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C-reactive protein in critically ill cancer patients with sepsis: influence of neutropenia

Pedro Póvoa^{1,2*}, Vicente Ces Souza-Dantas³, Márcio Soares^{3,4} and Jorge IF Salluh^{3,4}

Abstract

Introduction: Several biomarkers have been studied in febrile neutropenia. Our aim was to assess C-reactive protein (CRP) concentration in septic critically ill cancer patients and to compare those with and without neutropenia.

Methods: A secondary analysis of a matched case-control study conducted at an oncologic medical-surgical intensive care unit (ICU) was performed, segregating patients with severe sepsis/septic shock. The impact of neutropenia on CRP concentrations at admission and during the first week of ICU stay was assessed.

Results: A total of 154 critically ill septic cancer patients, 86 with neutropenia and 68 without, were included in the present study. At ICU admission, the CRP concentration of neutropenic patients was significantly higher than in non-neutropenic patients, 25.9 ± 11.2 mg/dL vs. 19.7 ± 11.4 mg/dL ($P = 0.009$). Among neutropenic patients, CRP concentrations at ICU admission were not influenced by the severity of neutropenia ($< 100/\text{mm}^3$ vs. $\geq 100/\text{mm}^3$ neutrophils), 25.1 ± 11.6 mg/dL vs. 26.9 ± 10.9 mg/dL ($P = 0.527$). Time dependent analysis of CRP from Day 1 to Day 7 of antibiotic therapy showed an almost parallel decrease in both groups ($P = 0.335$), though CRP of neutropenic patients was, on average, always higher in comparison to that of non-neutropenic patients.

Conclusions: In septic critically ill cancer patients CRP concentrations are more elevated in those with neutropenia. However, the CRP course seems to be independent from the presence or absence of neutropenia.

Introduction

The C-reactive protein (CRP) is a marker of inflammation and is elevated in a wide variety of acute and chronic inflammatory conditions. CRP is synthesized by the liver in response to interleukin-6 (IL-6) and is a member of the pentameric family of acute phase reactants. CRP is a sensitive and specific marker of inflammation and is used to monitor the response to treatment in a variety of conditions. CRP is also used as a prognostic marker in a variety of conditions. CRP is elevated in a wide variety of acute and chronic inflammatory conditions. CRP is synthesized by the liver in response to interleukin-6 (IL-6) and is a member of the pentameric family of acute phase reactants. CRP is a sensitive and specific marker of inflammation and is used to monitor the response to treatment in a variety of conditions. CRP is also used as a prognostic marker in a variety of conditions.

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Table 1 Baseline patients' characteristics and comparison between neutropenic and non-neutropenic patients

	All Patients	Neutropenic	Non neutropenic	P-value
N	154	86	68	
Age (yrs)	48.5 ± 18.1	47.0 ± 17.8	50.4 ± 18.4	0.248
Gender (M/F)	94/60	54/32	40/28	0.622
Type of cancer				0.569
Solid	49	29	20	
Hematologic	105	57	48	
Previous radiotherapy	36	21	15	0.731
Previous Chemotherapy	112	72	40	0.001
Previous surgery	6	1	5	0.049
Non-invasive Ventilation	15	14	1	0.002
Invasive mechanical Ventilation	135	74	61	0.493
Vasopressors	112	62	50	0.842
Type of infection				0.007
Pneumonia	63	28	35	
Peritonitis	15	7	8	
Urinary	3	0	3	
Blood stream infections	8	4	4	
Skin/Soft tissue infections	7	4	3	
CNS infections	1	0	1	
Other infections	57	43	14	
SAPS II (points)	62.2 ± 16.8	62.2 ± 16.7	62.5 ± 16.8	0.827
SOFA (Day 1) (points)	11.4 ± 3.9	11.6 ± 4.1	11.2 ± 4.1	0.591
Sepsis severity				0.899
Sepsis	10 (6.5%)	6 (7%)	4 (5.9%)	
Severe sepsis	29 (18.8%)	17 (19.8%)	12 (17.6%)	
Septic shock	111 (74.7%)	63 (73.3%)	52(76.5%)	
Total white cell count (/mm ³)	1,400 (14,636)	352 (909)	22,100 (35,900)	< 0.001
Temperature (°C)	37.0 ± 1.5	37.2 ± 1.5	36.8 ± 1.5	0.119
CRP (Day 1) (mg/dL)	23.6 ± 11.6	25.9 ± 11.2	19.7 ± 11.4	0.009
Duration of mechanical ventilation (days)	6.0 (9.0)	6.0 (8.0)	6.0 (9.0)	0.616
ICU length of stay (days)	7.0 (10.3)	7.0 (12.0)	8.0 (10.0)	0.699
Hospital length of stay (days)	18.5 (23.6)	20.5 (25.0)	16.5 (21.0)	0.111
ICU mortality	111 (72.1%)	60 (69.8%)	51 (75.0%)	0.472
Hospital mortality	122 (79.2%)	65 (75.6%)	57 (83.8%)	0.211

Values expressed as N (%), mean ± standard deviation or median (interquartile range) according to type of data and data distribution; abbreviations: CNS, central nervous system; CRP, C-reactive protein; ICU, intensive care unit; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment score

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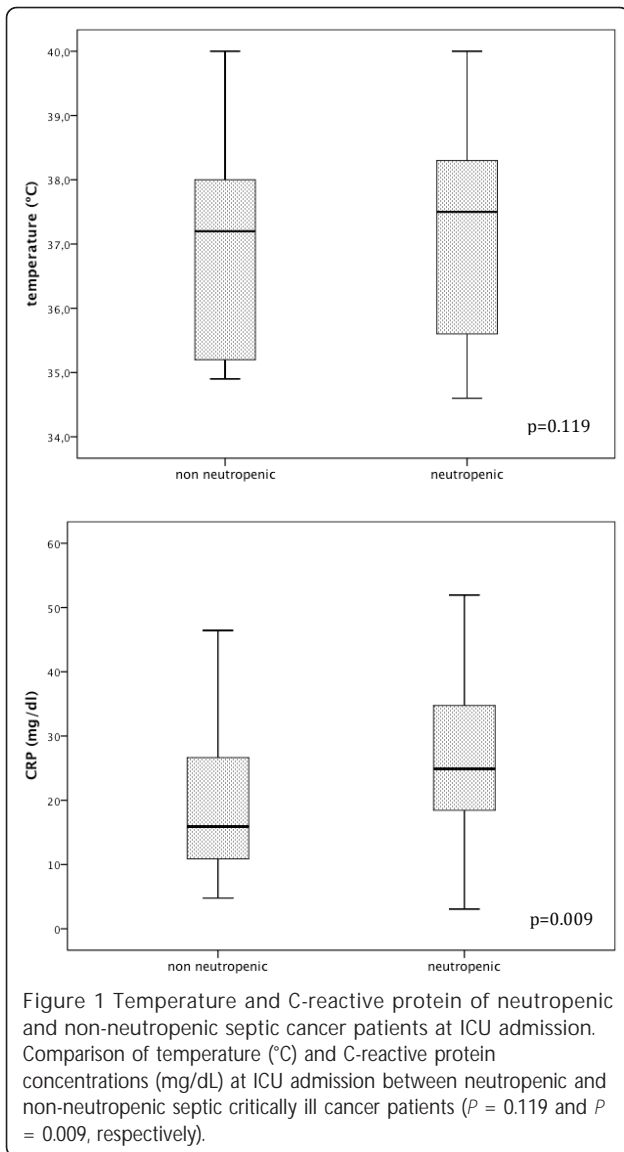


Figure 1 Temperature and C-reactive protein of neutropenic and non-neutropenic septic cancer patients at ICU admission. Comparison of temperature (°C) and C-reactive protein concentrations (mg/dL) at ICU admission between neutropenic and non-neutropenic septic critically ill cancer patients ($P = 0.119$ and $P = 0.009$, respectively).

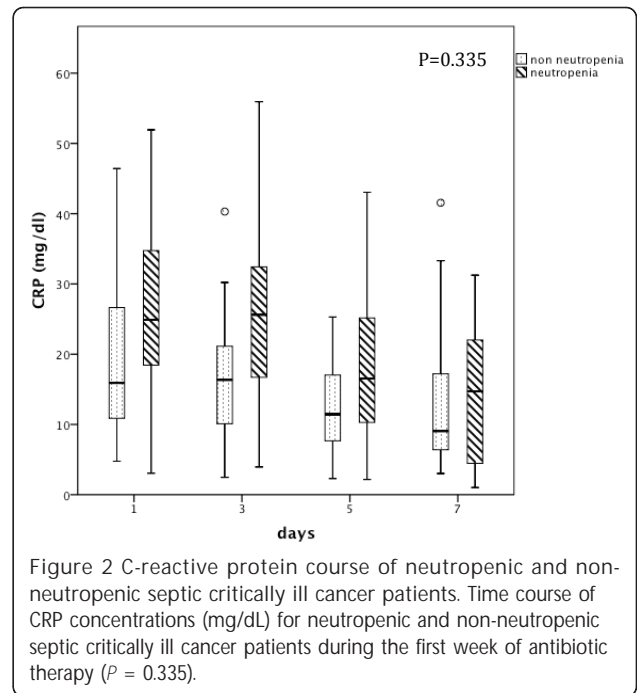


Figure 2 C-reactive protein course of neutropenic and non-neutropenic septic critically ill cancer patients. Time course of CRP concentrations (mg/dL) for neutropenic and non-neutropenic septic critically ill cancer patients during the first week of antibiotic therapy ($P = 0.335$).

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Key messages

- **Highly ill cancer patients with febrile neutropenia should be treated with antimicrobial agents.**
- **C-reactive protein and procalcitonin are useful markers for the diagnosis of infection in neutropenic patients.**
- **CRP and procalcitonin are useful markers for the diagnosis of infection in neutropenic patients.**

Abbreviations

CRP: C-reactive protein; ICU: intensive care unit; IL: interleukin; IQR: interquartile range; MV: mechanical ventilation; SAPS II: Simplified Acute Physiology Score (SAPS) II; SIRS: systemic inflammatory response syndrome; SOFA: Sequential Organ Failure Assessment; WCC: white cell count.

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Authors' contributions

PP, VCSD, MS and JIFS contributed to the study conception and design, carried out and participated in data analysis and drafted the manuscript. VCSD, MS and JIFS participated in acquisition of data. All authors read and approved the final version of the manuscript.

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Competing interests

PP has received honoraria and served as advisor of Astra Zeneca, Ely-Lilly, Gilead, Janssen-Cilag, Merck Sharp & Dohme, Novartis and Pfizer and received an unrestricted research grant from Brahms and Virogates. VCSD, MS and JIFS have no competing interests to declare.

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