

DYNAMIC LACTATE INDICES AS PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS

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Alistair Nichol^{1,3}, Michael Bailey¹, Moritoki Egi², Ville Pettila¹, Craig French^{5,4}, Edward Stachowski⁶, Michael C Reade⁴, David James Cooper^{1,3} and Rinaldo Bellomo^{1,4,7*}

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Supervised by VS 王瑞芳

INTRODUCTION

- Dynamic lactate indices predict patient outcome more accurately than static indices
- Static indices V.S. dynamic indices
 - Not only **magnitude** but also **duration** and **trend over time**
- High "Static" lactate concentration has been demonstrated to relate to higher hospital mortality.
- Dynamic lactate concentration had **not** been investigated in large heterogeneous cohort study

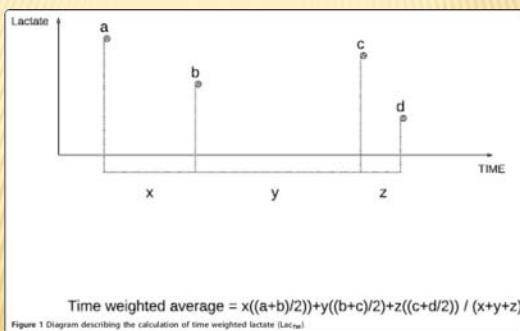
MATERIAL AND METHOD-1

- 5041 patients with 36673 lactate measurements
- Four center intensive care unit database in Australian university hospitals
- Enrolled patient from Jan. 2000 to Oct. 2004
- Inclusion criteria
 - At least two lactate value collected over first 24 hours of ICU admission
- Timing of measurement was decided by care team
- Primary outcome
 - Hospital and ICU mortality

MATERIAL AND METHOD-2

- Six lactate indices related to first 24 hours of ICU admission
 - Static
 - LAC adm- admission lactate
 - LAC max24- maximum lactate
 - LAC min24- minimum lactate
 - Dynamic
 - LAC_{tw24}- time weighted lactate
 - LAC_{Δ24}- absolute change in lactate
 - LAC_{%Δ24}- percentage change in lactate

TIME WEIGHTED AVERAGE



RESULT-1

Variable	Non survivors (n = 274)	Survivors (n = 4067)	P value
Male sex	59% (174)	62% (1510)	0.11
APACHE II score	24.7 (8.0)	13.3 (6.7)	< 0.0001
Age (yr)	65.7 (16.0)	59.7 (18.9)	< 0.0001
Mechanical ventilation rate	66% (81.7)	60% (244.0)	< 0.0001
Surgical patients	32% (18.7)	31% (208.5)	< 0.0001
Diagnosis at admission			
Cardiac and vascular	27% (85.3)	24% (97.8)	0.04
Thoracic and respiratory	20% (71.1)	18% (71.9)	0.16
Trauma	2% (2.7)	4% (14.6)	< 0.0001
Neurological	18% (17.5)	12% (48.5)	< 0.0001
Gastrointestinal tract diseases	13% (12.8)	21% (87.3)	< 0.0001
Other	19% (18.8)	16% (67.1)	0.04
Hospital stay (days)	10 (4 to 25)	15 (8 to 30)	< 0.0001
ICU stay (days)	3.0 (2.0 to 8.0)	3.0 (2.0 to 5.2)	< 0.0001
Number of measurements	8 (5 to 10)	7 (5 to 9)	< 0.0001
LAC _{adm} (mmol.L ⁻¹)	3.20 (1.41 to 3.66)	1.41 (1.02 to 1.87)	< 0.0001
LAC _{max} (mmol.L ⁻¹)	6.21 (1.66 to 6.73)	0.30 (1.18 to 0.24)	0.006
LAC _{min} (mmol.L ⁻¹)	1.7% (-4.9% to 4.7%)	-2.2% (-1.5% to 2.7%)	< 0.0001
LAC _{tw24} (mmol.L ⁻¹)	2.28 (1.45 to 4.28)	1.0 (1.08 to 2.49)	< 0.0001
LAC _{%Δ24} (mmol.L ⁻¹)	1.34 (0.92 to 2.16)	1.00 (0.74 to 1.31)	< 0.0001
LAC _{tw24} (mmol.L ⁻¹)	3.44 (1.99 to 6.20)	3.02 (1.37 to 3.28)	< 0.0001

APACHE II, Acute Physiology and Chronic Health Evaluation II; LAC_{adm}, admission lactate; LAC_{tw24}, time weighted lactate; LAC_{max}, maximum lactate; LAC_{min}, minimum lactate; LAC_{%Δ24}, 24h lactate; LAC_{tw24}, percentage change in lactate in the first 24 hours

RESULT-2

Table 2 Change in RAW (AUC-ROC) for indices of lactate homeostasis in the first 24 hours and mortality

NAME	Hosp AUC-RAW	P-value*	ICU AUC-RAW	P-value*
LAC _{admission}	0.68 ± 0.014		0.703 ± 0.017	
LAC _{tw24}	0.58 ± 0.016	0.0003	0.572 ± 0.022	< 0.0001
LAC _{Δ24}	0.54 ± 0.016	< 0.0001	0.542 ± 0.022	< 0.0001
LAC _{max24}	0.694 ± 0.014	< 0.0001	0.769 ± 0.016	< 0.0001
LAC _{min24}	0.705 ± 0.014	< 0.0001	0.769 ± 0.016	< 0.0001
LAC _{ratio24}	0.683 ± 0.014	0.002	0.713 ± 0.018	0.15
LAC _{tw24} and LAC _{Δ24}	0.710 ± 0.01	< 0.0001	0.763 ± 0.01	< 0.0001

*compared to LAC_{admission}
 AUC-RAW, Unadjusted Area Under Curve; LAC_{admission}, admission lactate; LAC_{tw24}, time weighted lactate; LAC_{max24}, maximum lactate; LAC_{min24}, minimum lactate;
 LAC_{Δ24}, delta lactate-change in lactate in the first 24 hours; LAC_{ratio24}, percentage delta lactate/percentage change in lactate in the first 24 hours; Hosp, hospital mortality; ICU intensive care unit mortality

RESULT-3

Table 3 Multivariate models for the prediction of hospital and ICU mortality

Effect	Hospital mortality	P-value	ICU mortality	p-value
	Odds ratio (95% CI)		Odds ratio (95% CI)	
APACHE II score	1.13 (1.11 to 1.14)	< 0.0001	1.13 (1.11 to 1.15)	< 0.0001
Age (yr)	1.02 (1.02 to 1.03)	< 0.0001	1.01 (1.00 to 1.03)	0.004
LAC _{admission} (mmol/L ²)	1.37 (1.29 to 1.45)	< 0.0001	1.43 (1.35 to 1.52)	< 0.0001
LAC _{Δ24} (mmol/L ²)	1.15 (1.10 to 1.20)	< 0.0001	1.18 (1.13 to 1.24)	< 0.0001
Diagnosis*		< 0.0001		< 0.0001
Mechanical ventilation	1.93 (1.52 to 2.45)	< 0.0001	2.81 (1.95 to 4.05)	< 0.0001
Hospital*		0.0001		0.006
Admission date (decreased risk per year)	0.91 (0.83 to 0.99)	0.04	0.88 (0.78 to 1.00)	0.05
Surgical patients	0.67 (0.53 to 0.84)	0.0007	0.80 (0.59 to 1.08)	0.15
Number of measurements	0.98 (0.95 to 1.01)	0.23	1.01 (0.97 to 1.04)	0.76
Female v male	0.96 (0.81 to 1.14)	0.66	0.99 (0.79 to 1.23)	0.90

*categorical variable, odds ratios excluded
 APACHE II, Acute Physiology and Chronic Health Evaluation; LAC_{admission}, time weighted lactate; LAC_{Δ24}, delta lactate-change in lactate in the first 24 hours

DISCUSSION-1

- ✗ LAC_{tw24} and LAC_{Δ24}
 - + Most predictive, independent indices of hospital mortality
- ✗ Every 1 mmol⁻¹ increase in LAC_{tw24} and LAC_{Δ24}, the risk of hospital death increased by 37% and 15%.
- ✗ No evidence of lactate and mortality differed significantly between those with and without sepsis
 - + No significant interaction between sepsis and LAC_{tw24} or sepsis and LAC_{Δ24}

DISCUSSION-2

- ✗ Limitations are
 - + Retrospective study design
 - + Therapeutic interventions affect lactate level
 - ✗ Epinephrine
 - ✗ Metformin
 - ✗ High-volume hemofiltration with lactate-buffered fluid
- ✗ Further research may prospectively conduct, identify interventions affect lactate level.

CONCLUSION

- ✗ Higher LAC_{tw24} and LAC_{Δ24} associated with greater hospital mortality, superior to static measurement.
- ✗ Dynamic measures doesn't have routine role in clinical practice
- ✗ Clinicians should be alert to patient with rapid raised lactate level.

BACK TO CLINICAL USE

- ✗ 如同作者提及, Retrospective study 的 bias 較多, 無法控制 intervention.
- ✗ Static lactate value 對於預測 mortality 已經是 significant 的, 而較強的 predictive capacity 對於臨床是否有幫助?

✘ Thank you for your attention!!

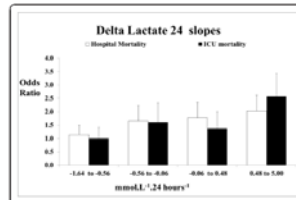


Figure 2 Adjusted* odds ratios for Lac_{24h} reference the lowest quintile. * adjusted for APACHE II, diagnosis, age, gender, ventilation, surgery, admission date, hospital number, measurements, 95% CI, 95% confidence interval, APACHE II Physiology and Chronic Health Evaluation II, Lac_{24h}, delta change in lactate in the first 24 hours; Lac_{24h} change in the first 24 hours.

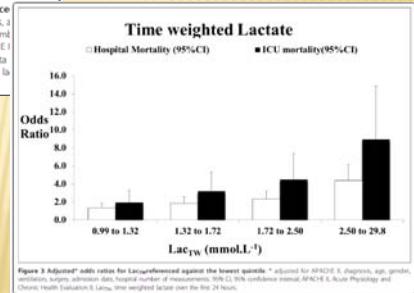


Figure 3 Adjusted* odds ratios for Lac_{TW} reference against the lowest quintile. * adjusted for APACHE II, diagnosis, age, gender, ventilation, surgery, admission date, hospital number of measurements, 95% CI, 95% confidence interval, APACHE II Acute Physiology and Chronic Health Evaluation II, Lac_{TW}, time weighted lactate over the first 24 hours.