

# Serum Lactate Thresholds in the Diagnosis of Septic Shock in Patients with Cirrhosis: Validation of the Sepsis-3 Guidelines

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## BACKGROUND

The 2016 Sepsis-3 guidelines adjusted the septic shock definition and criteria to better represent known pathophysiology and patient outcomes. One significant change was the lowering of serum lactate cutoff (2 mmol/L) to include patients with higher risk-adjusted hospital mortality<sup>1</sup>. However, this increased hospital mortality has not been investigated in patients with known derangements in lactate metabolism and hemodynamics such as those with cirrhosis<sup>2</sup>.

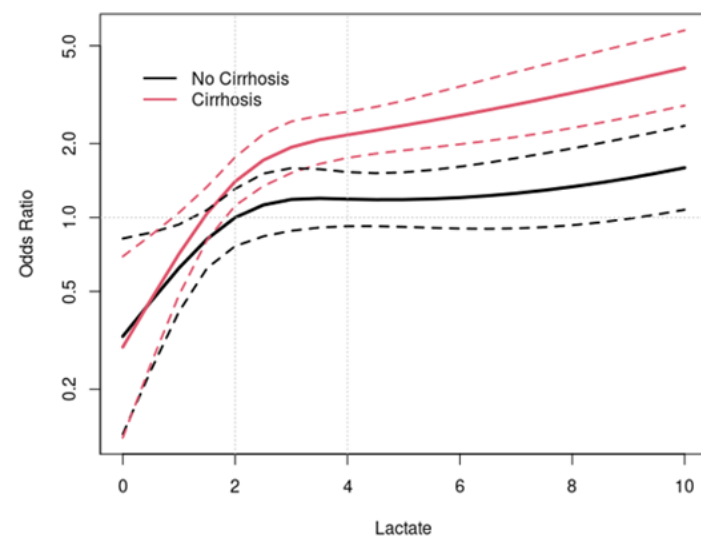
## METHODS

Retrospective cohort study of patients admitted to a Mayo Health System ICU for treatment of septic shock between 2006 and 2021 identified using a validated ICU Datamart<sup>3</sup>. Patients with documented infection source and who received vasopressors to maintain mean arterial pressure (MAP) greater than 65 mmHg were included (N=1,609). Patients with cirrhosis documented on imaging and ICD codes (N=856) were compared to patients without cirrhosis (N=753). Subgroups were created based on ICU-admission lactate levels, and in-hospital mortality was compared.

## RESULTS

For cirrhosis and non-cirrhosis groups, ICU admission lactates between 2-4 mmol/L were associated with significantly increased in-hospital mortality. In a logistic regression model adjusting for age and gender, the interaction between presence of cirrhosis and lactate >4 mmol/L on in-hospital mortality was not statistically significant. Continuous variable analysis was performed in both groups, demonstrating a relative plateauing of mortality risk after admission lactates increase past 2 mmol/L.

**FIGURE 1: In-Hospital Mortality Odds Ratio by ICU Admission Lactate**



Plot of in-hospital mortality Odds Ratio by ICU admission lactate for both cirrhosis and non-cirrhosis groups.

**TABLE 1: Group Comparison**

	No Cirrhosis (N=753)	Cirrhosis (N=856)	Adj. P value
<b>Age, y</b>			0.010
Median (Q1, Q3)	62.6 (52.8, 71.5)	60.2 (51.4, 67.8)	
Mean (SD)	61.1 (14.7)	59.4 (13.2)	
<b>Gender</b>			0.823
Female	294 (39.0%)	330 (38.6%)	
Male	459 (61.0%)	526 (61.4%)	
<b>Any Positive Culture during ICU</b>			0.328
No	158 (21.0%)	197 (23.0%)	
Yes	595 (79.0%)	659 (77.0%)	
<b>Pulmonary infiltrates</b>			0.759
No	310 (41.2%)	347 (40.5%)	
Yes	443 (58.8%)	509 (59.5%)	

**TABLE 2: Non-Cirrhosis Group Outcomes**

	Lactate (mmol/L) <=2 (n=280)	2-4 (n=213)	>4 (n=260)	Adj. P value
<b>Hospital Death</b>				0.002
No	232 (82.9%)	162 (76.1%)	182 (70.0%)	
Yes	48 (17.1%)	51 (23.9%)	78 (30.0%)	

- In the cirrhosis group, admission ICU lactate 2-4 mmol/L had significantly higher risk of in-hospital mortality compared to <=2 (p=0.041).
- In the non-cirrhosis group, ICU admission lactate 2-4 mmol/L had near-significant increase in risk of in hospital mortality compared to <=2 (p=0.062).
- Interaction test was performed between cirrhosis and non-cirrhosis groups and was found to be insignificant, allowing us to combine both groups to determine overall effect of lactate 2-4 mmol/L on in-hospital mortality, which was statistically significant (p=0.003).
- Despite suggestive difference in mortality between the lactate >4 mmol/L subgroups (non-cirrhosis 30.0%, cirrhosis 47.6%), after adjusting for age and gender there was no significant interaction between presence of cirrhosis and lactate >4 mmol/L on in-hospital mortality.

**TABLE 3: Cirrhosis Group Outcomes**

	Lactate (mmol/L) <=2 (n=287)	2-4 (n=302)	>4 (n=267)	Adj. P value
<b>Hospital Death</b>				<0.001
No	224 (78.0%)	213 (70.5%)	140 (52.4%)	
Yes	63 (22.0%)	89 (29.5%)	127 (47.6%)	

## CONCLUSION

**These findings support the ongoing use of lactate cutoff > 2 mmol/L in the diagnosis of septic shock in patients with cirrhosis.**

## REFERENCES

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