

The new Sepsis Marker Presepsin is Superior for Prognosis and Disease Monitoring compared to Procalcitonin

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Background: Soluble CD14 subtype (sCD14-ST, presepsin) serves as a mediator of the response to lipopolysaccharid from infectious agents. First evidence suggested that presepsin may be utilized as sepsis marker. **The aim of the study** was to examine the diagnostic and prognostic validity of presepsin in emergency patients with sepsis.

Methods: 140 patients presenting at the emergency room (ER) 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 PATHFAST Presepsin. 119 healthy volunteers served as control group. Primary endpoint was death within 30 days. The combined endpoint “major adverse event” (MAE) consisted of at least either the primary or at least one of the secondary endpoints intensive care, mechanical ventilation or dialysis.

Results

Reference values. Presepsin concentrations of the control group and the patient group are displayed in Tab. 1.

Tab. 1: Presepsin levels in 119 healthy individuals and 140 patients

	Healthy individuals	Patients with sepsis
Min – Max, ng/L	60.1 – 365.0	338 – 15757
Mean (95% CI), ng/L	159.4 (148.1 – 170.7)	2433 (1593 – 3272)
Upper Reference Limit	280 ng/L	non-parametric percentile method (CLSI C28-A3)

Diagnostic validity. For discrimination between low grade sepsis and severe sepsis presepsin showed the highest significance level reaching $p < 0.0001$ that was superior to IL-6, C-reactive protein (CRP) and procalcitonin (PCT) and comparable to those of the clinical scores (Tab. 2). Similar results (data not shown) were obtained for discrimination between survivors (N=117) and non-survivors (N=23).

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

	Low grade sepsis (N=91)		Severe sepsis (N=55)		P-value*
	Median	95% CI	Median	95% CI	
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
Presepsin, 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

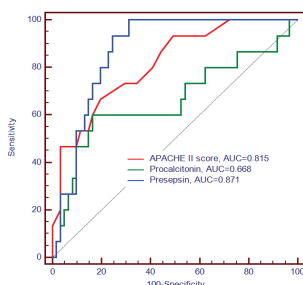


Fig. 2: ROC curves of presepsin, PCT and APACHE II score (30-day mortality)

Tab. 3: Quartiles of presepsin or PCT and mortality

Quartile	1 st	2 nd	3 rd	4 th
Presepsin (ng/L)	177 – 512	524 – 927	950 – 1810	1850 – 15757
Mortality ($p < 0.0001$)	2.7%	8.6%	17.1%	39.4%
PCT (ng/ml)	0.10 – 0.38	0.39 – 1.73	1.76 – 7.0	8.1 – 292
Mortality ($p = 0.9816$)	26.7%	8.1%	8.3%	24.3%

Disease monitoring. All patients received antimicrobial therapy. In patients without occurrence of MAEs within 30 days after admission (N=104) the both marker levels decreased from baseline to 72 hours in the majority of the patients. In the patient group who experienced MAEs (N=36), both markers showed an increasing tendency. This effect was more pronounced for presepsin (Fig. 2).

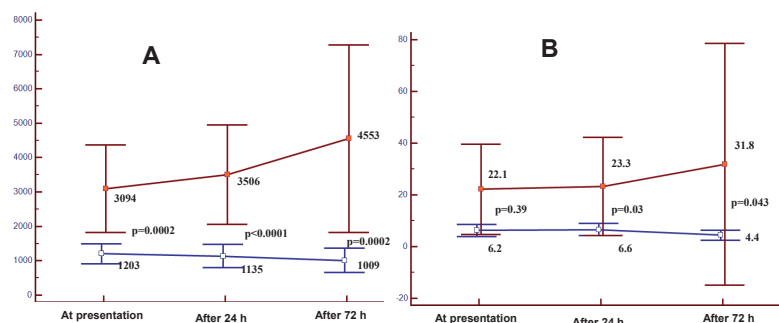


Fig. 2: Course of presepsin (A) and PCT (B) during microbial therapy in patients with worse outcome (red line, N=36) and favourable outcome (blue line, N=104) (mean values, error bars: 95% CI)

Prognostic validity. The 30-day mortality ranged from 2.7% to 39.4% between the 1st and the 4th quartile (Tab. 4). Presepsin demonstrated a stronger relationship with 30-day mortality than procalcitonin. Receiver operating curve analysis of presepsin, procalcitonin and APACHE II score revealed AUCs of 0.878 (95% CI: 0.801-0.934), 0.668 (95% CI: 0.570-0.757) and 0.815 (95% CI: 0.709-0.895), respectively (Fig. 3).

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 presepsin (sCD14-ST).

Tab. 5: Improved risk prediction by combining clinical scores and presepsin c-statistic and Net Reclassification Index (NRI)

	AUC alone	AUC with presepsin	NRI
APACHE II	0.815	0.905	54.38%
GCS	0.763	0.931	76.91%
MEDS	0.819	0.936	62.67%
SOFA	0.747	0.917	55.75%

Presepsin decision thresholds

Decision thresholds could be established for diagnostic differentiation of sepsis grades and mortality prediction in septic patients presenting at the ER (Tab. 4).

Tab. 4: Presepsin decision thresholds

Presepsin, ng/L	< 200	200-300	300-500	500-1000	≥ 1000
Sepsis progression and mortality risk	Very low	Low	Moderate	High	Very high
Clinical results:	< 200	200-300	300-500	500-1000	≥ 1000
Sepsis, n (%)	3 (3.5)	9 (10.6)	18 (21.1)	29 (34.1)	26 (30.6)
Severe sepsis, n (%)	0	0	5 (12.5)	11 (27.5)	24 (60.0)
Septic shock, n (%)	0	0	0	4 (26.7)	11 (73.3)
30-day death, n (%)	0	0	0	5 (21.7)	18 (78.3)

Conclusion

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