Prediction of intensive care unit mortality: Interest of serum lactates

Prédiction de la mortalité en réanimation : Intérêt des lactates

Chiheddine Ben Maaouia, Faten Haddad, Asma Ben Souissi, Hajer Arfaoui, Amani Ben Hadj Youssef, M'hamed Sami Mebazaa

Service d'anesthésie réanimation, CHU Mongi Slim, Tunis, Tunisie. Faculté de médecine de Tunis.

Abstract

Background: Many prognostic indices have been developed to assess clinical status and predict the probability of death in the intensive care unit (ICU) but none have perfect sensitivity or specificity.
Aim: to evaluate the prognostic value of admission lactate in patients admitted to ICU.
Methods: A cohort, observational, prospective study was carried out in the intensive care unit (ICU) of Mongi Slim Hospital, la Marsa, over 12 months period. Arterial blood lactate (ABL) was measured in ICU admission (H0), then 6 hours (H6), 12 hours (H12), 24 hours (H24) and 48hours (H48) after admission. Prognostic scores were calculated 24 hours after the admission. We also recorded biological data, hemodynamic parameters, and the evolution during the stay in intensive care. Primary endpoint was ICU mortality.
Results: We included 135 patients. The average age was 47.22 ± 16.88 years with a sex-ratio of 1.75. ICU mortality was 48%. The mean ABL at admission was 3.05 ± 2.63 mmol/l, higher in the dead group with a statistically significant difference.
Prognostic value of lactate at admission was less powerful than severity indices in this study but remains excellent with an AUC >0, 7 defining « cut-off » values with a good sensitivity and specificity. In multivariate analysis, initial lactate > 2 mmol/l was found to be an independent predictive factor of ICU mortality with an Odd Ratio [IC 95%] =1.16 [1.07 – 3.6]; p=0.04.
Conclusions: Monitoring lactatemia in ICU could allow better identification of patients at high risk of death and the reassessment of therapeutic efficacy.

Key words: Lactates – Mortality – Organ Dysfunction Scores – Prognosis – Intensive care unit - Morbidity

Résumé

Introduction: De nombreux indices pronostiques ont été développés pour évaluer l'état clinique et prédire la probabilité de décès en unité de soins intensifs (USI) mais aucun n'a une sensibilité ou une spécificité parfaite.
Objectif: évaluer la valeur pronostique du lactate à l'admission chez les patients admis en réanimation.
Méthodes: Une étude de cohorte, observationnelle et prospective a été réalisée dans l'USI de l'hôpital Mongi Slim, la Marsa, sur une période de 12 mois. Le lactate sanguin artériel a été mesuré à l'admission (H0), puis à H6, à H12, à H24 et à H48 après l'admission. Les scores pronostiques ont été calculés. Le critère principal était la mortalité en USI.
Résultats: Nous avons inclus 135 patients. L'âge moyen était de 47,22 ± 16,88 ans avec un sex-ratio de 1,75. La mortalité en USI était de 48 %. Le taux de lactates moyen à l'admission était de 3,05 ± 2,63 mmol/l, significativement plus élevé dans le groupe décédé.
La valeur pronostique du lactate à l'admission était moins puissante que les indices de sévérité dans cette étude mais reste excellente avec une ASC >0,7 définissant des valeurs seuils avec une bonne sensibilité et spécificité. En analyse multivariée, le lactate initial > 2 mmol/l était prédictif de mortalité en USI avec un Odd Ratio [IC 95%] =1,16 [1,07 – 3,6] ; p=0,04.
Conclusion: Le suivi de la lactatémie en réanimation pourrait permettre une meilleure identification des patients à haut risque de décès et la réévaluation de l'efficacité thérapeutique.

Mots clés: Lactates - Mortalité – Scores de dysfonction d'organes – Pronostic – Unités de soins intensifs- Morbidité.

Correspondance
Chiheddine Ben Maaouia
Service d'anesthésie réanimation, CHU Mongi Slim, Tunis, Tunisie. Faculté de médecine de Tunis.
Email: benmaaouia.chiheb@hotmail.fr

INTRODUCTION

Despite medical progress, mortality in intensive care unit (ICU) remains high with variability; this is around 17% for all-round resuscitation, the 26% in septic patients, can reach 50% in the event of associated shock (1). Any patient admitted to intensive care is therefore a real challenge not only for the medical team but also for the entire health system.

Lactate long considered a metabolic waste and synonymous with cellular hypoxia and anaerobiosis, is currently considered a central and main player in energy metabolism (2).

The contribution of lactate monitoring in intensive care has been widely described in the literature. Indeed, this biomarker has been proposed for several decades as a reliable prognostic tool and an independent factor of morbidity and mortality (3).

However, studies differ on the different aspects of lactatemia in intensive care; some point the superiority of a single measure on admission in precise timing over repeated measures.

The main aim of this study was to assess the prognostic value of arterial lactate during the first 24 hours in all patients admitted to ICU regardless of their initial pathologies.

Secondarily, to determine a cut-off for lactatemia on admission predictive of mortality in ICU, to evaluate the predictive value of the different other aspects (statics and dynamics) of lactatemia during the first 24 hours on morbidity and ICU mortality and to compare the diagnostic performance of arterial lactate with the various severity indices predicting mortality in ICU.

METHODS

Study design

A cohort, observational, prospective study was carried out in the ICU of Mongi Slim Hospital, La Marsa, Tunisia between July 2019 and June 2020. The study was approved by the hospital's scientific council and the Ethics committee.

Patient selection and enrolment criteria

All patients older than 18 years admitted to the ICU were eligible for study inclusion. Were not included, patients transferred from another hospital structure.

Patients were excluded from participating in the study if they died within the first 24 hours following their arrival in ICU, if their medical charts revealed implausible or their lactate data incomplete and if they have been transferred to another ICU.

Data acquisition

For all patients admitted to our department, the following variables were recorded at admission: age, sex, weight, comorbidities, cause of admission, prognostic score ; Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score (SAPS II), Glasgow Coma Scale (GCS),Injury Severity Score (ISS) for trauma patients, need for hemodynamic support, mechanical ventilation (MV), renal failure defined according to the KDIGO criteria (4), and we noted the stay in ICU.

The laboratory values evaluated were: leukocytes, platelet count, serum creatinine, arterial blood gas, sodium and potassium, bilirubin, prothrombin time.

While the physiological parameters measured were: heart rate, medium arterial tension, and diuresis.

Outcomes measures

The primary outcome was ICU mortality. Secondary outcomes included ICU length of stay (LOS), need of MV, requirement for vasopressors and organ dysfunction.

Patients were stratified according to survival to ICU discharge in two groups: SURVIVOR or NOT SURVIVOR.

Measurements of Lactate levels

Lactate concentrations were measured at H0, H6, H12, H24, and H48 systematically from an arterial blood sample with a heparinized syringe. The analysis was performed instantly in the department.

We have also studied other aspects of hyperlactatemia such as:

- Lactate clearance (LC) at H6, H12 and H24 for which we used formula $\frac{Lactate\ level\ at\ admission - lactate\ level\ at\ time\ point}{Lactate\ level\ at\ admission} * 100\%$
- Persistent Hyperlactatemia defined as a lactate level greater than or equal to 2 mmol/l throughout the first 24 hours despite adequate management.
- Lactate Area Score defined by the sum of the areas under the curves of a series of lactates samples taken at H0, H6, H12, H24 using the trapezoid rule (5).

Statistical analyses

We used IBM SPSS Statistics v.26 for statistical analysis. The Kolmogorov- Smirnov test was used to assess the distribution of data. Descriptive results are given as: quantitative ones are presented as mean ± standard deviation (SD) for normally distributed parameters and as median with 25-75% interquartile range (IQR), while qualitative ones were expressed by absolute numbers and percentage.

Comparison between the study groups was performed using the Chi-square test (X^2) of Fisher's exact test. We compared the prognostic value of different aspects of lactatemia and to the other severity scores using receiver operating characteristic (ROC) curves. Threshold values were determined by considering values that yielded the greatest sensitivity and specificity by calculating the Youden Index.

The association between the different prognostic scores, lactate levels and ICU mortality was determined by univariate and multivariate logistic regression. Results were reported as odd ratio (OR) and 95% confidence interval (CI). A p value < 0.05 was considered statically significant.

RESULTS

General population characteristics

During the study period, 235 eligible patients were enrolled in the study. We excluded 100 patients, leaving 135 patients who were included, 95 (71.1%) of whom presented surgical pathology (49 (51%) were post traumatic patients) and 39 (28.9%) presented medical pathology. Patients' characteristics are summarized in Table 1.

The overall mortality was 48% of included patients and it was much higher in case of sepsis than in trauma (78% vs. 30.6%). The comparison of the survivor group (70 patients) and not survivor group (65 patients) revealed that the average age was significantly higher in the non-survivor (53.9±16.5 vs. 41±14.7 years, p<0.001). The non-survivor patients were predominantly male (58.5% vs. 41.5%) and had higher prevalence of arterial hypertension and diabetes (30.8% vs. 12.9%, p=0.01; 30, 8% vs. 15.7%, p=0.03 respectively). Upon admission in ICU, non –survivor patients were clinically more serious as evidenced by severity scores which were significantly higher: the mean

SOFA score was 8.98±3.2 vs. 5.2±3.2; p<0.001, the mean APACHE II score was 22.35±8.06 vs. 12.39± 6.56; p<0.001 and the mean ISS II score was 51.7±15.9 vs. 28.8±13.5, p<0.001); they needed more vasopressor (76.9% vs.48.6%; p<0.001) , required MV (89.2% vs. 55% ;p<0.001) and had more organ dysfunction such as renal failure (30.8% vs. 5.7%;p<0.001).

Table 1. General characteristics, vital signs, laboratory parameters and outcomes of the population: subgroup analysis stratified by intensive care unit mortality

Characteristics	Population (n=135)	Survivor (n=70)	Non Survivor (n=65)	p
Age (years)	47.2 ± 16.9	41.0 ± 14.7	53.9 ± 16.6	$<10^{-3}$
Masculine Gender	86 (63.7 %)	48 (68.6 %)	38 (58.5 %)	0.222
Diabetes	31 (23 %)	11 (15.7 %)	20 (30.8 %)	0.038
HT*	29 (21.5 %)	9 (12.9 %)	20 (30.8 %)	0.011
SOFA† score	7.0 ±3.7	5.2 ± 3.2	8.98 ± 3.2	$<10^{-3}$
APACHE‡ II score	17.13 ±8.87	12.29 ± 6.56	22.35 ± 8.06	$<10^{-3}$
ISS§ II score	39.9 ±16.64	28.8 ± 13.5	51.7 ± 15.9	$<10^{-3}$
GCS‖	11.7 ± 4.1	12.3 ± 4.0	11.4 ± 4.3	0.211
MBP¶ (mmHg)	88.2 ±13.5	91.3 ± 13.7	84.8 ± 12.6	0.005
pH	7.29 ± 0.15	7.31 ± 0.13	7.26 ± 0.17	0.033
HCO3- (mmol/l)	18.25 ± 5.55	19.41 ± 5.09	17 ± 5.8	0.011
Leucocytes (10^3/mm3)	14.8 ± 7.6	12.7 ± 5.1	17.01 ± 9	0.001
Platelets (10^3/mm3)	221 ± 126.3	217 ± 109.6	225.2 ±142.8	0.711
PT** (%)	66.3 ± 19.8	72.7 ± 16.7	59.3 ± 20.6	$<10^{-3}$
Bilirubin (mmol/l)	12[8 ; 21.4]	9.65[6 ; 20]	14.7[9.2 ;23.4]	0.019
Creatinine (µmol/l)	126 ± 110	85.65 ±76.59	169.24±124.03	$<10^{-3}$
Mechanical ventilation	97 (71.8 %)	39 (55.7 %)	58 (89.2 %)	$<10^{-3}$
Oligo-anuria	24 (17.8 %)	4 (5.7 %)	20 (30.8 %)	$<10^{-3}$
Organ dysfunction	67 (49.6 %)	17 (24.3 %)	50 (76.9 %)	$<10^{-3}$
Vasopressor use	84 (62.2 %)	34 (48.6 %)	50 (76.9 %)	0.001

HT*: Hypertension, SOFA†: Sequential Organ Failure Assessment, APACHE II‡: Acute Physiology and Chronic Health Evaluation II, ISS II§: Injury Severity Score, GCSII: Glasgow Coma Scale, MBP: Median Blood Pressure, PT**: The prothrombin level.

Lactate study

Lactate values during the first 24 hours were significantly higher in the non-survivor group (Table 2).

Table 2. Study of the different aspects of lactatemia during the first 24 hours

Characteristics	Population (n=135)	Survivor (n=70)	Non survivor (n=65)	p
Lactate at H0 (mmol/l)	3.05 ± 2.63	2.11 ± 1.55	4.06 ± 3.15	$<10^{-3}$
Lactate at H6 (mmol/l)	2.7 ± 2.61	1.86 ± 1.69	3.60 ± 3.09	$<10^{-3}$
Lactate at H12 (mmol/l)	3.04 ± 2.35	2.13 ± 2.1	3.5 ± 2.3	0.013
Lactate at H24 (mmol/l)	1.72 ± 1.88	1.04 ± 0.74	2.46 ± 2.41	$<10^{-3}$
Lactatemia >2 mmol/L	73 (54%)	26 (37.1 %)	47 (70.8 %)	$<10^{-3}$
Lactatemia > 4 mmol/L	36 (26.7%)	11 (15.7 %)	25 (38.5 %)	$<10^{-3}$
Lactate Clearance H6(%)	20 [21.3 ;39.1]	16.06[0 ; 39.1]	23.7[-34.8 ;40.2]	0.526
Lactate Clearance H12 (%)	42.8[-2.4 ; 65]	57.5[30.3 ;73.5]	34.2[-7.8 ; 58.8]	0.016
Lactate Clearance H24 (%)	62.5[29.4 ; 73]	70.45[51.5 ;76.5]	54.6[18.2 ; 70]	0.015
Persistent hyperlactatemia	68 (50.4 %)	25 (35.7 %)	43 (66.2 %)	$<10^{-3}$
Lactate Area Score (mmol/l/h)	54.55 ± 48	35.5 ± 27.76	75.02 ± 56.2	$<10^{-3}$

The median arterial blood lactate was 4.06±3.15 at H0, 3.6±3.09 after 6 hours and 2.46± 2.41 after 24 hours. While in the survivor group it was 2.11±1.55 at H0, 1.86±1.69 at H6 and 1.04± 0.74 at H24.

LC was 23.7% (IQR,-34.8% to 40.2%) and 16% (IQR 0%-39.1%) after 6 hours (p=0.5) , 34.2% (IQR -7.8% to 58.8%) and 57.5% (IQR 30.3% to 73.5%) after 12 hours (p=0.01) and 54.6% (IQR 18.2% to 70%) and 70% (IQR 51% to 76.5%) after 24 hours (p=0.01) in non- survivors and survivors, respectively.

The Lactate Area Score was also significantly higher for patients who died compared with survivor group (p<0.001).

ICU mortality was 26 % for admission lactatemia between 0-2 mmol/l, 59.5 % for lactatemia between 2-4 mmol/l, and 69.4 % for lactatemia superior to mmol/l.

The ROC- area under the curve (AUC) for prediction of ICU mortality by the values of lactate at different time sampling was 0.721 for Lactate at H0 (95% confidence interval 0.63-0.8, p<0.001). According to the ROC analysis, a threshold value of Lactate at H0 of 2 mmol/l for the prediction of ICU mortality was calculated (sensitivity 72%, specificity 63%, NPV 62%, PPV 73% and HR 4.42 [2.13-9.14]).

The ROC curve for lactate clearance to predict ICU mortality showed an AUC of 0.668 for 12 H LC and 0.662 for 24H LC with 95% confidence interval of 0.533-0.803 (p=0.018) and 0.535 – 0.970 (p=0.02) respectively.

The area under the ROC of Lactate Area Score to predict mortality was 0.775 (95% IC [0.697 – 0.854], p< 0.001). The optimal cut-off to predict ICU mortality was 43% (Se=72% Sp=63%, PPV=71%, NPV=73% and HR=6.5 [3.07 – 13.76]).

The diagnostic performance of the different aspects of lactatemia in predicting mortality is shown in Table 3.

Table 3. Area under curve of the receiver-operating-characteristics and optimal cut-off for lactate associated to intensive care unit mortality

	AUC*	Cut-off	Sensitivity	Specificity	PPV†	NPV‡
Lactate at H0 (mmol/l)	0.721	2mmol/l	72%	63%	72%	62%
Lactate clearance H12	0.668	36%	73%	57%	57%	73%
Lactate clearance H24	0.662	64%	61%	62%	60%	62%
Lactate area score	0.775	43%	71%	63%	71%	73%

AUC*: Area Under Curve, PPV†: Positive Predictive Value, NPV‡: Negative Predictive Value.

Comparison of Lactate diagnostic performance and the Severity scores

The best discriminative power in our study population was that of ISS II with an AUC of 0.862 followed by that of APACHE II, SOFA, Lactate at H0, Lactate Area Score, 12H LC and then 24H LC (Table 4).

Table 4. Diagnostic and Prognostic performance of Lactate and Severity scores according to Area under curve of ROC

ICU* mortality predictive factors	AUC	p
ISS† II Score	0.862	$<10^{-3}$
APACHE‡ II Score	0.827	$<10^{-3}$
SOFA§ Score	0.798	$<10^{-3}$
Lactate at H0	0.721	$<10^{-3}$
Lactate clearance at H12	0.668	0.018
Lactate clearance at H24	0.662	0.022
Persistent hyperlactatemia	0.652	0.002
Lactate Area Score	0.775	$<10^{-3}$

ICU*: Intensive care unit, ISS† II: Injury Severity Score, APACHE II‡: Acute Physiology and Chronic Health Evaluation II, SOFA§: Sequential Organ Failure Assessment.

We selected the cut-off values of the different predictive factors of ICU mortality through ROC curve analysis (Figure 1).

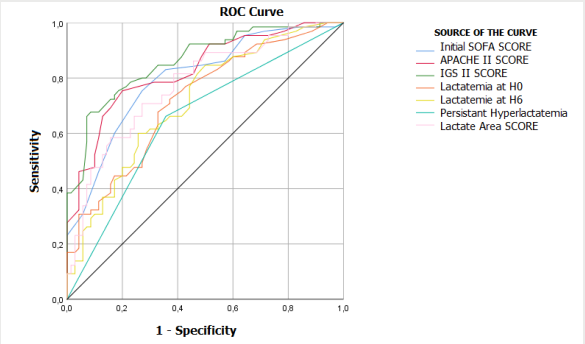

Figure 1. Comparison of prognostic performance of lactate at admission and the severity scores

After multivariate logistic regression model analysis lactate concentration at H0 greater than 2 mmol/l was shown to be an independent predictor of ICU mortality (AHR 1.16 [1.07 – 3.6], p=0.04). All the predictive factors of ICU mortality in univariate and multivariate analysis are summarized in Table 5.

Table 5. Univariate and Multivariate analysis

Intensive care unit mortality predictive factors	Univariate analysis		Multivariate analysis	
	HR CI 95%	p	AHR CI 95%	p
Age ≥ 55 years	5.639 (2.56 – 12.42)	$>10^{-3}$	3.94 (1.24-12.5)	0.02
SOFA* Score≥8	8.220 (3.8 – 17.8)	$>10^{-3}$		
APACHE† II Score ≥18	12.25 (5.42 – 27.62)	$>10^{-3}$		
ISS‡ II Score ≥33.5	9.33 (3.98 – 21.85)	$>10^{-3}$		
Lactate at H0 > 2 mmol/l	4.42 (2.13 – 9.15)	$>10^{-3}$	1.16 (1.07 – 3.6)	0.04
LC§ H12 < 36%	3.66 (1.3 – 10.3)	0.012		
LC§ H24 <64%	2.35 (0.88 – 6.3)	0.08		
Lactate Area Score > 43 mmol/l/h	6.5 (3.07 – 13.76)	$>10^{-3}$		
Persistent hyperlactatemia	3.51 (1.73 – 7.15)	10^{-3}		
Emergency surgery	4.06 (1.8 – 9.1)	10^{-3}	8.85 (1.8 – 43.5)	0.007
HCO^{3-} < 20 mmol /l	2.66 (1.3 – 5.5)	0.007		
Mechanical ventilation	6.58 (2.63 – 16.44)	10^{-3}	18.2 (3.7 – 43.8)	<0.001
Oligo-anuria	7.33 (2.35 – 22.9)	10^{-3}		
Vasopressor use	3.53 (1.67 – 7.42)	0.001		
HRII > 110 bpm	1.86 (0.93 – 3.71)	0.07		
PaO2 /FiO2 < 300	2.7 (1.34 – 5.43)	0.005		
Dose vasopressor > 0.75 mg/h	3.26 (1.13 – 8.09)	0.01	3.9 (1.15 – 13.2)	0.03
leukocytes > 15.10^3 elements/mm^3	2.57 (1.26 – 5.25)	0.008	6.5 (1.8 – 23.7)	0.005
Bilirubin > 17 Umol/l	3.28 (1.61 – 6.68)	0.001	1.1 (1 – 9.8)	0.03
Potassium > 5 mmol/l	3.45 (0.67 – 17.7)	0.11		

SOFA*: Sequential Organ Failure Assessment, APACHE†: Acute Physiology and Chronic Health Evaluation, ISS‡: Injury Severity Score, LC§:Lactate clearance, HRII: Heart Rate.

DISCUSSION

This prospective study evaluated the association between the different aspects of hyperlactatemia and prognosis in critically ill patients showing that a high single arterial blood lactate measurement at admission in ICU is independently associated with an increased ICU mortality (AHF 1.16) and sustained elevation in lactate is a reflect of adverse clinical outcome.

Looking at the literature, the contribution of lactate monitoring in time-sensitive pathologies has been widely described beginning with Broder et al in 1964 who have demonstrated that lactate is strongly associated with mortality, leaving room for large series of studies demonstrating that lactate is an independent factor of morbi-mortality (6).

A recent study that included 145 patients admitted to ICU without taking into account the underlying pathology, a lactate level greater than 2.1 mmol/l on admission was an independent factor of mortality (AHR= 1.28 CI 95%[1.07 – 1.53]). All patients whose lactatemia exceeded the threshold had higher severity scores and required hemodynamic support and mechanical ventilation (7).

Soliman et al included 433 patients, 45% of whom had serum lactate > 2 mmol/l, ICU mortality was around 23% and lactate has been recognized as a prognostic independent factor of mortality (AHR=2.97) and was strongly associated with organ dysfunction mainly renal failure as evidenced by the higher SOFA score in patients with hyperlactatemia, more frequent use of vasopressor and mechanical ventilation (8). These patients had a shorter ICU LOS explained by a higher mortality.

In our study, ICU mortality is all the more important as the lactatemia is high comforting the idea of Bou Cheb and Ferreruela that mortality follows lactate level on admission in a linear fashion (9,10).

No consensus in the literature regarding the cut-off value of lactate has been retained. Several values have been reported by studies. The majority have found cut-offs between 2 and 2.5 mmol/l (7,11,12).

On a retrospective cohort, Rishu et al found a discriminative lactate threshold of 1.35 mmol/l and concluded that a "relative hyperlactatemia" defined between 1.35 and 2 mmol/l was associated with 30% mortality constituting an independent factor of mortality (AHR= 1.6) (13). Our study is complementary to that of Rishu, aimed at alerting the medical team that any patient admitted to ICU with normal lactatemia remains at high risk of death.

Yong Joo et al reported a cut-off 2.6 mmol/l as an independent predictive factor (AHR=1.09) with an AUC of 0.711, Se = 56% and Sp = 74% (14). This study joins that of Smith et al who objectified for a value greater than 2 mmol/l an AUC of 0.78, Se of 69% and a Sp of 77% and also that of Del Porta who concluded that a threshold of 2 mmol/l was significantly associated with ICU mortality with un AUC of 0.662 (12,15). These findings are closer to ours; we found an AUC of 0.721 defining an optimal cut-off of 2 mmol/l at admission (Se= 72%, Sp= 63%, PPV=72% and NPV=62%).

This unique measure remains the subject of controversy in the literature; some authors consider it to be a static variable that cannot therefore be correlated with prognosis. In fact, Pal et al in a large study of 5995 patients found that hyperlactatemia greater that 2 mmol/l on admission had an AUC of 0.6 and PPV of only 5.4% (16).

Thus, the most recent studies tend to assess different aspects of lactate on admission and underscore the value of monitoring the decrease in lactate in order to assess the effectiveness of treatment.

A new concept of therapeutic objective including lactate at admission had recently emerged: Lactate clearance or Lactate clearance goal-directed therapy, however, the time interval and the percentage of clearance differ: LC < 36% or < 10% at 6 hours (17,18), LC < 32.8% at 12 hours (19) or LC < 50% at 24 hours (20).

Ferreruela et al found that the best interval for measuring clearance was H12 defining a threshold of 35% with an AUC of 0.67, sensitivity of 90% and a specificity of 42% (10). The same result was noted in the Haas study which found an area under the curve of 0.91 for LC at H12 defining a threshold of 32.8% (19).

These results are consistent with those of our cohort; LC at H6 was not significant, this could be explained by the fact that a threshold of 2 mmol/l was considered to calculate the clearance while most of the studies included only patients whose serum lactate exceeded 4 mmol/l (18,21). Furthermore, we found a significant association between ICU mortality and LC at H12 with an AUC of 0.66 determining a threshold of 36% (Se=73% and Sp= 57%). A LC at H12 below 36% multiplies the risk of death by 3.5. The lactate area score indicates the persistence and severity of the hyperlactatemia during the first hours reflective the degree and duration of the hypoxia and the extent of tissue damage indicating treatment failure (22–25). In our study, we found a significant association of lactate area score and ICU mortality with an AUC of 0.775 greater than that of LC at H12 (0.663), or LC at H24 (0.657) and Lactate at H0 (0.721), thus joining the literature. We also defined an optimal cut-off of 43 mmol/h to predict ICU mortality (Se= 71%, Sp=63%). A value above 43 mmol/l multiplies the risk of death by 6.5.

Limitations

Our study has some limitations notably the small size of our sample compared to the literature. Indeed, studies of this type requite a larger sampling with a multicenter participation. Another limitation is the inhomogeneity of the population; our cohort seems very heterogeneous because any pathology has its own physiopathology as well as its own complications. A third limitation is the study of ICU mortality only. This attitude is increasingly questionable in the literature because it underestimates mortality. Most of the work on this subject studies ICU and In-hospital mortality. This limit was dictated by logistical constraints and the difficulty of monitoring patients after their discharge.

CONCLUSION

ICU mortality remains a global health scourge. The ability to stratify patients based on risk of death in the earliest phase of their disease can help clinician to manage more effectively and avoid unnecessary additional costs in a failing sanitary system.

Lactate has been proposed as a diagnostic biomarker and a reliable prognostic index; however, literature diverge concerning the cut-off, the timing of sampling and the prognostic value of the other lactate indicators but they all agree on the interest of monitoring lactate levels to guide resuscitations measures in order to normalize lactatemia.

REFERENCES

1. Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. Lancet Respir Med. 2014;2(5):380-6.
2. Collange O, Tacquard C, Lactatémie en anesthésie et réanimation, physiologie et monitorage, Conférence d'essentiel du congrès de la SFAR, 2016.
3. Baysan M, Baroni GD, van Boekel AM, Steyerberg EW, Arbous MS, van der Bom JG. The Added Value of Lactate and Lactate Clearance in Prediction of InHospital Mortality in Critically Ill Patients With Sepsis. Crit Care Explor. 2020;2(3):e0087.
4. Ichai C, Vinsonneau C, Souweine B, Armando F, Canet E, Clec'h C, et al. Insuffisance rénale aiguë en périopératoire et en réanimation (à l'exclusion des techniques d'épuration extrarénale). Anesthésie & Réanimation. 2016;2(3):184-205.
5. Kim YA, Ha EJ, Jhang WK, Park SJ. Early blood lactate area as a prognostic marker in pediatric septic shock. Intensive Care Med. 2013;39(10):1818-23..
6. Broder G, Weil MH. Excess lactate: an index of reversibility of shock in human patients. Science (New York, NY). 1964;143(3613):1457-9.
7. Gutiérrez HB, Concepción YA, Pérez JS, Lara YD, López FMR, Contreras PR. Prognostic Value of Serum Lactate Levels in Critically Ill Patients in an Intensive Care Unit. J Crit Care Med (Targu Mures). 2020;6(1):59-64.
8. Soliman HM, Vincent JL. Prognostic value of admission serum lactate concentrations in intensive care unit patients. Acta clin Belg. 2010;65(3):176-81.
9. Bou Chebl R, El Khuri C, Shami A, Rajha E, Faris N, Bachir R, et al. Serum lactate is an independent predictor of hospital mortality in critically ill patients in the emergency department: a retrospective study. Scand J Trauma Resusc Emerg Med. 2017;25(1):69.
10. Ferreruela M, Raurich JM, Ayestarán I, Llompart-Pou JA. Hyperlactatemia in ICU patients: Incidence, causes and associated mortality. J Crit Care. 2017;42:200-5.
11. Nichol AD, Egi M, Pettila V, Bellomo R, French C, Hart G, et al. Relative hyperlactatemia and hospital mortality in critically ill patients: a retrospective multi-centre study. Crit Care (London, England). 2010;14(1):R25.
12. Smith I, Kumar P, Molloy S, Rhodes A, Newman PJ, Grounds RM, et al. Base excess and lactate as prognostic indicators for patients admitted to intensive care. Intensive Care Med. 2001;27(1):74-83.
13. Rishu AH, Khan R, Al-Dorzi HM, Tamim HM, Al-Qahtani S, Al-Ghamdi G, et al. Even mild hyperlactatemia is associated with increased mortality in critically ill patients. Crit Care (London, England). 2013;17(5):R197.
14. Park YJ, Kim DH, Kim SC, Kim TY, Kang C, Lee SH, et al. Serum lactate upon emergency department arrival as a predictor of 30-day in-hospital mortality in an unselected population. PloS one. 2018;13(1):e0190519.
15. del Portal DA, Shofer F, Mikkelsen ME, Dorsey PJ, Jr., Gaieski DF, Goyal M, et al. Emergency department lactate is associated with mortality in older adults admitted with and without infections. Acad Emerg Med. 2010;17(3):260-8.
16. Pal JD, Victorino GP, Twomey P, Liu TH, Bullard MK, Harken AH. Admission serum lactate levels do not predict mortality in the acutely injured patient. J Trauma. 2006;60(3):583-7; discussion 7-9.
17. Walker CA, Griffith DM, Gray AJ, Datta D, Hay AW. Early lactate clearance in septic patients with elevated lactate levels admitted from the emergency department to intensive care: time to aim higher? J Crit Care. 2013;28(5):832-7.
18. Nguyen HB, Loomba M, Yang JJ, Jacobsen G, Shah K, Otero RM, et al. Early lactate clearance is associated with biomarkers of inflammation, coagulation, apoptosis, organ dysfunction and mortality in severe sepsis and septic shock. J Inflamm (Lond). 2010;7:6.
19. Haas SA, Lange T, Saugel B, Petzoldt M, Fuhrmann V, Metschke M, et al. Severe hyperlactatemia, lactate clearance and mortality in unselected critically ill patients. Intensive Care Med. 2016;42(2):202-10.
20. Morales C, Ascuntar J, Londoño JM, Niño CD, León JP, Bernal E, et al. Lactate clearance: prognostic mortality marker in trauma patients. J Colombian Journal of Anestesiology. 2019;47:41-8.
21. Odom SR, Howell MD, Silva GS, Nielsen VM, Gupta A, Shapiro NI, et al. Lactate clearance as a predictor of mortality in trauma patients. J Trauma Acute Care Surg. 2013;74(4):999-1004.
22. Kim YA, Ha EJ, Jhang WK, Park SJ. Early blood lactate area as a prognostic marker in pediatric septic shock. Intensive Care Med. 2013;39(10):1818-23.
23. Wang H, Li Z, Yin M, Chen XM, Ding SF, Li C, et al. Combination of Acute Physiology and Chronic Health Evaluation II score, early lactate area, and N-terminal prohormone of brain natriuretic peptide levels as a predictor of mortality in geriatric patients with septic shock. J Crit Care. 2015;30(2):304-9.
24. Yu G, Yoo SJ, Lee SH, Kim JS, Jung S, Kim YJ, et al. Utility of the early lactate area score as a prognostic marker for septic shock patients in the emergency department. Acute Crit Care. 2019;34(2):126-32.
25. Khodashahi R, Sarjamee S. Early lactate area scores and serial blood lactate levels as prognostic markers for patients with septic shock: a systematic review. Infect Dis (Lond). 2020;52(7):451-63.