PATHFAST Presepsin in Patients with SIRS and Early Sepsis in the Emergency Department

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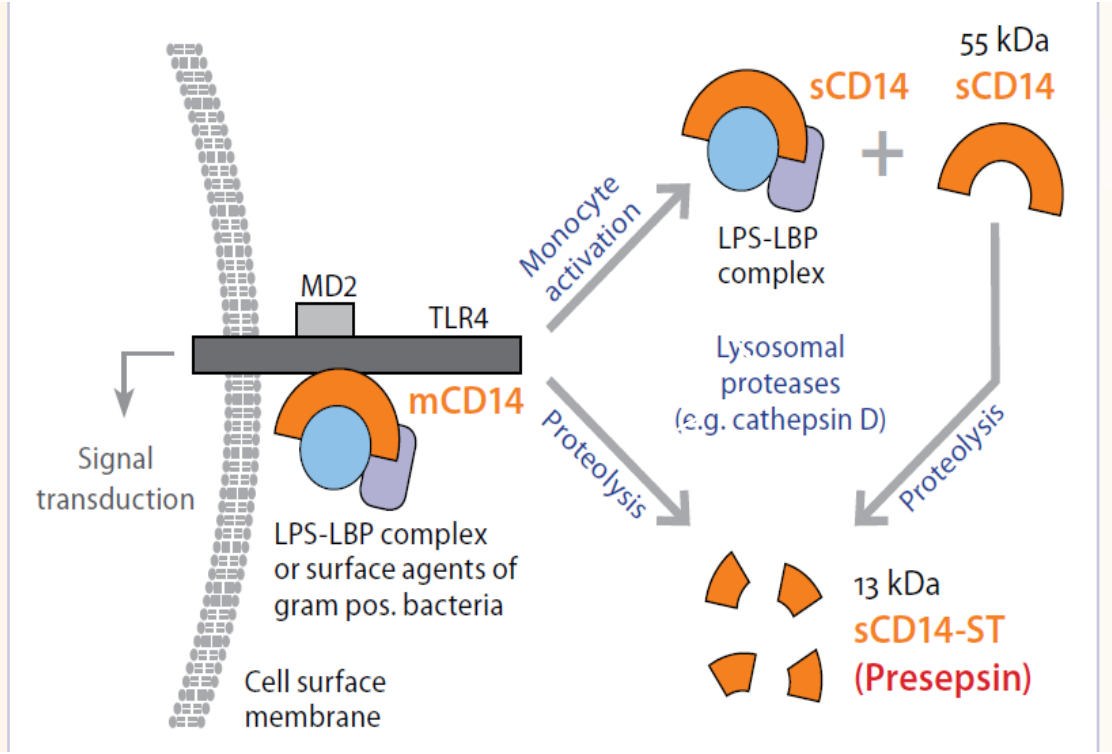
Objective of the study

to examine the suitability of presepsin for diagnosis and prognosis in patients suspicious of sepsis admitted to the emergency room

New Marker of sepsis: PRESEPSIN

Secretion mechanism of Presepsina



mCD14: membrana CD14; sCD14: soluble CD14;sCD14-ST:soluble CD14 subtipo (=Presepsina); LPS:lipopolisacáridos;LBP:lipopolisacáridos unidos a proteínas;TLR4: receptor tipo toll; MD2: Co –proteína de TLR4 , PG: Poliglicanos

Study design

Methods:

- The study was performed as a single-center, non-randomized, non-blinded observation of consecutive emergency patients admitted between November 2012 and February 2013 to Rebagliati Hospital, Lima, Peru.
- The study was approved by the local ethics committee.
- All patients provided informed consent prior to enrollement.

Patients:

- 123 patients at age 18 years or older

Control goup:

- *123 healthy volunteers served as blood donors formed the control group* (31 females and 92 males, aged 18 to 56 years, mean 35 years)

Study design

Primary endpoint:

- death within 30 days.

Secondary endpoints:

- intensive care
- Mechanical ventilation
- dialysis

Combined endpoint:

- at least one event (either the primary or at least one of the secondary endpoints)

Characteristics of the study population

		Total n=123	SIRS n=9	Sepsis n=74	Severe sepsis/sept. shock n=40
Demography					
	Age; median(min-max)	67(21-95)	34(27-64)	69(24-94)	70(21-95)
	Male; %	45.5	22.2	41.9	57.5
Medical history					
	Stroke; n, %	21, *17.1*	0, *0*	15, *20.3*	06, *15.0*
	Diabetes; n, %	15, *12.2*	0, *0*	12, *16.2*	03, *07.5*
	Kidney disease n, %	20, *16.3*	0, *0*	8, *10.8*	12, 30.*0*
	Lithiasis; n, %	12, *9.8*	5, *44.4*	4, *5.4*	3, *7.5*
	Liver disease; n, %	7, 5.7	0, *0*	2, *2.7*	5, *12.5*
	Fibrosis of the lung; n, %	7, 5.7	0, *0*	4, *5.4*	3, *7.5*
	Others, n, %	9, *7.3*	1, *11.1*	4, *5.4*	4, *10.0*
Infective focus					
	Urinary tract; n, %	42, *34.1*	0, *0*	33, *44.6*	9, 22.*5*
	Lung; n, %	35, 30.*7*	0, *0*	20, *27.0*	15, *37.5*
	Abdomen; n, %	23, *20.1*	0, *0*	14, *18.9*	9, 22.*5*
	Central venous catheter; n, %	5, *4.4*	0, *0*	2, *2.7*	3, *7.5*
	Skin; n, %	5, *4.4*	0, *0*	4, *5.4*	1, *2.0*
	Others, n, %	4, *3.5*	0, *0*	1, *1.4*	3, *7.5*
APACHE II score					
	24 h; median (95% CI)	13 (10-15)	3 (2-4)	11 (9-12)	18 (15-21)
	72 h; median (95% CI)	9 (9-11)	2(0-3)	8 (6-9)	16 (13-18)
Presepsin (pg/ml)					
	0 h; median (95% CI)	690 (556-955)	304 (175-477)	544 (457-688)	2037 (1482-3668)
	8 h; median (95% CI)	700 (563-1014)	320 (184-635)	536 (453-706)	2134 (1403-4119)
	24 h; median (95% CI)	637 (538-886)	260 (214-333)	572 (450-657)	2428 (1252-4334)
	72 h; median (95% CI)	623 (475-888)	244 (158-830)	472 (391-596)	2020 (1037-5109)
Outcome					
	30-days death; n, %	24, *19.5*	0, *0*	7, *9.5*	17, *42.5*
	Combined endpoint; n, %	35, *28.5*	0, *0*	11, *14.9*	24, *60.0*

Laboratory analysis

Presepsin was determined in EDTA plasma samples using the chemiluminiscent enzyme inmunoassay POC assay

PATHFAST Presepsin

(LSI Medience Corporation, Tokyo, Japan)

The PATHFAST system

The PATHFAST system

Presepsin in healthy controls and patients

	Controls n=123	**Patients n=123**
Min – Max, ng/L	58.0 – 339.0	103.0 – 13036.0
Mean (95% CI), ng/L	**130.2** (120.6 – 139.8)	**1946.1** (1447.1 – 2445.1)
Upper Refence Limit	**243 ng/L**	non-parametric percentile method (CLSI C28-A3)

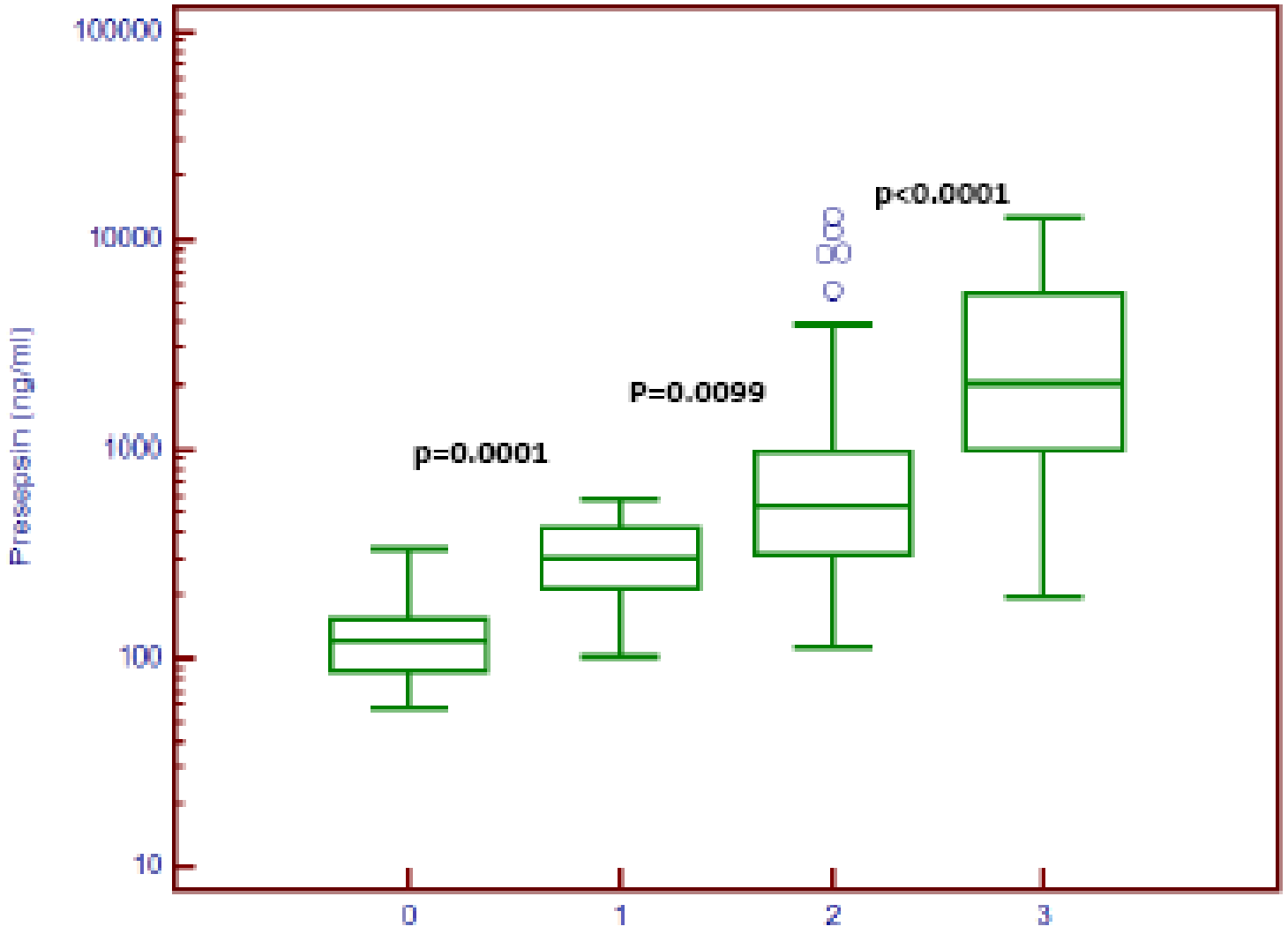
Presepsin levels compared to APACHE II score

	Presepsin at admission Median (IQR)	APACHE II score after 24 hours Median (IQR)
SIRS, n=9	304 (219-428)	3 (2-4)
Sepsis, n=74	544 (319-984)	11 (7-16)
Severe sepsis, n=34	1994 (1061-5331)	18 (15-21)
Septic shock, n=6	2796 (1004-5583)	24 (23-24)

Presepsin in survivors and decedents during 72 hours

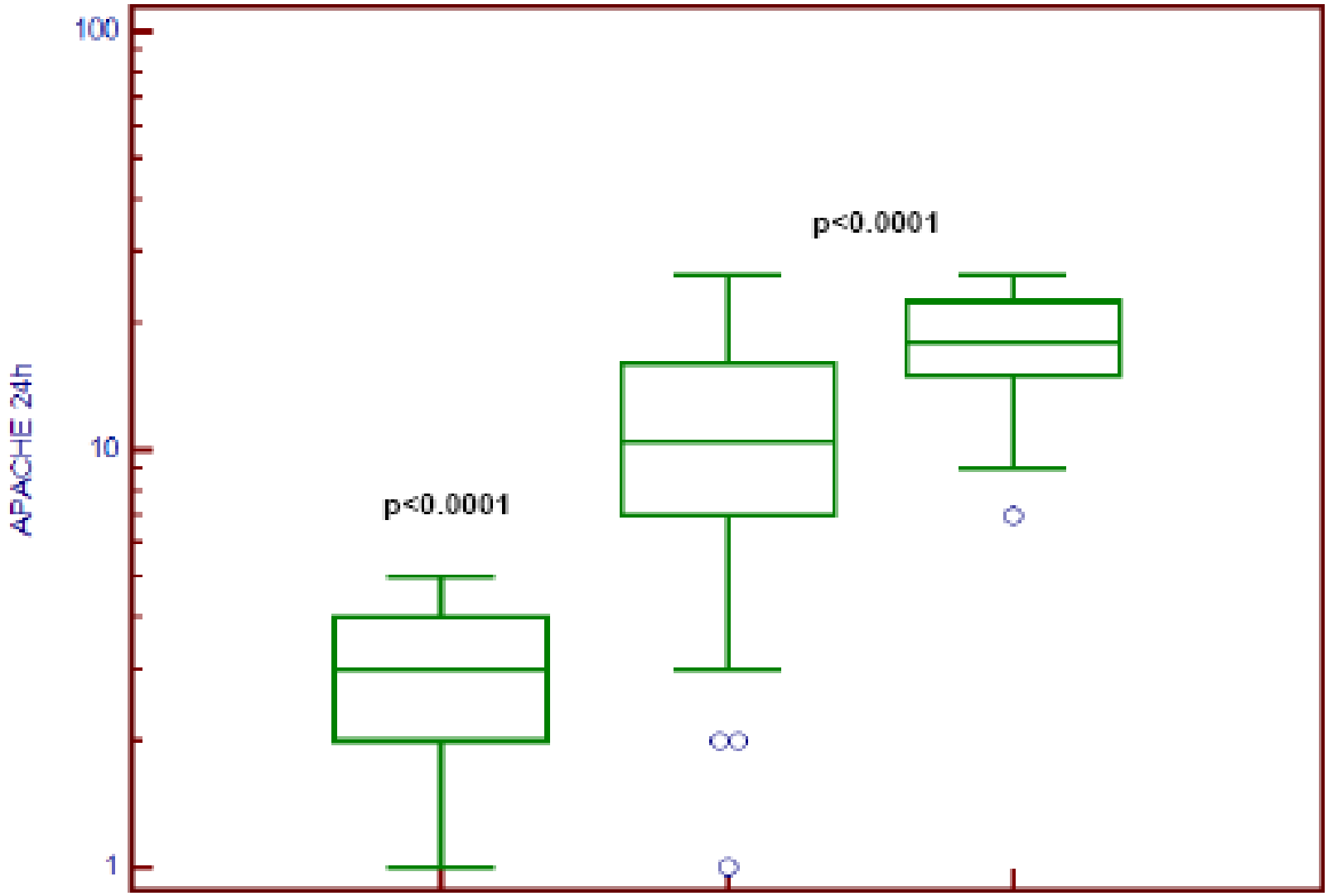
Presepsin Median (IQR), pg/ml	Baseline	8 hours	24 hours	78 hours
Survivors	590 (345-1396)	622 (367-1912)	574 (336-1610)	533 (324-1246)
Non-survivors	1763 (705-6616)	1859 (1001-5744)	1731 (809-4586)	2056 (811-5540)
p-value	0.0046	0.0005	0.0033	0.0013

Presepsin values in controls, patients with SIRS, sepsis (low grade) and severe sepsis or septic shock at admission



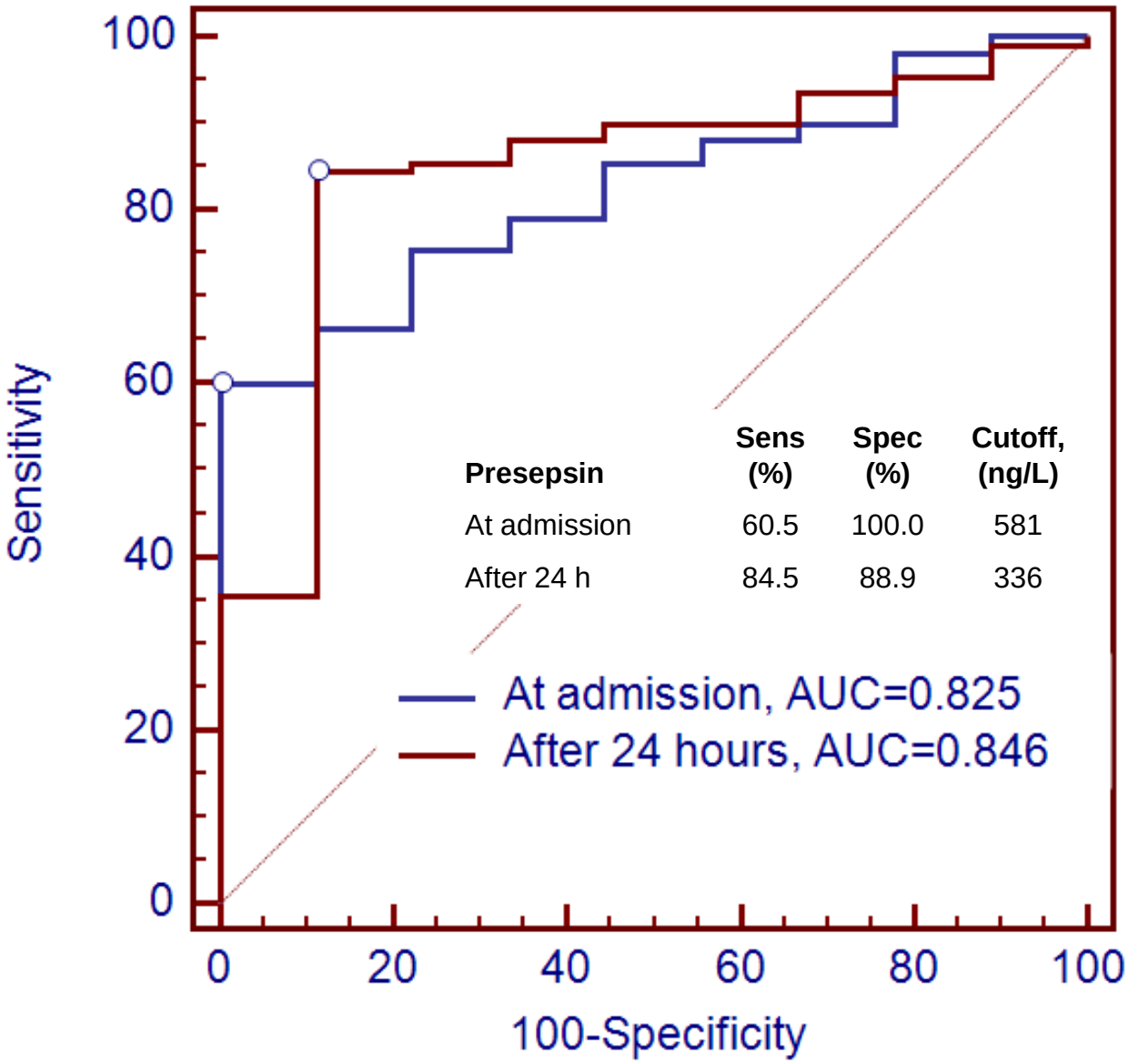
0 = controls (n=123), 1=SIRS (n=9), 2=sepsis (n=74), 3=severe sepsis or septic shock (n=40)

APACHE II score 24 hours after admission in patients with SIRS, sepsis (low grade) and severe sepsis or septic shock



0=SIRS (n=9), 1=sepsis (n=74), 2=severe sepsis or septic shock (n=40)

ROC analysis of presepsin for discrimination between SIRS and sepsis

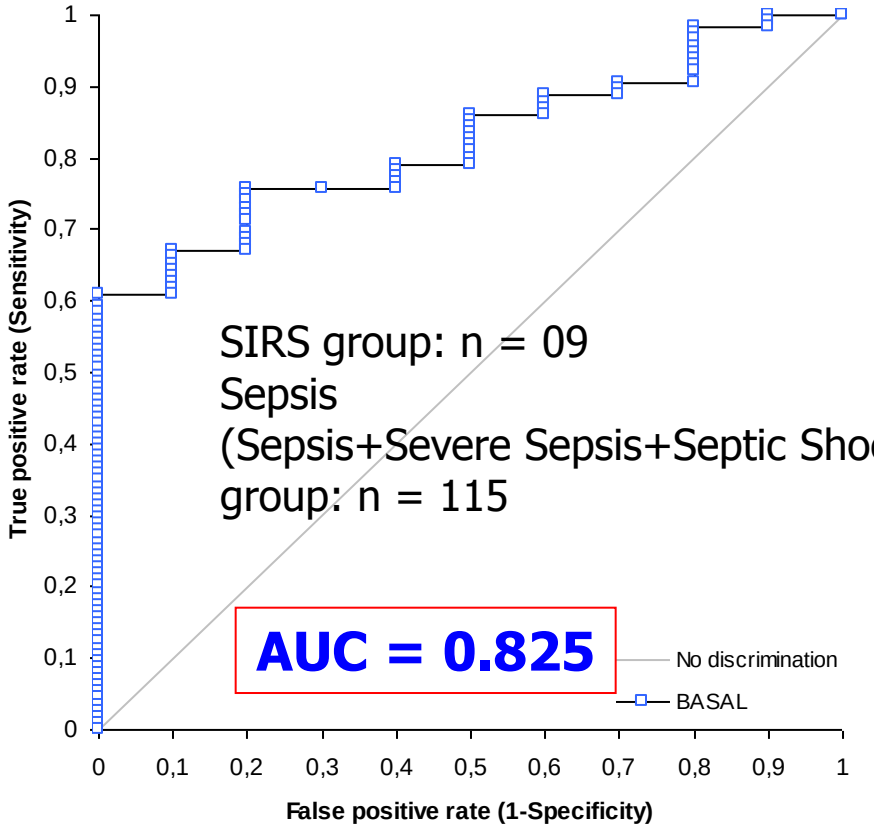


Presepsin	Sens (%)	Spec (%)	Cutoff, (ng/L)
At admission	60.5	100.0	581
After 24 h	84.5	88.9	336

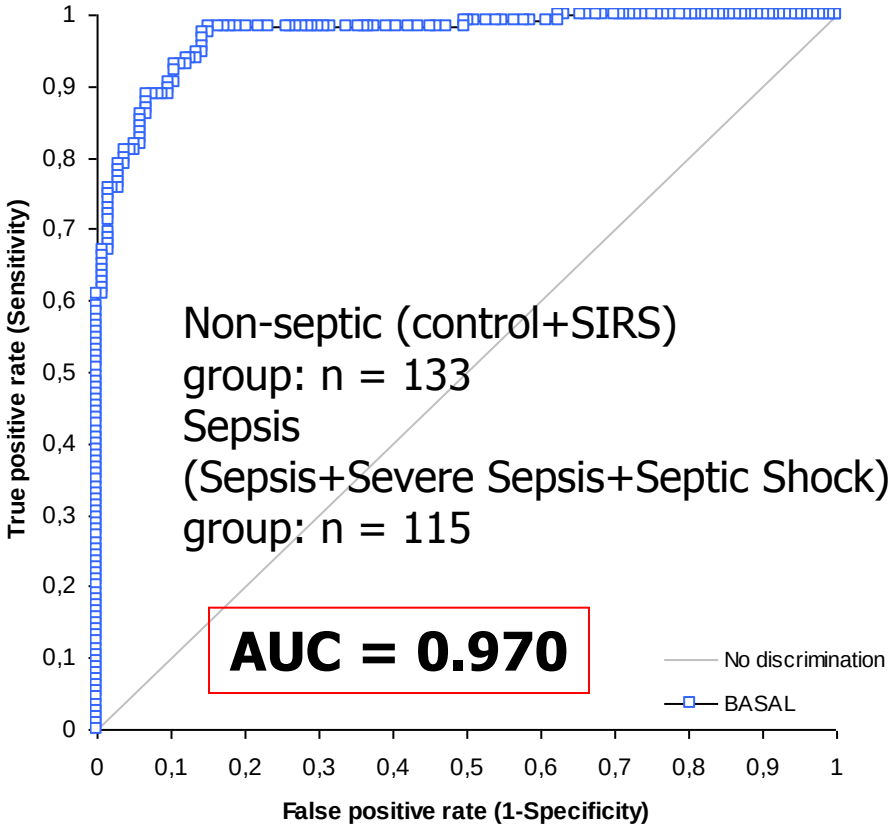
Early Diagnosis of Sepsis

On admission

SIRS vs Sepsis

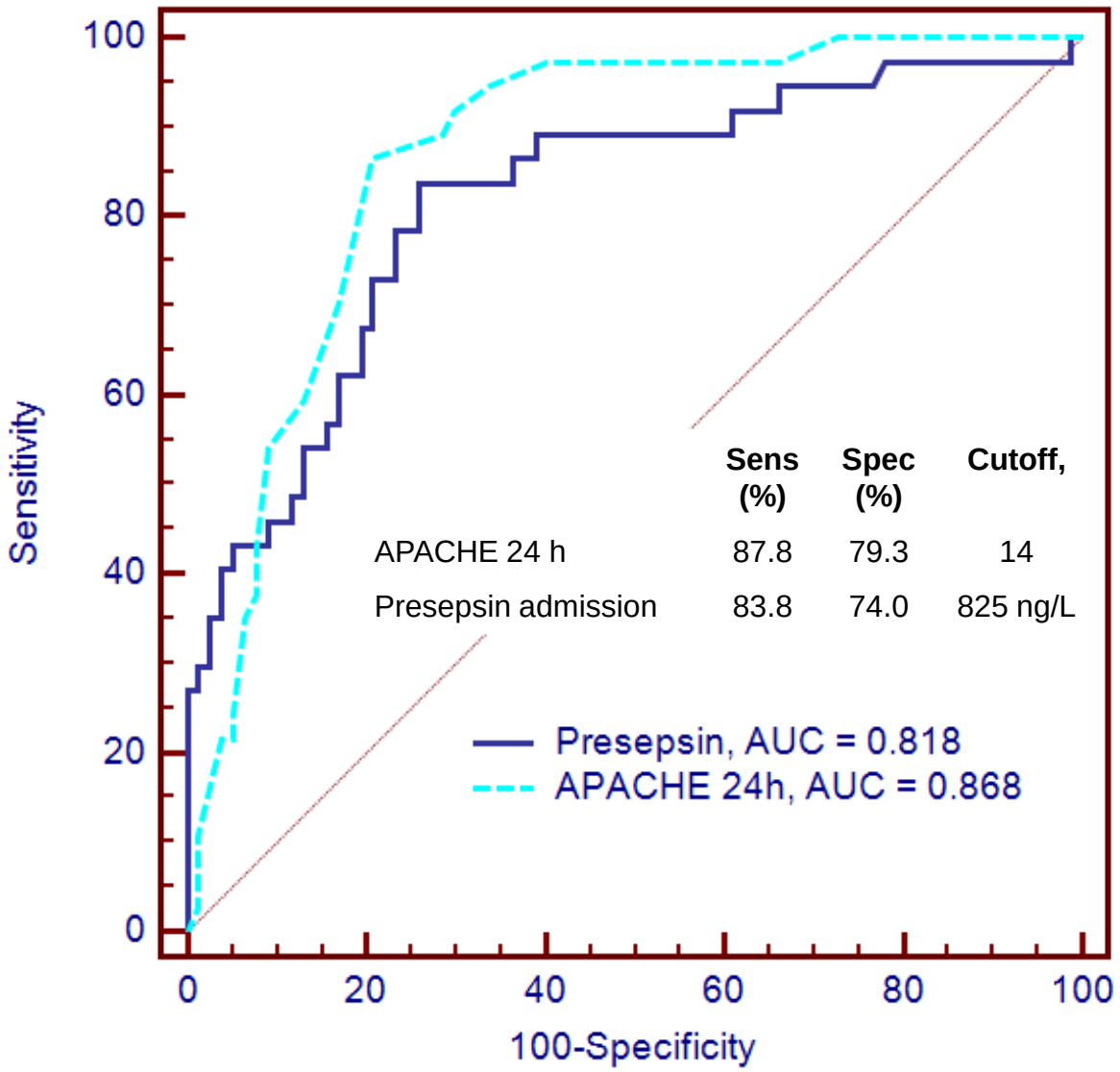


Non-septic vs Sepsis

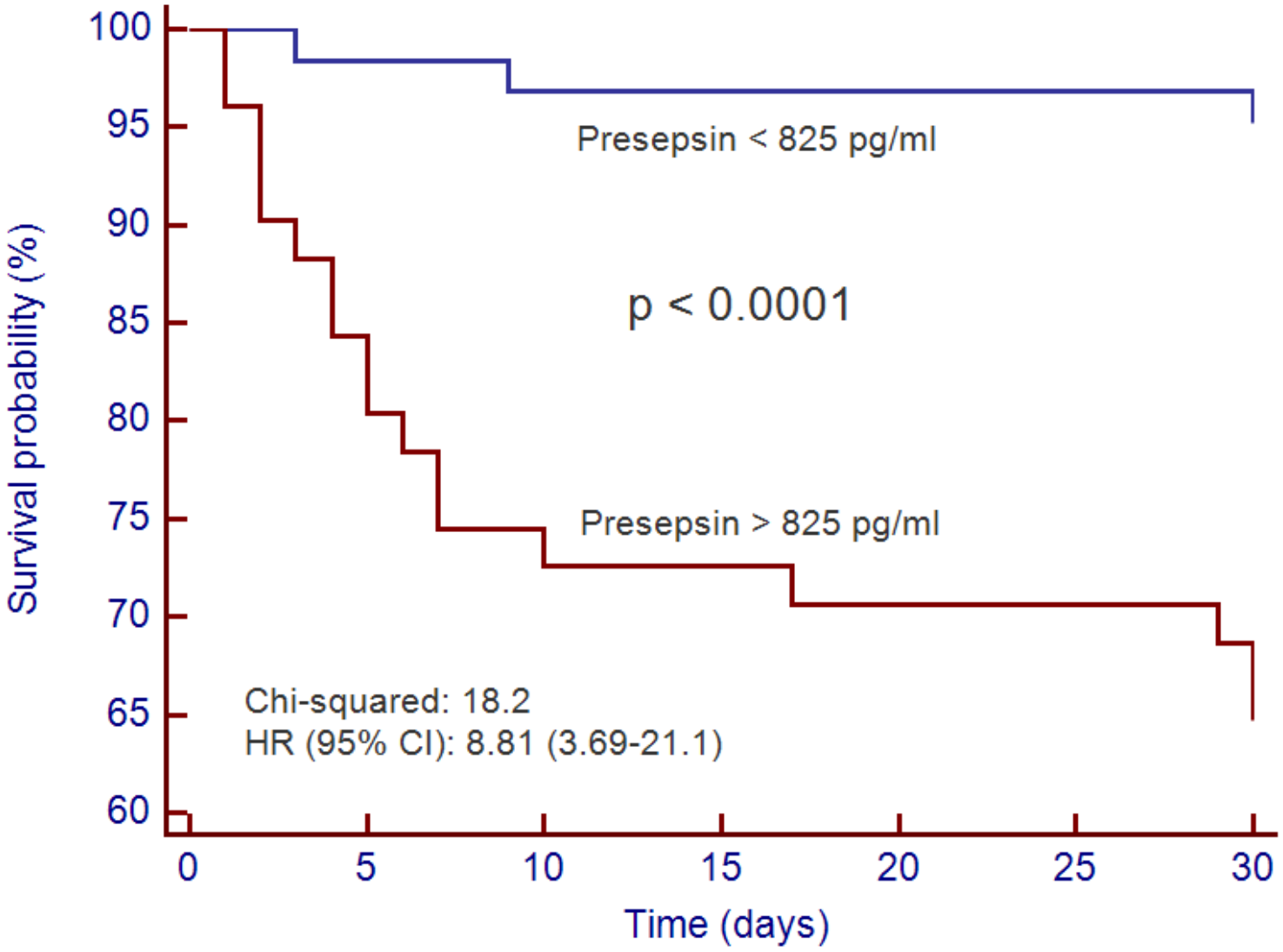


According to AUC evaluation, Presepsin can be used to distinguish septic patients from non-septic or SIRS patients

Outcome prediction (combined endpoint, n=37) in patients with sepsis (n=114) Presepsin at admission, APACHE II score after 24 hours

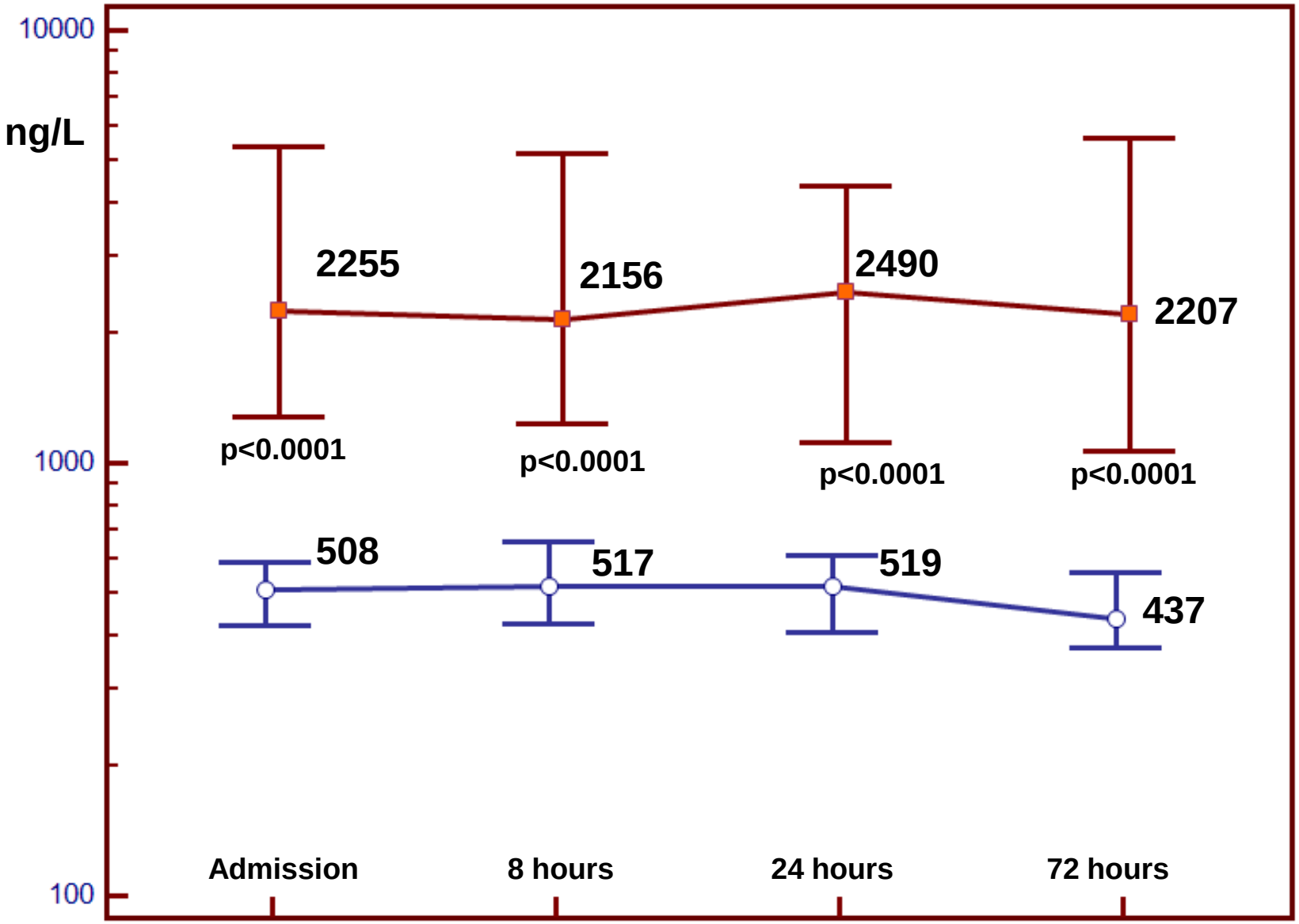


Kaplan-Meier survival analysis of baseline presepsin for outcome prediction (30 days mortality)



Presepsin (median, 95% CI) in the course of the disease

blue line: favourable outcome, n=74; red line: worse outcome (combined endpoint), n=40



Presepsin decision thresholds for risk stratification and outcome prediction

Risk	Low	Moderate	High	Very high
Presepsin, ng/L	**< 300**	**300 – 500**	**500 – 1000**	**> 1000**
Healthy controls, n (%)	113 (**91.8**)	10 (**8.1**)	0 (**0.0**)	0 (**0.0**)
SIRS, n (%)	4 (**44.4**)	5 (**55.5**)	0 (**0.0**)	0 (**0.0**)
Sepsis (low grade), n (%)	6 (**8.1**)	24 (**32.4**)	26 (**35.1**)	18 (**24.3**)
Severe sepsis/shock, n (%)	0 (**0.0**)	4 (**10.0**)	6 (**15.0**)	30 (**75.0**)
30-day death, n (%)	0 (**0.0**)	4 (**16.6**)	6 (**25.0**)	14 (**58.3**)
Combined endpoint, n (%)	1 (**2.4**)	3 (**7.3**)	6 (**14.6**)	31(**46.3**)

Conclusion

Presepsin demonstrated a strong relationship with disease severity and outcome. Presepsin provided reliable discrimination between SIRS and sepsis as well as prognosis and early prediction of 30-day mortality and combined endpoint already at admission. Moreover, presepsin values showed close association to the course of the disease.

The PATHFAST system allows the quantitative determination of presepsin also in whole blood samples and **may improve the management of patients presenting with early sepsis in the emergency room.**