ABSTRACT

EVALUATION OF PROCALCITONIN ACCURACY FOR THE DISTINCTION BETWEEN GRAM-NEGATIVE AND GRAM-POSITIVE BACTERIAL SEPSIS IN BURN PATIENTS

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INTRODUCTION

Sepsis is the main cause of death in burns. Early institution of antimicrobial therapy is crucial to optimize outcomes but superfluous therapy increases adverse events, microbial resistance, and costs.

Blood cultures are the gold standard for diagnosis but can take 48 to 72 hours.

Therefore, biomarkers are used to help sepsis diagnosis and distinction between Gram-negative and Gram-positive bacterial cause. The aim of this work is to evaluate Procalcitonin PCT accuracy for this distinction in burn patients.

THE METHODS

A retrospective observational study of adult septic burn patients was elaborated, accounting patients with ≥15% total burn surface area admitted from January 2011 to December 2014 at Coimbra's Burn Unit in Portugal. A statistical analysis was done, evaluating the correlation between PCT levels on the day of the first positive blood culture and microbiological data for Gram-negative and Grand-positive bacteria. Patients with mixed bacterial and/or fungal blood cultures were excluded. Data were summarized by quartiles statistics. Blood cultures were positive in 189 patients: 75 (39.7%) showed growth for Gram-negative and 114 (60.3%) for Gram-positive bacteria.

The sample under analysis was composed 438 burn patients. Among these patients, 249 (56.8%) did not fulfill American Burn Association sepsis criteria neither had any growth in their blood cultures during their stay at Coimbra's Burn Unit. These results were deemed to serve as controls.

Blood cultures were positive in 189 (43.2%) patients; among from these, 75 patients (39.7%) showed growth for Gram-negative bacteria and 114 (60.3%) showed growth for Gram-positive bacteria

RESULTS

Table 1: Age, Gender distributions were studied for statistical significance

		Controls	Gram-Negative Sepsis	Gram-Positive Sepsis	*P*
Number of Patients		249	75	114	—
Age (years)	Median	62.0	66.0	69.0	
	Q1–Q3	45.5–78.0	44.5–79.5	47–80.0	.392*
Sex	Males	152 (61%)	41 (55%)	70 (61%)	
	Females	97 (49%)	34 (45%)	44 (39%)	.578†
Procalcitonin (ng/ml)	Median	0.20	0.75	0.32	.000*
	Q1–Q3	0.11–0.84	0.35–4.15	0.16–0.87	

*Kruskall–Wallis test.
†Chi-square test.

On the day of the first identification of microbiological growth in blood cultures, PCT levels were significantly higher in patients with Gram-negative bacteria comparing to controls and patients with Gram-positive bacteria; the differences between controls and Gram-positive infected patients did not reach statistical significance

Table 2: Pairwise comparisons for PCT levels between sepsis groups

Comparison	*P*
Gram-negative septic patients vs controls	.000
Gram-negative septic patients vs Gram-positive septic patients	.000
Gram-positive septic patients vs controls	.153

Mann–Whitney test with Bonferroni-corrected *P*-values.

Subgroup analysis was performed including the most frequent Gram-negative and Gram-positive microorganisms responsible for sepsis in this sample of patients.

Figure 1: Box-plots for procalcitonin levels in controls (*n* = 249), Gram-negative (*n* = 75), and Gram-positive (*n* = 114) sepsis patients groups

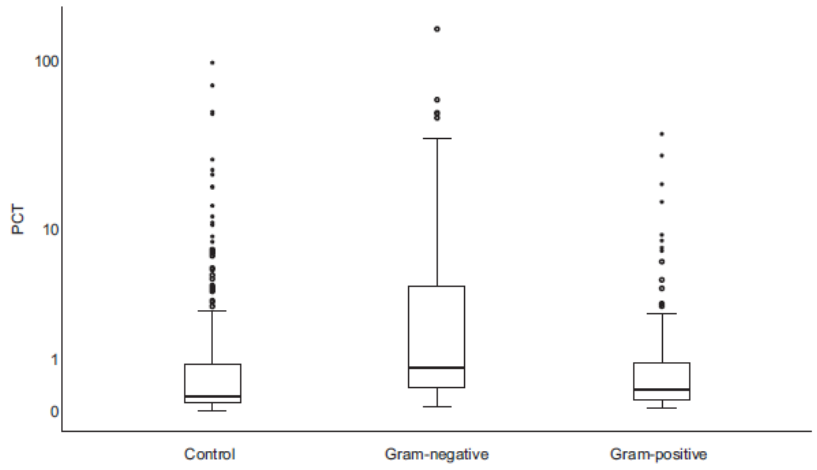
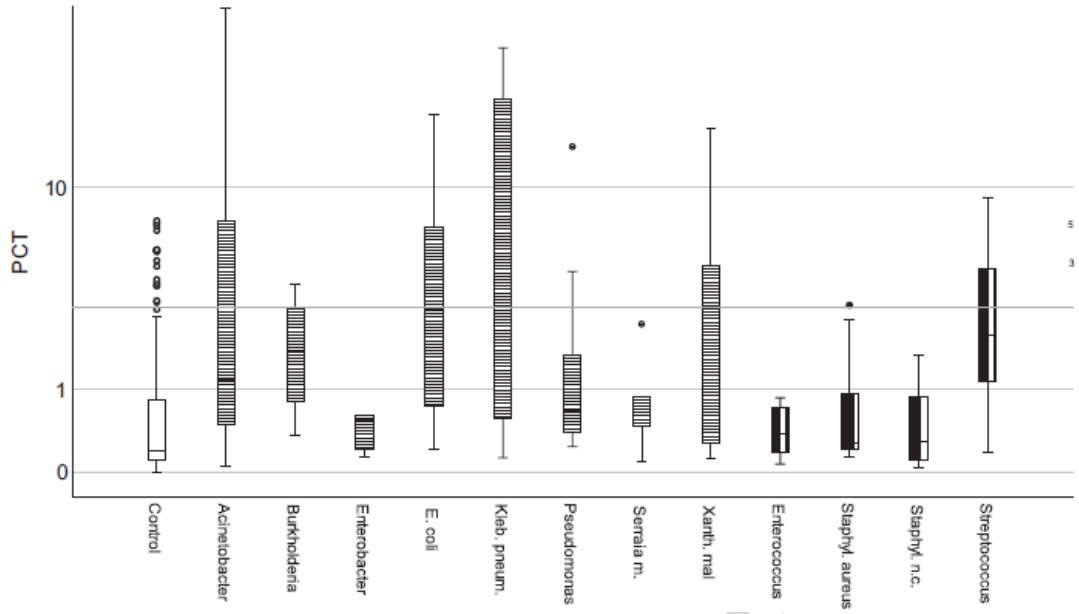


Figure 2: Box-plots for procalcitonin levels in Gram-negative and Gram-positive bacterial sepsis subgroups



In the Gram-negative group, the mostly frequently isolated agent was *Pseudomonas aeruginosa*, as it would be expected according to its great prevalence in many burn units, followed by *Acinetobacter* spp. and other nonfermentative bacteria, including *Burkholderia cepacia* and *Stenotrophomonas maltophilia*.

The Enterobacteriaceae were also very common, namely *Escherichia coli, Enterobacter* spp.*, Klebsiella pneumonia, Serratia marcescens, Proteus mirabilis*, etc.

From the Gram-positive group, *Staphylococcus epidermidis*, *Staphylococcus hominis* and other coagulase-negative species of Staphylococci, were the most isolated from the blood samples.

Sensitivity, specificity, positive predictive value, and negative predictive value of procalcitonin cutoffs were evaluated for the distinction between Gram-negative and Gram-positive sepsis in burn patients.

The statistical analysis of PCT levels on the first day of microbiological identification in blood samples in this sample of extensively burned patients confirmed previous reports demonstrating significantly higher values in the presence of Gram-negative bacteria comparing with controls or patients with Gram-positive sepsis.

The difference was most pronounced when causative agents were glucose nonfermenting bacilli, particularly *Acinetobacter* and *Pseudomonas* spp., or Enterobacteriaceae rods, like *E. coli* or *K. pneumoniae*.

Receiver operating characteristic curve analysis showed accuracy for Gram-negative discrimination with area under the curve = 0.687.

On the other hand, a statistical difference in PCT levels was not found between PCT levels of patients with sepsis caused by Gram-positive bacteria and control patients, with the exception of patients with sepsis caused by *Streptococcus* spp.

CONCLUSIONS

To the authors' knowledge, the present work, with 189 septic burn patients, from an homogenous population, corresponds to the largest sample already analyzed in medical literature regarding this subject. It confirms previous reports and, moreover, it further details subgroups differences.

The results obtained were consistent with medical literature even though there is not yet a full understanding of the mechanisms involved in cytokines activation following microbial insult. Very high PCT levels (above 3.00 or 5.00 ng/ml) would usually be more associated with Gram-negative sepsis, with fair positive predictive value and negative predictive value, and good specificity. Furthermore in the great majority of the cases, PCT values under 0.5 ng/ml would not correspond to Gram-negative infections but to Gram-positive or fungal ones.

Cutoffs should be adapted to the idiosyncratic characteristics of each facility, depending on its nosocomial flora and its patients.

This retrospective study consistently showed the presence higher PCT levels in burn patients with Gram-negative sepsis, suggesting that PCT, while not precise, may help clinicians in the choice of the empirical antimicrobial therapy, while the definitive, gold standard, microbiological culture results and sensibility tests are not yet available.