PGY-1

**Critical Review Form**

 **Prognosis**

[Lara B, Enberg L, Ortega M, et al. Capillary refill time during fluid resuscitation in patients with sepsis-related hyperlactatemia at the emergency department is related to mortality. PLoS One. 2017 Nov 27;12(11):e0188548.](http://pmid.us/29176794)

**Objectives: "to determine the prevalence of abnormal CRT [capillary refill time] in patients with sepsis-related hyperlactatemia in early phase after ED admission, and its relationship with outcome." (p. 1)**

**Methods: This prospective, observational study was conducted in the ED of the University Hospital of the Pontificia Universidad Catolica de Chile, an academic institution. Consecutive adult patients presenting to the ED with sepsis and an elevated lactate (≥ 2 mmol/L) at arrival were eligible for inclusion. Patients who received IV fluid prior to ED arrival were excluded, as were those in whom CRT could not be assessed (Raynaud syndrome, severe hypothermia), patients requiring an emergent surgical procedure in the first hour, and patients with a DNR order.**

**All patients were treated by a standard protocol adapted from the** [**Surviving Sepsis Campaign guidelines**](https://www.sccm.org/SurvivingSepsisCampaign/Guidelines)**, including fluid resuscitation. CRT was measured immediately before and after fluid resuscitation was undertaken in the ED. All residents and staff physicians were trained in CRT measurement prior to the start of the study. Outcomes included** [**SOFA score**](https://www.mdcalc.com/sequential-organ-failure-assessment-sofa-score) **on day 2, need for and length of mechanical ventilation, ICU and hospital length of stay, and hospital mortality. A composite outcome of ICU length of stay ≥ 72 hours, need for mechanical ventilation ≥ 48 hours, need for renal replacement therapy, and in-hospital mortality was also assessed.**

**The authors originally planned to enroll 100 patients, but after stopping enrollment, 5 patients were found to meet exclusion criteria leaving 95 patients in the final analysis. The mean lactate level at presentation was 4.2 mmol/L, mean age was 67 years, and 47% were male.**

|  |
| --- |
| **Critical Review Form: Prognosis** |
| Guide | Comments |
| **Are the results valid?** |
| **Was the sample of patients representative?** *In other words, how were subjects selected and did they pass through some sort of “filtering” system which could bias your results based on a non-representative sample. Also, were objective criteria used to diagnose the patients with the disorder?* | Yes. The authors chose to only include those patients presenting with sepsis (requiring a documented or suspected source of infection and SIRS criteria) and a lactate that was elevated above 2 mg/dL. Patients meeting these criteria are typically resuscitated based on serial lactate measurements, and the authors wished to evaluate the use of CRT as a surrogate measure of perfusion over time. While the diagnosis of sepsis is not entirely objective, there is no alternative, more objective way of diagnosing these patients. Further the method used to make this diagnosis in the study is similar to real-world practice. |
| **Were the patients sufficiently homogeneous with respect to prognostic risk?** *In other words, did all patients share a similar risk from during the study period or was one group expected to begin with a higher morbidity or mortality risk?* | Yes. Despite likely including a wide range of illness severity in this cohort, this range is typical of patients with severe sepsis. This typically includes patients with hypoperfusion, but who are hemodynamically stable, and those with hemodynamic instability requiring vasopressors. In this study, the mean lactate at admission was 4.3 ± 2.5 mmol/L. It is unclear how many patients required vasopressors or mechanical ventilation. |
| **Was follow-up sufficiently complete?** *In other words, were the investigators able to follow-up on subjects as planned or were a significant number lost to follow-up?* | Yes. All outcomes were measured in-hospital and there appears to be outcome data for all included patients. |
| **Were objective and unbiased outcome criteria used?** Investigators should clearly specify and define their target outcomes before the study and whenever possible they should base their criteria on objective measures. | Yes. All of the outcomes measured were highly objective. |
| **What are the results?** |
| **How likely are the outcomes over time?***For the defined follow-up period, how likely were subjects to have the outcome of interest?*  | * Baseline CRT (prior to initial fluid resuscitation) was not associated with a significant increased risk of the composite outcome (28% for the abnormal CRT group vs 24% in the normal CRT group) or in-hospital mortality (21% vs. 11%).
* Patients with an abnormal CRT after initial fluid resuscitation were at increased risk of the composite outcome (88% vs. 20%; RR 4.4, 95% CI 2.7-7.4) and in-hospital mortality (63% vs. 9%; RR 6.7, 95% CI 2.9 to 16) compared to this with a normal CRT.
* Patients with normal CRT after FR were more likely to normalize or decrease lactate levels than those with abnormal CRT (77 vs. 38%, p = 0.01).
 |
| **How precise are the estimates of likelihood?***In other words, what are the confidence intervals for the given outcome likelihoods?* | See above. This was a fairly small study and the 95% confidence intervals associated with the outcomes were fairly wide. |
| **How can I apply the results to patient care?** |
| Were the study patients and their management similar to those in my practice?  | Possibly. This study was conducted in Chile, where comorbidities and risk factors may exist in difference proportions than in patients in the US. Nearly one third of included patients had an intra-abdominal source of infection. This is likely more typical of patients in our surgical ICU, but likely quite different than those in the typical medical ICU, or in the general ICUs of smaller community hospitals. |
| Was the follow-up sufficiently long? | Mostly yes. All outcomes measured in the study were in-hospital outcomes (death, need for mechanical ventilation, need for renal replacement therapy). The authors did not look at need for vasopressors/vasopressor-free days and did not look at long-term outcomes including functional status. |
| Can I use the results in the management of patients in my practice?  | No. While this study demonstrated an association between abnormal CRT following initial fluid resuscitation and adverse outcomes, it is unclear how this information should be used in clinical practice. Further evidence will need to evaluate how CRT can be used to guide resuscitation and will need to evaluate whether this is a better method of evaluating perfusion than serial lactate measurements. |

**Limitations:**

1. **Several reporting issues were noted inconsistent with** [**STROBE guidelines for reporting in observational studies**](https://www.equator-network.org/reporting-guidelines/strobe/)**:**
	1. **Dates of enrollment not provided**
	2. **Key prognostic factors were not reported, including how many patients required vasopressors and how many required mechanical ventilation.**
	3. **No** [**primary outcome**](http://pmid.us/26528658) **was identified.**
	4. **No information provided as to how a desired sample size of 100 patients was chosen.**
2. **Despite planning to enroll 100 patients, the authors ended up with only 95 in the analysis due to exclusion of 5 patients.**

**Bottom Line:**

**This observational study found that patients with an abnormal CRT following initial fluid resuscitation were at increased risk of the composite outcome of ICU length of stay ≥ 72 hours, need for mechanical ventilation ≥ 48 hours, need for renal replacement therapy, and in-hospital mortality (RR 4.4, 95% CI 2.7-7.4).**