SEPTICYTE® RAPID IN SEPSIS CASES WITH MALIGNANCY OR TREATED WITH ANTINEOPLASTICS/IMMUNOSUPPRESSANTS

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the signature diagnostics for sepsis

INTRODUCTION

SeptiCyte® RAPID is a host immune response assay using peripheral blood gene expression markers to provide a probability of sepsis in patients presenting with systemic inflammation (SI). The purpose of the study was to evaluate the performance of SeptiCyte® RAPID in sepsis patients having systemic inflammation (SI), and a hematological malignancy (HM) or metastatic malignancy (MM) or those treated with antineoplastics or immunosuppressants.

Immunexpress has conducted a study with well characterized, bio-banked, clinical samples, in collaboration with researchers at Academic Medical Center and Utrecht Medical Center, NL and Seattle Children's Hospital, US. The study used samples from adults & children, and data from microarray, NGS and PCR.

METHODS

The adult microarray data (MARS:NCT01905033) were derived from patients with a primary infection likelihood of "culture proven" sepsis or "NA" (SIRS, i.e. systemic inflammatory response syndrome) (n=341). These adults had either HM/ MM or not, or were treated with either corticosteroids/antineoplastic therapies. The pediatric NGS data (GAPPSS:NCT02728401) (n=63) were derived from patients post cardiopulmonary bypass (PCPB) (n=28) resulting in SIRS without infection, or with clinical severe sepsis syndrome (CSSS).

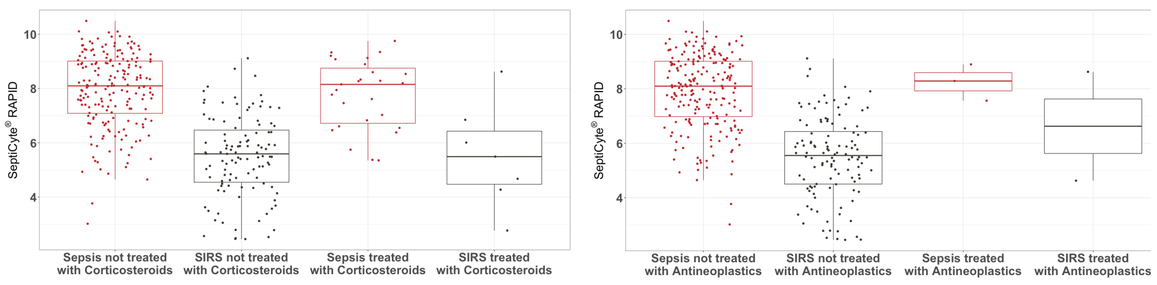
Pediatric PCR data (NGS subset, n=41) included PCPB (n=12) and CSSS cohorts with or without the studied treatment/disease. Instead of an MM group, the pediatric cohort had a 'malignancy' group apart from HM to match the adult data. Diagnostic performance was compared using the area under the receiver operating characteristic curves (ROC-AUC) & ROC test. ROC curves were compared to evaluate whether there was a statistically significant drop in performance of SeptiCyte® RAPID in the population with or without the studied treatments/disease.

RESULTS

Performance of SeptiCyte® RAPID in adult cases of sepsis treated with or without corticosteroids was above an AUC of 0.83 regardless of whether the sepsis group was compared relative to SIRS cases treated with corticosteroids or not. Using pediatric NGS data, the AUC for CSSS cases on immunosuppressants relative to PCPB was 1.00, and for CSSS cases not on immunosuppressants relative to PCPB was 0.97. Using pediatric PCR data, the AUC for sepsis cases on immunosuppressants relative to PCPB was 0.98 & for CSSS cases not on immunosuppressants relative to PCPB was 0.96. Performance of SeptiCyte® RAPID in adult sepsis cases with HM vs. SIRS cases without HM was AUC=0.9. Comparatively, in a sepsis cohort without HM vs. SIRS cases without HM, the performance was AUC=0.88.

SeptiCyte® RAPID performance in adult sepsis cases with MM vs. SIRS cases without MM was AUC=0.95, & in sepsis cases without MM vs. SIRS without MM was AUC=0.88. SeptiCyte® RAPID performance in adult sepsis cases with MM vs. SIRS cases with MM was AUC=0.88 as compared to sepsis cases without MM vs. SIRS cases with MM at AUC=0.89. SeptiCyte® RAPID performance in adult sepsis cases administered anti-neoplastics vs. SIRS without AND was AUC=0.97 and in sepsis cases not administered AND vs. SIRS without AND was at AUC=0.88. SeptiCyte® RAPID AUC in the pediatric cohort for both NGS & PCR data, regardless of treatment/ disease or not, was above 0.96. ROC test p-values did not show a decrease in performance in treated/diseased group relative to untreated/ group without disease in both adult and pediatric data.

Figure 1: Distribution of SeptiCyte® RAPID scores in the adult cohort (MARS microarry data)
A.) Corticosteroid treatment B.) Treatment with anti-neoplastic drugs



Treatments under consideration were Corticosteroids or anti-neoplastic drugs in addition to treatments provided based on standard of care. Since there are only 2 cases in the SIRS group for treatment with anti-neoplastic drugs, this group is excluded from the ROC analysis.

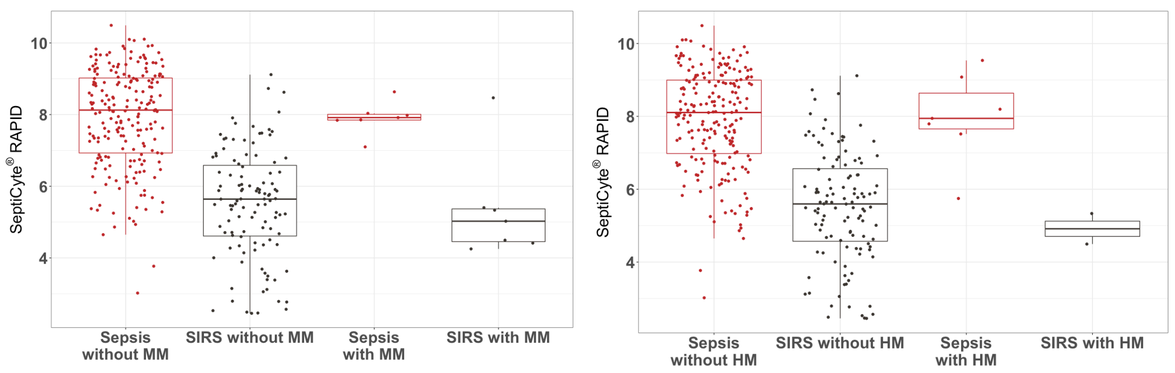
The Performance of SeptiCyte® RAPID in Adults Does Not Drop in the Treated or Malignant Group

Area Under Curve for Various Sepsis vs SIRS Comparisons [microarray data]

Sepsis Cases Treated* or With HM/MM versus		Sepsis Cases NOT Treated* or With HM/MM versus	
SIRS without corticosteroids	0.87	SIRS without corticosteroids	0.88
SIRS with corticosteroids	0.83	SIRS with corticosteroids	0.85
SIRS without AND	0.97	SIRS without AND	0.88
SIRS without HM	0.90	SIRS without HM	0.88
SIRS without MM	0.95	SIRS without MM	0.88
SIRS with MM	0.88	SIRS with MM	0.89

*Treatments under consideration were corticosteroid or anti-neoplastic drugs in addition to treatments provided based on standard of care
AND: anti-neoplastic drugs; HM: Hematological malignancy; MM: metastatic malignancy
Mean ROC test p-value between groups = 0.55
Note: The comparison lacked sufficient number of SIRS cases with AND and HM. This can be tested in a broader population of patients.

Figure 2: Distribution of SeptiCyte® RAPID scores in the adult cohort (MARS microarry data)
A.) Metastatic malignancy B.) Hematologic malignancy



Since there are only 2 cases in the SIRS group with a hematologic malignancy, this group is excluded from the ROC analysis.

The Performance of SeptiCyte® RAPID in Children Does Not Drop in the Treated or Malignant Group

Area Under Curve for Various Sepsis vs SIRS Comparisons [NGS data]

Sepsis Cases Treated* or with Malignancy Versus		Sepsis Cases NOT Treated* or with Malignancy Versus	
SIRS without immunosuppressant	1.00	SIRS without immunosuppressant	0.97
SIRS without AND	1.00	SIRS without AND	0.97
SIRS without HM	1.00	SIRS without HM	0.98
SIRS without malignancy	1.00	SIRS without malignancy	0.97

Area Under Curve for Various Sepsis vs SIRS Comparisons [PCR data]

Sepsis Cases Treated* or with Malignancy Versus		Sepsis Cases NOT Treated* or with Malignancy Versus	
SIRS without immunosuppressant	0.98	SIRS without immunosuppressant	0.96
SIRS without AND	1.00	SIRS without AND	0.96
SIRS without HM	1.00	SIRS without HM	0.96
SIRS without malignancy	1.00	SIRS without malignancy	0.96

*Treatments under consideration were immunosuppressants or anti-neoplastic drugs in addition to treatments provided based on standard of care
AND: anti-neoplastic drugs; HM: Hematological malignancy; MM: metastatic malignancy
Mean ROC test p-value between groups for both NGS and PCR data = 0.3
Note: The pediatric cohort unlike the adult data does not have sufficient SIRS cases with the condition/ treatment in question to be included in this analysis.
For the pediatric cohort, this question can be assessed in a broader population of patients. Some patients had both PCR and NGS data.
The PCR cohort represents a subset of the data from patients on whom NGS data was also available.

CONCLUSIONS

- **Malignancy or treatment with anti-neoplastics or immunosuppressants does not significantly alter the performance of SeptiCyte® RAPID for distinguishing between sepsis and SIRS in adults, infants, children and adolescent patients.**
- **These results are platform independent across PCR, NGS and microarray data.**

SeptiCyte® RAPID