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Diagnosis and Severity Prediction of Bacterial Infections and Sepsis Using a 29-Gene Host-Response Test from Whole Blood

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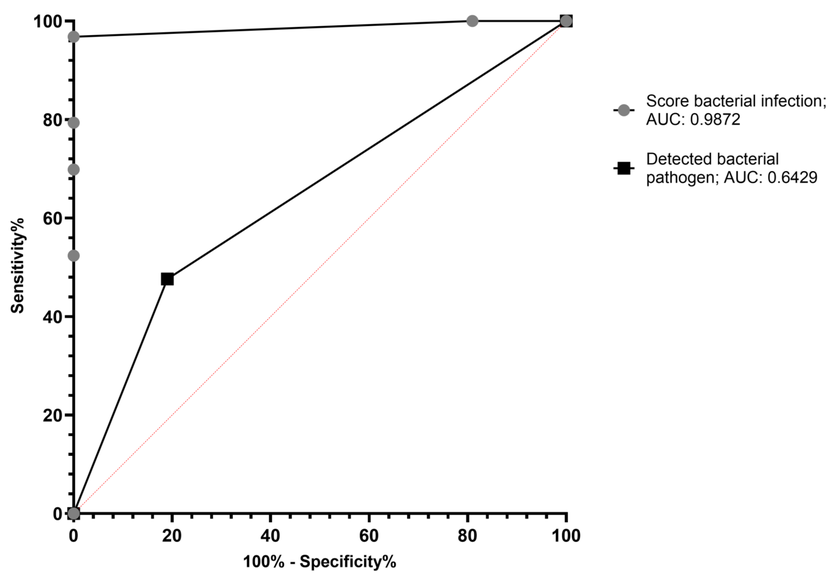
Background

Sepsis remains a major challenge in clinical practice due to variable symptoms and delays in pathogen identification. Host-response profiling has emerged as a promising tool for the diagnosis of infection and prediction of those at high risk of poor outcome. This study evaluates the performance of a 29-gene host-response mRNA expression test in patients with suspected sepsis.

Methods

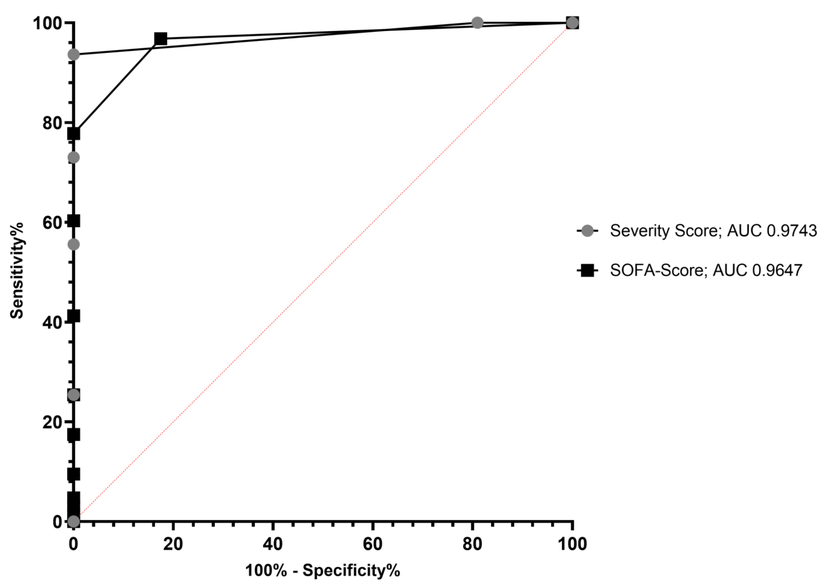
Patients presenting to the emergency room (ER) with suspected sepsis were enrolled in the SEPTICISION study (DRKS00028972). Whole blood (2.5 ml) was collected in PAXgene Blood RNA tubes whenever a blood culture was obtained. This interim analysis analyzed 29 mRNA targets (TriVerity®, Inflammatix) in 63 patients. Expression levels were categorized by machine learning classifiers into three scores (likelihood of bacterial infection, viral infection and illness severity), each ranging from 0-50 and falling into one of five interpretation bands (Very Low, Low, Moderate, High, Very High). Results were compared to clinical data, diagnostic findings, clinical scores (SOFA, NEWS-2), and patient outcomes. Ground truth was established by blinded infectious disease (ID) specialist clinical adjudication. Diagnostic and prognostic performance were assessed using area under the curve of receiver operating characteristics (AUC), and interpretation band specific calculation of sensitivity and specificity.

A: Bacterial Infection (based on retrospective clinical evaluation)



	Sensitivity%	95% CI	Specificity%	95% CI
> 0.5000	100.0	94.25% to 100.0%	19.05	11.25% to 30.41%
> 1.500	96.83	89.14% to 99.44%	100.0	94.25% to 100.0%
> 2.500	79.37	67.83% to 87.52%	100.0	94.25% to 100.0%
> 3.500	69.84	57.64% to 79.76%	100.0	94.25% to 100.0%
> 4.500	52.38	40.27% to 64.22%	100.0	94.25% to 100.0%

B: Sepsis (based on retrospective clinical evaluation)



	Sensitivity%	95% CI	Specificity%	95% CI
> 0.5000	100.0	94.25% to 100.0%	19.05	11.25% to 30.41%
> 1.500	93.65	84.78% to 97.50%	100.0	94.25% to 100.0%
> 2.500	73.02	60.97% to 82.42%	100.0	94.25% to 100.0%
> 3.500	55.56	43.32% to 67.15%	100.0	94.25% to 100.0%
> 4.500	25.40	16.28% to 37.34%	100.0	94.25% to 100.0%

Table A: Accuracy of the TriVerity Bacterial Score vs. retrospective adjudication of bacterial infection by an infectious disease specialist

Interpretation Band	Ground Truth: bacterial infection	Ground Truth: no bacterial infection	Sensitivity	Specificity	Likelihood Ratio (LR)
Very High	31	2	60.78%	83.33%	3.65
High	10	1	19.61%	91.67%	2.35
Moderate	3	3	5.88%	75.00%	0.24
Low	5	6	90.20%	50.00%	0.20
Very Low	2	0	96.08%	0.00%	-

Table B: Accuracy of the TriVerity Illness Severity Score vs. retrospective assessment of sepsis[1]

Interpretation Band	Ground Truth: sepsis	Ground Truth: no sepsis	Sensitivity	Specificity	Likelihood Ratio (LR)
Very High	6	10	54.55%	80.77%	2.83
High	1	18	9.09%	46.15%	0.17
Moderate	2	9	18.18%	28.85%	0.26
Low	2	11	81.82%	21.15%	0.86
Very Low	0	4	100.00%	7.69%	0

[1], infection with organ dysfunction/SOFA-Score ≥ 2

Results

The host-response panel demonstrated higher accuracy for bacterial infection prediction (AUC 0.987) compared to microbiological bacterial detection (AUC 0.643, Figure 1A). The AUC was 0.974 for prediction of clinically adjudicated sepsis, comparable to SOFA score (AUC 0.965, Figure 1B). Sensitivity of the Very Low and specificity of the Very High bacterial interpretation band were 83.3% and 96.1%, respectively, and were 80.8% and 100.0% for the TriVerity disease severity outer Very High and Very Low bands (Table)

Conclusion

This interim analysis in patients with suspected sepsis highlights the high diagnostic and prognostic accuracy of the TriVerity test for the diagnosis of bacterial infections and prediction of disease severity. Accuracy of the TriVerity test for identifying bacterial infections was superior compared to traditional microbiological methods. Larger patient cohorts and further validation are required to confirm these findings.

DZIF Deutsches Zentrum für Infektionsforschung

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Inflammatix

Inflammatix™ performed gene expression analysis and machine learning for host response targets (TriVerity test) from whole blood

Additional information on patients‘ characteristics is displayed in the abstract (see QR code).

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