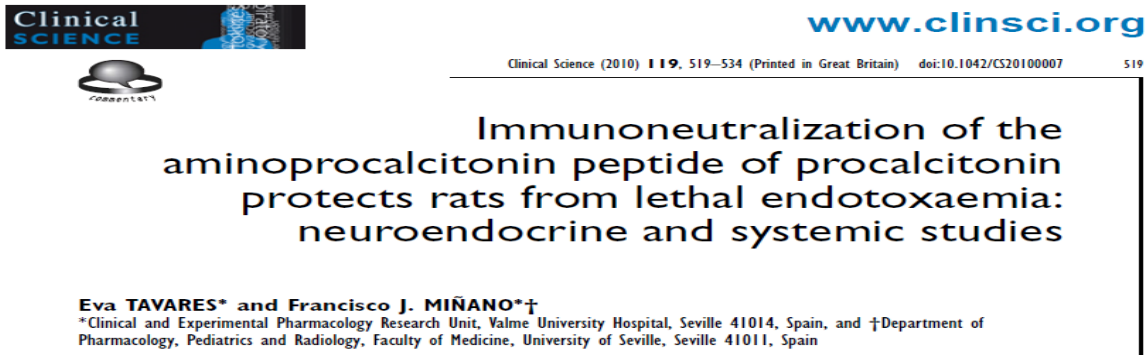
PCT v diagnostice sepse – Con

Miroslav Průcha
Klinická imunologie , Nemocnice Na Homolce, Praha

Ostrava, 23. ledna 2014

PCT

- Fyziologie PCT ????
- Produkován více druhy buněk…
- Stimuly různé... infekce, trauma, autoimunita … obecně zánět
- Ale také ATG… transplantovaní
- Toxicita PCT - mortalita – blokace PCT



Clinical SCIENCE

www.clinsci.org

Clinical Science (2010) 119, 519–534 (Printed in Great Britain) doi:10.1042/CS20100007

Immunoneutralization of the aminoprocalcitonin peptide of procalcitonin protects rats from lethal endotoxaemia: neuroendocrine and systemic studies

Eva TAVARES* and Francisco J. MIÑANO*†
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PCT – proč ne ?

- Různý fenotyp sepse – pacient X původce, klinický obraz
- Různé cílové skupiny pacientů
- Různá vypovídací schopnost PCT (robustnost biomarkeru)
- Falešně pozitivní a falešně negativní výsledky
- Kdy „mám potřebu verifikovat exaktně“ sepsi?

PCT – proč ne

- Cutt off

3,0

0,5

2,0

0,7

1,5

Procalcitonin-guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: A randomized trial*

Jens U. Jensen, MD, PhD; Lars Hein, MD; Bettina Lundgren, MD, DMSc; Morten H. Bestle, MD, PhD; Thomas T. Mohr, MD, PhD; Mads H. Andersen, MD; Klaus J. Thornberg, MD; Jesper Løken, MD; Morten Steensen, MD; Zoe Fox, MD, PhD; Hamid Tousi, MD; Peter Søe-Jensen, MD; Anne Ø. Lauritsen, MD; Ditte Strange, MD; Pernille L. Petersen, MD; Nanna Reiter, MD; Søren Hestad, MD; Katrin Thormar, MD; Paul Fjeldborg, MD; Kim M. Larsen, MD; Niels E. Drenck, MD; Christian Østergaard, MD, PhD, DMSc; Jesper Kjær, MSc; Jesper Grarup, DVM; Jens D. Lundgren, MD, DMSc; for The Procalcitonin And Survival Study (PASS) Group

9 interdisciplinárních jednotek intenzivní péče v Dánsku

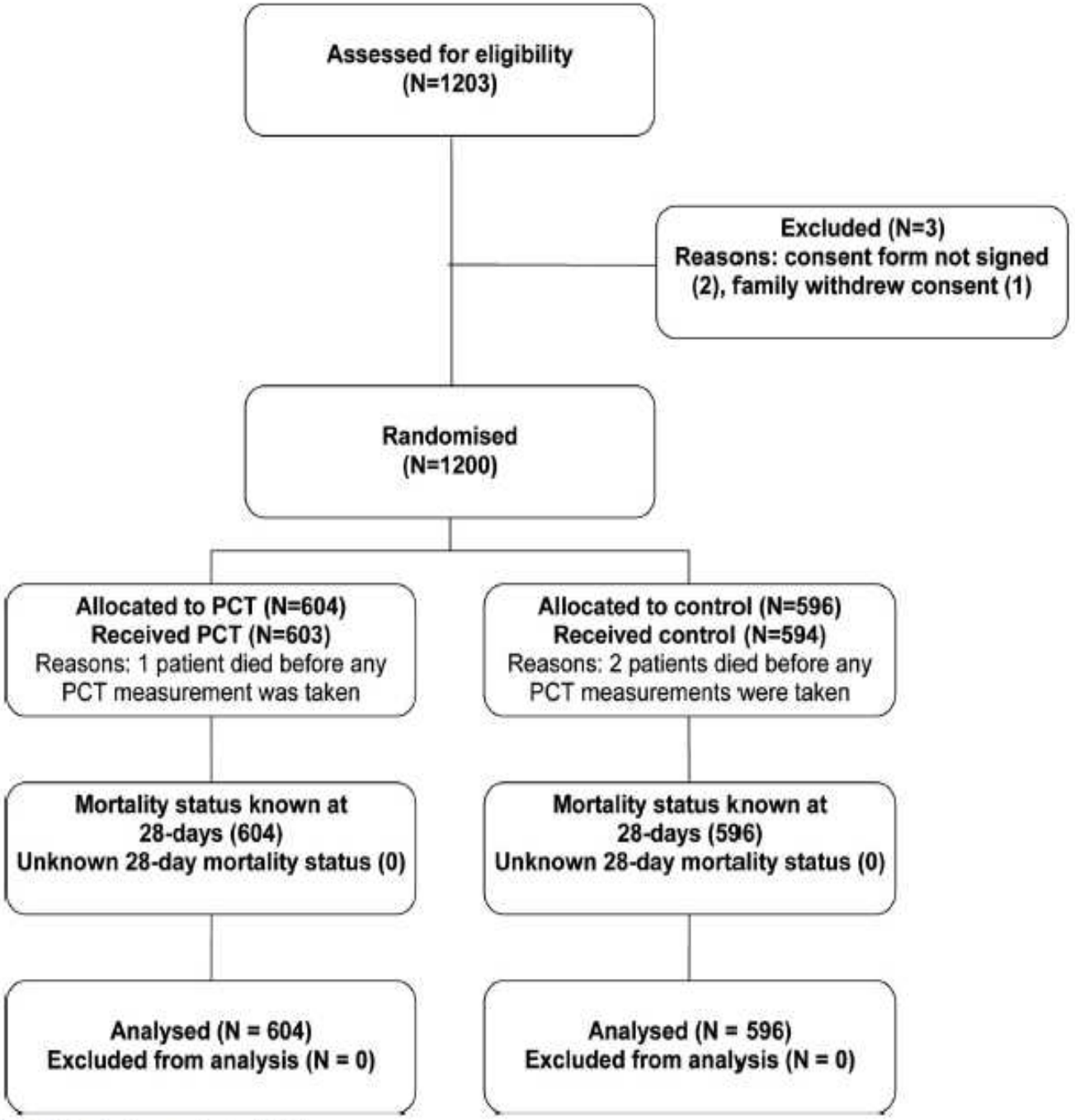
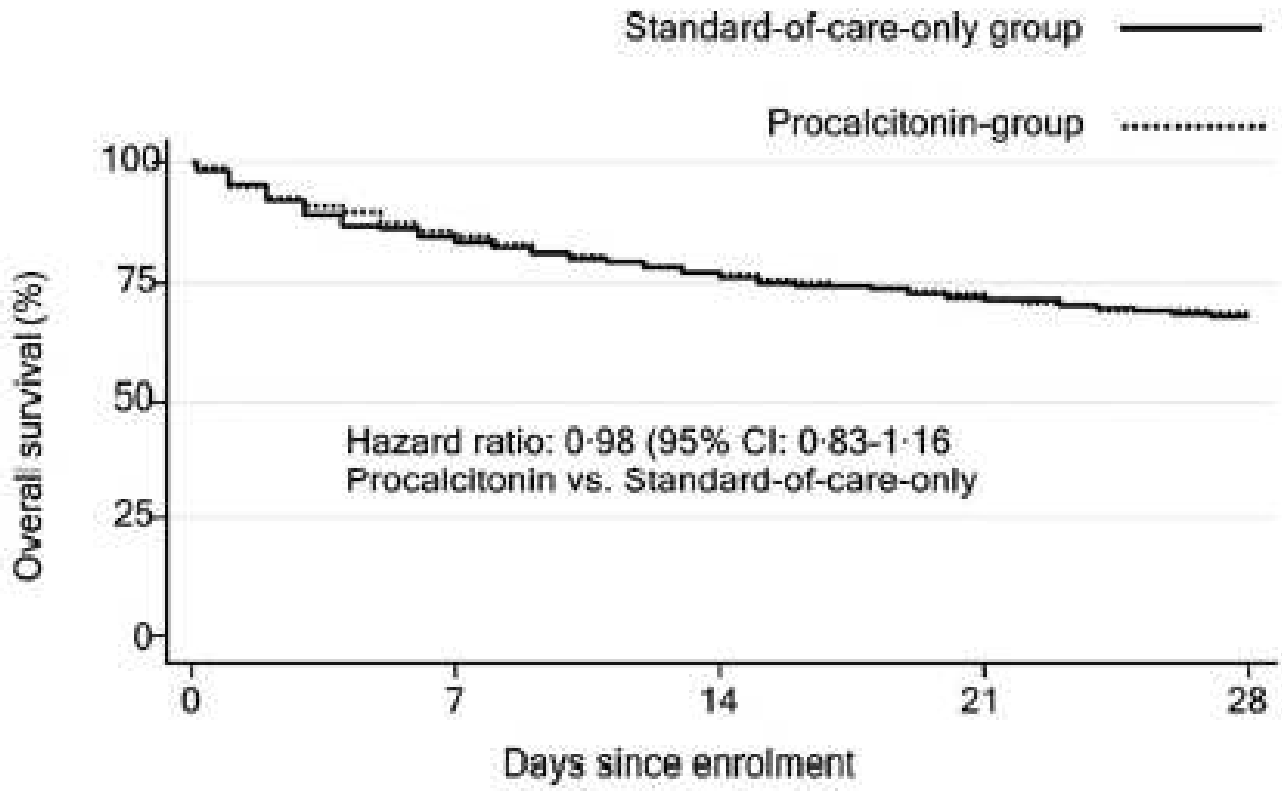


Figure 2. Trial profile. *PCT*, placebo-controlled trial.



Number at risk:

Procalcitonin	604	518	466	436	414
Standard-of-care	596	505	458	429	405

Figure 3. Kaplan-Meier estimates of 28-day survival. The analysis is based on the intention-to-treat population. The log-rank test *p* value was.80. The overall nonadjusted hazard ratio is displayed. Subgroup analysis of seven predefined subgroup separators was made (described in "Results" section). *CI*, confidence interval.

Table 4. Organ failure and infection during follow-up

	Standard-of-Care-Only (n = 596)	Procalcitonin-Guided (n = 604)	Absolute Difference (95% Confidence Interval, Standard-of-Care Only vs. Procalcitonin-Guided)	p
Need for organ support, no. (%)				
ICU days[a] with mechanical ventilation	2861 (60.7)	3569 (65.5)	−4.9% (−6.7% to −3.0%)	<.0001
Mechanical ventilation on last ICU day (1200 days followed)	196 (32.9)	196 (32.5)	0.4% (−4.9% to 5.7%)	.87
ICU days[a] with vasopressors/inotropics	1393 (29.5)	1564 (28.7)	0.8% (−1.0% to 2.6%)	.86[b]
Patients with vasopressors/inotropics at discharge/death (1200 days followed)	122 (20.5)	113 (18.7)	1.8% (−2.7% to 6.3%)	.44
ICU days[a] with estimated glomerular filtration rate <60 mL/1.73 m^2	2187 (46.4)	2796 (51.3)	−5.0% (−6.9% to −3.0%)	.33[c]
Patients with estimated glomerular filtration rate <60 mL/1.73 m^2 at discharge/death	256 (43.0)	278 (46.0)	−3.1% (−8.7% to 2.5%)	.28
ICU days[a] spent with dialysis treatment	982 (20.8)	1214 (22.3)	−1.5% (−3.1% to 0.1%)	.31[d]
Patients in treatment with dialysis at discharge/death	86 (14.4)	84 (13.9)	0.5% (−3.4% to 4.5%)	.80
Other organ failure measures, no. (%)				
ICU days[a] with bilirubin >1.2 mg/dL	900 (19.1)	809 (14.9)	4.2% (2.8% to 5.7%)	.83[e]
Patients with bilirubin >1.2 mg/dL at discharge/death	82 (13.8)	76 (12.6)	1.2% (−2.7% to 5.0%)	.55
ICU days[a] spent with Glasgow Coma Score ≤13	387 (8.2)	361 (6.6)	1.6% (0.6% to 2.6%)	.52[f]
Patients with Glasgow Coma Score ≤13 at discharge/death	50 (8.4)	61 (10.1)	−1.7% (−5.0% to 1.6%)	.31
Infection/host response by clinical assessment[h], no. (%)				
ICU days[a] with severe sepsis/septic shock	924 (19.6)	1097 (20.1)	−0.6% (−2.1% to 1.0%)	.33[g]
ICU survivors with infection clinically judged[h] at the time of discharge (n = 819)	282 (69.6)	288 (69.6)	−0.1% (−6.2% to 6.4%)	.98

Table 2. Consumption of antimicrobials during follow-up

Consumption of Antimicrobials	Standard-of-Care-Only (n = 596)	Procalcitonin-Guided (n = 604)	*p*
Piperacillin/tazobactam used within 28 days (DDD)	1893	2925	—
Proportion of days[a] followed when piperacillin/tazobactam was used	0.00 (0.00–0.33)	0.11 (0.00–0.56)	<.001
Meropenem used within 28 days (DDD)	2174	2480	—
Proportion of days[a] followed when meropenem was used	0.00 (0.00–0.00)	0.00 (0.00–0.07)	.23
Cefuroxime used within 28 days (DDD)	4369	3390	—
Proportion of days[a] followed when cefuroxime was used	0.11 (0.00–0.39)	0.04 (0.00–0.29)	<.001
Ciprofloxacin used within 28 days (DDD)	6210	8382	—
Proportion of days[a] followed when ciprofloxacin was used	0.21 (0.00–0.71)	0.33 (0.04–0.88)	<.001
Number (%) intensive care unit days spent with at least three antimicrobials	2721 (57.7%)	3570 (65.5%)	.002

DDD, defined daily dose administered within 1–28 days.

[a]This comparison was made with complete follow-up for 28 days (if patients were discharged from the intensive care unit, they were followed for antimicrobial use in all hospital admissions in Denmark).

Crit Care Med. 2011 Sep;39(9):2048-58. doi: 10.1097/CCM.0b013e31821e8791.

Procalcitonin-guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: a randomized trial.

Jensen JU, Hein L, Lundgren B, Bestle MH, Mohr TT, Andersen MH, Thornberg KJ, Løken J, Steensen M, Fox Z, Tousi H, Søe-Jensen P, Lauritsen AØ, Strange D, Petersen PL, Reiter N, Hestad S, Thormar K, Fjeldborg P, Larsen KM, Drenck NE, Ostergaard C, Kjær J, Grarup J, Lundgren JD; Procalcitonin And Survival Study (PASS) Group.

Collaborators (167)

Author information

Abstract

OBJECTIVE: For patients in intensive care units, sepsis is a common and potentially deadly complication and prompt initiation of appropriate antimicrobial therapy improves prognosis. The objective of this trial was to determine whether a strategy of antimicrobial spectrum escalation, guided by daily measurements of the biomarker procalcitonin, could reduce the time to appropriate therapy, thus improving survival.

DESIGN: Randomized controlled open-label trial.

SETTING: Nine multidisciplinary intensive care units across Denmark.

PATIENTS: A total of 1,200 critically ill patients were included after meeting the following eligibility requirements: expected intensive care unit stay of ≥ 24 hrs, nonpregnant, judged to not be harmed by blood sampling, bilirubin <40 mg/dL, and triglycerides <1000 mg/dL (not suspensive).

INTERVENTIONS: : Patients were randomized either to the "standard-of-care-only arm," receiving treatment according to the current international guidelines and blinded to procalcitonin levels, or to the "procalcitonin arm," in which current guidelines were supplemented with a drug-escalation algorithm and intensified diagnostics based on daily procalcitonin measurements.

MEASUREMENTS AND MAIN RESULTS: The primary end point was death from any cause at day 28; this occurred for 31.5% (190 of 604) patients in the procalcitonin arm and for 32.0% (191 of 596) patients in the standard-of-care-only arm (absolute risk reduction, 0.6%; 95% confidence interval [CI] -4.7% to 5.9%). Length of stay in the intensive care unit was increased by one day (p = .004) in the procalcitonin arm, the rate of mechanical ventilation per day in the intensive care unit increased 4.9% (95% CI, 3.0-6.7%), and the relative risk of days with estimated glomerular filtration rate <60 mL/min/1.73 m was 1.21 (95% CI, 1.15-1.27).

CONCLUSIONS: Procalcitonin-guided antimicrobial escalation in the intensive care unit did not improve survival and did lead to organ-related harm and prolonged admission to the intensive care unit. The procalcitonin strategy like the one used in this trial cannot be recommended.

Demagog .cz aneb jak si s námi „hrají “

Sepse ne, ale těžká sepse ano.....

Jaimes et al. BMC Anesthesiology 2013, 13:23
http://www.biomedcentral.com/1471-2253/13/23

BMC Anesthesiology

RESEARCH ARTICLE Open Access

A latent class approach for sepsis diagnosis supports use of procalcitonin in the emergency room for diagnosis of severe sepsis

Fabián A Jaimes[1,6,7*], Gisela D De La Rosa[2], Marta L Valencia[1], Clara M Arango[1,3], Carlos I Gomez[3], Alex Garcia[4], Sigifredo Ospina[5], Susana C Osorno[1] and Adriana I Henao[1]

Abstract

Background: Given the acknowledged problems in sepsis diagnosis, we use a novel way with the application of the latent class analysis (LCA) to determine the operative characteristics of C-reactive protein (CRP), D-dimer (DD) and Procalcitonin (PCT) as diagnostic tests for sepsis in patients admitted to hospital care with a presumptive infection.

Methods: Cross-sectional study to determine the diagnostic accuracy of three biological markers against the gold standard of clinical definition of sepsis provided by an expert committee, and also against the likelihood of sepsis according to LCA. Patients were recruited in the emergency room within 24 hours of hospitalization and were follow-up daily until discharge.

Results: Among 765 patients, the expert committee classified 505 patients (66%) with sepsis, 112 (15%) with infection but without sepsis and 148 (19%) without infection. The best cut-offs points for CRP, DD, and PCT were 7.8 mg/dl, 1616 ng/ml and 0.3 ng/ml, respectively; but, neither sensitivity nor specificity reach 70% for any biomarker. The LCA analysis with the same three tests identified a "cluster" of 187 patients with several characteristics suggesting a more severe condition as well as better microbiological confirmation. Assuming this subset of patients as the new prevalence of sepsis, the ROC curve analysis identified new cut-off points for the tests and suggesting a better discriminatory ability for PCT with a value of 2 ng/ml.

Conclusions: Under a "classical" definition of sepsis three typical biomarkers (CRP, PCT and DD) are not capable enough to differentiate septic from non-septic patients in the ER. However, a higher level of PCT discriminates a selected group of patients with severe sepsis.

Demagog cz……
Aneb jak si s námi „hrají“ ve studiích

The Value of Serum Procalcitonin Level for Differentiation of Infectious from Noninfectious Causes of Fever After Orthopaedic Surgery

By Sabina Hunziker, MD, Thomas Hügle, MD, Katrin Schuchardt, MD, Isabelle Groeschl, MD, Philipp Schuetz, MD, Beat Mueller, MD, Walter Dick, MD, Urs Eriksson, MD, and Andrej Trampuz, MD

Investigation performed at the Departments of Orthopaedic Surgery and Traumatology, University Hospital Basel, Basel, Switzerland

Background: Early diagnosis of postoperative orthopaedic infections is important in order to rapidly initiate adequate antimicrobial therapy. There are currently no reliable diagnostic markers to differentiate infectious from noninfectious causes of postoperative fever. We investigated the value of the serum procalcitonin level in febrile patients after orthopaedic surgery.

Methods: We prospectively evaluated 103 consecutive patients with new onset of fever within ten days after orthopaedic surgery. Fever episodes were classified by two independent investigators who were blinded to procalcitonin results as infectious or noninfectious origin. White blood-cell count, C-reactive protein level, and procalcitonin level were assessed on days 0, 1, and 3 of the postoperative fever.

Results: Infection was diagnosed in forty-five (44%) of 103 patients and involved the respiratory tract (eighteen patients), urinary tract (eighteen), joints (four), surgical site (two), bloodstream (two), and soft tissues (one). Unlike C-reactive protein levels and white blood-cell counts, procalcitonin values were significantly higher in patients with infection compared with patients without infection on the day of fever onset ($p = 0.04$), day 1 ($p = 0.07$), and day 3 ($p = 0.003$). Receiver-operating characteristics demonstrated that procalcitonin had the highest diagnostic accuracy, with a value of 0.62, 0.62, and 0.71 on days 0, 1, and 3, respectively. In a multivariate logistic regression analysis, procalcitonin was a significant predictor for postoperative infection on days 0, 1, and 3 of fever with an odds ratio of 2.3 (95% confidence interval, 1.1 to 4.4), 2.3 (95% confidence interval, 1.1 to 5.2), and 3.3 (95% confidence interval, 1.2 to 9.0), respectively.

Conclusions: Serum procalcitonin is a helpful diagnostic marker supporting clinical and microbiological findings for more reliable differentiation of infectious from noninfectious causes of fever after orthopaedic surgery.

Level of Evidence: Diagnostic Level II. See Instructions to Authors for a complete description of levels of evidence.

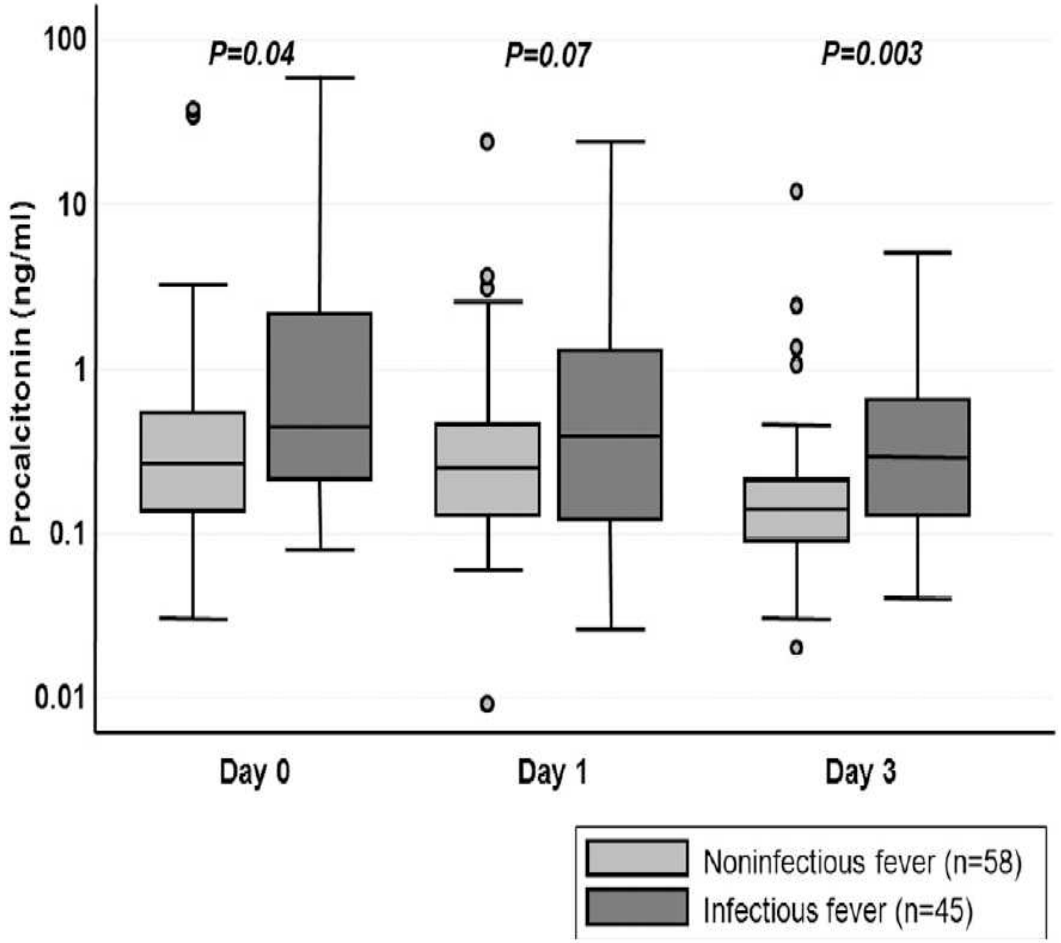

P=0.04
P=0.07
P=0.003
100
10
1
0.1
0.01
Procalcitonin (ng/ml)
Day 0
Day 1
Day 3
Noninfectious fever (n=58)
Infectious fever (n=45)

Fig. 1-C

TABLE II Laboratory Parameters in Patients with Postoperative Fever of Infectious and Noninfectious Origin

Parameter	Noninfectious Fever* (N = 58)	Infectious Fever* (N = 45)	Area Under Receiver-Operating Characteristic Curve†	P Value
White blood-cell count *(×10⁹/L)*				
Day 0	8.3 (7.2-10.8)	9.6 (8.4-11.8)	0.62 (0.50-0.73)	0.04
Day 1	8.2 (6.6-10.2)	8.9 (7.3-11.0)	0.57 (0.45-0.69)	0.24
Day 3	7.8 (6.6-9.6)	7.9 (6.6-10.9)	0.53 (0.41-0.66)	0.59
C-reactive protein level *(mg/L)*				
Day 0	129 (85-190)	179 (79-227)	0.56 (0.44-0.68)	0.26
Day 1	110 (77-182)	160 (86-234)	0.59 (0.47-0.71)	0.15
Day 3	66 (33-115)	80 (39-140)	0.56 (0.44-0.68)	0.31
Procalcitonin *(ng/mL)*				
Day 0	!! 0.27 (0.13-0.55)	!! 0.34 (0.17-1.66)	0.62 (0.51-0.73)	0.04
Day 1	!! 0.26 (0.13-0.46)	!! 0.44 (0.14-1.53)	0.62 (0.48-0.75)	0.07
Day 3	!! 0.14 (0.09-0.21)	!! 0.30 (0.13-0.66)	0.71 (0.57-0.85)	0.003

*The values are given as the median with the interquartile range in parentheses. †The values are given as the mean with the 95% confidence interval in parentheses.

Am J Emerg Med. 2013 Jun;31(6):935-41. doi: 10.1016/j.ajem.2013.03.008. Epub 2013 Apr 17.

Role of procalcitonin in the diagnosis of infective endocarditis: a meta-analysis.

Yu CW, Juan LI, Hsu SC, Chen CK, Wu CW, Lee CC, Wu JY.

Author information

Abstract

BACKGROUND: Infective endocarditis (IE) is a diagnostic challenge. We aimed to systemically summarize the current evidence on the diagnostic value of procalcitonin (PCT) in identifying IE.

METHODS: We searched EMBASE, MEDLINE, Cochrane database, and reference lists of relevant articles with no language restrictions through September 2012 and selected studies that reported the diagnostic performance of PCT alone or compare with other biomarkers to diagnose IE. We summarized test performance characteristics with the use of forest plots, hierarchical summary receiver operating characteristic curves, and bivariate random effects models.

RESULTS: We found 6 qualifying studies that included 1006 episodes of suspected infection with 216 (21.5%) confirmed IE episodes from 5 countries. Bivariate pooled sensitivity, specificity, positive likelihood ratios, and negative likelihood ratios were 64% (95% confidence interval [CI], 52% -74%), 73% (95% CI 58%-84%), 2.35 (95% CI 1.40-3.95), and 0.50 (95% CI 0.35-0.70), respectively. Of the 5 studies examining C-reactive protein (CRP), the pooled sensitivity, specificity, positive likelihood ratios, and negative likelihood ratios were 75% (95% CI 62%-85%), 73% (95% CI 61%-82%), 2.81 (95% CI 1.70-4.65), and 0.34 (95% CI 0.19-0.60), respectively. The global measures of accuracy, area under the receiver operating characteristic curve (AUC) and diagnostic odds ratio (dOR), showed CRP (AUC 0.80, dOR 8.55) may have higher accuracy than PCT (AUC 0.71, dOR 4.67) in diagnosing IE.

CONCLUSIONS: Current evidence does not support the routine use of serum PCT or CRP to rule in or rule out IE in patients suspected to have IE.

PMID: 23601504 [PubMed - indexed for MEDLINE]

Imunokompromitovaní pacienti

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Can procalcitonin differentiate *Staphylococcus aureus* from coagulase-negative staphylococci in clustered gram-positive bacteremia?

William Shomali, Ray Hachem *, Anne-Marie Chaftari, Ramez Bahu, Gilbert El Helou, Ying Jiang, Alex Hanania, Ruth Reitzel, Issam Raad

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ABSTRACT

Procalcitonin (PCT) and pro-adrenomedullin (ProADM) have been proposed as diagnostic and prognostic biomarkers of infection. Between July 2009 and January 2012, we studied the role of these biomarkers in 163 patients with clustered gram-positive and gram-negative bacteremia. PCT levels were significantly higher in patients with *Staphylococcus aureus* and gram-negative bacteremia than those with coagulase-negative staphylococci (CoNS) isolated from blood cultures ($P = 0.29$ and <0.001, respectively). ProADM levels were only significantly higher in patients with gram-negative bacteremia (median 1.46 nmol/L) than those with CoNS (median 1.01 nmol/L) ($P = 0.04$). Among patients with CoNS, PCT, and ProADM, levels failed to differentiate blood contamination (medians 0.24 ng/mL and 0.97 nmol/L) from true bacteremia (medians 0.26 ng/mL and 1.14 nmol/L) ($P = 0.51$ and 0.57, respectively). In cancer patients, PCT (and to a lesser extent, ProADM) was useful in differentiating CoNS from *S. aureus* and gram-negative bacteremia.

PCT and ProADM levels in different groups.

Group	N	Median PCT (range) (ng/mL)	*P* value PCT, ProADM
CoNS	95	0.25 (0.075–43.8)	
CoNS contamination	69	0.24 (0.075–43.8)	0.51, 0.57
CoNS true bacteremia	26	0.26 (0.075–14.1)	
S. aureus bacteremia	24 (21*)	0.85 (0.075–47.4)	0.029, 0.08**
Gram negative bacteremia	44 (42*)	0.78 (0.075–129.3)	<0.001, 0.04**

CoNS contamination	0,24	0,075-43,8	!!
CoNS true bacteremia	0,26	0,075-14,1	!!

PCT – proč ne

The Lancet Infectious Diseases, Volume 13, Issue 5, Pages 426 - 435, May 2013
doi:10.1016/S1473-3099(12)70323-7 Cite or Link Using DOI
This article can be found in the following collections: Infectious Diseases (Infectious diseases-other)
Published Online: 01 February 2013

< Previous Article | Next Article >

Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis

Christina Wacker Cand Med [a], Anna Prkno Cand Med [a], Prof Frank M Brunkhorst MD [*b], Prof Peter Schlattmann PhD [*a]

Sensitivita 0, 77 **Specificita 0,79**

Findings

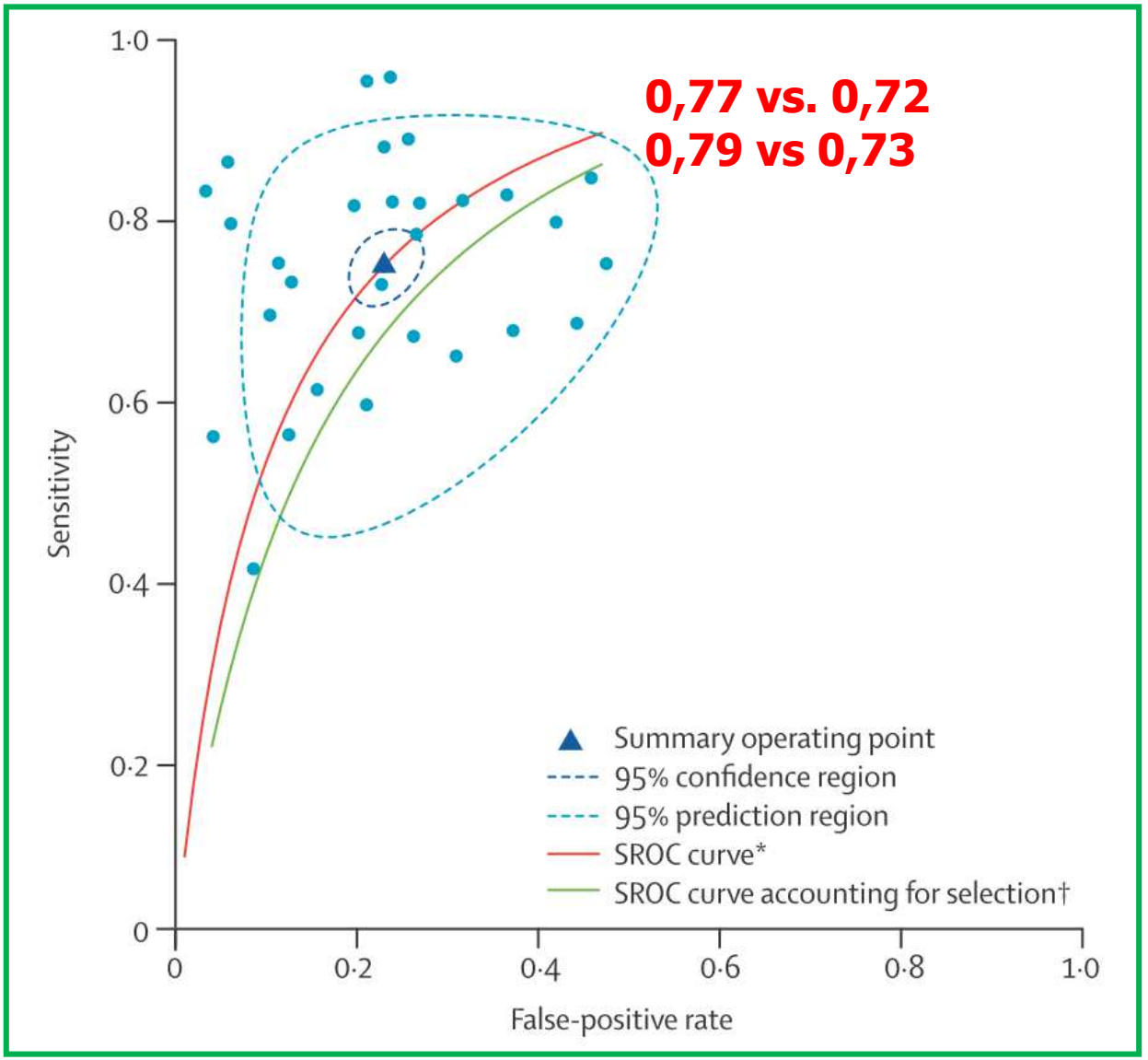
Our search returned 3487 reports, of which 30 fulfilled the inclusion criteria, accounting for 3244 patients. Bivariate analysis yielded a mean sensitivity of 0·77 (95% CI 0·72–0·81) and specificity of 0·79 (95% CI 0·74–0·84). The area under the receiver operating characteristic curve was 0·85 (95% CI 0·81–0·88). The studies had substantial heterogeneity (I^2=96%, 95% CI 94–99). None of the subgroups investigated—population, admission category, assay used, severity of disease, and description and masking of the reference standard—could account for the heterogeneity.

Interpretation

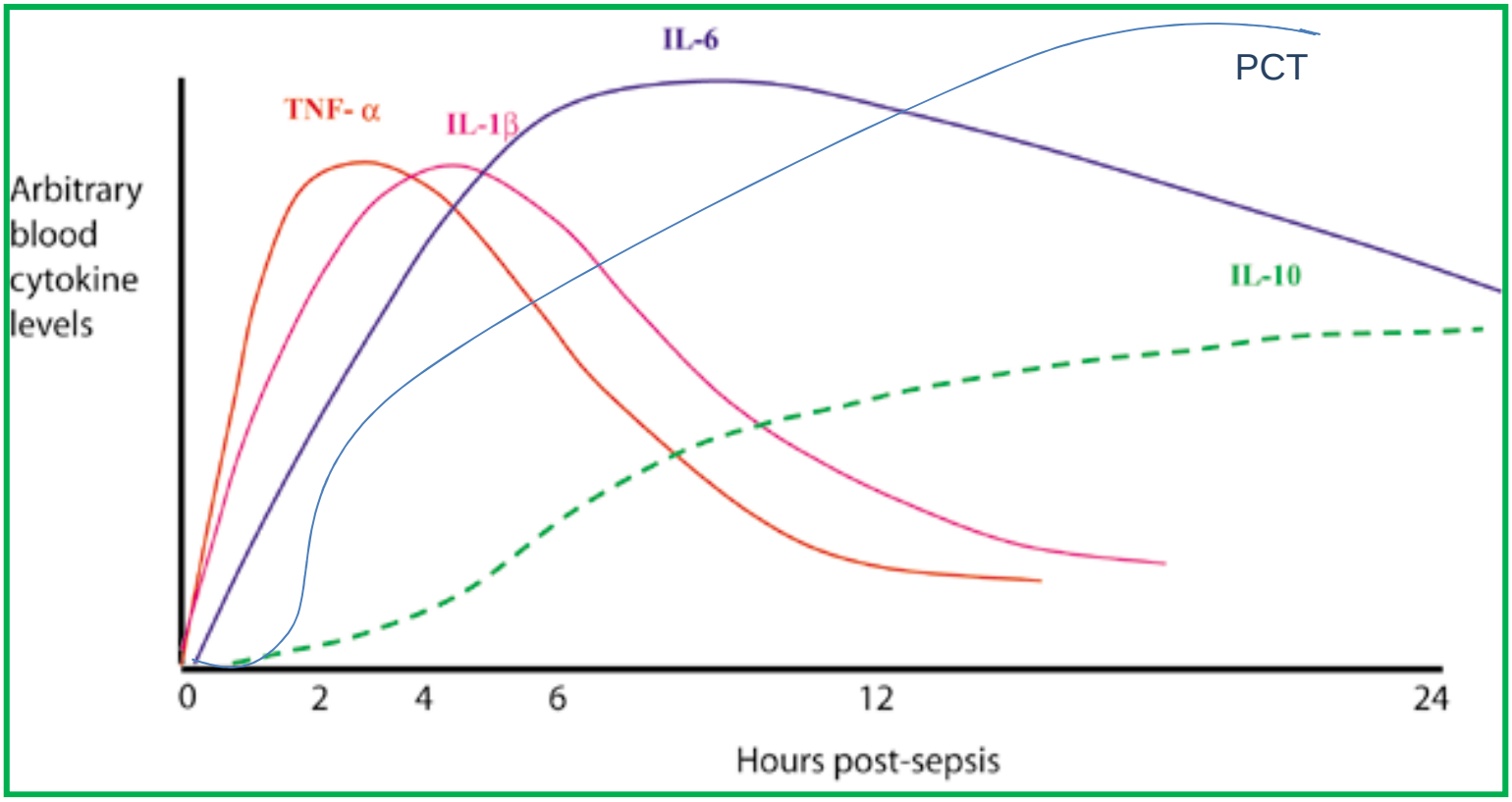
Procalcitonin is a helpful biomarker for early diagnosis of sepsis in critically ill patients. Nevertheless, the results of the test must be interpreted carefully in the context of medical history, physical examination, and microbiological assessment.

Funding

Ministry of Education and Research, the Deutsche Forschungsgemeinschaft, Thuringian Ministry for Education, Science and Culture, the Thuringian Foundation for Technology, Innovation and Research, and the German Sepsis Society.


0,77 vs. 0,72
0,79 vs 0,73
1·0
0·8
0·6
0·4
0·2
0
Sensitivity
0
0·2
0·4
0·6
0·8
1·0
False-positive rate
Summary operating point
95% confidence region
95% prediction region
SROC curve*
SROC curve accounting for selection†

Časový průběh produkce různých biomarkerů



2012 Balíčky péče

Initial resuscitation Bundle – hlavní změna nových Guidelines

První 3 hodiny od zjištění diagnózy

- odeber laktát
- odeber 2 hemokultury během 45 minut
- nasaď širokospektrá ATB během první hodiny
- podání krystaloidů v bolusu minimálně 30 ml/kg v případě hypotenze a/nebo laktátu > 4 mmol/l - **okamžitě - nezávisle na přijetí na ICU**

Surviving Sepsis Campaign

ERIC
EARLY RECOGNITION IS CRITICAL

Prvních 6 hodin

- Podání vasopresorů k dosažení MAP ≥ 65 mmHg – pokud nebylo dosaženo pomocí tekutinové resuscitace, 1. lékem volby je norepinephrine **(1B)**

- V případě přetrvávající arteriální hypotenze přes tekutinovou resuscitaci a/nebo laktátu ≥ 4 mmol/l
  - zavedení centrálního žilního katétru
  - CVP 8-12 mmHg,
  - ScvO2 – cílem je ≥ 70% nebo SvO2 ≥ 65% **(1C)**

- dosažení normalizace laktátu s použitím EGDT, pokud není dostupná centrální monitorace žilní oxygenace **(2C)**

- výdej moči ≥ 0,5 ml/kg/hod

ERIC
EARLY RECOGNITION IS CRITICAL

Surviving Sepsis Campaign

Otázka kterou řešíme u lůžka: – kdy a u koho použít PCT ???

- **Různé fenotypy sepse**
- **Nejasný zdroj a nejasná diagnóza**
- **Diferenciace podle cílových skupin pacientů ,**
- **Různé cutoff**
- **Imunokompromitovaní pacienti**
  – pacienti s imunosupresivní terapií

Quenot et al. Annals of Intensive Care 2013, 3:21
http://www.annalsofintensivecare.com/content/3/1/21

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Role of biomarkers in the management of antibiotic therapy: an expert panel review II: clinical use of biomarkers for initiation or discontinuation of antibiotic therapy

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Abstract

Biomarker-guided initiation of antibiotic therapy has been studied in four conditions: acute pancreatitis, lower respiratory tract infection (LRTI), meningitis, and sepsis in the ICU. In pancreatitis with suspected infected necrosis, initiating antibiotics best relies on fine-needle aspiration and demonstration of infected material. We suggest that PCT be measured to help predict infection; however, available data are insufficient to decide on initiating antibiotics based on PCT levels. In adult patients suspected of community-acquired LRTI, we suggest withholding antibiotic therapy when the serum PCT level is low (<0.25 ng/mL); in patients having nosocomial LRTI, data are insufficient to recommend initiating therapy based on a single PCT level or even repeated measurements. For children with suspected bacterial meningitis, we recommend using a decision rule as an aid to therapeutic decisions, such as the Bacterial Meningitis Score or the Meningitest®; a single PCT level ≥0.5 ng/mL also may be used, but false-negatives may occur. In adults with suspected bacterial meningitis, we suggest integrating serum PCT measurements in a clinical decision rule to help distinguish between viral and bacterial meningitis, using a 0.5 ng/mL threshold. For ICU patients suspected of community-acquired infection, we do not recommend using a threshold serum PCT value to help the decision to initiate antibiotic therapy; data are insufficient to recommend using PCT serum kinetics for the decision to initiate antibiotic therapy in patients suspected of ICU-acquired infection. In children, CRP can probably be used to help discontinue therapy, although the evidence is limited. In adults, antibiotic discontinuation can be based on an algorithm using repeated PCT measurements. In non-immunocompromised out- or in- patients treated for RTI, antibiotics can be discontinued if the PCT level at day 3 is < 0.25 ng/mL or has decreased by >80-90%, whether or not microbiological documentation has been obtained. For ICU patients who have nonbacteremic sepsis from a known site of infection, antibiotics can be stopped if the PCT level at day 3 is < 0.5 ng/mL or has decreased by >80% relative to the highest level recorded, irrespective of the severity of the infectious episode; in bacteremic patients, a minimal duration of therapy of 5 days is recommended.

Keywords: Infection; Sepsis; Emergency medicine; Biomarkers; Procalcitonin; C-reactive protein; Pancreatitis; Meningitis; Pneumonia