Délka léčby antibiotiky- jak ji zkrátit?

Colours of Sepsis 2020

Marcela Káňová

Antibiotikum – nejčastější lék na ICU

ATB má předepsáno denně více jak 70 % pacientů na ICU empiricky nebo cíleně

U více jak 50 % pacientů zbytečně nepotvrzena infekční etiologie

Obtížná dif dg sepse X SIRS neinfekčního původu

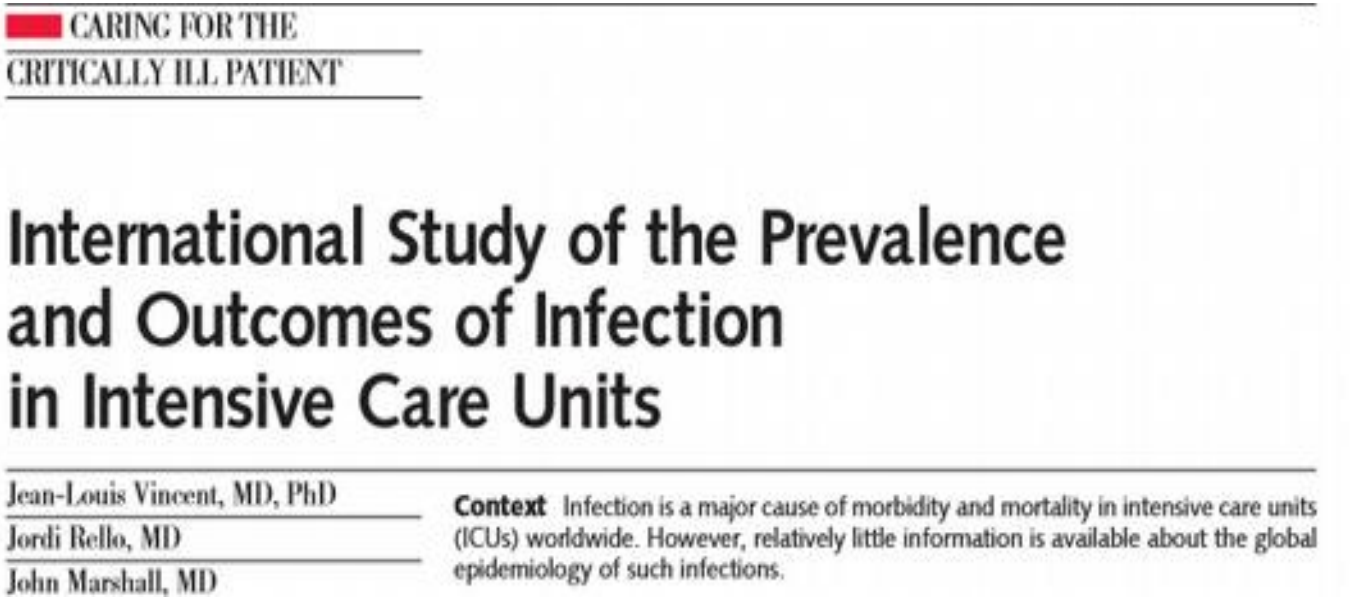
quick SOFA: dechová frekvence 22/min a více, alterace vědomí, systolický tlak 100 mmHg a méně

Sepse- incidence 6 % všech hospitalizovaných pacientů

25 % ICU pacientů (sepse, severe sepsis, septický šok)

Vysoká mortalita (30 %, severe sepis 50 %)

18mil, sepsí celosvětově/rok
Tj cca 5,4 mil úmrtí



CARING FOR THE CRITICALLY ILL PATIENT

International Study of the Prevalence and Outcomes of Infection in Intensive Care Units

Jean-Louis Vincent, MD, PhD
Jordi Rello, MD
John Marshall, MD

Context Infection is a major cause of morbidity and mortality in intensive care units (ICUs) worldwide. However, relatively little information is available about the global epidemiology of such infections.

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/312503854

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock

Article in Critical Care Medicine · January 2017

Časné zahájení ATB terapie při podezření na sepsi redukuje mortalitu **do 1 hodiny** (silné dop.)

Nesprávně zvolená empirická ATB terapie naopak prodlužuje pobyt na ICU, zhoršuje mortalitu

CONFERENCE REPORTS AND EXPERT PANEL

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Časné zahájení ATB terapie při podezření na sepsi
Redukuje mortalitu

Vzestup spotřeby ATB 2010-2015 o
30%

Nature 2015

Nespravn… …apie naopak
prodlužuje pobyt na ICU, zhoršuje mortalitu

Intensive Care Med
https://doi.org/10.1007/s00134-019-05520-5

REVIEW

Rationalizing antimicrobial therapy in the ICU: a narrative review

Jean-François Timsit[1,2*], Matteo Bassetti[3], Olaf Cremer[4], George Daikos[5], Jan de Waele[6], Andre Kallil[7], Eric Kipnis[8], Marin Kollef[9], Kevin Laupland[10], Jose-Artur Paiva[11], Jesús Rodríguez-Baño[12], Étienne Ruppé[2,13], Jorge Salluh[14], Fabio Silvio Taccone[15], Emmanuel Weiss[16,17] and François Barbier[18]

Nadměrná spotřeba ATB

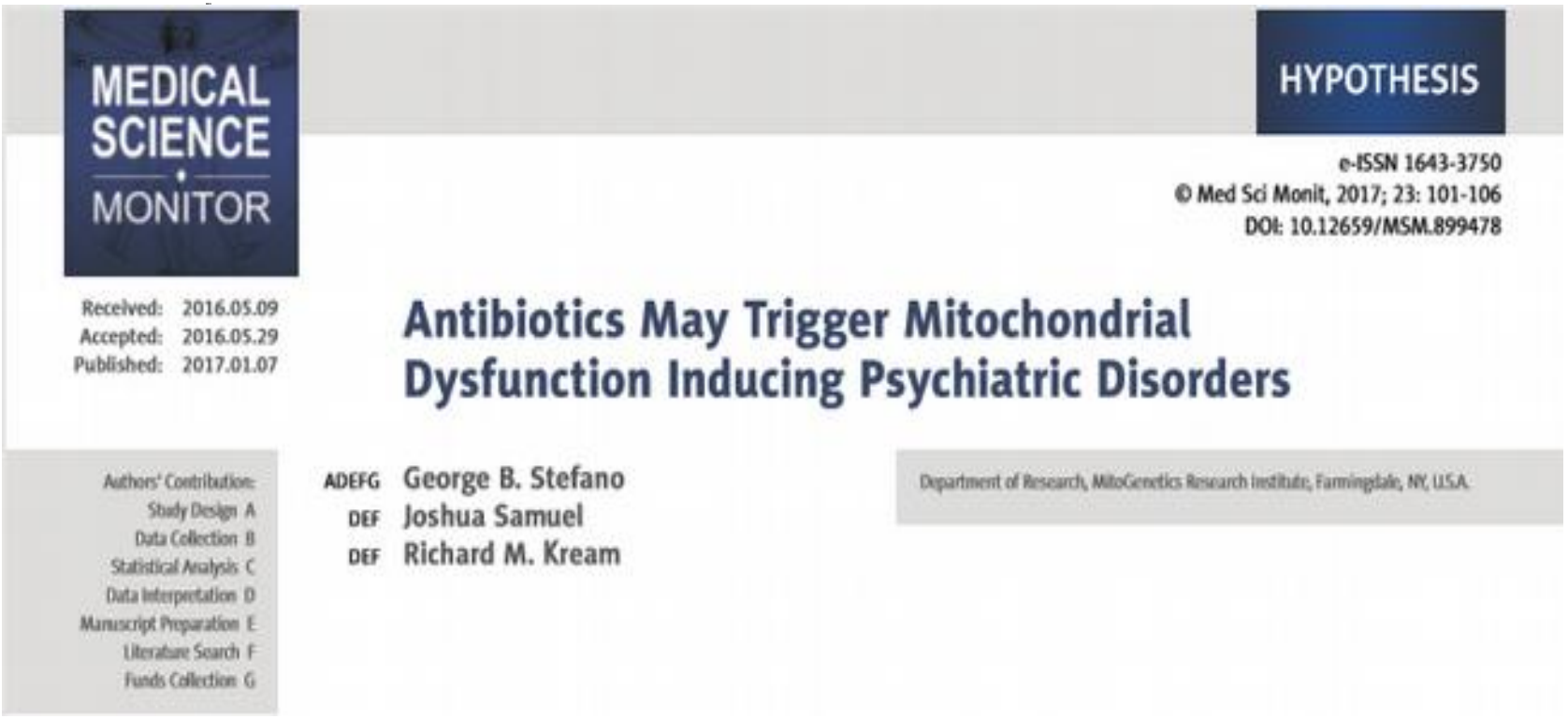
Selekční tlak
MDRB multirezistentní kmeny

Postižení mikrobiomu
Clostridium diff
NÚ ATB- nefrotoxicita, ototoxicita

Published in final edited form as:
Sci Transl Med. 2013 July 3; 5(192): 192ra85. doi:10.1126/scitranslmed.3006055.

Bactericidal Antibiotics Induce Mitochondrial Dysfunction and Oxidative Damage in Mammalian Cells

Sameer Kalghatgi[1], Catherine S. Spina[1,2,3], James C. Costello[1], Marc Liesa[3], J Ruben Morones-Ramirez[1], Shimyn Slomovic[1], Anthony Molina[3,4], Orian S. Shirihai[3], and James J. Collins[1,2,3,*]



Review

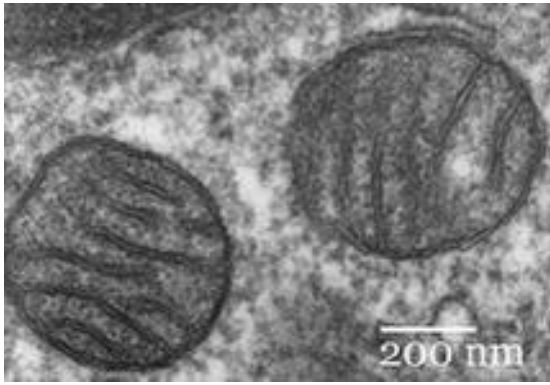
Public Health Genomics

Public Health Genomics 2017;20:257–273
DOI: 10.1159/000485095

Received: August 16, 2017
Accepted: October 16, 2017
Published online: December 15, 2017

Antibiotics-Induced Obesity: A Mitochondrial Perspective

Melisa J. Andrade[a] Chinchu Jayaprakash[a] Smitha Bhat[a]



Antibiotic drug piperacillin induces neuron cell death through mitochondrial dysfunction and oxidative damage

Shan Jiang[1*], Tong Li[1*], Xiao Zhou[2], Wenjun Qin[1], Zijun Wang[1], Yi Liao[3]

De eskalace….

A general principle of “start broadly, narrow quickly, if they don’t need it get rid of it” Akrami 2016

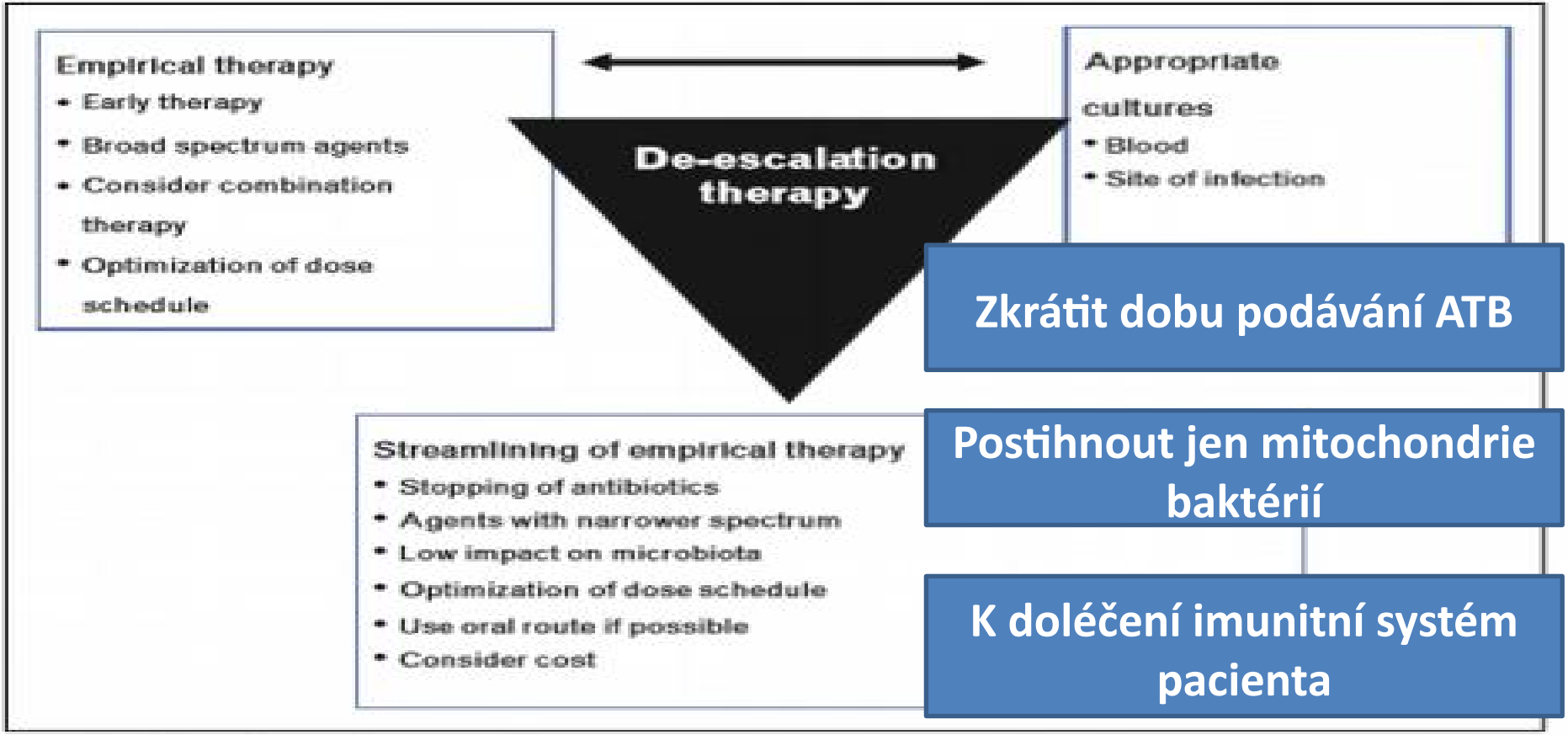
Surviving Sepsis Campaign 2016:
Antimicrobial regimen should be reassed daily for potential deescalation (Grade1B)

... užívej jen indikovaná ATB po indikovanou dobu…

Antibiotic de-escalation in the ICU: how is it best done?

Curr Opin Infect Dis 2015, 28:193–198

Jose Garnacho-Montero[a,b,c], *Ana Escoresca-Ortega*[a], *and Esperanza Fernández-Delgado*[a]



Zkrátit dobu podávání ATB

Postihnout jen mitochondrie baktérií

K doléčení imunitní systém pacienta

Jak zkrátit či ukončit terapii ATB? Podle čeho se řídit?

Rychlé dg testy

PCR (polymerase chain reaction)

PNA FISH (peptide nucleic acid fluorescence)

MALDI TOFF (mass spectromectry)

Nucleid acid PCR

Biomarkery

PCT

start za 2-4hod, max 12-24 hod, t1/2 24-35hod

PSEP (sCD14-ST)

vzestup do 1 hodiny, max 3 hod

BDG

GM

Cut off

PCT x PSEP

Brodská H, Malíčková K, Adámková V et al. Significantly higher procalcitonin levels could differentiate gram-negative sepsis form gram-positive and fungal sepsis. **Clin Exp Med 2013**

- **PCT ng/ml (medián)u sepsí**
- G- 8,9 ng/ml
- G+ 0,73 ng/ml
- Smíšené 0,58 ng/ml

Lu B, Zhang Y, Li C et al. The utility of presepsin in diagnosis and risk stratification for the emergency patients with sepsis. **Am J Emerg Med 2018**

- **PSEP pg/ml (medián) u sepsí**
- G- 1128 pg/ml
- G+ 1070 pg/ml
- Smíšené 1757 pg/ml
- Mykotické 922 pg/ml

Journal of Critical Care 40 (2017) 197–201

Contents lists available at ScienceDirect

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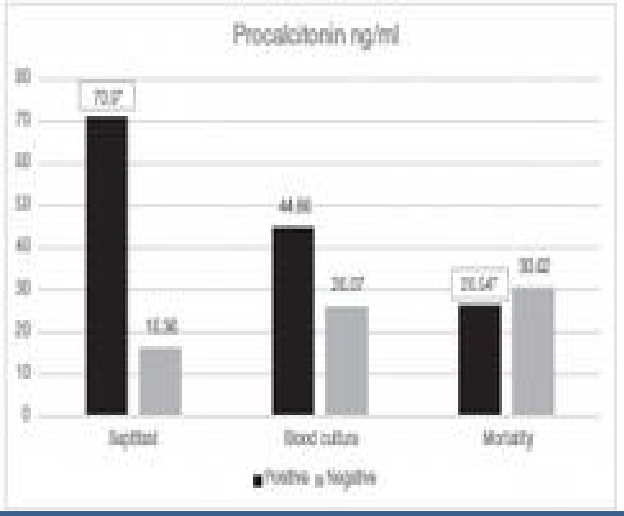
journal homepage: www.jccjournal.org

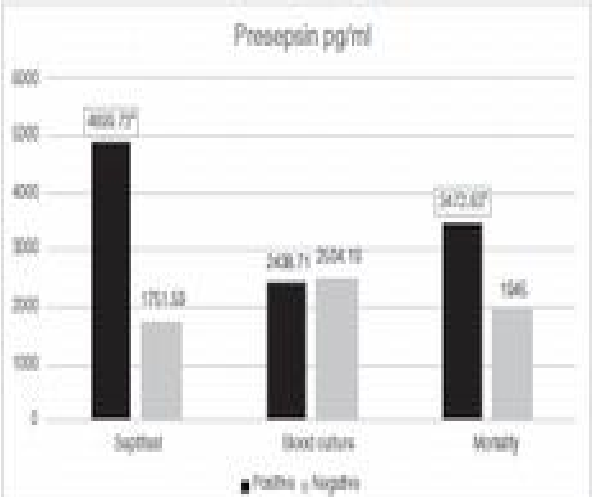
Use of presepsin and procalcitonin for prediction of SeptiFast results in critically ill patients☆

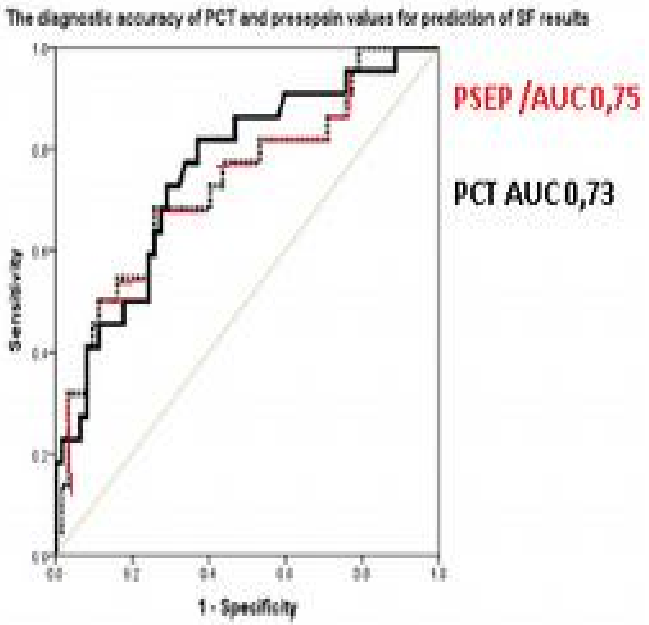
Dunja Mihajlovic, MD, PhD, Teaching Assistant [a,*], Snezana Brkic, MD, PhD, Full Professor [b], Arsen Uvelin, MD, PhD, Assistant Professor [a], Biljana Draskovic, MD, PhD, Full Professor [c], Vladimir Vrsajkov, MD, PhD [a]

[a] Medical faculty, University of Novi Sad, Clinical center of Vojvodina, Emergency center, Department of anesthesia and reanimation, Novi Sad, Serbia
[b] Medical faculty, University of Novi Sad, Clinical center of Vojvodina, Clinic for infectious diseases, Novi Sad, Serbia
[c] Medical faculty, University of Novi Sad, Institute of Child and Adolescent Health Care of Vojvodina, Clinic of Pediatric Surgery, Novi Sad, Serbia

Cíl: Zda PSEP a PCT mohou predikovat výsledky BC a SeptiFast (PCR)
A tím pomoci vyselektovat pacienty pro provedení SF v praxi







PSEP i PCT jsou dobrými prediktory pozitivní baktériemie

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

14. We suggest that measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients
(weak recommendation, low quality of evidence**).**

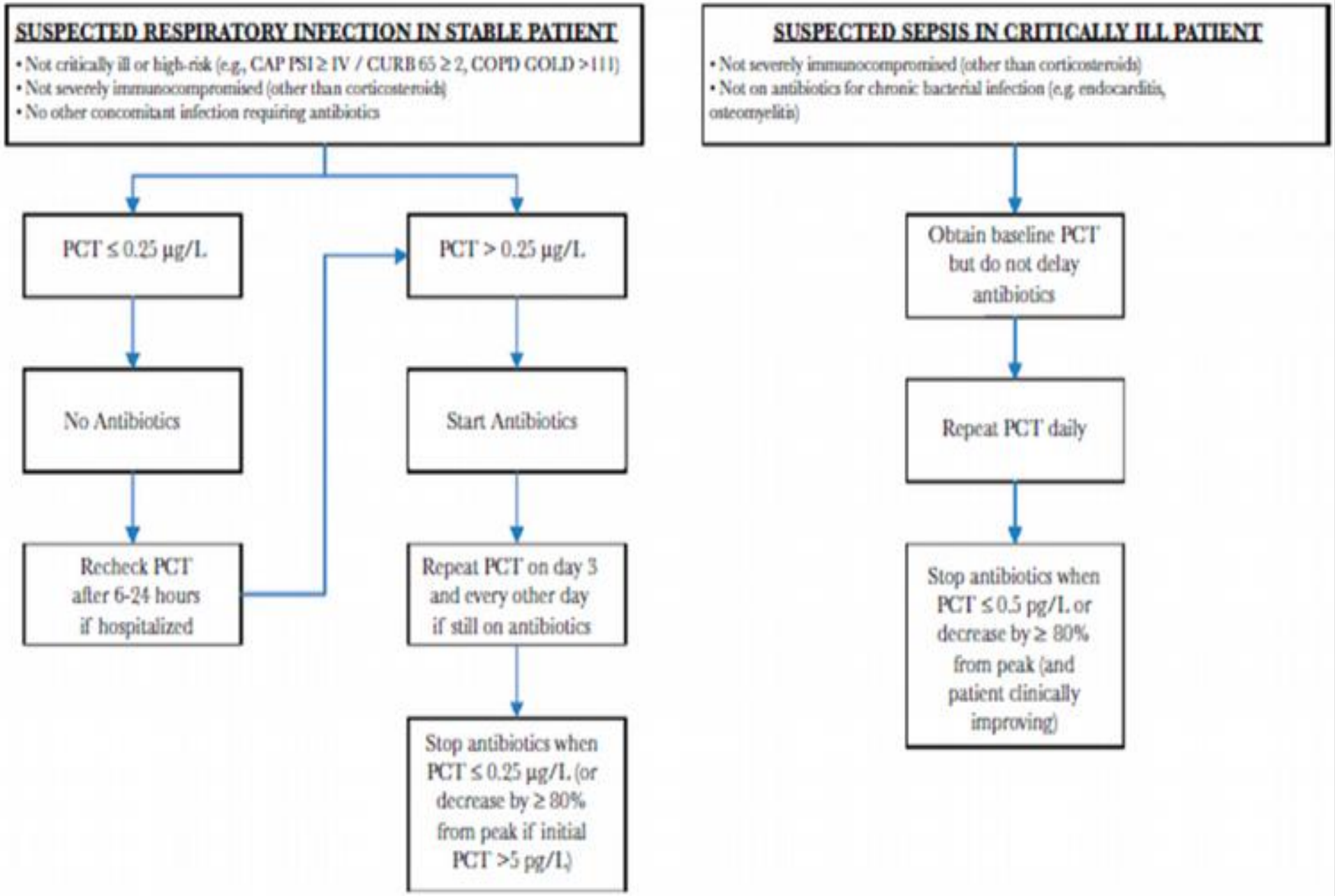
15. We suggest that procalcitonin levels can be used to support the discontinuation of empiric antibiotics in patients who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection
(weak recommendation, low quality of evidence**)**.

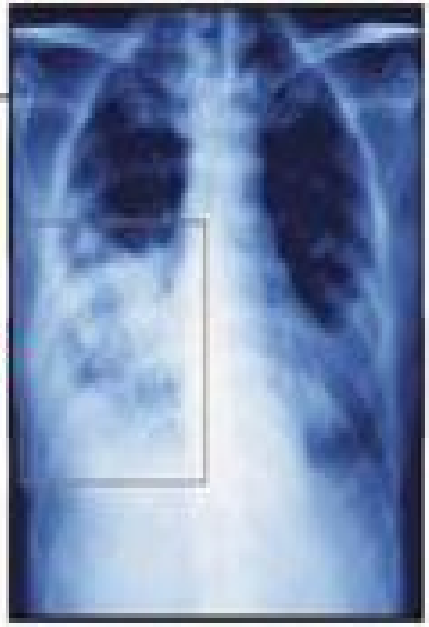
Procalcitonin Randomized Controlled Trials for Infections in Critically Ill Adult Patients

[Reference] Trial Name	Setting (Country)	Number and Type of Infection	PCT Algorithm	Exclusion Criteria	Reduction Outcomes	Clinical Outcomes
Nobre (2008) [17]	1 Medical-Surgical ICU (Switzerland)	79 patients with severe sepsis/septic shock min 3dny	Discontinuation only: stop antibiotics if PCT decreased 90% from initial value, but not before day 3 (if baseline <1 μg/L) or day 5 (if baseline ≥1)	Organisms or conditions requiring prolonged duration of therapy, severe viral or parasitic infections, antibiotics started >48 hours before enrollment, severely immunocompromised, withholding of life support	4 day reduction in median duration of antibiotic therapy ($P = .003$)	No different in mortality and recurrent infection; reduced ICU LOS by 2 days ($P = .03$)
Hochreiter (2009) [28]	1 Surgical ICU (Germany)	110 patients with suspected or confirmed sepsis min 3dny	Discontinuation only: stop antibiotics if PCT <1 μg/L or decrease to 25%–35% of initial value over 3 days	Antibiotics started before ICU admission, therapy limitation due to goals of care	Mean 5.9 vs 7.9 days ($P < .001$) 6 vs 8 dní	No difference (treatment success, ICU LOS, SOFA score, hospital mortality)
Schroeder (2009) [29]	1 Surgical ICU (Germany)	27 patients with severe sepsis min 3dny	Discontinuation only: stop antibiotics if PCT <1 μg/L or decrease to <35% of initial value over 3 days	Antibiotics started before ICU admission	Mean 6.6 vs 8.3 days ($P < .001$) 6,6 vs 8,3 dny	No difference (SAPS II or SOFA score, ICU stay, hospital mortality)
Stolz (2009) [26] ProVAP	7 ICUs in 3 hospitals (Switzerland, United States)	101 patients with ventilator-associated pneumonia min 3dny VAP	Discontinuation only: after 72 hours, antibiotic cessation strongly encouraged (<0.25 μg/L), encouraged (0.25–0.5 or decrease by ≥80%), discouraged (>0.5 or decrease by <80%), strongly discouraged (>1)	Pregnant, enrolled in another trial, immunosuppressed, coexisting extrapulmonary infection requiring antibiotics for >3 days	13 vs 9.5 antibiotic-free days alive 28 days after ventilator-associated pneumonia onset (overall 27% reduction in antibiotic therapy, $P = .038$) dlouhá th	No difference (mechanical ventilation-free days, ICU-free days alive, hospital LOS, 29-day mortality)
Boudama (2010) [30] PRORATA	5 medical ICUs and 2 surgical ICUs (France)	621 patients with suspected infection	Initiation and Discontinuation: antibiotics strongly discouraged (<0.25 μg/L), discouraged (0.25–0.5), encouraged (0.5–1), strongly encouraged (≥1) (daily PCT measurements). Discontinuation also if PCT decreased ≥80% from peak	Pregnancy, bone marrow transplant, or neutropenic, infections requiring long-term antibiotics, poor chance of survival, and do-not-resuscitate orders	Mean 11.6 vs 14.3 days of therapy ($P < .0001$) dlouhá th	No difference in noninferiority analysis (28-day and 60-day mortality), but trend towards increased 60-day mortality (+3.8%). No difference in infection relapse or superinfection, mechanical ventilation, ICU and hospital LOS PCT protokol dodržen jen z 53% !

(Year) [Reference] Trial Name	Setting (Country)	Number and Type of Infection	PCT Algorithm	Exclusion Criteria	Antibiotic Reduction Outcomes	Clinical Outcomes
Shehabi (2014) [31] ProGUARD	11 ICUs (Australia)	394 patients with suspected sepsis	Discontinuation only: stop antibiotics if PCT <0.1 μg/L, or 0.1–0.25 and infection is highly unlikely, or subsequent PCT declines >90% from baseline (daily PCT measurements)	Antibiotics for surgical prophylaxis or proven infection requiring >3 weeks of therapy, fungal or viral infections, immunosuppressed, cardiac surgery or trauma or heat stroke within 48 hours, medullary thyroid or small cell lung cancer, not expected to survive, pregnancy	Nonsignificant trend: median 9 vs 11 days of antibiotic therapy (P = .58)	No difference (ventilation time, ICU and hospital LOS, hospital and 90-day mortality)
de Jong (2016) [32] SAPS	ICUs at 15 hospitals (Netherlands)	1546 patients with suspected or proven infection	Discontinuation only: stop antibiotics if PCT decreased to ≥80% of peak value, or ≤0.5 μg/L (daily PCT measurements)	Antibiotics for prophylaxis only or gut decontamination, expected ICU stay <24 hours, severe immunosuppression, severe viral or parasitic or tuberculosis infections, moribund, chronic infection (eg, endocarditis)	Median antibiotic consumption of 7.5 vs 9.3 daily defined doses (P < .0001), median treatment duration 5 vs 7 days (P < .0001)	Decreased 28-day mortality (20% vs 25%, P = .0122) and 1-year mortality (36% vs 43%, P = .0188). No difference in hospital and ICU LOS or requirement for additional antibiotics within 28 days. But 5% vs 3% rate of reinfection by same pathogen (P = .0492)

Algoritmus užití PCT v řízení ATB terapie





PCT (ng/ml)

Likelihood of bacterial infection

Recommendation for antibiotic treatment

iniciace i deeskalace

10.0
7.5
5
2.5
1.0
0.75
0.5
0.25
0.1
0.075
0.05
0.025

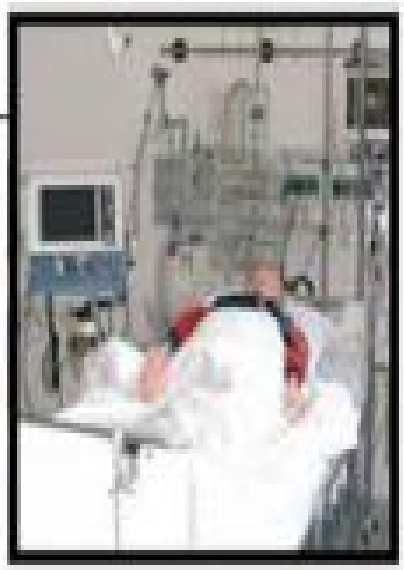
very likely
likely
unlikely
very unlikely

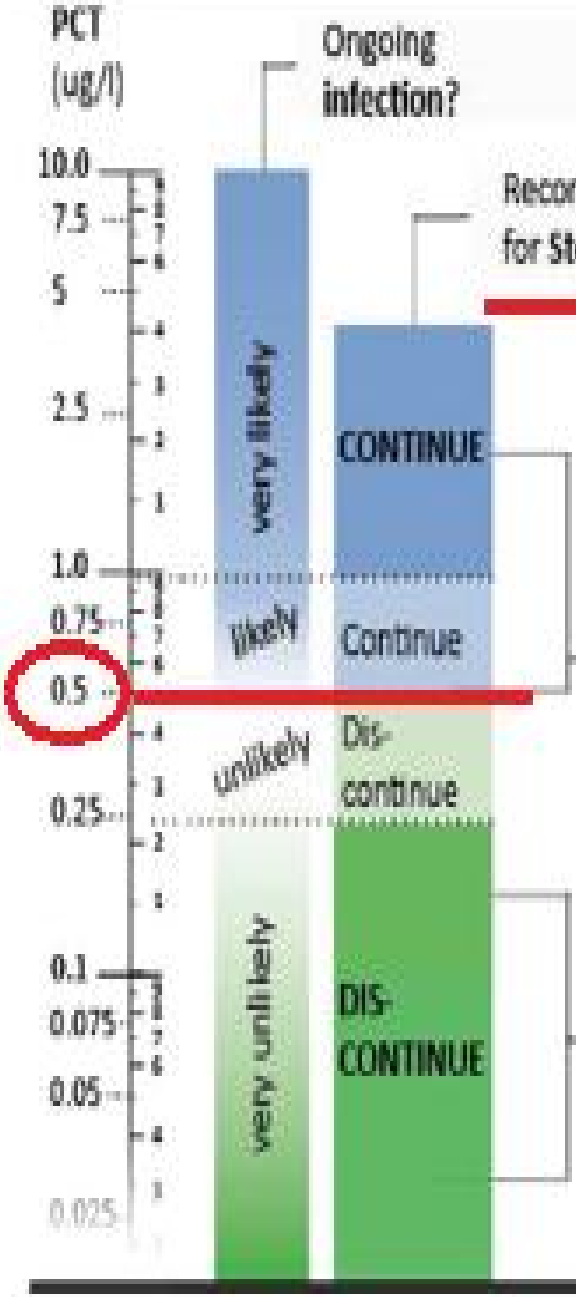
YES!
Yes
No
NO!

Important considerations and overruling criteria

- Consider the course of PCT (dynamic monitoring)
- If antibiotics are initiated:
  - Repeat PCT on days 3, 5, 7; stop antibiotics using the same cut offs
  - if peak PCT levels are very high, then stop when 80-90% decrease of peak
  - If PCT remains high, consider treatment failure

- If Antibiotics are withheld, control PCT after 6-24 hours
- Initial antibiotics can be considered in case of:
  - Respiratory or hemodynamic instability, severest comorbidities, ICU admission
  - PCT < 0.1 ug/L: CAP with PSI V or CURB >3, COPD with GOLD IV
  - PCT < 0.25 ug/L: CAP with PSI IV & V or CURB >2, COPD with GOLD III & IV





Important considerations
and overruling criteria

- Consider the course of PCT
- If antibiotics are continued:
  - Daily measurement of PCT, discontinue antibiotics when PCT decreases >80% of the peak level or an absolute PCT value <0.5ng/ml is reached.
  - If PCT remains high, consider treatment failure.

- Always consider clinical course of patients in addition to PCT levels.
- If Antibiotics are discontinued, close clinical evaluation is recommended.

Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis

Lancet Infect Dis 2018; 18: 95–107

Philipp Schuetz*, Yannick Wirz*, Ramon Sager*, Mirjam Christ-Crain, Daiana St
Jean Chastre, Florence Tubach, Kristina B Kristoffersen, Olaf Burkhardt, Tobias We
Djillali Annane, Konrad Reinhart, Ann R Falsey, Angela Branche, Pierre Damas, M
Carolina F Oliveira, Vera Maravić-Stojković, Alessia Verduri, Bianca Beghé, Bin Cao
Jos A H van Oers, Albertus Beishuizen, Armand R J Girbes, Evelien de Jong, Matthi

Summary

Background In February, 2017, the US Food and Drug Adm procalcitonin for guiding antibiotic therapy in patients with acute data from 26 randomised controlled trials was designed to assess with acute respiratory infections from different clinical settings.

26 studií, 6 708 pacientů s ak resp infektem
Prim outcome- mortalita
Sec outcome- ATB side effects

PCT sk. redukce mortality
Nejvíce u ICU

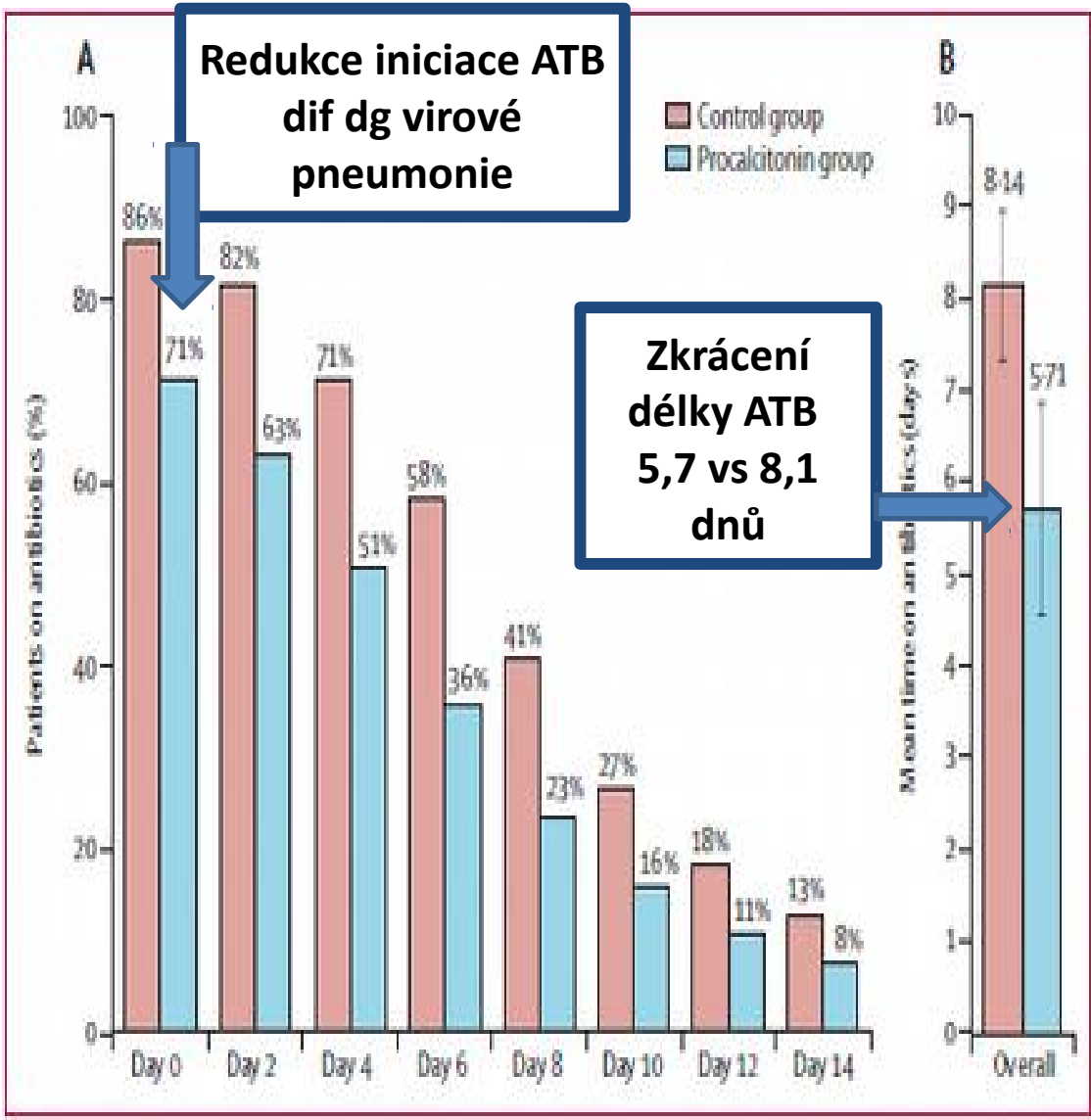
PCT protokol bezpečný

	Control (n=3372)	Procalcitonin group (n=3336)
Overall		
30-day mortality	336 (10%)	286 (9%)
Treatment failure	841 (25%)	768 (23%)
Length of ICU stay, days	13·3 (16·0)	13·7 (17·2)
Length of hospital stay, days	13·7 (20·6)	13·4 (18·4)
Antibiotic-related side-effects	336/1521 (22%)	247/1513 (16%)
Setting-specific outcomes		
Intensive care unit	1233	1214
30-day mortality	273 (22%)	229 (19%)
Length of ICU stay, days	14·8 (16·2)	15·3 (17·5)
Length of hospital stay, days	26·3 (26·9)	25·8 (23·9)
Disease-specific outcomes		
Ventilator-associated pneumonia	186	194
30-day mortality	29 (16%)	23 (12%)
Treatment failure	51 (27%)	44 (23%)
Length of ICU stay, days	23·5 (20·5)	21·8 (19·1)
Length of hospital stay, days	33·8 (27·6)	32·0 (23·1)

Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis

Philipp Schuetz*, Yannick Wirz*, Ramon Sager*, Mirjam Christ-Crain, Daiana Stolz, Michael Tamm, Lila Bouadma, Charles E Luyt, Michel Wolff

	Control (n=3372)	Procalcitonin group (n=3336)
Overall		
Initiation of antibiotics	2894 (86%)	2351 (70%)
Duration of antibiotics, days†	9·4 (6·2)	8·0 (6·5)
Total exposure of antibiotics, days‡	8·1 (6·6)	5·7 (6·6)
Setting-specific outcomes		
Intensive care unit	1233	1214
Initiation of antibiotics	1224 (99%)	1116 (92%)
Duration of antibiotics, days†	9·5 (7·4)	8·8 (7·8)
Total exposure of antibiotics, days‡	9·5 (7·4)	8·1 (7·9)
Ventilator-associated pneumonia	186	194
Initiation of antibiotics	186 (100%)	193 (100%)
Duration of antibiotics, days†	13·1 (7·9)	10·8 (8·7)
Total exposure of antibiotics, days‡	13·1 (7·9)	10·8 (8·7)



Redukce iniciace ATB dif dg virové pneumonie

Zkrácení délky ATB 5,7 vs 8,1 dnů

PCT redukuje spotřebu ATB, snižuje NÚ ATB, zlepšuje přežití

Published in final edited form as:
J Hosp Med. 2018 May 01; 13(5): 336–342. doi:10.12788/jhm.2905.

Shorter Versus Longer Courses of Antibiotics for Infection in Hospitalized Patients: A Systematic Review and Meta-Analysis

Stephanie Royer, MD[1,2,3,*], **Kimberley M. DeMerle, MD**[1], **Robert P. Dickson, MD**[1], and **Hallie C. Prescott, MD, MSc**[1,4]

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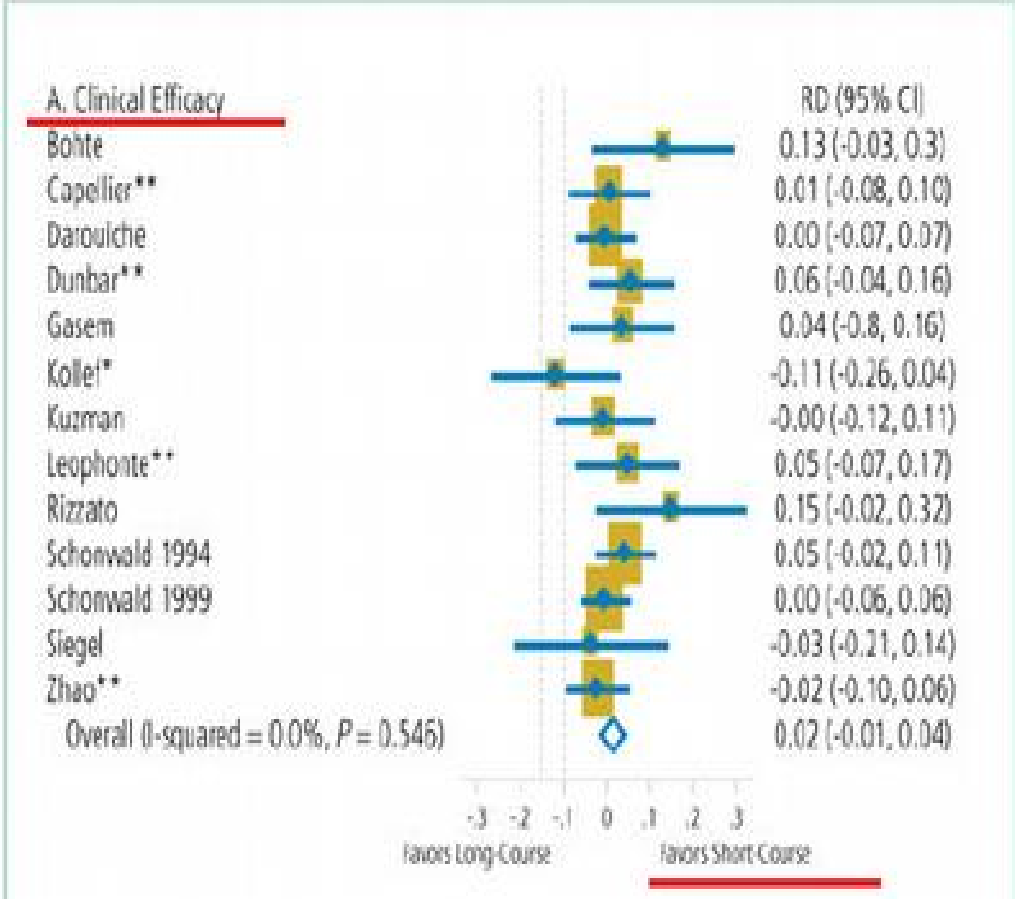
[2]Division of Hospital Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

[3]Department of Internal Medicine, University of Cincinnati, Cincinnati, Ohio



Conclusion

Shorter courses of ATB is safe

Including dg pneumonia, UTI, intra-abdominal inf

Without adverse effect on infection recurrence

Limited data- secondary infection or MDR organisms

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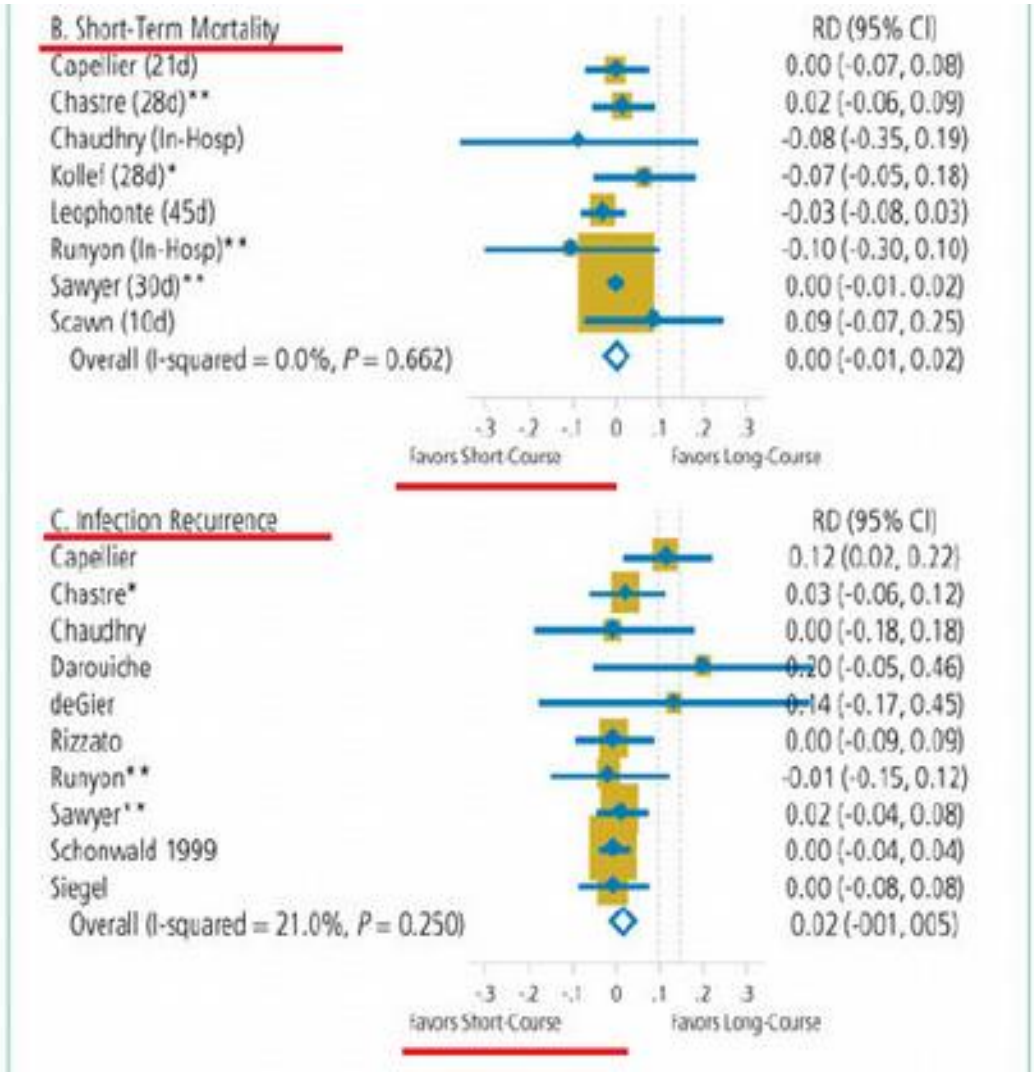

Jak je bezpečné zkrátit ATB terapii?

CAP (3) 5 dní
VAP (7) 8 dní
c-UTI (5) 7dní
IAI 5 dní

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Shorter Versus Longer Courses of Antibiotics for Infection in Hospitalized Patients: A Systematic Review and Meta-Analysis

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[1]Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan

[2]Division of Hospital Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

[3]Department of Internal Medicine, University of Cincinnati, Cincinnati, Ohio

Závisí na

lokalizaci infekce,
dostupnosti pro ATB,
pro chirurga
délce pobytu na ICU
kolonizaci MDR kmeny
přítomnosti
imunodeficitu

Jak je bezpečné zkrátit ATB terapii?

CAP (3) 5 dní
VAP (7) 8 dní
c-UTI (5) 7dní
IAI 5 dní

Intensive Care Med
https://doi.org/10.1007/s00134-018-5088-x

ORIGINAL

Short-course antibiotic therapy for critically ill patients treated for postoperative intra-abdominal infection: the DURAPOP randomised clinical trial

Philippe Montravers[1,18*], Florence Tubach[2], Thomas Lescot[3], Benoit Veber[4], Marina Esposito-Farèse[5], Philippe Seguin[6], Catherine Paugam[7], Alain Lepape[8], Claude Meistelman[9], Joel Cousson[10], Antoine Tesniere[11], Gaetan Plantefeve[12], Gilles Blasco[13], Karim Asehnoune[14], Samir Jaber[15], Sigismond Lasocki[16], Herve Dupont[17] and For the DURAPOP Trial Group

Zkracování ATB terapie: short course 4-5 dní u lehkých až středně závažných intra-abdominal-infekcí IAI

X pro závažné pooperační IAI (MODS)

ICU pacienti, infekční pooperační komplikace
Podmínkou je adekvátní ošetření zdroje

8 vs 10 dní

Kratší trvání ATB terapie efektivní a bezpečné

VIRULENCE
2017, VOL. 8, NO. 6, 658–672
https://doi.org/10.1080/21505594.2016.1226721

Taylor & Francis
Taylor & Francis Group

REVIEW

Antifungal stewardship considerations for adults and pediatrics

Rana F. Hamdy[a], Theoklis E. Zaoutis[b], and Susan K. Seo[c]

[a]Division of Infectious Diseases, Children's National Health System, Washington, DC, USA; [b]Division of Infectious Diseases, Department of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; [c]Department of Medicine, Infectious Disease Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA

IFI: 20 % sepsí (především Candida ICI, ¾ C albicans, ¼ nonalbicans- C glabrata, tropicalis)

Mortalita vysoká až 60%

Obtížná diagnostika, zpožděná terapie

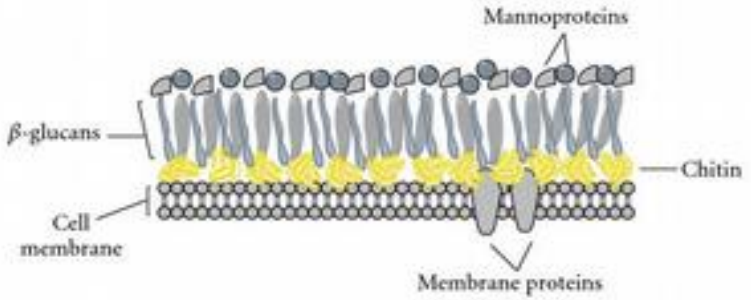
Empirická terapie při klinickém podezření:
teploty, hemodynamická nestabilita

RF ICI: ATB , CŽK, PEV, RRT, kortikosteroidy, onkolog nemocní, břišní chirurgie, pancreatitida…

Nadužívání antimykotik
Toxické
Drahé
NÚ, interakce
Nárůst rezistence (albicans- nonalbicans kmeny)

Antifungal stewardship

1. **Mikroskopie**
2. **Hemokultury**
   (pozdě, false negat až 50%)
3. **MALDI TOFF, PNA FISH**



Biomarkery
1,3- BDG, CAGTA
GM

BDG- early panfugal marker
Senzitivita 0,75 (¼ ICI falešně negat)
Falešná pozitivita (krevní deriváty, album,in, RRT, betalaktám ATB…)
Skvělá negat prediktivní hodnota:
Možná deeskalace

Jaffal et al. Ann. Intensive Care (2018) 8:49
https://doi.org/10.1186/s13613-018-0392-8

Annals of Intensive Care

RESEARCH Open Access

De-escalation of antifungal treatment in critically ill patients with suspected invasive *Candida* infection: incidence, associated factors, and safety

Karim Jaffal[1], Julien Poissy[1,2,3], Anahita Rouze[1,2,3], Sébastien Preau[1,2,3], Boualem Sendid[2,3,4], Marjorie Cornu[2,3,4] and Saad Nseir[1,2,3*]

Intensive Care Med (2017) 43:1668–1677
DOI 10.1007/s00134-017-4932-8

190 pacientů
20 % deeskalace

Z 13dní
na 6 dní

SEVEN-DAY PROFILE PUBLICATION

Biomarker-based strategy for early discontinuation of empirical antifungal treatment in critically ill patients: a randomized controlled trial

Anahita Rouzé[1,2,3], Séverine Loridant[1,2,4], Julien Poissy[1,2,3], Benoit Dervaux[5,6], Boualem Sendid[1,2,4], Marjorie Cornu[1,2,4] and Saad Nseir[1,2,3*] for the S-TAFE study group

109 pacientů
BDG

Zkrácení
z 13 na 6 dní

VIRULENCE
2017, VOL. 8, NO. 6, 658–672
https://doi.org/10.1080/21505594.2016.1226721

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REVIEW

Antifungal stewardship considerations for adults and pediatrics

Rana F. Hamdy[a], Theoklis E. Zaoutis[b], and Susan K. Seo[c]

[a]Division of Infectious Diseases, Children's National Health System, Washington, DC, USA; [b]Division of Infectious Diseases, Department of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; [c]Department of Medicine, Infectious Disease Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Antifungal de- escalation (ICI)
Echinocandin or amphotericin to fluconazole

Within 5-7 days

BDG + a PCT –

(≥80 pg/ml)(<2ng/ml)

=

Invazívní kandidóza

(PPV 96%)

Giacobbe et al. Critical Care (2017) 21:176
DOI 10.1186/s13054-017-1763-5

Critical Care

RESEARCH Open Access

Combined use of serum (1,3)-β-D-glucan and procalcitonin for the early differential diagnosis between candidaemia and bacteraemia in intensive care units

Daniele Roberto Giacobbe[1*†], Malgorzata Mikulska[1†], Mario Tumbarello[2], Elisa Furfaro[1], Marzia Spadaro[1], Angela Raffaella Losito[2], Alessio Mesini[1], Gennaro De Pascale[3], Anna Marchese[4], Marco Bruzzone[5], Paolo Pelosi[6,7], Michele Mussap[8], Alexandre Molin[8], Massimo Antonelli[3], Brunella Posteraro[9], Maurizio Sanguinetti[10], Claudio Viscoli[1], Valerio Del Bono[1] and on behalf of ISGRI-SITA (Italian Study Group on Resistant Infections of the Società Italiana Terapia Antinfettiva)

Abstract

Background: This study aimed to assess the combined performance of serum (1,3)-β-D-glucan (BDG) and procalcitonin (PCT) for the differential diagnosis between candidaemia and bacteraemia in three intensive care units (ICUs) in two large teaching hospitals in Italy.

Methods: From June 2014 to December 2015, all adult patients admitted to the ICU who had a culture-proven candidaemia or bacteraemia, as well as BDG and PCT measured closely to the time of the index culture, were included in the study. The diagnostic performance of BDG and PCT, used either separately or in combination, was assessed by calculating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and positive and negative likelihood ratios (LR+ and LR–). Changes from pre-test probabilities to post-test probabilities of candidaemia and bacteraemia were inferred from Fagan's nomograms.

Results: One hundred and sixty-six patients were included, 73 with candidaemia (44%) and 93 with bacteraemia (56%). When both markers indicated candidaemia (BDG ≥80 pg/ml and PCT <2 ng/ml) they showed higher PPV (96%) compared to 79% and 66% for BDG or PCT alone, respectively. When both markers indicated bacteraemia (BDG <80 pg/ml and PCT ≥2 ng/ml), their NPV for candidaemia was similar to that of BDG used alone (95% vs. 93%). Discordant BDG and PCT results (i.e. one indicating candidaemia and the other bacteraemia) only slightly altered the pre-test probabilities of the two diseases.

Conclusions: The combined use of PCT and BDG could be helpful in the diagnostic workflow for critically ill patients with suspected candidaemia.

Keywords: *Candida*, Bloodstream infections, BSI, Sepsis, Fungal antigens, Non-culture-based methods, Biomarker, Critically ill patients

RESEARCH ARTICLE

Increased presepsin levels are associated with the severity of fungal bloodstream infections

Yuuki Bamba, Hiroshi Moro*, Nobumasa Aoki, Takeshi Koizumi, Yasuyoshi Ohshima, Satoshi Watanabe, Takuro Sakagami, Toshiyuki Koya, Toshinori Takada, Toshiaki Kikuchi

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PLOS ONE, 2018

Results

Presepsin was increased in 11 patients with fungal bloodstream infections. Serial measurement of presepsin levels demonstrated a prompt decrease in 7 patients in whom treatment was effective, but no decrease or further increase in the patients with poor improvement.

Conclusions

Cut off 560 pg/ml

Plasma presepsin levels increased in patients with fungal bloodstream infection, with positive association with the disease severity. Presepsin could be a useful biomarker of sepsis secondary to fungal infections.

Retrospective data from ClinicalTrials.gov ID: NCT03584594 study in ICU patients with candidemia and control bacteriemia group from University Hospital and City Hospital in Ostrava (Czechia)

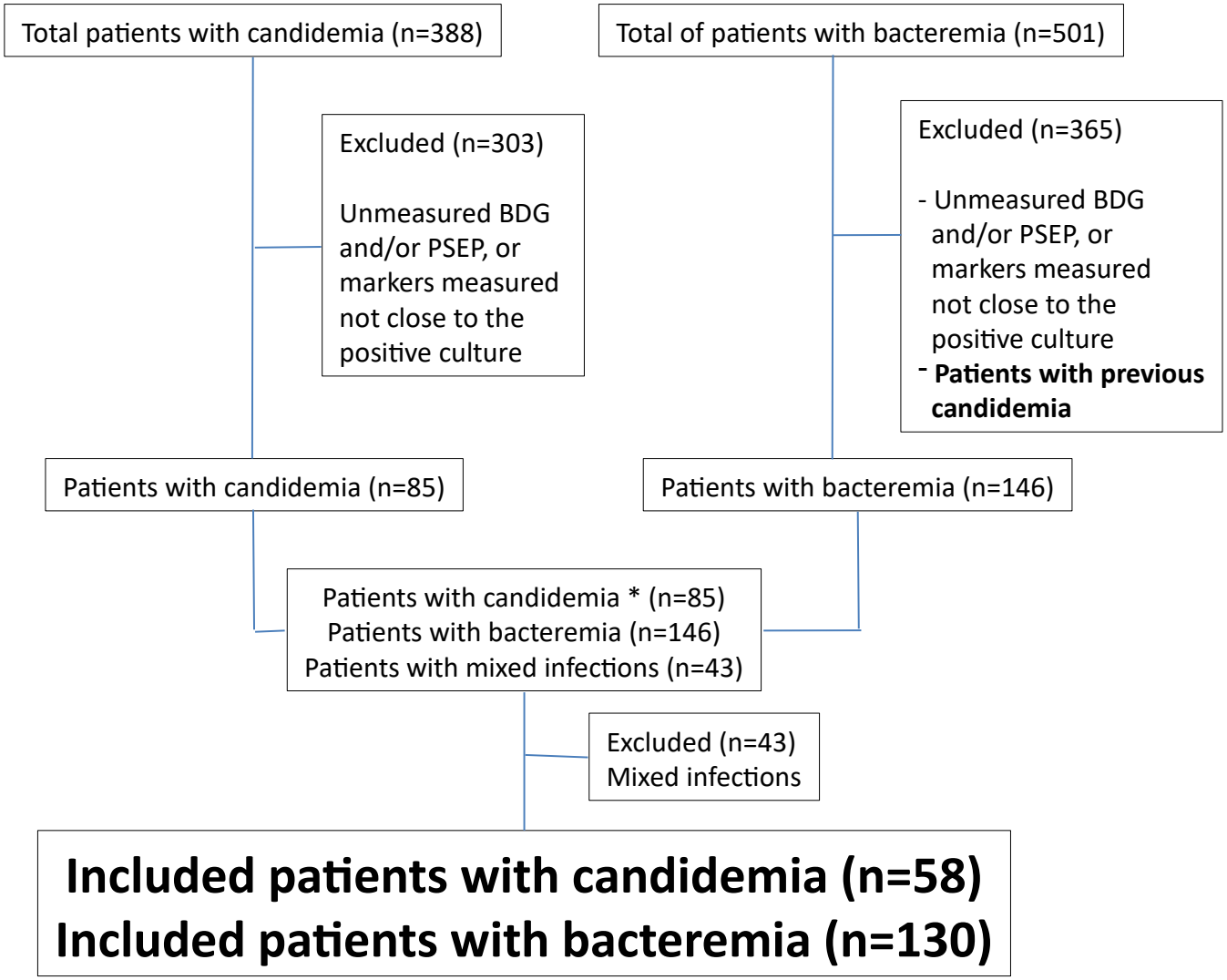
We used 2 biomarkers PSEP and 1,3-BGG

- **PSEP** measured 24 hours before or after the *Candida* spp. positive blood culture
- Values of serum **BDG** measured 48 hours before or after the *Candida* spp. positive blood culture

Sequential Organ Failure Assessment (SOFA) score of 2 or more who were admitted to our ICU´s from January 2018 to November 2019. Exclusion criteria were age <18 years, and a SOFA score of <2

Dobiáš R.

Inclusion criteria of 889 ICU patients with positive blood culture during the period 2018-2019

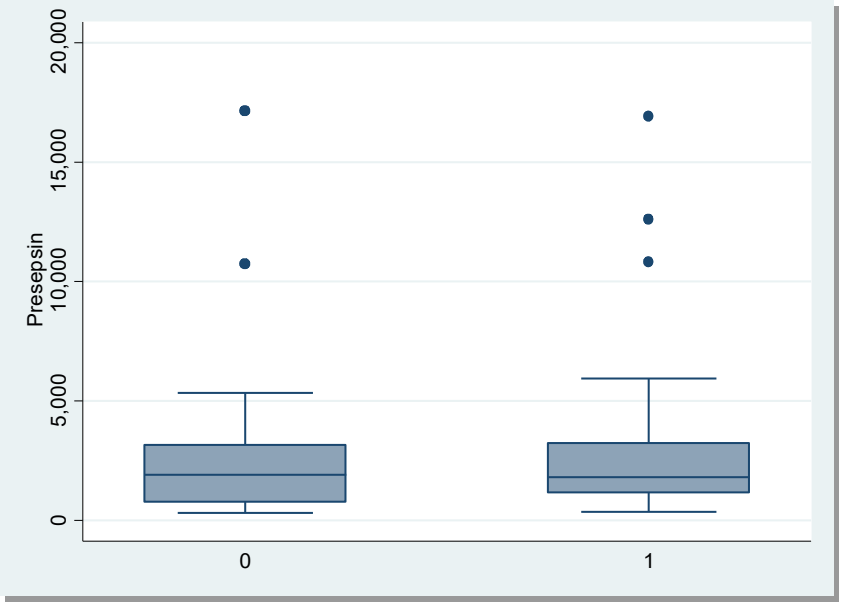


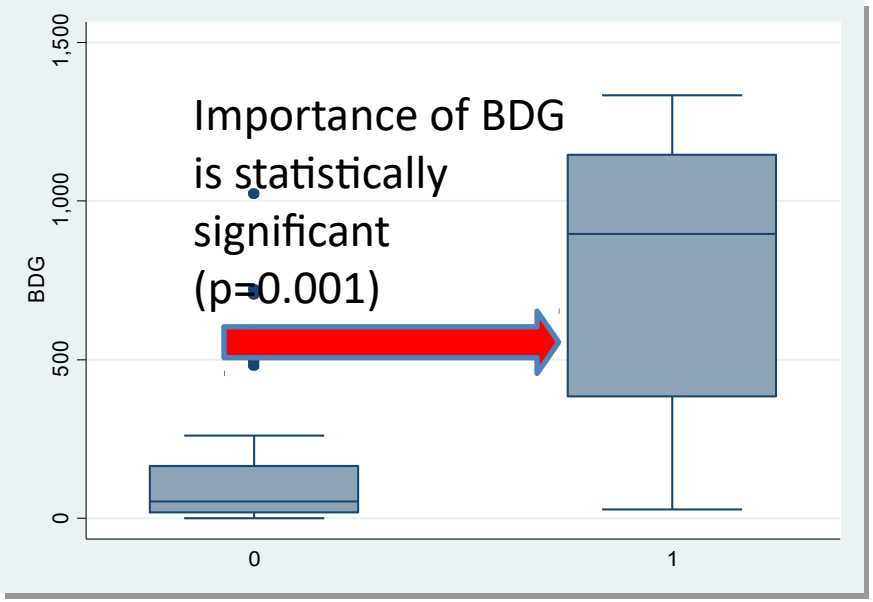
* 20% of included patients with candidemia (17/85) had previous bacteremia not meeteing inclusion criteria

ICU patients with positive blood culture during the period 2018-2019
Included patients with candidemia (n=58)
Included patients with bacteremia (n=130)

Elevation of serum BDG indicates invasive candidiasis

In combination of high levels of PSEP can indicate sepsis due to Candida species

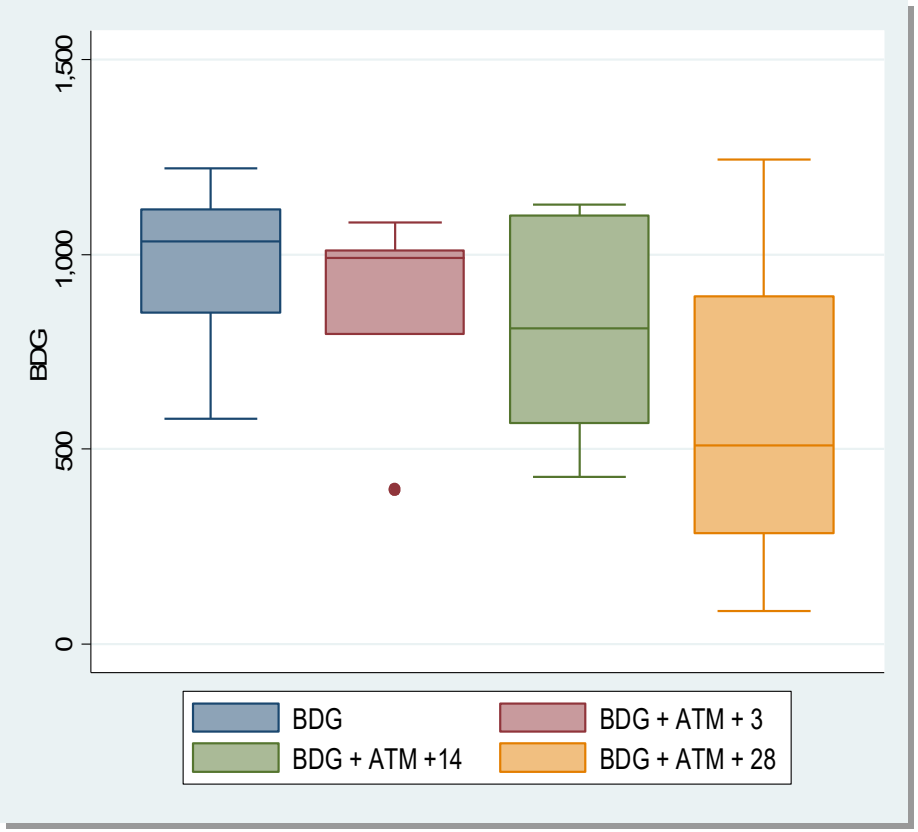


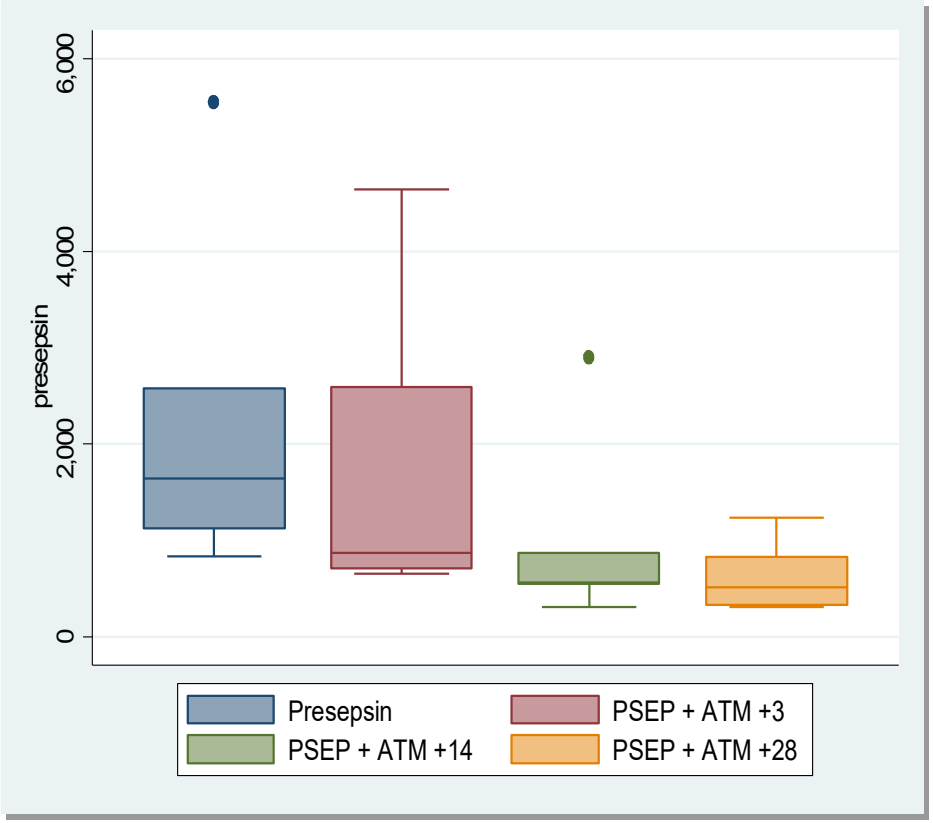


Double positivity (BDG+PSEP)
Specificity of 79.4 %

Single negativity (BDG)
NPV of 82.8 %

5 patient was measured in 4 time points of BDG and PSEP

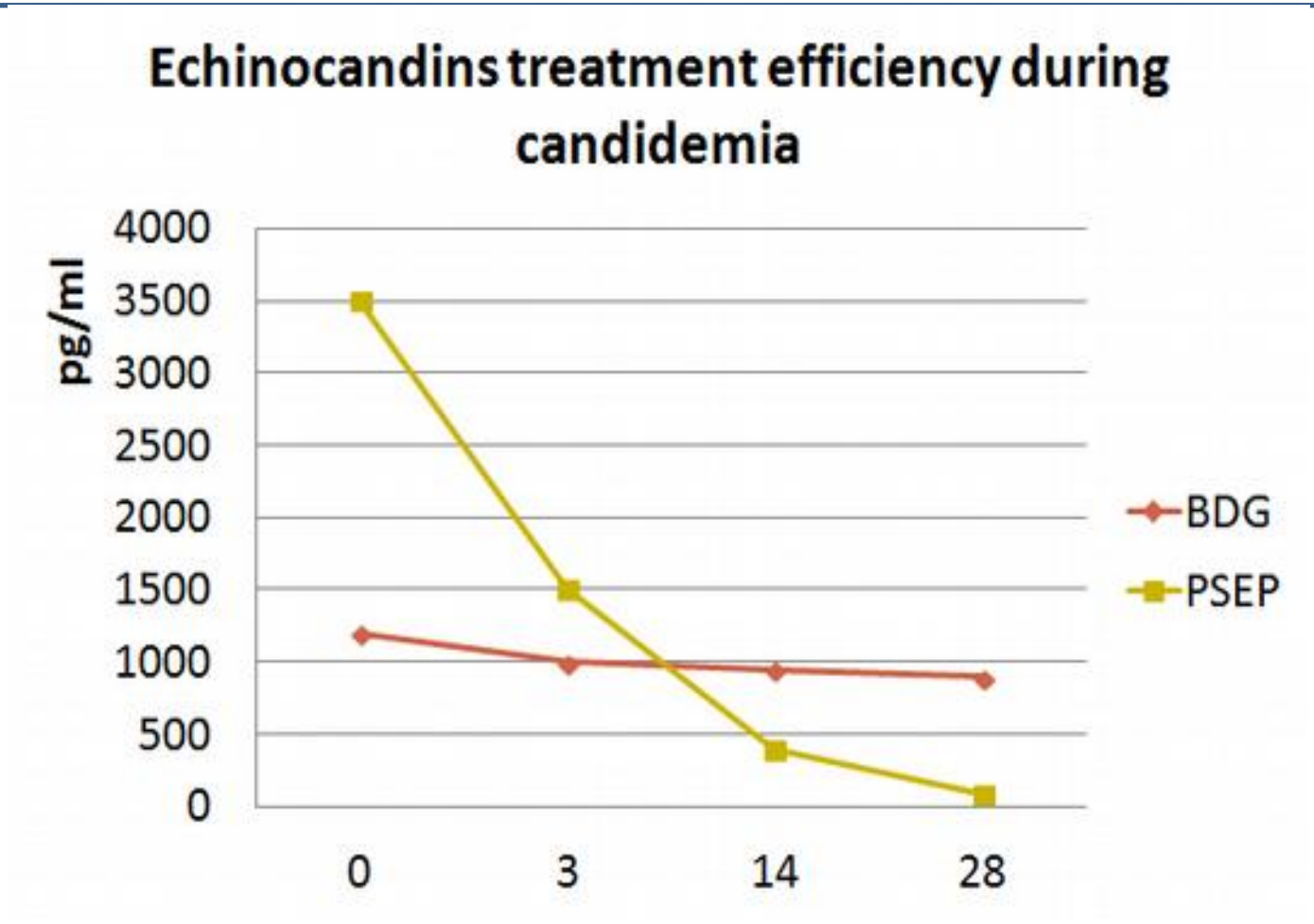




The statistically significant decrease (p = 0. 043) in the concentrations of BDG begins only after 28 days of the antimycotic treatment

The statistically significant decrease in the concentrations of PSEP begins early, after 14 days (p=0.043) of the antimycotic treatment and persists after 28 days (p=0.043).

Could we use decreasing of PSEP concentration in antifungal therapy by echinocandins for possible de-escalation to azole therapy?



Kombinace pozitivního BDG a pozitiv PSEP
by mohl lépe predikovat kvasinkovou sepsi
než kombinace BDG a PCT

Pokles PSEP se zdá dá využít k deeskalaci antimykotik

“start broadly, narrow quickly,
if they don’t need it get rid of it”

As soon as possible

DĚKUJI ZA POZORNOST