Dual-cohort independent validation of a novel 12-mRNA score for sepsis prognosis

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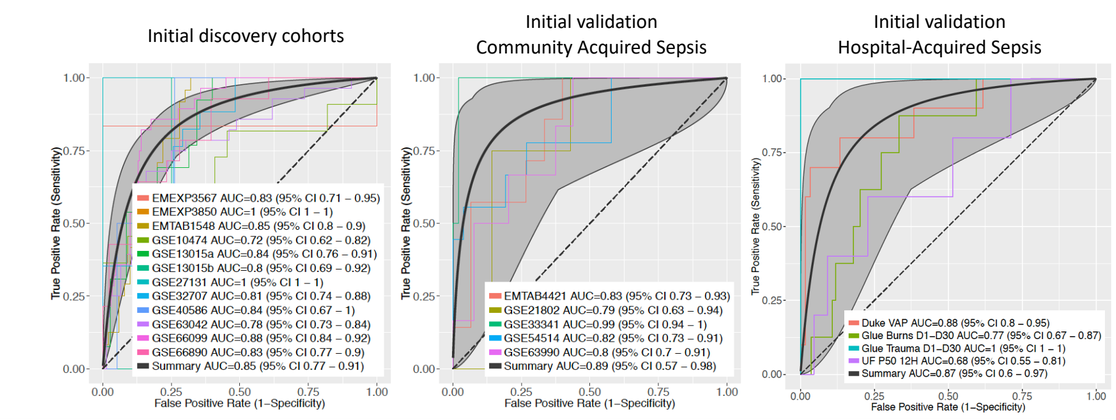
Inflammatix
Advanced Host-Response Diagnostics

Background

We recently described a 12-mRNA host-response signature score that predicts 28-day mortality (Sweeney et al., Nat Comms, 2018), both alone (AUROC mean 0.89) and in linear combination with risk-stratification tools such as SOFA (mean boost in AUROC 0.10) across 9 validation cohorts.



Materials and methods

These are pilot results of two separate multisite Greek cohorts: (1) the Greek Sepsis Forum (or 'GSF'), patients with sepsis according to Sepsis-2 criteria enrolled at ICU admission; and (2) the 'PROMPT' study, patients with one SIRS criteria and suspected infection enrolled at ED admission. Whole blood was drawn (PAXgene® RNA tubes) at enrollment. We then extracted RNA (Qiagen QIAcube®) and quantitated the 12 mRNAs in batches using the NanoString nCounter® platform. We converted the 12 mRNAs into a single score as previously described (difference of geometric means). The 12-mRNA score was used to calculate AUROCs for mortality prediction, both alone and combined with clinical risk scores (qSOFA and SOFA).

Results: PROMPT study (emergency dept.)

Population	ED patients with 1+ SIRS and suspected infection
Size	N=112
Age	63.1 +/- 21.8
qSOFA ≥ 2	13 (12%)
Delta-SOFA ≥ 2	55 (48%)
SOFA	1.7 +/- 1.9
Mortality	10 (9%)

Measure	AUROC for 30-day mortality
12-mRNA score	0.87
qSOFA	0.71
qSOFA + 12-mRNA	0.89 (+ 0.18)
SOFA	0.85
SOFA + 12-mRNA	0.92 (+ 0.07)
APACHE II	0.82
APACHE II + 12-mRNA	0.91 (+ 0.09)

Several other markers measured at admission in this population and were not predictive of mortality (total N reflects missingness)

- Lactate, N=63, AUROC = 0.63
- PCT, N=81, AUROC = 0.55
- CRP, N=109, AUROC = 0.39

Results: Greek Sepsis Forum study (ICU)

Population	ICU admission with sepsis
Size	N=29
Age	68.5 +/- 13.2
qSOFA ≥ 2	19 (65%)
Delta-SOFA ≥ 2	20 (69%)
SOFA	6 +/- 4.9
Mortality	9 (31%)

Measure	AUROC for 30-day mortality
12-mRNA score	0.82
qSOFA	0.68
qSOFA + 12-mRNA	0.86 (+ 0.18)
SOFA	0.92
SOFA + 12-mRNA	0.96 (+ 0.04)

Conclusions

The 12-mRNA host-response signature continues to show validity for the prognosis of 28-day mortality in patients with suspected sepsis at ED and ICU admission. This is true both alone and in combination with standard prognostic scores such as qSOFA and SOFA.

Improved risk stratification in combination with clinical risk scores may allow for improved resource utilization, in particular by ruling out patients likely not to benefit from clinical intervention. Accurate immune-based prognostic enrichment may also be useful in interventional clinical trials for sepsis therapies.

The 12-gene score is being commercially developed into a rapid, POC test by Inflammatix as part of the HostDx™ Sepsis panel. Further study is warranted prior to clinical use.

References

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