

**Critical Appraisal Worksheet – Diagnosis**  
**Eastern Virginia Medical School EM Journal Club**

<b>Presenter:</b> Katy Deljoui	<b>Date:</b> 02/29/2010
--------------------------------	-------------------------

<p><b>Article Citation</b>          Jones et.al. Lactate Clearance vs Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy : A Randomized Clinical Trial. <i>JAMA</i>. 2010; 303(8) :739-746</p>
---

<p><b>Clinical Scenario:</b>          Pt brought in to the ED from nursing home for change in MS. On arrival, febrile, tachycardic and hypotensive. Urine looks grossly infected. Suspect sepsis and start resuscitation according to goal-directed guidelines. Check CVP for adequacy of preload, MAP for measure of perfusion pressure. Traditionally, adequate oxygen delivery to the tissues determined by ScvO<sub>2</sub>, but cumbersome. Would lactate clearance be an equally good - yet easier to use - indicator of proper tissue oxygen delivery?</p>
---

<b>Are the Results Valid?*</b>	
<b>Questions</b>	<b>Comments</b>
Did all patients receive the diagnostic test being evaluated and a reference standard?	No, they didn't receive both; they got either one or the other. Half the pts had their lactate clearance calculated, while the other half had their ScvO <sub>2</sub> measured.
Was there an independent, blind comparison with a reference standard?	The "reference standard" (based on previous studies) is ScvO <sub>2</sub> measurements. However, there is no "gold standard" at the present time. Several recent studies comparing various biochemical markers to try and find a gold standard (Il 6, Il 8, TNF, Caspase, d-dimer, etc) This study compared the reference standard ScvO <sub>2</sub> to lactate clearance measurements.
Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice?	Yes, because the inclusion criteria for the study sample were broad (age >17 with severe sepsis or septic shock) and the exclusion criteria were not overly stringent (pregnancy, need for surgery, directives). Plus, variety of co-morbidities at baseline. A large number of patients in clinical practice would fall within that spectrum.
Did the results of the test being evaluated influence the decision to perform the reference standard?	No. There were 2 pre-planned interim safety analyses performed during the study, and the results of those analyses did not warrant terminating the study and going back to the reference standard.
Were the methods for performing the test described in sufficient detail to permit replication?	<p>The lactate clearance was defined as:  <math display="block">\frac{[\text{Lactate initial} - \text{Lactate delayed}]}{[\text{Lactate Initial}]} \times 100.</math>                     Lactate initial = measured at the beginning of resuscitation                      Lactate delayed = measured at the end of "at least 2 hours" (?)</p> <p>Used venous samples.                      Bases, on facility, did either POC or sent to hospital lab.</p>

<b>What are the Results?*</b>	
<b><i>Questions</i></b>	<b><i>Comments</i></b>
Are the sensitivity and specificity and/or likelihood ratios presented or data necessary for their calculation provided?	No, but this is due to the design of the study. This is a non inferiority trial and the goal was to show that using lactate clearance instead of ScvO2 would NOT increase mortality by a certain amount called the inferiority margin (set as -10%). Mortality in the lactate group was 17% compared to 23% in ScvO2 group. The difference is 6% with a CI of -3 to 15%. So, at worst, using lactate clearance might increase mortality by 3% when compared to ScvO2, which is well below the threshold of 10%...
<b>How Can the Results Apply to Patient Care?*</b>	
<b><i>Questions</i></b>	<b><i>Comments</i></b>
Will the reproducibility of the test result and its interpretation be satisfactory in my setting?	Yes, but would just have to clarify two points. First, when does the delayed lactate need to be drawn (what does it mean to say “at least 2 hours after the start of resuscitation?? 2 hrs after? 3hrs after? 4 hrs after?) Second, would we use POC lactate or send it to the lab? Does it matter? Are studies out there showing they are equivalent?
Were the study patients similar on critical characteristics to my patients or those we want to generalize to?	If we refer to baseline characteristics in tables 1 and 2, yes. The study patients were people with signs of systemic inflammation, suspected infection, and multiple co-morbidities... just like our septic patients. See tables 1 & 2.
<b>Will the results change my management?</b>	<b>Possibly, serial lactate levels could provide clinicians with a data regarding patient responses to fluid resuscitation and other measures. In ‘borderline’ patients this could help to guide need for further interventions such as CVP lines. The placement of a CVP line for ScvO2 is not without risk and could possibly be avoided. Also delays in timely placement of CVP’s is not uncommon in busy ED and having access to an easier test such as a serial lactate may provide useful information with comparatively minimal risk to the patient.</b>
<b>Will patients be better off as a result of the test?</b>	<b>In theory, yes. Lactate measurements are simpler than ScvO2 measurements, so healthcare providers are more likely to adhere to guidelines recommending lactate measurements... And, better adherence to guidelines typically means better care for the patient.</b>
<b>Do the results of this study fit with other available evidence?</b>	<b>See literature search and attached table.</b>