Title: The association of Syndecan-1 with inflammation, endothelial cell signaling, illness severity and organ dysfunction in sepsis.

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Abstract
Background:
Syndecan-1 (SYN) is a key component of the glycocalyx and serves as a biomarker of glycocalyx degradation. Prior studies, largely in the ICU and operative setting, have shown increased SYN levels in sepsis; there are few studies in the emergency department (ED) setting.

Objective:
To define the association of glycocalyx degradation measured by SYN with inflammation, endothelial cell signaling, sepsis severity, and organ dysfunction in ED patients with sepsis.

Method:
This is a prospective, observational study of a convenience sample of adult ED patients with suspected infection and non-infected ED controls, conducted from 9/2009 – 4/2014. We used ELISA and Luminex technologies to assay biomarkers of glycocalyx degradation (SYN), inflammation (IL-6, TNF-a) and endothelial cell signaling (E-selectin). We assessed sepsis severity by classification of sepsis syndromes of sepsis, severe sepsis, and septic shock and defined organ dysfunction by SOFA score. We compared means with t-tests, assessed

associations between biomarkers with spearman's correlation, and calculated area under the curve (AUC) values to assess diagnostic accuracy.

Result:
There were 200 patients included: 54 (27%) sepsis, 45 (23%) severe sepsis, 51 (26%) septic shock, and 50 (25%) were non-infected controls. Overall in-hospital mortality was 7% (14/200).

SYN in patients with sepsis was significantly lower than non-infected controls (2189± 2453 ng/mL vs 3039 +/-2929, $p < 0.05$). When assessing severity, we found the following mean SYN levels: sepsis (2570 ng/mL, 95% CI: 1775-3365), severe sepsis (2236, 1559-2913), septic shock (1743, 1172-2314).

SYN had a significant but weak AUC (0.60, 95% CI; 0.51 to 0.68) for septic shock prediction.

It was significantly correlated with IL-6 ($r = 0.23$, $p < 0.01$) and TNF-α ($r = 0.27$, $p < 0.005$), but not E-selectin ($r = 0.013$, $p = 0.84$) or SOFA score ($r = -0.024$, $p = 0.73$).

Conclusion:
Contrary to published literature, we found SYN levels to be significantly lower in sepsis upon presentation to the ED, in patients with septic shock. Circulating SYN levels were positively associated with inflammation, but not endothelial cell activation, or organ dysfunction. Theses findings are in conflict with reported data in OR and ICU. Further study is needed that investigate the discrepancy.