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Diagnostic and prognostic value of presepsin (soluble CD14 subtype) in emergency patients with early sepsis using the new assay PATHFAST Presepsin

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Background

CD14 is a membrane glycoprotein of monocytes/macrophages (mCD14) and serves as a pattern recognition moleclue in the innate immune response against microorganism. Upon activation of proinflammatory signaling cascade by CD14 is shedded of from the cell membrane resulting in soluble CD14 (sCD14). Clinical studies have revealed elevated sCD14 in sepsis but the marker was not established as a diagnostic tool. However, plasma protease activity generates also another particle from sCD14 called sCD14 subtype (sCD14-ST).
The aim of the study was to compare the diagnostic and prognostic validity of sCD14-ST to PCT, CRP and IL-6, correlate sCD14-ST with clinical scores and to examine the diagnostic efficacy and prognostic value of sCD14-ST for outcome in patients presenting with sepsis at an emergency room (ER).

Methods

146 patients presenting at the ER with sepsis were included. EDTA plasma samples were collected at first presentation, 24 hours, and 72 hours after admission, and were stored at -70°C until determination of sCD14-ST using the PATHFAST Presepsin assay. PCT, CRP and IL-6 were determined at the central lab using using commercial available kits following the instructions of the manufactorers. 119 healthy volunteers served as control group. The EDTA plasma samples obtained from this group (60 females and 59 males, aged 21 to 69 years, mean 42 years) were used for determination of the reference interval.

Results

Tab. 1: Reference range of sCD14-ST (presepsin) based on 119 healthy individuals in comparison sCD14-ST in patients with sepsis

	sCD14-ST (Presepsin) (pg/ml) in Healthy individuals	**sCD14-ST** (pg/ml) in patients with sepsis
Lowest – highest value	**60.1 – 365.0**	338 – 15757
Mean (95% CI)	**159.4 (148.1 – 170.7)**	2433 (1593 – 3272)
5th percentile	**62.2**	380
95th percentile	**319.8**	10653

The PATHFAST Presepsin assay revealved elevated concentrations of sCD14-ST in septic patients depending on the Severity of the disease compared to sCD14-ST concentration in healthy subjects (Tab. 1) .

Tab. 2: Biomarkers and clinical scores at baseline (admission)

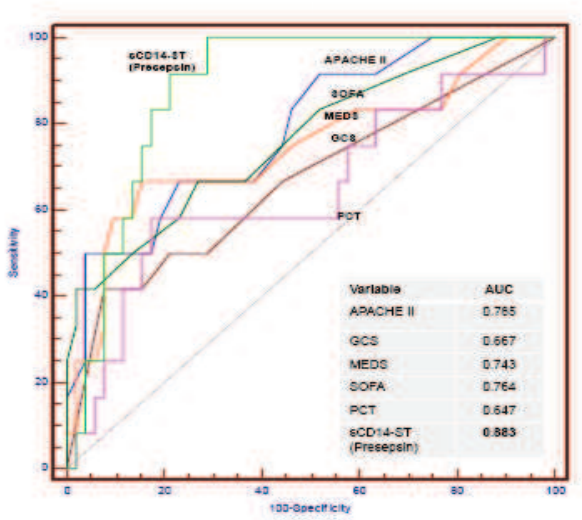
	Low grade sepsis (N=91)		Severes sepsis/septic shock (N=55)		
	Median	**95% CI**	**Median**	**95% CI**	**P-value***
IL-6, pg/ml	125	80 - 213	265	113 - 790	0.0123
CRP, mg/dl	148.3	93.7 - 190.4	195.7	125.1 - 260.8	0.0315
PCT, ng/ml	1.44	0.66 - 2.24	3.05	1.74 - 8.47	**0.0065**
sCD14-ST, pg/ml	782	559 - 932	1407	989 – 1868	**<0.0001**
APACHE II	14	11 - 17	23	20 – 27	<0.0001
GCS	15	15 - 15	14	11.0 - 14.5	<0.0001
MEDS	8	6 - 9	11	9.5 - 14.5	<0.0001
SOFA	4	3 - 5	6	5 – 8	0.0005

	Survivors (N=123)		Non-survivors (N=23)		
	Median	**95% CI**	**Median**	**95% CI**	**P-value***
IL-6, pg/ml	129	95 - 239	440	106 - 6174	0.0584
CRP, mg/dl	173,3	133,6 - 207,6	120,4	43,1 - 235,5	0.3824
PCT, ng/ml	1,84	1,23 - 2,73	2,07	0,31 - 21,23	**0.7452**
sCD14-ST, pg/ml	823	678 – 973	2124	1209 - 3604	**<0.0001**
APACHE II	16	14 – 19	28	23 – 35	<0.0001
GCS	15	15 – 15	8,5	3 - 14	<0.0001
MEDS	8	8 – 10	17	14 – 21	<0.0001
SOFA	4	4 - 5	8	5 – 13	0.0007

* Mann-Whitney *U*-test, two-sided

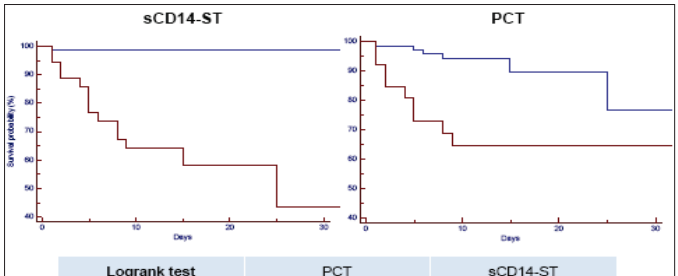
sCD14-ST (Presepsin) showed the highest significance level for discrimination between survivors and non-survivors (30-day-mortality) and between low grade sepsis and severe sepsis or septic shock reaching p < 0.0001 that was superior to IL-6, CRP and PCT and comparable to those of the clinical scores (Tab. 2).

Fig. 1: Comparison of ROC curves for 30 day mortality at admission by sCD14-ST (presepsin), and PCT and clin scores in septic patients with PCT ≥ 0.5 ng/ml wi with PCT ≥ 0.5 ng/ml



The ROC anaylsis showed superior risk prediction of sCD14-ST (presepsin) at admission for 30 day mortality in septic patients with PCT ≥ 0.5 ng/ml which was confirmed by Kaplan-Meier analysis (Fig. 1 and 2)

Fig. 2: Kaplan-Meier survival curves for sCD14-ST (cutoff 1622 pg/ml) and PCT (cutoff 13.43 ng/ml) (30 day mortality)



Logrank test	PCT	sCD14-ST
Chi-square	10.03	24.47
P	0.0015	< 0.0001
HR (95% CI)	0.221 (0.04 – 0.48)	0.036 (0.022 – 0.193)

C-statistic:

MEDS alone	**AUC = 0.743**
sCD14-ST alone	**AUC = 0.883**
MEDS and sCD14-ST in combination	**AUC = 0.936**

Net re-classification index NRI = 22.67% + 40.00% = 62.67%
23% of alive patients more are re-classified in the right direction than in the wrong direction and 40% more of dead patients are re-classified in the right direction than in the wrong direction by combining MEDS and sCD14-ST.

Conclusion

sCD14-ST (prespsin) is a promising novel diagnostic marker for sepsis. These preliminary results suggested that presepsin could be used for early diagnosis. sCD14-ST is superior in mortality prediction already at first presentation using the novel POC assay PATHFAST Presepin which allows reliable determination of sCD14-ST within 17 min from whole blood samples in the ER.