EGYPTIAN JOURNAL OF ANAESTHESIA
2024, VOL. 40, NO. 1, 179–183
https://doi.org/10.1080/11101849.2024.2331366

RESEARCH ARTICLE

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A comparative study between serum lactate level versus change in end tidal carbon dioxide level regarding assessment of hemodynamic instability in intensive care unit patients after cardiac surgeries

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ABSTRACT

Background: After cardiac surgeries, elevated lactate level is used as a marker of tissue hypoperfusion. Still, there is a search for other helpful markers of hemodynamic instability. Exhaled carbon dioxide has been recently studied as marker of cardiac output and tissue perfusion and may be considered a reliable alternative which is more convenient and real time.

Objectives: The main aim is to correlate between end tidal carbon dioxide ($ETCO_2$) and serum lactate level as indicators of hemodynamic instability in intensive care unit (ICU) patients after cardiac surgeries. The secondary objective is to correlate the measured parameters to the changes in the vital data and the resuscitation efforts.

Methods: A prospective cohort study that enrolled 51 adult patients admitted to ICU after cardiac surgeries. The serum lactate and $ETCO_2$ values as well as vital data and vasopressor doses were recorded on admission to ICU, after 2 hours and after 6 hours.

Results: The study shows insignificant weak positive correlation between Lactate and $ETCO_2$ levels at admission ($r = 0.172$, p value = 0.229), and insignificant negative weak correlation after 2 hours ($r = -0.148$, p value = 0.300) and after 6 hours ($r = -0.235$, p value = 0.096). Moreover, lactate level showed significant direct relation with the doses of vasopressors at admission, after 2 hours and after 6 hours postoperative (p value < 0.001 at all intervals). Whereas there was insignificant relation between $ETCO_2$ and doses of vasopressors at all intervals (p value = 0.23, 0.4 and 0.18 respectively).

Conclusion: In post-cardiac surgery ICU patients we detected no statistically significant relation between serum lactate and $ETCO_2$ as indicators of hemodynamic instability. The change in $ETCO_2$ over a period of time has failed so far to be of a beneficial value as a non-invasive real-time cardiac output monitoring parameter. In addition, serum lactate had strong correlation with changes in vital signs and resuscitation efforts.

ARTICLE HISTORY
Received 11 January 2024
Revised 23 February 2024
Accepted 2 March 2024

KEYWORDS
Carbon dioxide; cardiac surgery; hemodynamic; lactate

1. Introduction

Cardiac surgeries are a frequent surgical procedures and the intensive care management that follows usually involves significant complications that require early and rapid detection and management to minimise organ hypo-perfusion. Hemodynamic deteriorations are frequent but may initially be subtle, therefore they need rapid detection and targeted interventions [1].

Despite the growing availability of minimally invasive procedure of cardiac output monitoring, they are still not used as a main stream practice due to many factors, such as the increasing costs and the need for certain skills and equipment. For example, pulse contour analysis devices are expensive and not widely available. Trans-esophageal echocardiography is now frequently used in the operating theatre, but the technique is less suitable for monitoring in the ICU. Trans-thoracic echocardiography is of limited use postoperatively due to the poor cardiac window. Hence, there is always a search for less expensive and more simple methods [2].

$ETCO_2$ can reflect the pulmonary blood flow fluctuations provided that the ventilation parameters and the metabolic rate are relatively constant [3]. Several studies showed that $ETCO_2$ has an inverse correlation with serum lactate level in critically ill patients in ICU. A favourable characteristic for $ETCO_2$ is that it reflects the changes rapidly while serum lactate clearance is usually calculated on 6 hourly intervals and can be affected by other factors [4].

Furthermore, many cardio-pulmonary resuscitation (CPR) guidelines have included the measurement of $ETCO_2$ to reflect the efficiency of chest compressions and it can clearly mark the return of spontaneous circulation [5]. Studies have proven that $ETCO_2$ can

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Table 1. Association between doses of vasopressors and levels of lactate and $ETCO_2$ on different time intervals.

		Lactate at 0 hour (mmol/L)		$ETCO_2$ at 0 hour (mmHg)	
Time interval	Vasopressor dose	Mean ± SD	P value	Mean± SD	P value
On admission (0 hour)	Low	3.34 ± 2.15	<0.001*	33.41 ± 6.86	0.236
	High	6.72 ± 3.10		35.95 ± 8.05	
After 2 hours	Low	3.74 ± 1.60	<0.001*	37.97 ± 7.18	0.401
	High	7.37 ± 3.49		36.10 ± 8.43	
After 6 hours	Low	3.03 ± 1.57	<0.001*	38.68 ± 6.62	0.188
	High	5.92 ± 2.97		36.05 ± 7.22	

Test of significance: Independent Sample t test.

be used for monitoring hemodynamic changes in circulatory shock and it can predict fluid responsiveness after a bolus load or during passive leg raise (PLR) test [6].

2. Patients and methods

The study design is a prospective cohort study. It was conducted in Ain Shams University Hospitals, Cairo, Egypt, after Medical Ethical Committee approval and included post cardiac surgery patients undergoing elective surgeries including: coronary artery bypass grafting, mitral valve replacement, aortic valve replacement, atrial septal defect repair, left atrial myxoma removal and combined operations are included. The patients included are aged from 21 to 70 years old of both sexes. Written informed consent for data collection was obtained. The study started on the 28 of July 2022 and lasted one year. Patients having history of chronic respiratory or chronic liver or kidney diseases, patients having oncological diseases or having chest wall deformities and pregnant female patients were excluded from the study.

According to Wiryana et al. (2017) [7] who reported a statistically significant relation between lactate level and $ETCO_2$ in hemodynamically unstable patients, a sample size of more than 45 cases achieves the power of 90% to detect a Pearson correlation coefficient of at least 0.5 between $ETCO_2$ and lactate using a t-test for r with level of significance of 0.05. Thus we included 51 patients in the study with random sampling by computer generated program.

• Study Procedures: The patients were transferred to the ICU directly after the operation for stabilization. The patients were all ventilated and sedated. They were attached to a monitor including waveform infrared adsorption spectroscopy capnography module and the values of the $ETCO_2$ were obtained and documented at time of admission to ICU, after 2 hours and after 6 hours from admission. Arterial blood gases sample including serum lactate level were analyzed and the values were recorded at the same times of $ETCO_2$ recordings. Other hemodynamic values including mean arterial blood pressure heart and respiratory rate, temperature and oxygen saturation, in addition to the inotropic and vasopressors dosages were documented. A cutoff value of 0.1 mcg/kg/min of adrenaline, noradrenaline or both was set to evaluate the patients' needs for vasopressor and inotropic support; doses below the cutoff value were considered low while doses equal or more than the cutoff value were considered high.

• Statistical Package: After data collection and preparation, descriptive statistics were calculated for parametric numerical data. We used analytical statistics including independent sample t-test utilizing *p* value for level of significance, where a value of ≥ 0.05 is set to be insignificant, while a value of < 0.05 is set to be of statistical significance.

3. Results

Table (1) showed significant relation between the lactate level and vasopressor doses at all intervals where higher lactate levels were recorded among patients requiring high doses of vasopressors (=/> 0.1 mcg/kg/min of noradrenaline and/or adrenaline) compared with low levels (<0.1 mcg/kg/min of noradrenaline and/or adrenaline). There was also insignificant relation between vasopressors doses and $ETCO_2$ at all intervals.

Table (2) shows a significant direct moderate relation between serum lactate and heart rate (HR) at admission, and a moderate noteworthy negative correlation between serum lactate and mean arterial pressure (MAP) after 2 hours.

Table 2. Correlation between different quantitative variables and levels of lactate.

	Lactate (0 hour)		Lactate (2 hours)		Lactate (6 hours)	
Variable	Correlation co-efficient (r)	P value	Correlation co-efficient (r)	P value	Correlation co-efficient (r)	P value
Age	−0.030	0.837	0.092	0.520	0.044	0.759
Weight	0.189	0.184	0.079	0.581	0.040	0.783
MAP	−0.234	0.098	−0.403	0.003*	−0.074	0.606
HR	0.450	0.001*	0.274	0.052	0.237	0.093
Temperature	0.241	0.089	0.097	0.500	−0.156	0.275

Test of significance: Pearson correlation.

Table 3. Correlation between different quantitative variables and levels of $ETCO_2$.

	$ETCO_2$ (0 hour)		$ETCO_2$ (2 hours)		$ETCO_2$ (6 hours)	
Variable	Correlation co-efficient (r)	P value	Correlation co-efficient (r)	P value	Correlation co-efficient (r)	P value
Age	−0.159	0.264	−0.123	0.390	−0.250	0.077
Weight	0.070	0.626	0.027	0.850	−0.090	0.528
MAP	0.282	0.045*	0.135	0.344	−0.074	0.067
HR	0.284	0.043*	0.119	0.407	−0.011	0.941
Temperature	0.007	0.960	0.131	0.360	0.094	0.510

Test of significance: Pearson correlation.

Table (3) shows only a significant weak positive correlation with MAP and HR on admission.

Figure (1) shows insignificant weak positive correlation.

Figure (2) shows insignificant weak negative correlation.

Figure (3) shows insignificant weak negative correlation.

Table (4) shows significant change in the level of Lactate at admission, after 2 and 6 hours where the levels increased after 2 hours and then it decreased after 6 hours. It also shows significant change in the levels of $ETCO_2$ at admission, after 2 and 6 hours where the levels increased after 2 hours and continued to increase after 6 hours.

4. Discussion

The use of $ETCO_2$ as a tool for assessment of hemodynamic instability and fluid responsiveness has been studied widely but the results were variable. Many studies showed promising results [7–11], while others showed otherwise [12,13]. Most of the previous studies that proved significant relation between $ETCO_2$ and changes of the hemodynamic parameters were targeting fluid responsiveness at short periods of time to avoid variations of metabolism and ventilation parameters.

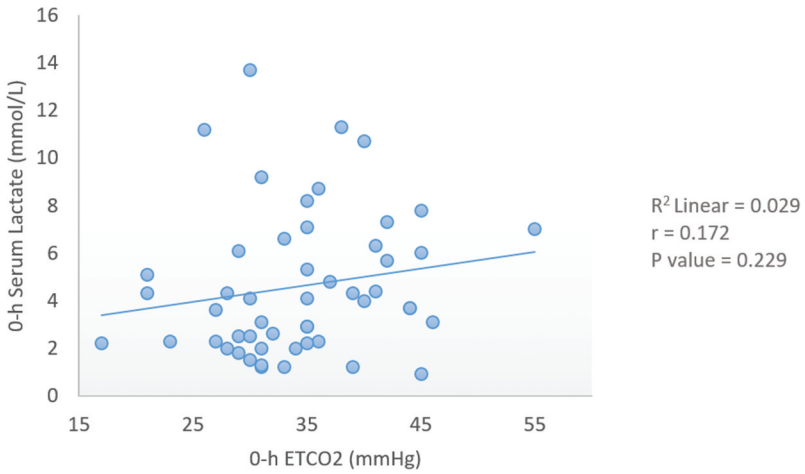

Figure 1. Correlation between levels of lactate and $ETCO_2$ on admission.

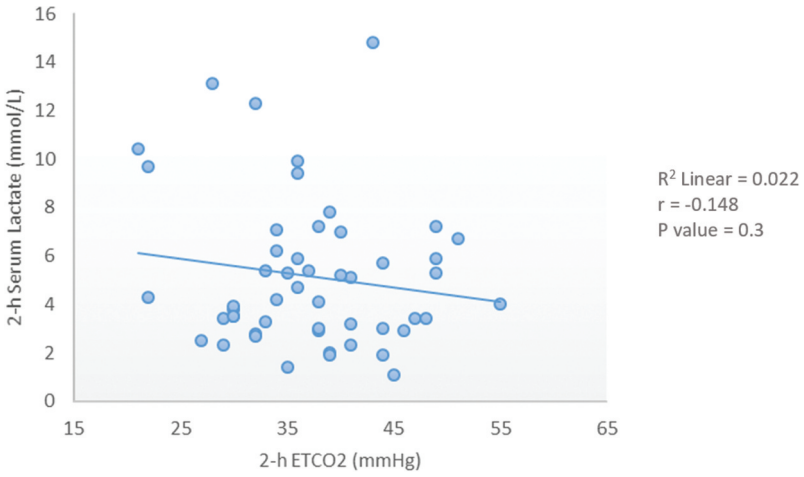

Figure 2. Correlation between levels of lactate and $ETCO_2$ after two hours.

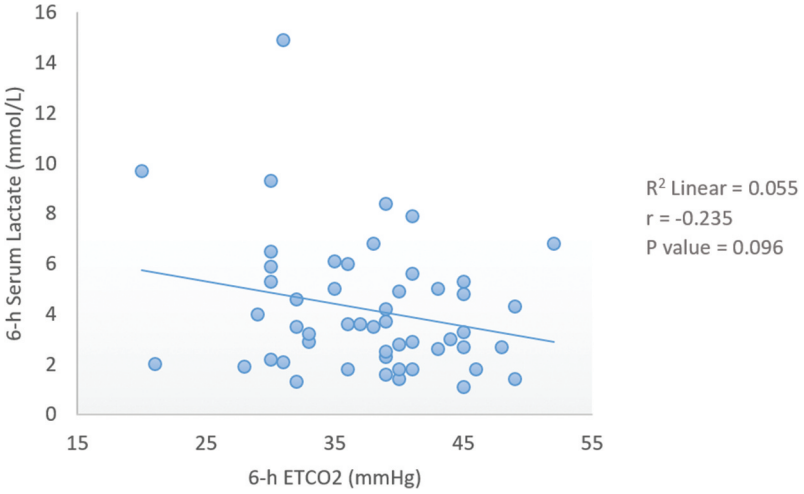

Figure 3. Correlation between levels of lactate and $ETCO_2$ after six hours.

Table 4. Lactate and $ETCO_2$ levels comparison at admission, after two and six hours.

	Lactate level (mmol/L)			$ETCO_2$ level (mmHg)		
Intervals	Mean ± SD	P value	Rank	Mean ±SD	P value	Rank
0 hour	4.6 ± 3.0	0.001*	AB	34.4 ± 7.4	0.019*	A
2 hours	5.2 ± 3.1		A	37.2 ± 7.7		B
6 hours	4.2 ± 2.6		B	37.7 ± 6.9		B

Test of significance: Repeated measure ANOVA.
Pairwise comparison was done using Bonferroni where different letters in rank indicates significant difference between groups, while similar letters indicate no statistically significant difference between groups.

Applying the previously tested results in common clinical scenarios and specific sub-population of ICU patients was needed to verify usefulness of measuring $ETCO_2$ as a supporting parameter or a substitute for conventional methods. To the best of our knowledge, we are the foremost to compare $ETCO_2$ with the conventional serum lactate level over an extended time period (6 hours) in post-cardiac surgery patients.

Our study showed no statistically significant direct relationship between $ETCO_2$ and serum lactate level: at time of admission to ICU ($r = 0.172$, p value = 0.229), after 2 hours ($r = -0.148$, p value = 0.300) and after 6 hours ($r = -0.235$, p value = 0.096). These results could be either due to the poor ability of $ETCO_2$ to predict the subtle hemodynamic changes in the direct post-operative period, or that they both could be reflecting such changes with a different pattern.

The support for the former argument, as demonstrated in a previous study by Jin et al. who suggested that $ETCO_2$ needs a wide drop of cardiac output (>40%) to be affected [14]. That may affect the ability of $ETCO_2$ to reflect subtle fluctuations in the flow of the pulmonary circulation.

The support for the latter argument is that the measured serum lactate levels in our study showed distinctive pattern of being relatively low on admission (mean = 4.6 ± 3.0 mmol/L) and starting to rise at 2 hours (mean = 5.2 ± 3.1 mmol/L) and then drop again at 6 hours (mean = 4.2 ± 2.6 mmol/L), while the values of $ETCO_2$ showed another distinctive pattern of steadily rising gradually throughout the postoperative period (mean = 34.4 ± 7.4 mmHg on admission, 37.2 ± 7.7 mmHg after 2 hours and 37.7 ± 6.9 mmHg after 6 hours).

We suggest that this trend can be explained by the patient's instability following withdrawal from the cardio-pulmonary bypass pump or their instability while being transported from OR to the ICU that leads to hemodynamic effects that are reflected late on the serum lactate level while affecting the $ETCO_2$ more rapidly making it detectable at time of admission and gradually improves over time. This goes in line with Hajjar et al. who stated that in post cardiac surgery patients, measuring serum lactate 6 hours after admission to ICU is a reliable marker for poor tissue perfusion and is a risk factor for poor outcomes [15]. It also goes in line with Hoff et al. who stated that $ETCO_2$ reflects immediate changes in the cardiac output [9].

Furthermore, our study showed that serum lactate levels have a better correlation with the patients' vital data (mean arterial pressure and heart rate). More obvious was the correlation between serum lactate and doses of vasopressors needed (p value < 0.001 at all measurement intervals), where lactate levels were higher among patients requiring higher doses of vasopressors. On the other hand, there was insignificant relation between $ETCO_2$ and doses of vasopressors at all measurement intervals (p value = 0.23, 0.4 and 0.18 at 0, 2 and 6 hours respectively).

Limitations of using $ETCO_2$ widely as a standard parameter of hemodynamic instability are that it is not applicable on patients with respiratory diseases in addition to the technical difficulties of measuring its level accurately in non-intubated patients. Moreover, three variables are affecting $ETCO_2$ at all times: (1) CO_2 production from tissues, (2) cardiac output and subsequent effect on pulmonary blood flow, and (3) ventilation in alveoli. As a result, $ETCO_2$ can reflect cardiac output more accurately provided that the ventilation parameters and CO_2 production are stable [16]. Such stability is difficult to achieve in the general ICU patient population.

5. Conclusion

In post-cardiac surgery ICU patients we detected no statistically significant relation between serum lactate and $ETCO_2$ as indicators of hemodynamic instability. The change in $ETCO_2$ over a period of time has failed so far to be of a beneficial value as a non-invasive real-time cardiac output monitoring parameter. In addition, serum lactate had strong correlation with changes in vital signs and resuscitation efforts.

As for future research recommendations, $ETCO_2$ needs to be compared with other dynamic real-time parameters such as pulse pressure variation (PPV), pulse contour analysis, velocity time integral (VTI) or trans-pulmonary thermos-dilution techniques. Furthermore, other data as fluid resuscitation and cumulative doses of cardio-vascular drugs could be considered during comparison.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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