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Abstract (Original Investigations)

Title: COMPARISON OF A CELLULAR HOST RESPONSE TEST TO PROCALCITONIN FOR EARLY DETECTION OF SEPSIS IN THOSE PRESENTING TO THE EMERGENCY DEPARTMENT WITH SIGNS OR SUSPICION OF INFECTION

Purpose: Those with sepsis, a common and costly condition, primarily present to the Emergency Department (ED), where they are masked among a much larger undifferentiated population of those with signs or suspicion of infection. A highly-sensitive rapid diagnostic with clinically actionable performance is needed to aid ED clinicians in their risk assessment of this large population. The objective of this study was to compare the potential of IntelliSep test to procalcitonin (PCT) in stratification of such a population for risk of sepsis and poor outcomes.

The IntelliSep test is a sepsis diagnostic that quantifies immune activation by measuring the biophysical properties of leukocytes from a whole blood sample in <10 minutes. The test provides a single score, the IntelliSep Index (ISI; 0.1-10.0), stratified into 3 interpretation bands based on the probability of sepsis: Band 1, Band 2, Band 3.

Methods: Adult patients presenting to the ED with signs or suspicion of infection were prospectively enrolled at multiple US sites (Feb. 2016 – Oct. 2021). The assay was performed on EDTA-anticoagulated blood within 5 hours of draw, and patients were followed by retrospective chart review for outcome information. Sepsis disease status was determined through retrospective physician adjudication. For this analysis, the population was subsampled to those with a PCT obtained at the same time as the ISI test.

Results: 847 subjects (adjudicated sepsis prevalence 20%) were included in the final analysis. Positive percent agreement (sensitivity) with the adjudicated sepsis disease state was 92 (87 - 96, 95% CI) and 75 (68 - 81, 95% CI) for ISI (Band 1) and PCT (< 0.5 ng/mL), respectively. Importantly, all subjects adjudicated as septic that suffered in-hospital mortality (n = 22) were in ISI Bands 2 or 3, while 3 of these patients had a PCT of < 0.5. Irrespective of adjudicated disease state, the ISI (cutoff: Band 1) achieved higher sensitivity vs. PCT (cutoff:< 0.5), in identifying those at risk of worsening (as measured by an increase in sequential organ failure assessment scores compared to presentation, 61% vs. 37%), need for ICU level of care (63% vs. 52%), and hospital length of stay > 3-days (65% vs. 45%). The two tests achieved comparable Negative Percent Agreement (specificity) for ISI Band 3 (87; 81-92, 95% CI) and PCT > 2 ng/mL (94; 89 - 97, 95% CI).

Conclusions: The ISI, a quantitative measure of immune activation, compared favorably to procalcitonin as an aid in the rapid assessment of sepsis risk for patients presenting to the ED with signs or suspicion of infection.

Clinical Implications: A highly-sensitive, rapid, and early indicator of activation of the host innate immunity has the potential to aid physicians in improving sepsis efficiency of care and outcomes.

Awards: Apply

Alfred Soffer Research
Awards:

Yes

Young Investigator Awards:

No

Grant Identification:

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Primary Category:

Biotechnology

Secondary Category:

Critical Care

06 Critical Care

6.17 Severe sepsis and septic shock

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Comparison of a Cellular Host Response Test to Procalcitonin for Early Detection of Sepsis in Those Presenting to the Emergency Department with Signs or Suspicion of Infection

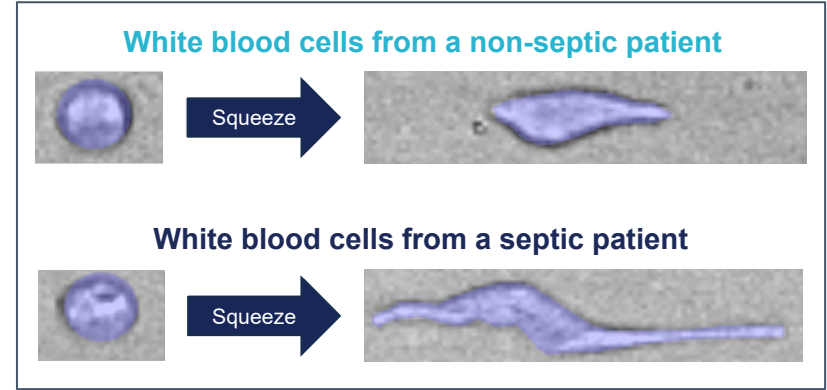


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Disclosure: CEO of Cytovale Inc. and has an equity interest in company whose device is the subject of this study.

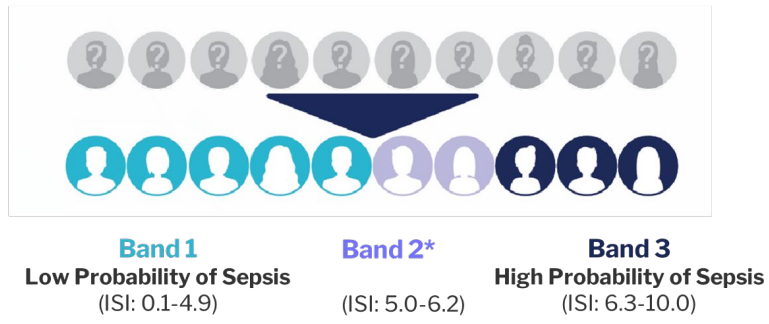
IntelliSep Test (FDA Cleared)



- FDA cleared, semi-quantitative test that assesses cellular host response to aid in the early detection of sepsis with organ dysfunction manifesting within the first 3 days after testing
- Microfluidic junction “squeezes” leukocytes from patient whole blood sample, allowing the discrimination of septic and non-septic patients through leukocyte deformability
- Generates an IntelliSep Index (ISI) value and discrete interpretation bands based on the probability of sepsis in less than 10 min

The IntelliSep Index

Full ISI Range: 0.1-10.0



**All results should be interpreted in the context of the other clinical observations and laboratory test results for the patient.*

Study Objective: Comparing IntelliSep to PCT

- Compare the potential of IntelliSep test to procalcitonin (PCT) in stratification of in those presenting to the Emergency Department (ED) with signs or suspicion of infection for risk of sepsis and poor outcomes using a meta-analysis of multiple clinical studies

Study Design

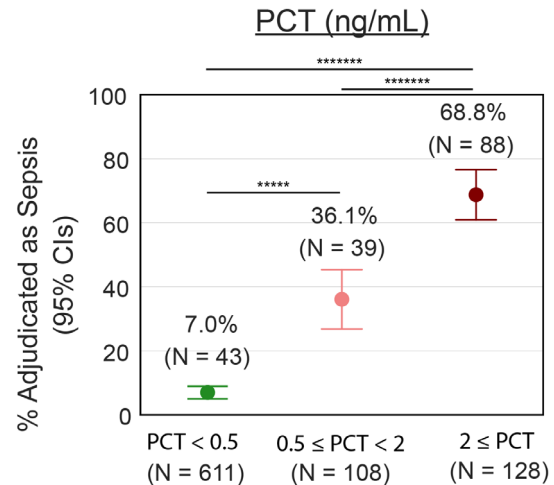
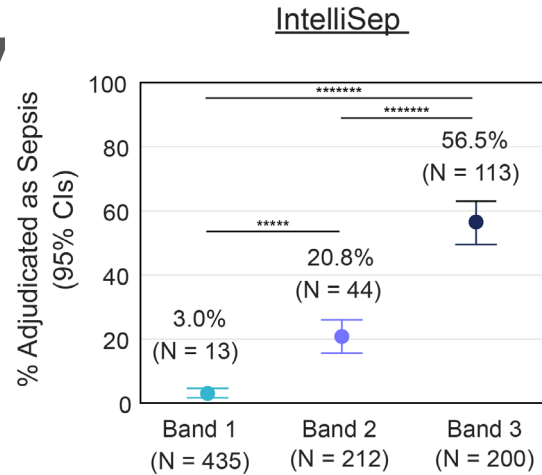
- Adult patients presenting to the ED with signs or suspicion of infection were prospectively enrolled at multiple US sites (Feb. 2016 – Oct. 2021[†])
- Assay performed on EDTA-anticoagulated blood within 5 hours of draw, and patients followed by retrospective chart review for outcome information.
- Sepsis status determined through blinded retrospective physician adjudication.
 - In a subset of cases, PCT data visible during adjudication
- Population subsampled to those with a PCT obtained at the same time as the ISI test.
 - 847 subjects (adjudicated sepsis prevalence 20%) in final analysis

[†]Meta-analysis of multiple clinical studies, inclusive of IntelliSep's clinical validation study and non-validation studies.

Study Results: Sepsis Probability

- The ISI achieved significantly higher Positive Percent Agreement (sensitivity) than PCT in this meta-analysis
- The two tests achieved comparable Negative Percent Agreement (specificity)

	IntelliSep Index	PCT
Population [N] & Adjudicated Sepsis Prevalence [%]	847; 20%	
Cutoffs (Low – High)	Band 1 & Band 3	< 0.5 & ≥ 2
Positive Percent Agreement (Sensitivity): <i>low vs. else</i>	92.4 (87.3 – 95.9)	74.7 (67.5 – 81.0)
Negative Percent Agreement (Specificity): <i>high vs. else</i>	87.1 (81.1 – 91.7)	94.1 (88.7 – 96.7)
Negative Predictive Value	97.0 (92.5 – 98.7)	93.0 (88.0 – 96.3)
Positive Predictive Value	56.5 (48.7 – 64.0)	68.8 (60.7 – 75.2)
Diagnostic Odds Ratio (LR+/LR-)	42.2	29.1

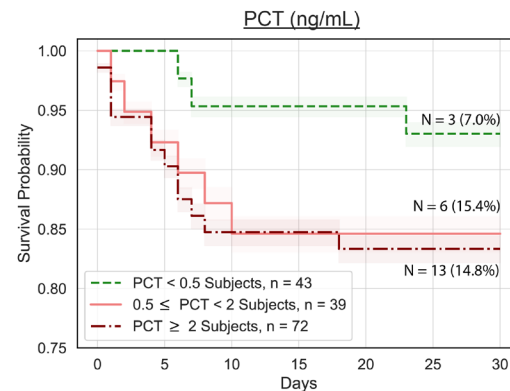
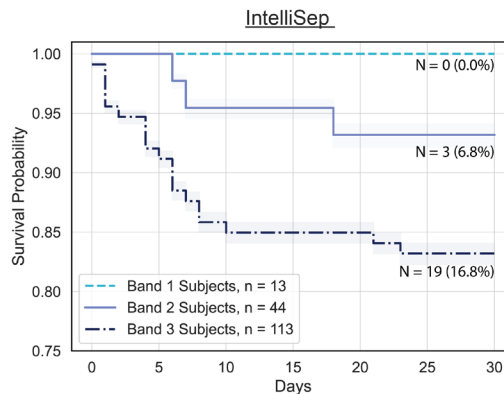


**** → p < 10⁻⁵,
 ***** → p < 10⁻⁶,
 ***** → p < 10⁻⁷

Study Results: Risk Stratification for Poor Outcomes

- All subjects adjudicated as septic that suffered in-hospital mortality (n = 22) were in ISI Bands 2 or 3, while 3 of these patients had a PCT of < 0.5
- ISI (Band 1 vs. else) achieved higher Positive Percent Agreement (sensitivity) vs. PCT (< 0.5 vs. else) for risk of worsening, need for ICU level of care, and hospital length of stay > 3-days

Study Subpopulation Adjudicated as Septic (n = 170)
30-day In-Hospital All-Cause Mortality



	Worsening (increase in SOFA scores compared to presentation)		Need for ICU Level of Care		Hospital Length of Stay > 3-days	
	IntelliSep Index	PCT	IntelliSep Index	PCT	IntelliSep Index	PCT
Positive Percent Agreement (Sensitivity): <i>low vs. else</i>	60.9 (53.7 – 67.9)	36.5 (29.6 – 43.7)	62.7 (55.0 – 70.0)	51.5 (43.7 – 59.2)	64.9 (59.5 – 69.6)	44.5 (39.0 – 49.5)
Negative Percent Agreement (Specificity): <i>high vs. else</i>	79.2 (72.7 – 84.7)	85.6 (79.6 – 90.1)	79.5 (72.4 – 85.1)	88.8 (83.0 – 93.1)	84.9 (80.7 – 88.3)	92.6 (89.3 – 95.0)

Study Conclusions & Clinical Implications

- In this study, the ISI, a quantitative measure of immune activation, compared favorably to procalcitonin as an aid in the rapid assessment of sepsis risk for patients presenting to the ED with signs or suspicion of infection.
- A highly-sensitive, rapid, and early indicator of activation of the host innate immunity has the potential to aid ED physicians in improving sepsis efficiency of care and outcomes.

Thank You!

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