pump cardiac surgery, for them to be considered interchangeable.

There are certain limitations of this study that should be noted. It has a rather homogeneous sample of cardiac surgery patients with stable operation period during which the highest lactate values do not exceed 4 mmol L^{-1}. Although the analysis of Reminiac et al. [11] shows that irrespective of the lactate concentration, CVL is sufficiently close to arterial lactate for the two values to be considered clinically interchangeable in critically ill patients, an extended study is required for cardiac surgery patients who develop higher blood concentrations of lactate.

In summary; venous blood gases are reliable and contain considerable information about the patient's metabolic, respiratory and circulatory condition [22]. If one chooses to measure central venous blood gases at any time point of on-pump cardiac surgery, the lactate values in this venous blood sample simultaneously measured by blood gas machines can replace arterial lactate measurement, which is accepted as "gold standard". It is known that frequent blood sampling both leads to iatrogenic anemia and increased costs. Therefore the interchangeable use of AL and CVL in cardiac surgery can help to reduce frequency of blood sampling resulting in less iatrogenic anemia and decreased costs.

Ethics Committee Approval: Approved
Conflict of Interest: None
Funding: None
Informed Consent: The patients' consent were obtained

REFERENCES

1. Bloom B, Pott J, Freund Y, Grundlingh J, Harris T. The agreement between abnormal venous lactate and arterial lactate in the ED: a retrospective chart review. Am J Emerg Med. 2014;32:596-600. https://doi.org/10.1016/j.ajem.2014.03.007
2. Higgins C. Lactate measurement: arterial versus venous blood sampling. Online Referencing acutecaretesting.org Jan 2017.
3. Swan H, Sanchez M, Tyndall CM, Koch C. Quality control of perfusion: monitoring venous blood oxygen tension to prevent hypoxic acidosis. J Thorac Cardiovasc Surg. 1990;99:868-72. https://doi.org/10.1016/S0022-5223(19)36902-8

4. Alves RL, Aragão e Silva AL, Kraychete NC, Campos GO, Martins Mde J, Módolo NS. Intraoperative lactate levels and postoperative complications of pediatric cardiac surgery. Paediatr Anaesth. 2012;22:812-17. https://doi.org/10.1111/j.1460-9592.2012.03823.x
5. Svenmarker S, Häggmark S, Ostman M. What is a normal lactate level during cardiopulmonary bypass? Scand Cardiovasc J. 2006;40:305-11. https://doi.org/10.1080/14017430600900261
6. Sun J, Chen H, Zheng J, Mao B, Zhu S, Feng J. Continuous blood pressure monitoring via non-invasive radial artery applanation tonometry and invasive arterial catheter demonstrates good agreement in patients undergoing colon carcinoma surgery. J Clin Monit Comput. 2017;31:1189-95. https://doi.org/10.1007/s10877-016-9967-9
7. Lin WQ, Wu HH, Su CS, et al. Comparison of Continuous Noninvasive Blood Pressure Monitoring by TL-300 With Standard Invasive Blood Pressure Measurement in Patients Undergoing Elective Neurosurgery. J Neurosurg Anesthesiol. 2017;29:1-7. https://doi.org/10.1097/ANA.0000000000000245
8. Murdoch IA, Turner C, Dalton RN. Arterial or mixed venous lactate measurement in critically ill children. Is there a difference? Acta Paediatr. 1994;83:412-3. https://doi.org/10.1111/j.1651-2227.1994.tb18131.x
9. Middleton P, Kelly A-M, Brown J, Robertson M. Agreement between arterial and central venous values for pH, bicarbonate, base excess, and lactate. Emerg Med J. 2006;23:622-4. https://doi.org/10.1136/emj.2006.035915
10. Lavery RF, Livingston DH, Tortella BJ, Sambol JT, Slomovitz BM, Siegel JH. The utility of venous lactate to triage injured patients in the trauma center. J Am Coll Surg. 2000;190:656-64. https://doi.org/10.1016/S1072-7515(00)00271-4
11. Réminiac F, Saint-Etienne C, Runge I, et al. Are central venous lactate and arterial lactate interchangeable? A human retrospective study. Anesth Analg. 2012;115:605-10. https://doi.org/10.1213/ANE.0b013e31825e703e
12. Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. Crit Care. 2004;8:R60-5. https://doi.org/10.1186/cc2423
13. Abramson D, Scalea TM, Hitchcock R, Trooskin SZ, Henry SM, Greenspan J. Lactate clearance and survival following injury. J Trauma. 1993;35:584-8. https://doi.org/10.1097/00005373-199310000-00014
14. Demers P, Elkouri S, Martineau R, Couturier A, Cartier R. Outcome with high blood lactate levels during cardiopulmonary bypass in adult cardiac operation. Ann Thorac Surg. 2000;70:2082-6. https://doi.org/10.1016/S0003-4975(00)02160-3
15. Kopterides P, Bonovas S, Mavrou I, Kostadima E, Zakynthinos E, Armaganidis A. Venous oxygen saturation and lactate gradient from superior vena cava to pulmonary artery in patients with septic shock. Shock. 2009;31:561-7. https://doi.org/10.1097/SHK.0b013e31818bb8d8
16. Weil M, Michaels S, Rackow E. Comparison of blood lactate concentrations in central venous, pulmonary artery and arterial blood. Crit Care Med. 1987;15:489-90. https://doi.org/10.1097/00003246-198705000-00006
17. Bellomo R, Kellum JA, Pinsky MR. Transvisceral lactate fluxes during early endotoxemia. Chest. 1996;110:198-204. https://doi.org/10.1378/chest.110.1.198
18. de Backer D, Creteur J, Zhang H, Norrenberg M, Vincent JL. Lactate production by the lungs in acute lung injury. Am J Respir Crit Care Med. 1997;156:1099-104. https://doi.org/10.1164/ajrccm.156.4.9701048
19. Bendjelid K, Treggiari MM, Romand JA. Transpulmonary lactate gradient after hypothermic cardiopulmonary bypass. Intensive Care Med. 2004;30:817-21. https://doi.org/10.1007/s00134-004-2179-7
20. Nascente AP, Assuncao M, Guedes CJ, et al. Comparison of lactate values obtained from different sites and their clinical significance in patients with severe sepsis. Sao Paulo Med J. 2011;129:11-6. https://doi.org/10.1590/S1516-31802011000100003
21. Iscra F, Gullo A,Biolo G. Bench-to-bedside review: lactate and the lung. Crit Care. 2002;6:327-9. https://doi.org/10.1186/cc1519
22. Widgren B, Ekhardt M. Blood Lactate: A Useful Analysis in Emergency Care. Online Referencing acutecaretesting.org July 2012.