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

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Abstract
Background:
Endocan is a novel biomarker whose production and excretion are specific to the endothelium. Endocan is proposed as a novel biomarker of endothelial signaling.

Objective:
To define the association of circulating endocan levels with inflammation, endothelial cell signaling, sepsis severity, and organ dysfunction (SOFA score) in Emergency Department (ED) patients with sepsis.

Method:
This was 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 Endocan, and biomarkers of 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 and Tukey's test, 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 analyzed: 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). When comparing patients with sepsis of any severity to non-infected controls, Endocan levels were significantly higher (24 ng/mL+/- 34 vs 0.41 ng/mL +/- 2.5, $p < 0.001$). We found the following mean Endocan levels: sepsis (17 ng/mL, 95%CI: 7.9-26), severe sepsis (30, 18-42), septic shock (30, 13-47) and control (0.4, 0-1.8). Endocan level in each sepsis severity were significantly higher than control ($p < 0.05$). Endocan had a significant and strong AUC (0.91, 0.87 - 0.98) for sepsis discrimination. Endocan was significantly correlated with IL-6 ($r = 0.23$, $p < 0.01$), TNF-α ($r = 0.27$, $p < 0.005$), E-selectin ($r = 0.45$, $p < 0.0001$) and SOFA score ($r = 0.66$, $p < 0.001$).

Conclusion;
Endocan was associated with sepsis, inflammation, endothelial cell signaling, and organ dysfunction. Further study of endocan as a sepsis biomarker may improve diagnostic strategies, and perhaps be used in endothelial-targeted therapies in sepsis.

Keywords
Degradation of glycocalyx, Biomarker, Endocan, Endothelial cell signaling, Sepsis.