Multi-marker Approach Using Procalcitonin, Presepsin, Galectin-3, and Soluble Suppression of Tumorigenicity 2 in Sepsis

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Background

- Timely diagnosis and risk stratification in sepsis are important to make appropriate and prompt treatment decisions.
- We investigated the prognostic utilities of emerging biomarkers in septic patients.

Material & Methods

- In a total of 157 septic patients (112 patients with sepsis; 45 patients with septic shock), procalcitonin (PCT), presepsin, galectin-3, and soluble suppression of tumorigenicity 2 (sST2) were measured **(Table 1).**
- The assay results were analyzed in relation to sepsis severity and 30-day mortality.

Table 1. Characteristics of study population

Variable	All patients (N = 157)
Sepsis criteria, n (%)	157 (100.0)
Sepsis, n (%)	112 (71.3)
Septic shock, n (%)	45 (28.7)
Patients enrollment	
Intensive care unit, n (%)	94 (59.9)
Emergency room, n (%)	63 (40.1)
Age (years), median [IQR]	70 [57.7 – 77.0]
Males, n (%)	95 (60.5)
Hospital stay (days), median [IQR]	16 [8 – 40]
In-hospital mortality, n (%)	40 (25.5)
30-day mortality, n (%)	34 (21.7)
Co-morbidities	
Hemato-oncologic, n (%)	31 (19.6)
Pulmonary, n (%)	29 (18.6)
Cerebrovascular, n (%)	28 (17.5)
Renal and genitourinary, n (%)	19 (12.4)
Gastrointestinal, n (%)	18 (11.3)
Cardiovascular, n (%)	16 (10.3)
Others, n (%)	16 (10.3)
eGFR by MDRD Study equation (mL/min/1.73 m²), median [IQR]	44.45 [20.83 – 81.33]
SOFA score range	2 – 11
	2 (45, 28.7%); 3 (32, 20.4%); 4 (26, 16.6%); 5 (14, 8.9%); 6 (13, 8.3%); 7 (12, 7.6%); 8 (6, 3.8%); 9 (3, 1.9%); 10 (3, 1.9%); 11 (3, 1.9%)
CRP (mg/dL), median [IQR]	12.54 [7.22 – 22.0]
WBC (x 10^9/L), median [IQR]	12.47 [8.18 – 17.10]
PCT (ng/mL), median [IQR]	6.19 [2.25 – 21.99]
Presepsin (pg/mL), median [IQR]	2,714.0 [1,479.3 – 4,129.7]
Galectin-3 (ng/mL), median [IQR]	30.8 [17.9 – 58.5]
sST2 (ng/mL), median [IQR]	214.5 [133.6 – 238.8]

Results

- PCT, presepsin, galectin-3, and sST2 increased significantly according to the sepsis severity (all $P < 0.01$) **(Table 2).**
- PCT, presepsin, galectin-3, and sST2 were all comparable for the prediction of septic shock **(Fig. 1).**
- Galectin-3 was a risk predictor for 30-day mortality (hazard ratio [HR] = 11.03, 95% confidence interval [CI] = 2.69 - 45.25) **(Table 3).**
- The risk of 30-day mortality increased stepwise as the number of biomarkers above cut-offs increased, and the highest risk was observed when all four biomarkers increased (HR = 3.3, 95% CI = 1.3 - 8.5).

Table 2. Comparison of PCT, presepsin, galectin-3, and sST2 between sepsis and septic shock

	Sepsis (N = 112)	Septic shock (N = 45)	*P**
Procalcitonin (ng/mL)	5.35 (1.52 – 14.00)	9.73 (4.03 – 35.13)	0.0053
Presepsin (pg/mL)	2,159.5 (1357.5 – 3743.5)	3,679.0 (2738.8 – 6335.5)	< 0.0001
Galectin-3 (ng/mL)	24.4 (15.3 – 54.6)	49.6 (29.4 – 81.3)	< 0.0001
sST2 (ng/mL)	205.4 (103.1 – 233.9)	237.3 (215.1 – 254.6)	< 0.0001

Data are expressed as median (interquartile range).
*Mann-Whitney U test.

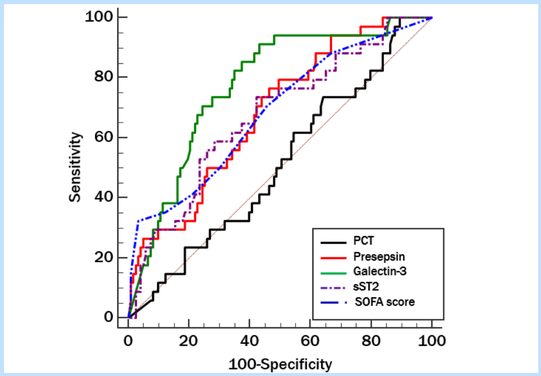
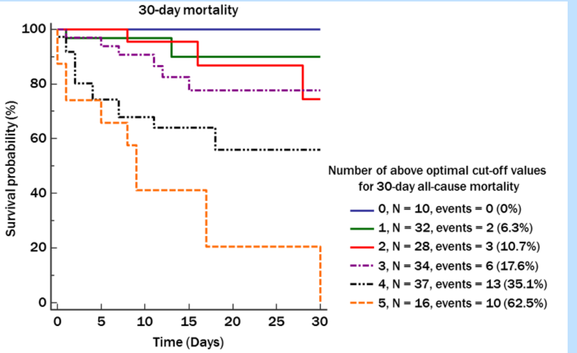


Figure 1. Comparison of the receiver operating characteristics curves to predict septic shock and 30-day mortality.

Table 3. Comparison of PCT, presepsin, galectin-3, and sST2 according to the 30-day mortality

	Total (N = 157)			30-day mortality	
	Survivor (N = 123)	Non-survivor (N = 34)	*P**	HR (95% CI)	*P*†
Procalcitonin (ng/mL)	6.19 (2.24 – 22.39)	6.61 (2.22 – 20.78)	NS	0.60 (0.33 – 1.08)	NS
Presepsin (pg/mL)	2,310.0 (1,375.8 – 3,920.2)	3,549.0 (2,493.7 – 8,242.7)	0.0011	2.25 (0.74 – 6.85)	NS
Galectin-3 (ng/mL)	24.5 (16.7 – 47.5)	58.6 (37.0 – 82.2)	< 0.0001	11.03 (2.69 – 45.25)	0.0009
sST2 (ng/mL)	209.5 (116.9 – 236.9)	237.3 (208.8 – 253.3)	0.0020	14.91 (0.93 – 240.4)	NS

Data are expressed as median (interquartile range).
*Mann-Whitney U test. Cox proportional-hazard regression using log-transformation of variables.
Abbreviations: NS, not significant



Group	1	2	3	4	5
0	-	-	-	-	-
1		1.5 (0.5 – 4.4)	2.4 (0.9 – 6.6)	6.2 (2.1 – 17.9)	14.5 (3.2 – 64.7)
2			1.6 (0.6 – 4.4)	4.1 (1.4 – 11.8)	9.6 (2.1 – 42.8)
3				2.6 (0.9 – 7.1)	6.1 (1.4 – 26.0)
4					2.3 (0.5 – 10.4)

Figure 2. Risk prediction by multimarker-approach using below/above cut-offs of PCT, presepsin, galectin-3, and sST2.

Conclusions

This is the first study that demonstrated the utility of PCT, presepsin, galectin-3, and sST2, as a single measurement or combination, for the prediction of disease severity and clinical outcome in sepsis. Multi-marker approach would be beneficial for the appropriate management of septic patients.

Abbreviations: IQR, interquartile range; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; SOFA, sequential organ failure assessment; PCT, procalcitonin; sST2, soluble suppression of tumorigenicity 2.

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[1] Singer et al. The Third International Consensus Definitions for Sepsis and Septick Shock (Sepsis-3). JAMA 2016;315:801-10