Usefulness of presepsin for assessment of sepsis in leukopenic patients.

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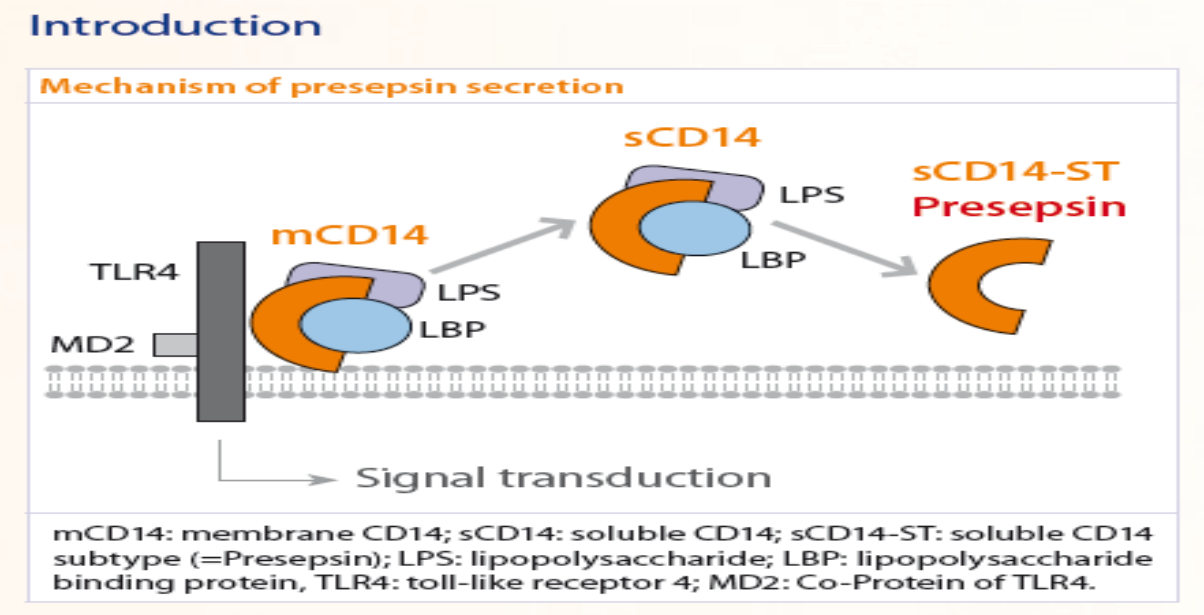
Background

2nd International Presepsin Workshop in Munich

- Presepsin is a new biomarker for early diagnosis of sepsis.

  Presepsin (sCD14-ST) is a soluble N-terminal fragment of the protein CD14 lipopolysaccharideebinding protein complex receptor produced in response to bacterial infections



Background

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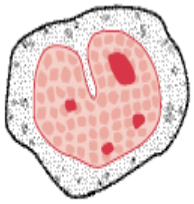
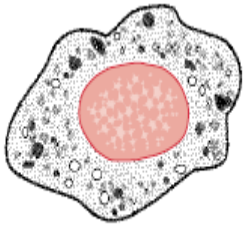
- **CD14 is presented in macrophage, monocyte, and granulocyte cells and their cell membranes**

Neutrophil

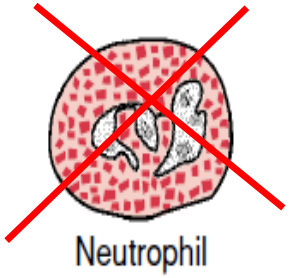


Monocyte

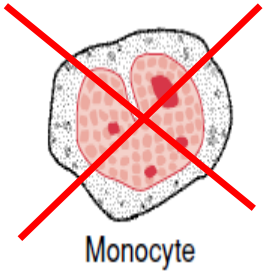


Macrophage

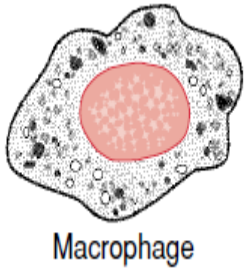
Data on possibility of use of presepsin for diagnosis of sepsis in severe leukopenic, especially neutropenic, patients are absent



Neutrophil



Monocyte



Macrophage

?

Background

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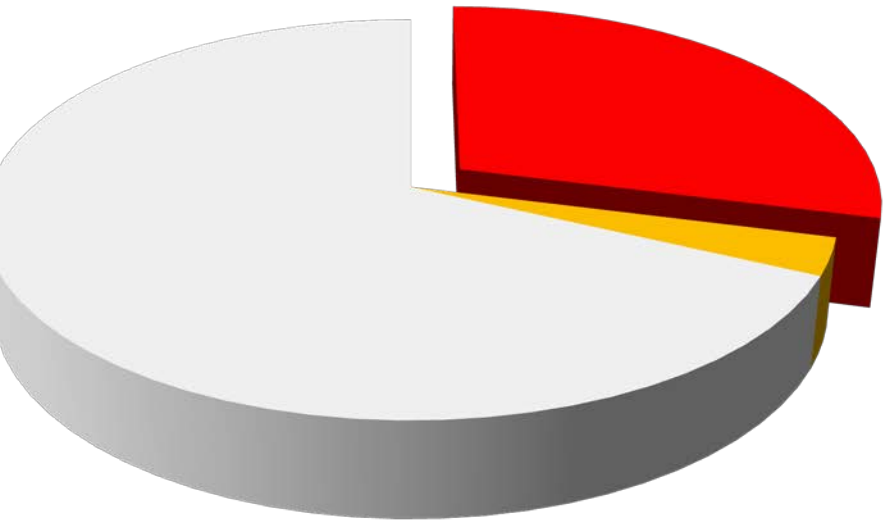
In EORTC-trial 859 febrile neutropenic cancer patients were included

(Viscoli C et al. Clin Microbiol Infect 2006; 12: 212-6.)

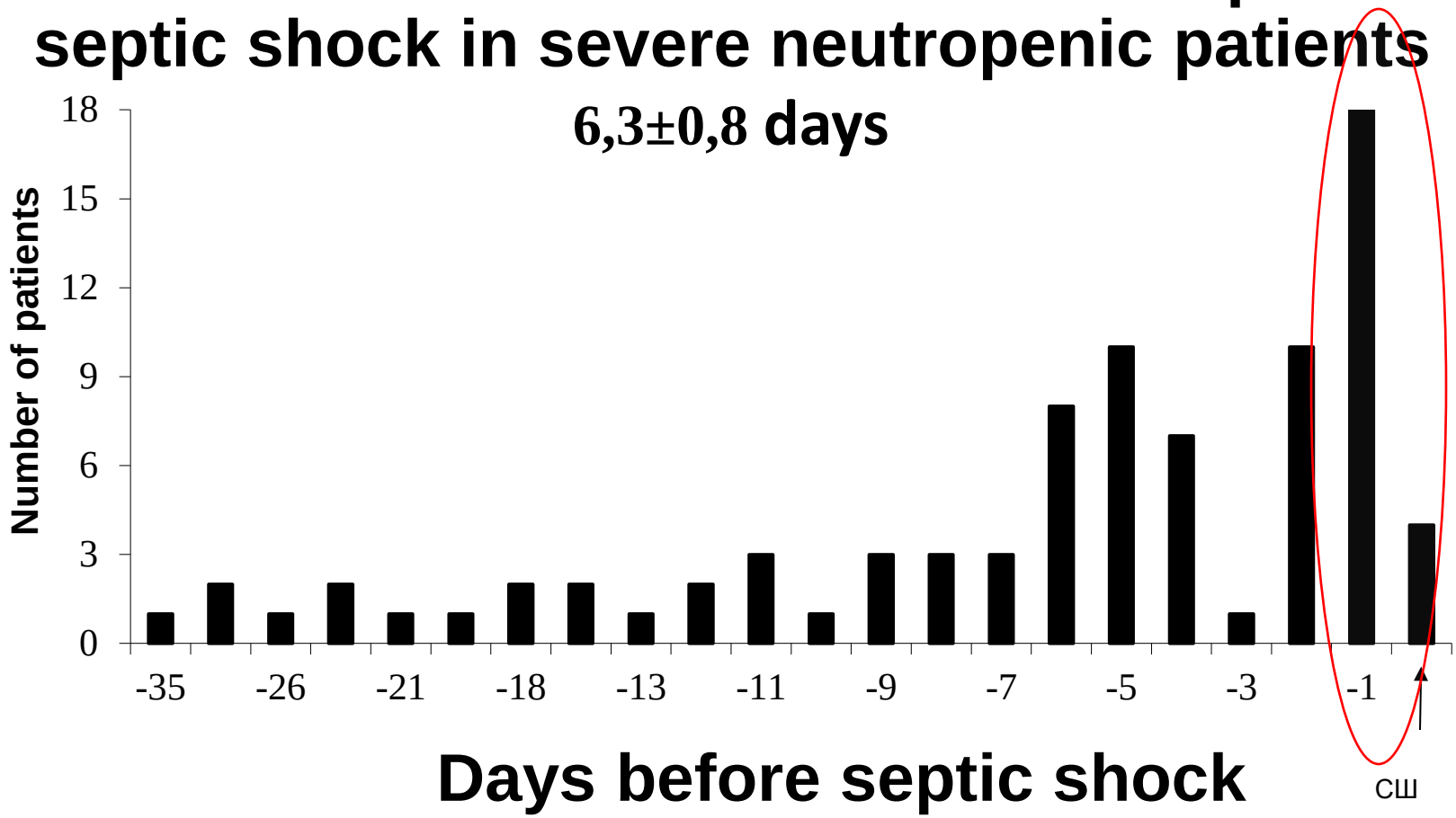


Bacteriemia **29%**

Microbiological documented infection without bacteraemia **3%**

Unknown **68%**

Time between onset of fever and development of septic shock in severe neutropenic patients

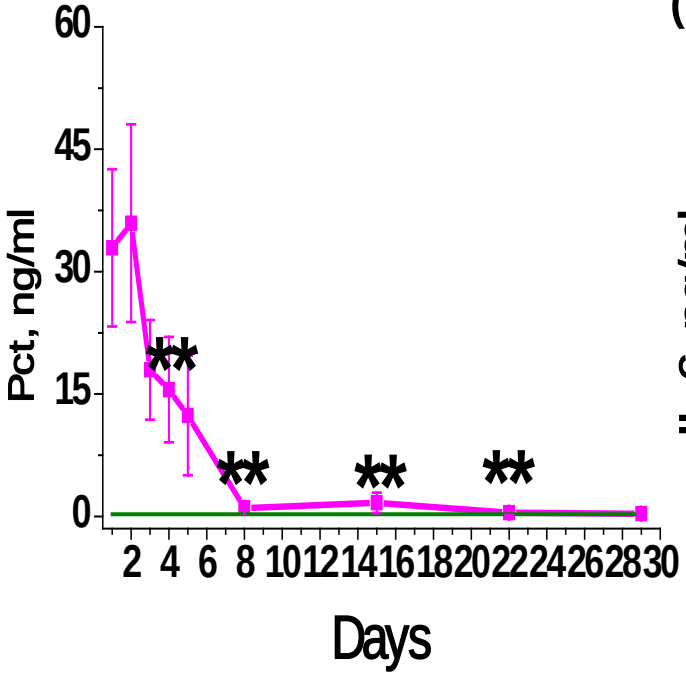


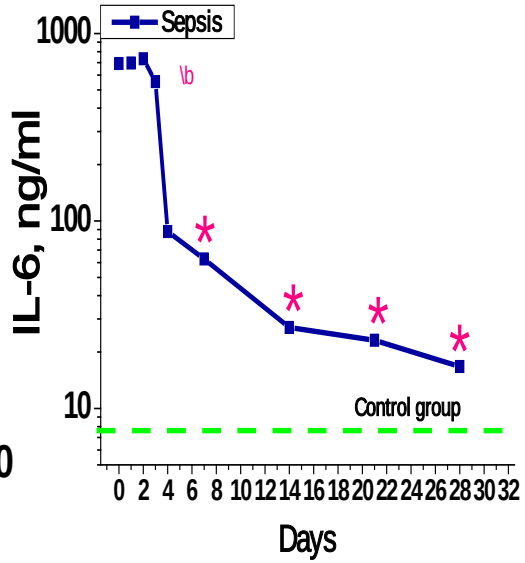
33% of neuropenic patients had fever only 1 day before onset of septic shock

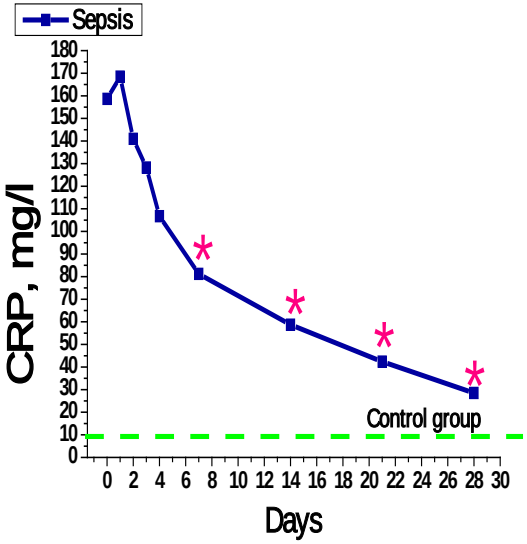
Galstyan 2003

PCT, IL-6 and CRP in neutropenic patients with sepsis

(Krechetova, 2011)







Purpose

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To evaluate whether presepsin is a useful biomarker for assessing the severity of sepsis and organ dysfunction in leukopenic patients with septic shock.

Materials and methods

Data from the Russian Clinical Trial of Mesenchymal Cells in Patients with Septic Shock and severe Neutropenia (*RuMCeSS)*

ClinicalTrials.gov
Protocol Registration System

Send message to ClinicalTrials.gov PRS

Help us improve: PRS Survey

Protocol Registration Receipt NCT01849237
05/08/2013

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Protocol Records are made available to the public through the ClinicalTrials.gov web site within 2 to 5 days of release, following system validation and quality assurance review. **Records that contain Results may take up to 30 days.**

Tip: Use the "Download PDF" link to get a printable record confirming the registration of this trial.

Russian Clinical Trial of Mesenchymal Cells in Patients With Septic Shock and Severe Neutropenia

This study is currently recruiting participants.
Verified by Elena N.Parovichnikova, National Research Center for Hematology, Russia, May 2013

Sponsor:	National Research Center for Hematology, Russia
Collaborators:	
Information provided by (Responsible Party):	Elena N.Parovichnikova, National Research Center for Hematology, Russia
ClinicalTrials.gov Identifier:	NCT01849237

The presepsin levels in infection

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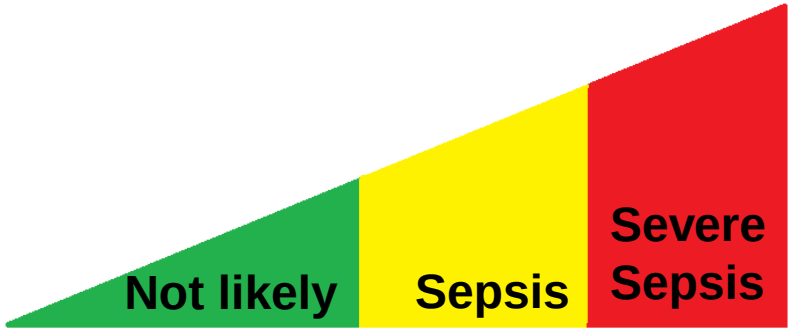
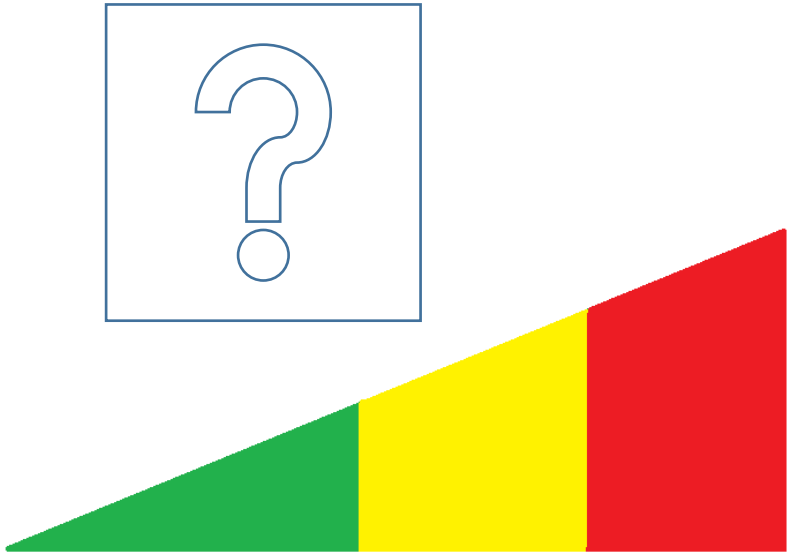
Patients without leukopenia



Presepsin (pg/ml) 500 1000

Takahashi G. et al.,2013 in press

Patients with leukopenia



Presepsin ? ?

Patients *(n=32)*

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Inclusion criteria (control group) *(n=12)*

- Hematological malignances
- Non-terminal malignance with a life expectancy of 6 months
- Absolute neutrophil count less than $0.5*10^9$/l
- Absence of signs of an infection

Inclusion criteria (main group) *(n=20)*

- Hematological malignances
- Non-terminal malignance with a life expectancy of 6 months
- Absolute neutrophil count less than $0.5*10^9$/l
- Septic shock (American College of Chest Physicians/Society of Critical Care Medicine criteria)

12 neutropenic patients without infection

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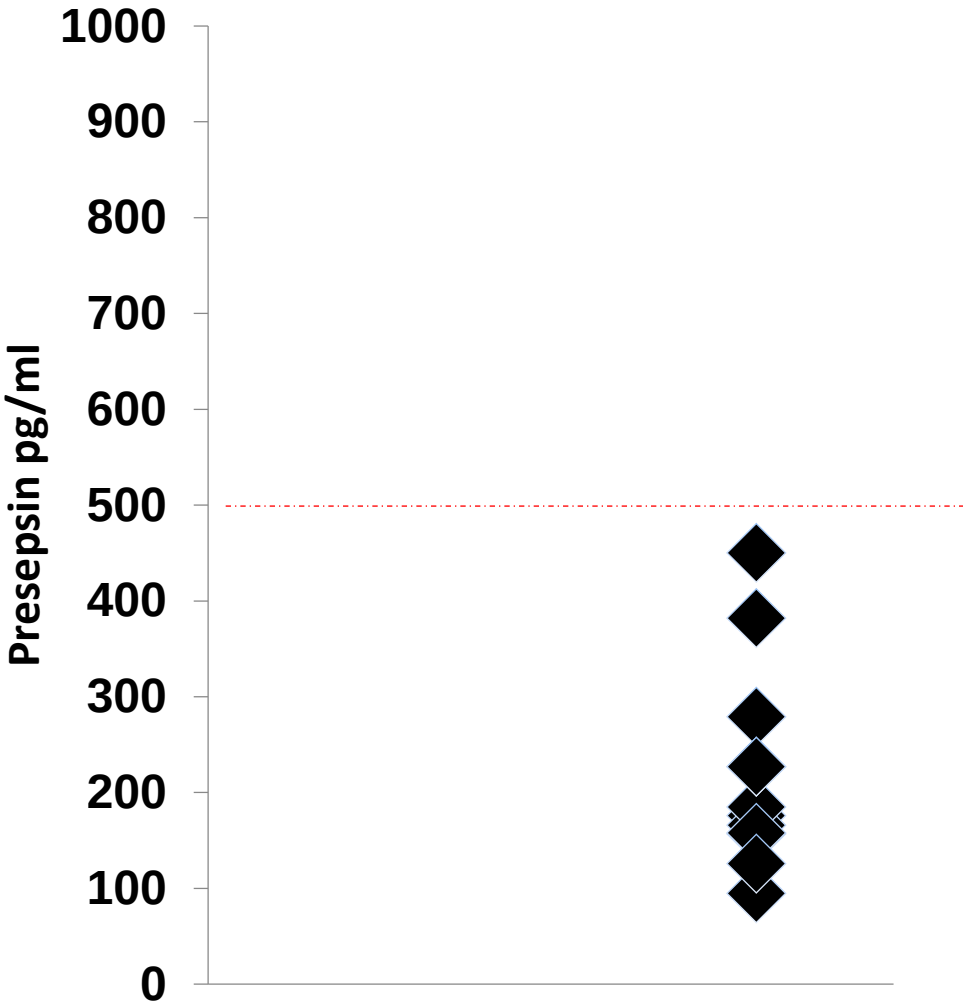
Underlying disease	N (%)
Non-Hodgkin's lymphoma	4
Multiple myeloma	4
Acute myeloid leukemia	1
Acute Lymphoid leukemia	3
Demographic Data	
Male/Female (n)	9/3
Age (years)	23-66 (median 47)



Characteristics of patients with septic shock

Underlying disease	N 20 (%)
Acute myeloid leukemia	8 (41)
Non-Hodgkin's lymphoma	8 (35)
Multiple myeloma	3 (18)
Myelodysplastic syndrome	1 (6)
Demographic and Clinical Parameters	
Male/Female (n)	11/9
Age (years)	30-81 (median 55)
APACHE II score	29 (21-43)

Study design

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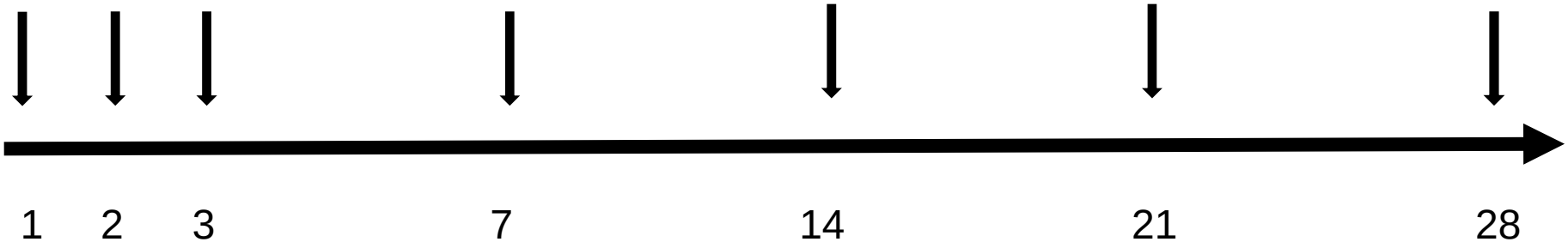
- PSP
- PCT
- IL-6
- CRP
- SOFA
- APACHE II



Days from onset of Septic shock

Blood presepsin levels in patients with septic shock

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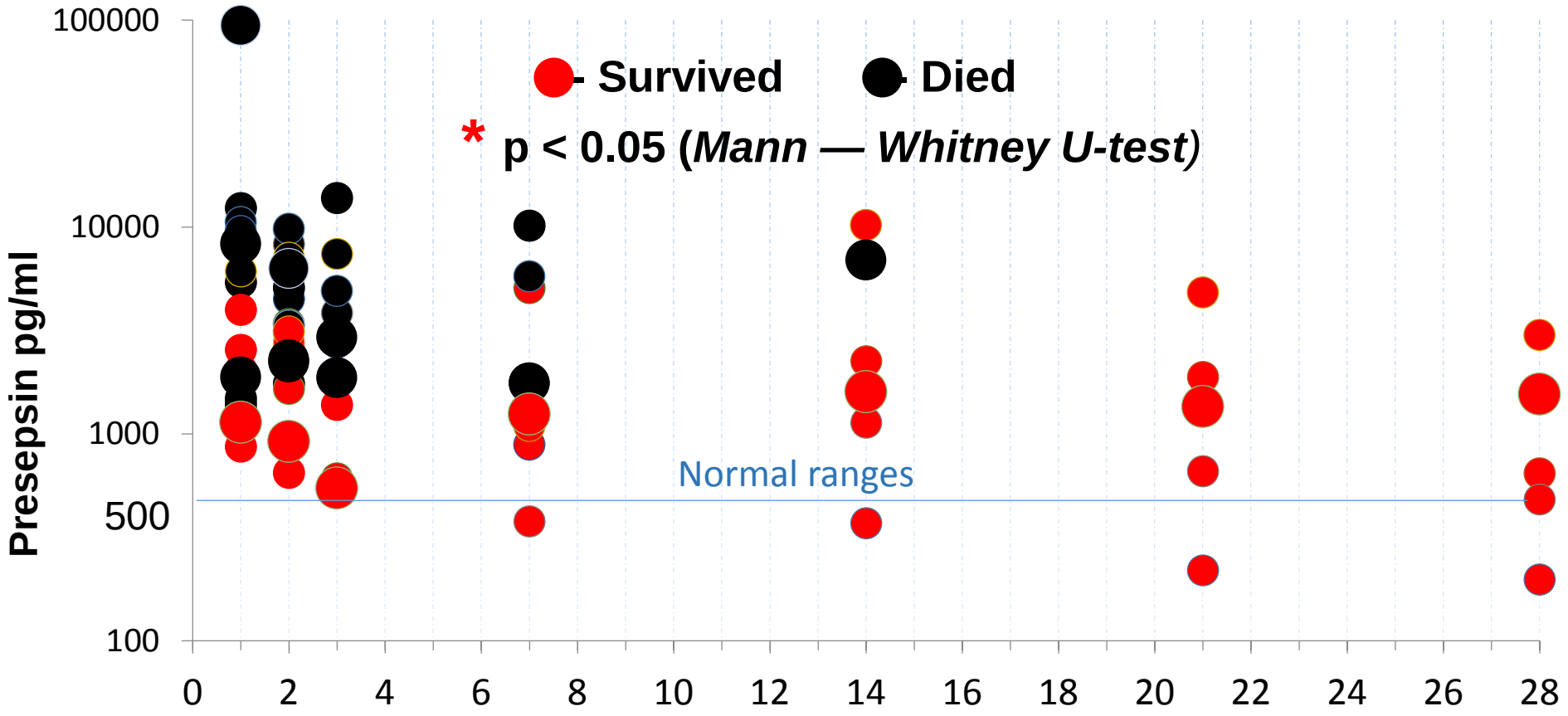
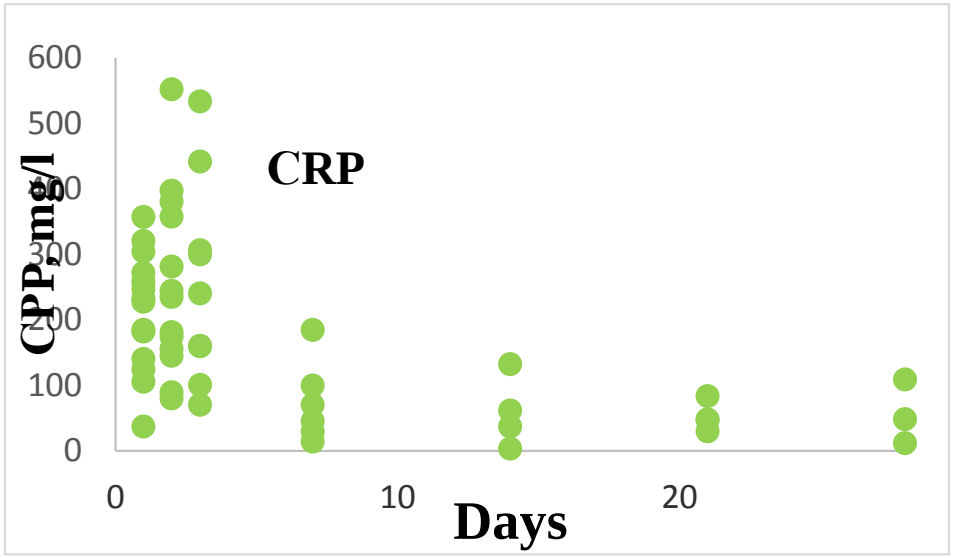


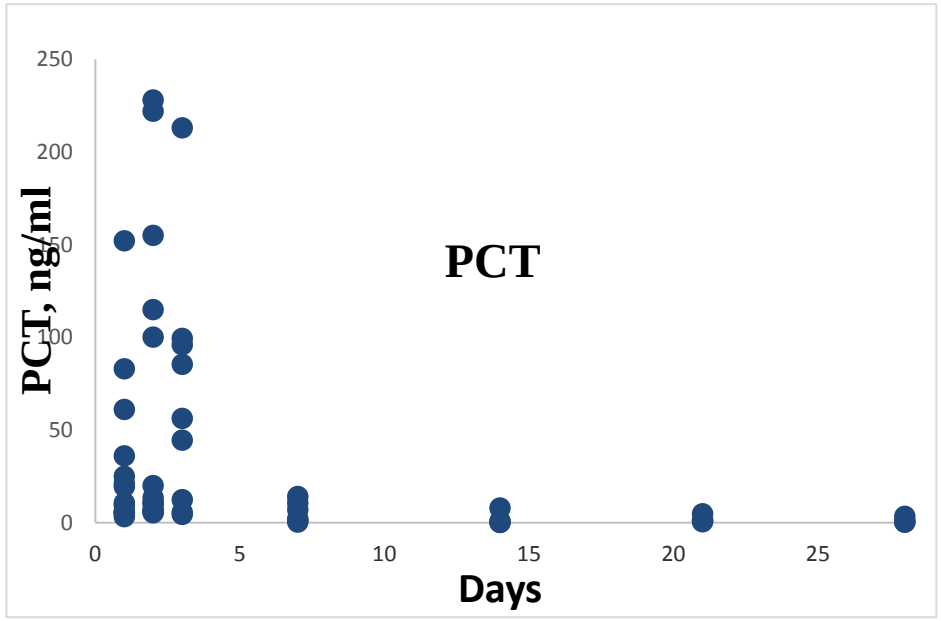
Days of shock	1	2	3	7	14	21	28
Survived	2051	1649*	1380*	1095*	1601*	1358	645
Died	6108	4497	3842	3777	6935	-	-

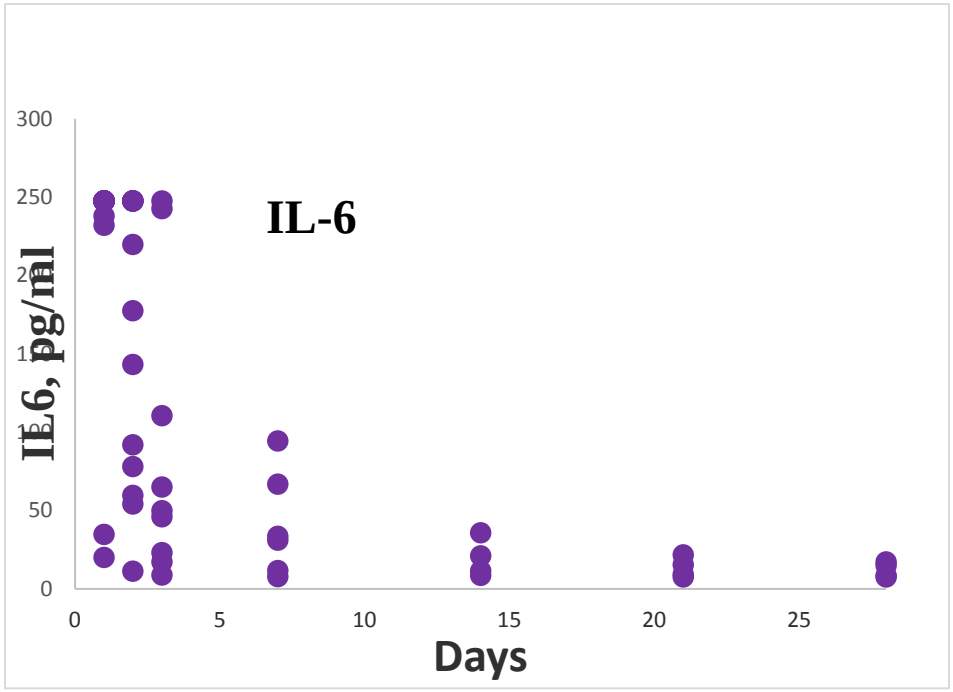
Presepsin and etiology of sepsis

Patient	Pathogen	Type of pathogen	sCD14, pg/ml
1	Kl. Pneumoniae	Gram negative	9564
2	E. coli	Gram negative	1559
3	E. faecium	Gram positive	8304
4	Sphingobacterium multivorum	Gram negative	6935
5	C krusei	Fungi	90 400
6	P. aeruginosa	Gram negative	10594
7	A baumanii, Kl pneumoniae	Gram negative	12342
8	E.Coli	Gram negative	868
9	E. faecium, P. aeruginosa	Gram positive + Gram negative	13816
10	Klebsiella pneumoniae	Gram negative	10154
11	A baumanii,Kl pneumoniae, S hominis	Gram negative+ Grampositive	3979
12	P. aeruginosae	Gram negative	2765
13	Klebsiella pneumoniae	Gram negative	6108
14	P aeruginosae, E.coli	Gram negative	10245

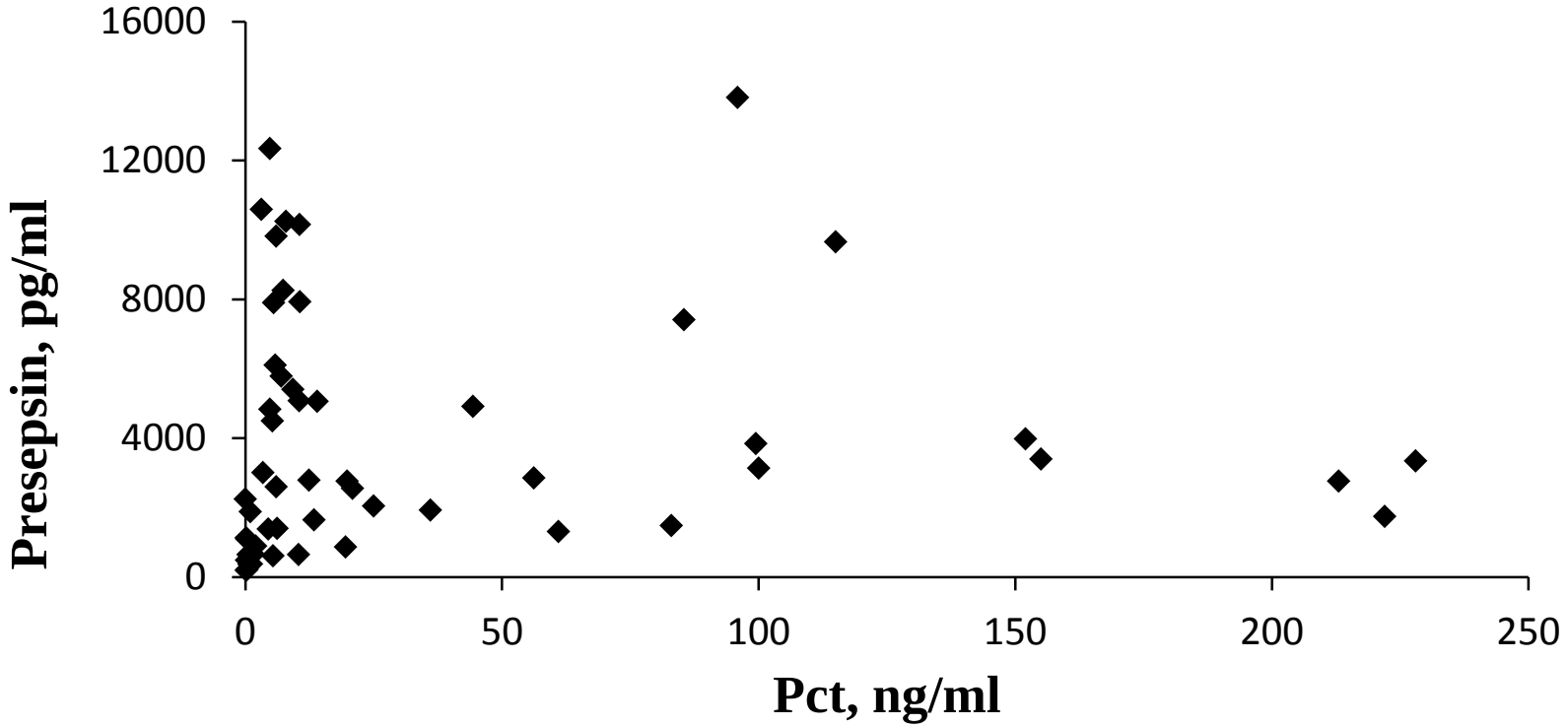
Inflammatory markers in patients with septic shock



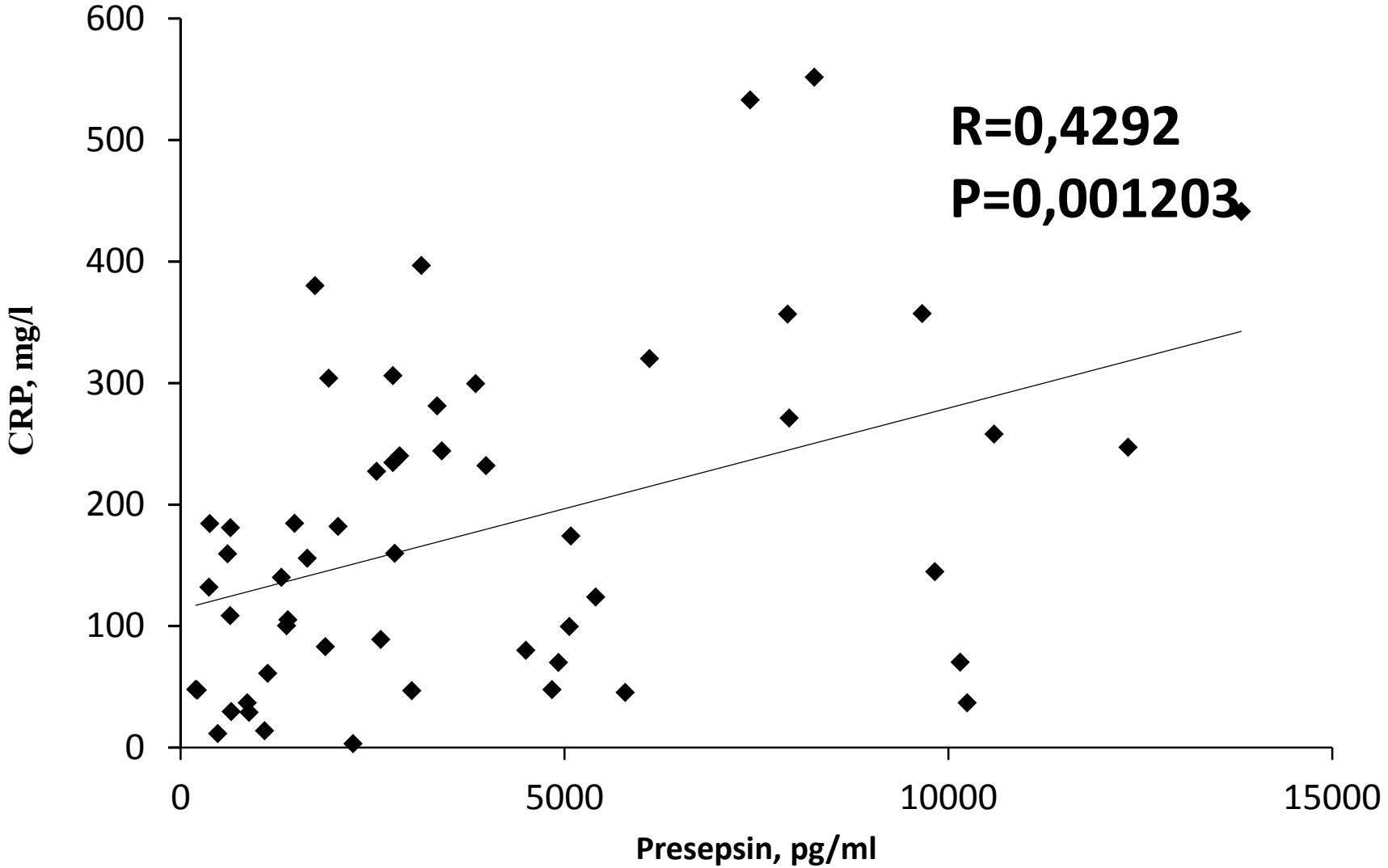




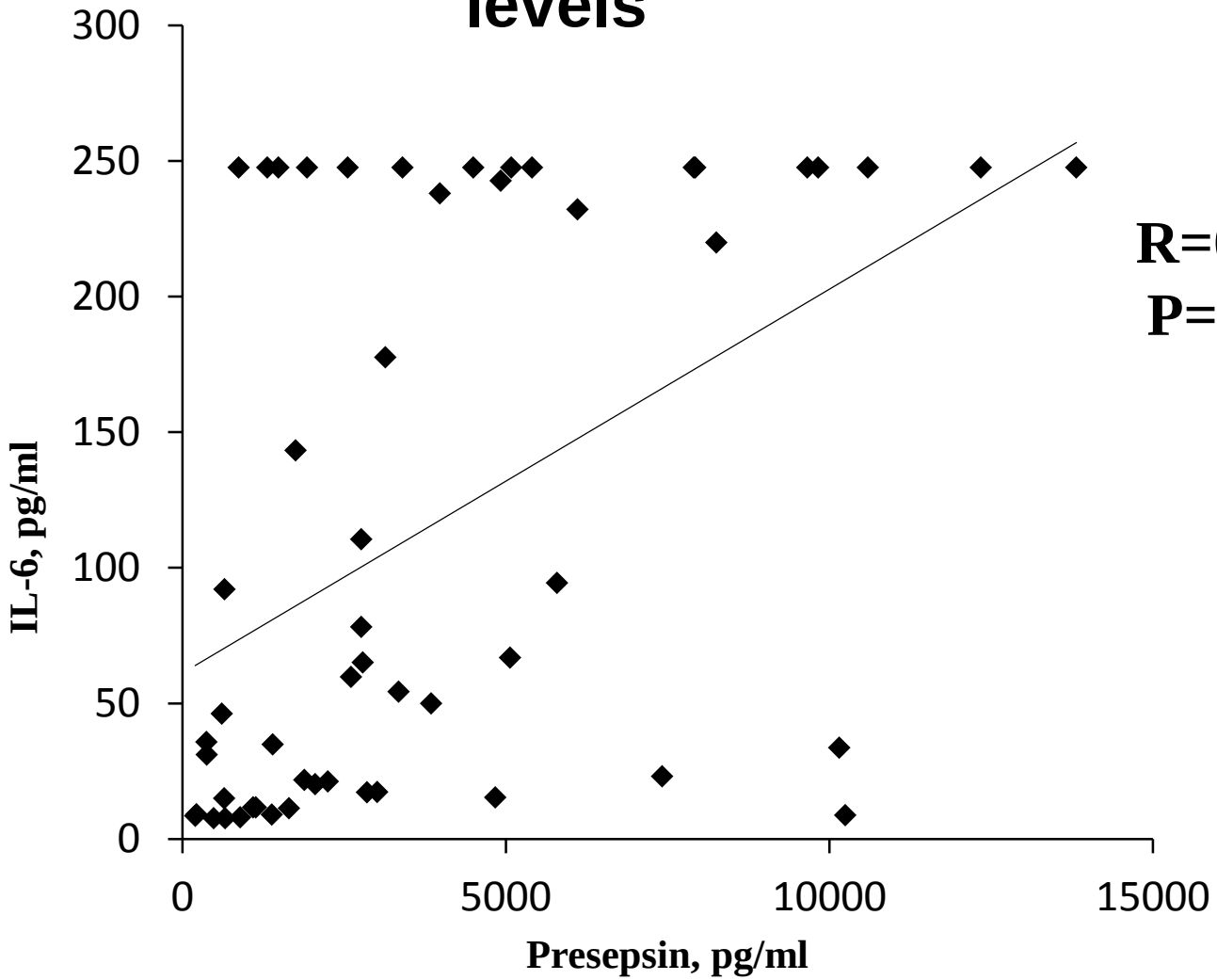
Correlation between plasma presepsin and serum procalcitonin levels



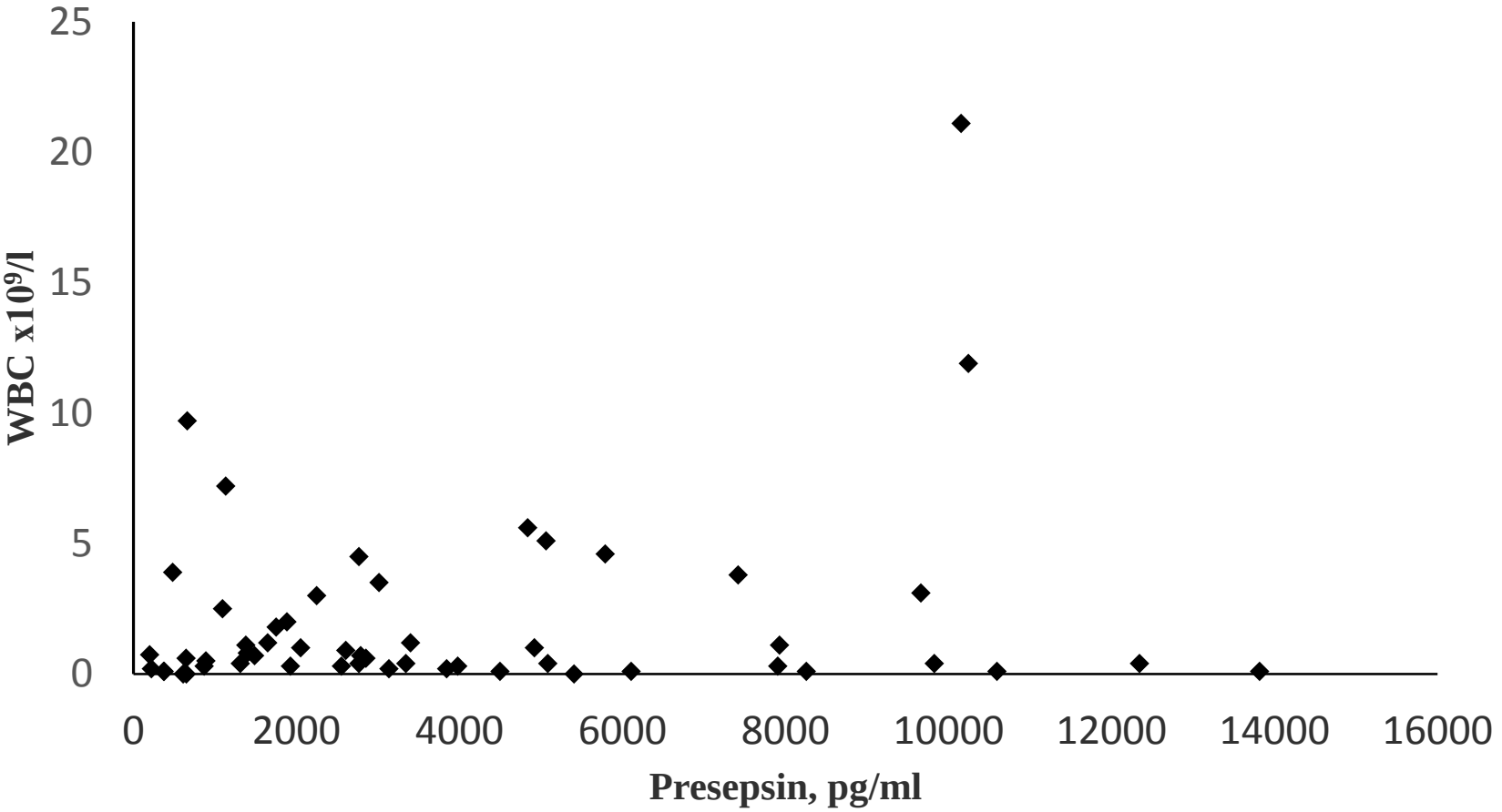
Correlation between plasma presepsin and serum CRP levels



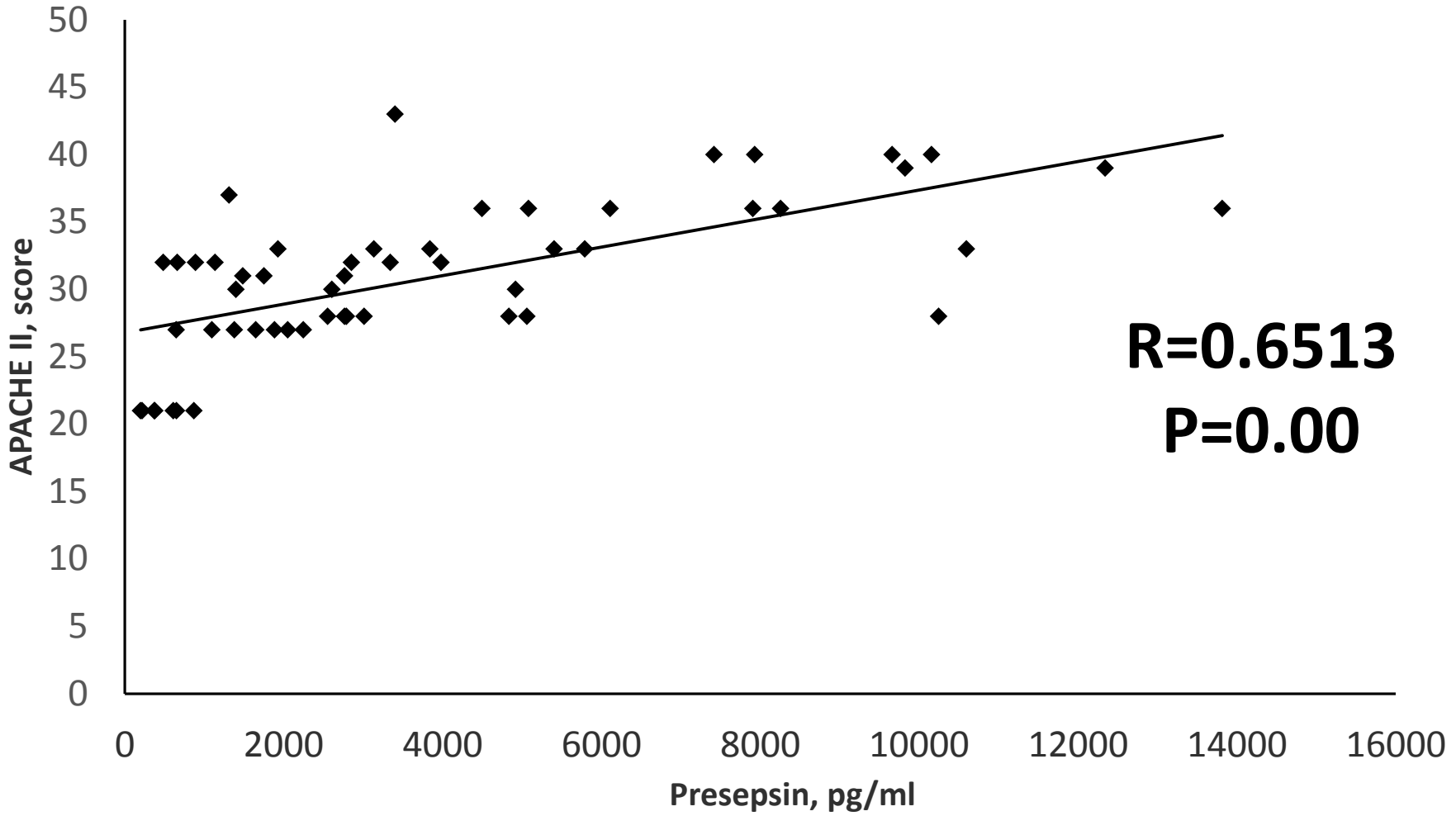
Correlation between plasma presepsin and serum IL-6 levels



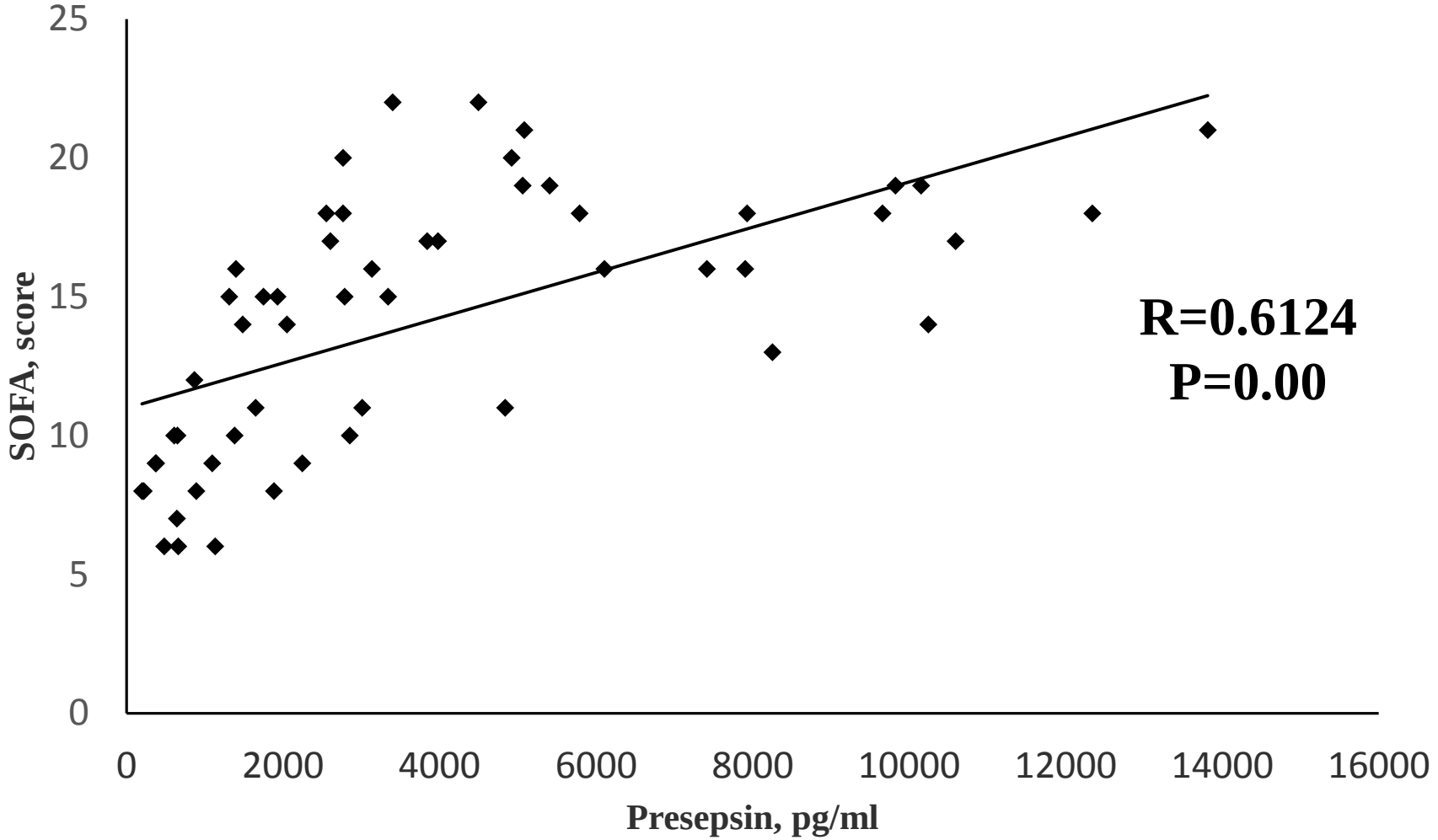
Correlation between plasma presepsin and WBC



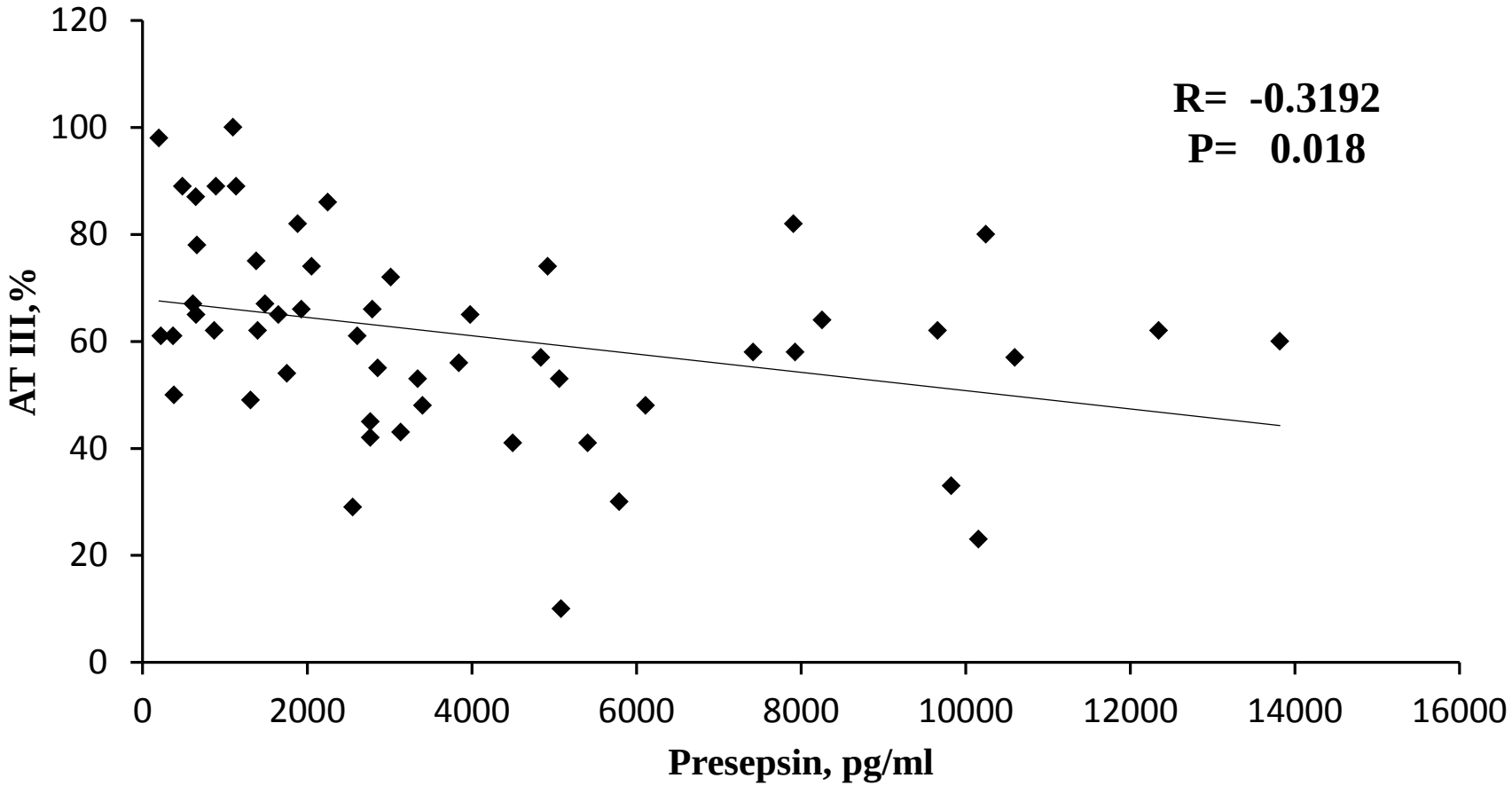
Correlation between plasma presepsin and APACHE II



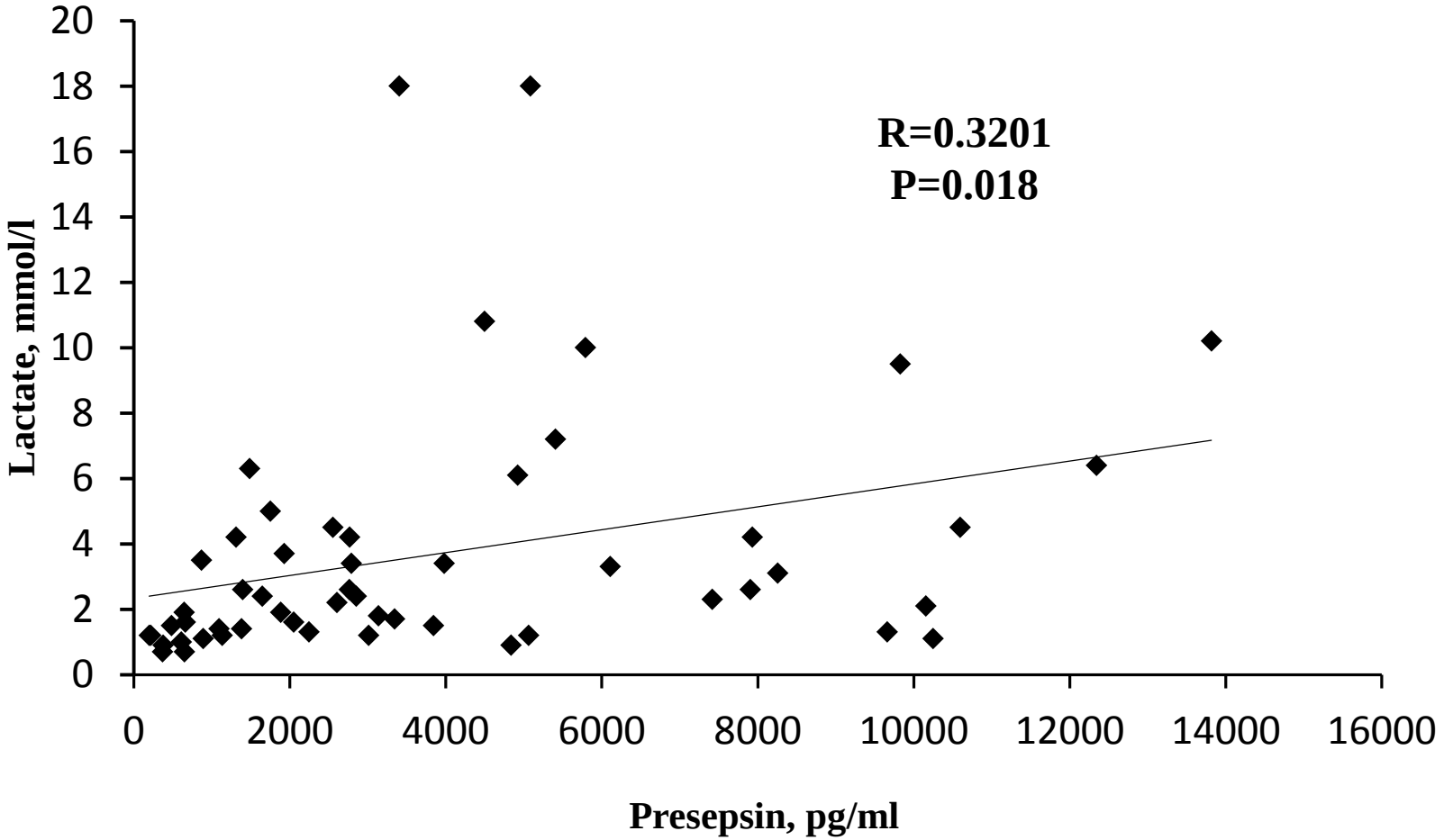
Correlation between plasma presepsin and SOFA



Correlation between plasma presepsin and plasma antithrombin activity



Correlation between plasma presepsin and arterial blood lactate concentration



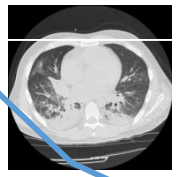
Case report # 1

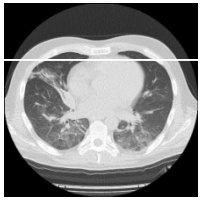
- **Patient A., 33 yo**
- **Acute myeloid leukaemia**
- **At admission 23.10.2013: Hb= 106 g/l, WBC= 70x10^9/l, Plt= 19x10^9/l**
- **Induction chemotherapy Cytarabine + Rubomycine (7+3) (23.11 - 29.11.2013).**

After 5 days

T=39-40^{0}C, WBC 0.3x10^9/l Pneumonia. Acute respiratory failure

- **Antibiotics – imipenem, colistin, vancomycine**
- **10.11.2013 – septic shock (APACHE II = 32)**





41
40,5
40
39,5
39
38,5
38
37,5
37
36,5
36

Noradrenaline

10.11.2013 11.11.2013 12.11.2013 13.11.2013 14.11.2013 15.11.2013 16.11.2013 17.11.2013 18.11.2013 19.11.2013 20.11.2013 21.11.2013 22.11.2013 23.11.2013 24.11.2013 25.11.2013 26.11.2013

Mechanical ventilation

ARF

Septic shock

Sepsis

Imipenem

Colistin

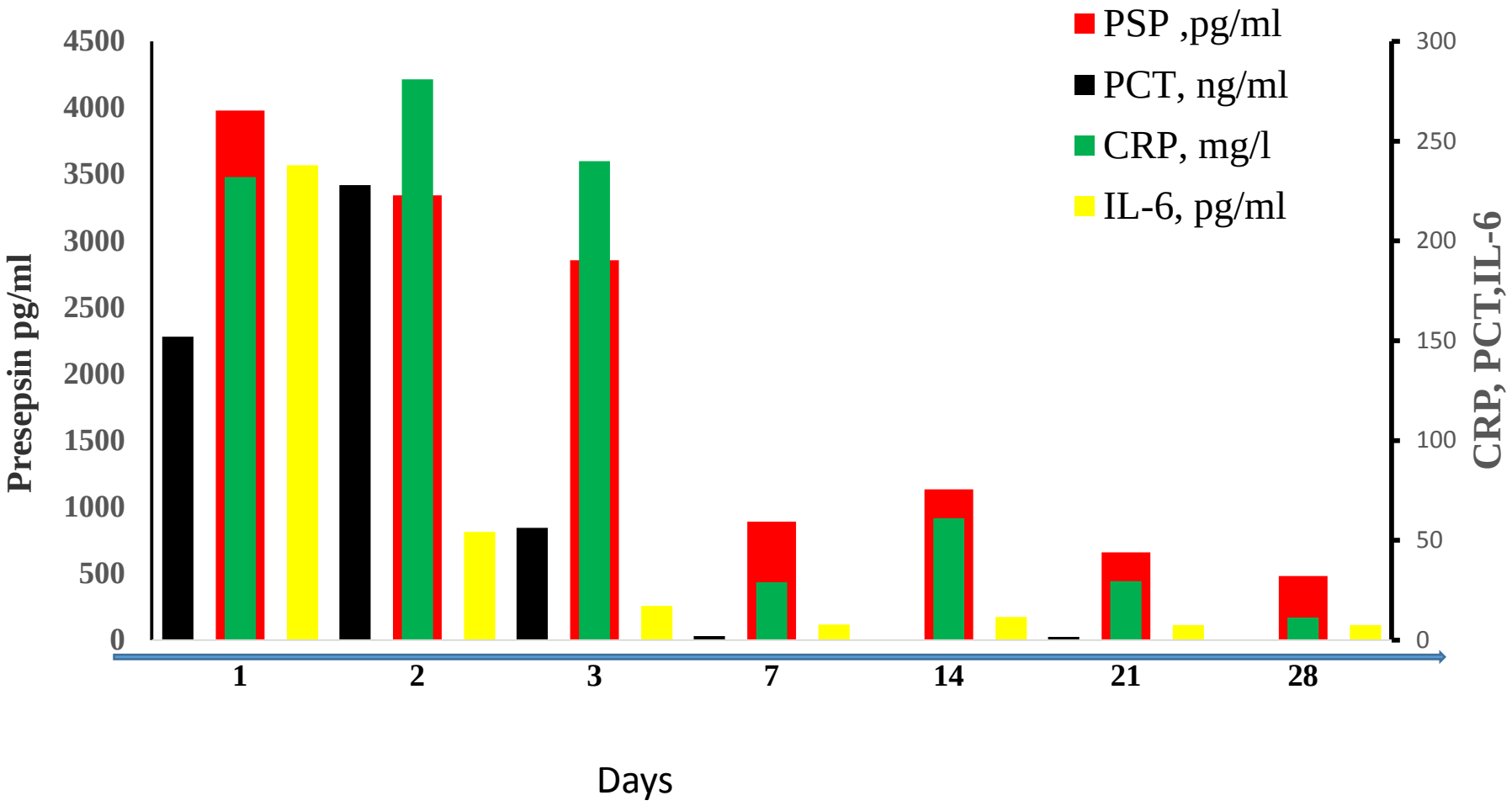
Vancomycine

Tygicycline

Blood: Ac. baumannii, Kl. pneumonia, Staph. hominis

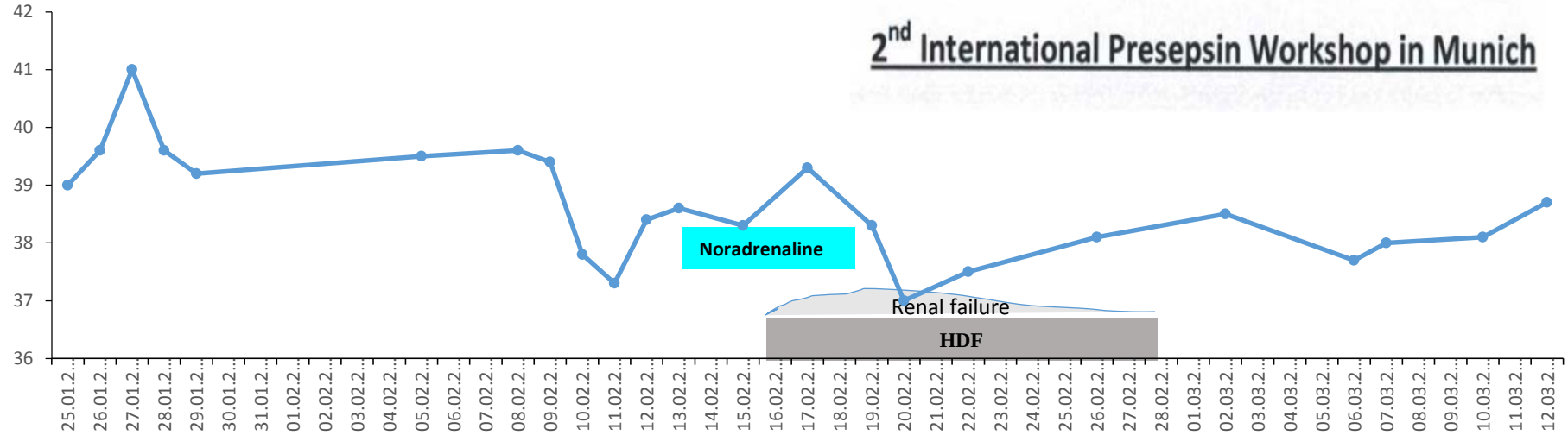
Blood: sterile

Inflammatory markers in patient with septic shock



Case report # 2

- **Patient Z..,31 yo.**
- **Acute myeloid leukaemia**



Mechanical ventilation

Sepsis

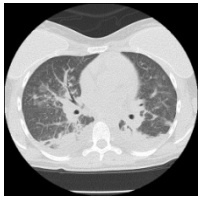
Septic shock

Doripenem

Colistin

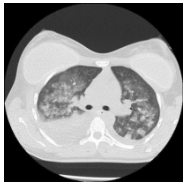
Phosphomycine

Daptomycine

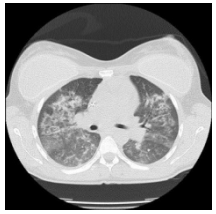


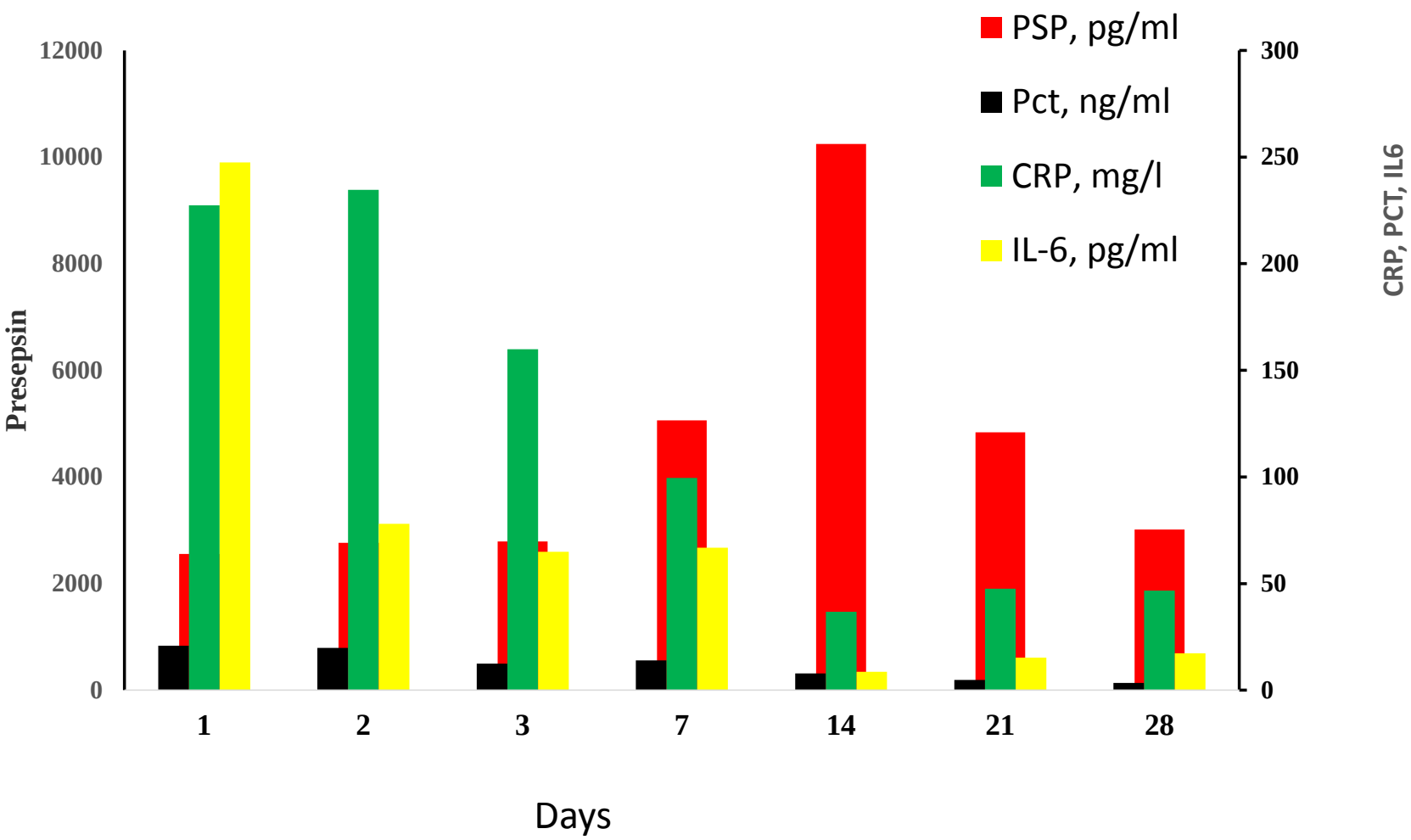
Blood, BAL:
Ps. aeruginosae

Blood,
Ps. aeruginosae
+ S aureus



Blood, BAL
Sterile




PSP, pg/ml
Pct, ng/ml
CRP, mg/l
IL-6, pg/ml
Presepsin
CRP, PCT, IL6
12000
10000
8000
6000
4000
2000
0
300
250
200
150
100
50
0
1
2
3
7
14
21
28
Days

CONCLUSION

- Despite a leukopenia and neutropenia, plasma presepsin levels can be used for an assessment of severity of septic shock and organ dysfunction.
- Blood concentrations of presepsin may be very high in patients with not only bacteraemia but also with fungaemia.
- Presepsin may be be more specific marker of an infection, than PCT, CRP and IL-6
- Presepsin can be used as discriminator of infection and non-infection origin in haematological patients