Daha Kısa Tedaviler Mümkün mü?

İntraabdominal İnfeksiyonlar

Dr. A. Seza İnal
Çukurova Üniversitesi Tıp Fakültesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji ABD

İntraabdominal Enfeksiyonların Sınıflandırması

- Toplumda Edinilmiş
  - Primer peritonit
  - Sekonder peritonit (spontan, posttravmatik)

- Sağlık hizmetler ile ilişkili
  - Kontinü Ambulatuvar Peritoneal Diyaliz (CAPD)
  - Sekonder peritonit (Postoperatif)
  - Tersiyer peritonit
    - Rekürren/Persistan enfeksiyon

İntraabdominal İnfeksiyonlar

- Komplike
- Ankomplike

İntraabdominal İnfeksiyonlar

Nedeni:

- Gastrointestinal kanal bütünlüğünün
  - Bozulması
  - İnflamasyonu

  Daha seyrek olarak:
  - Jinekolojik
  - Üriner sistem

İntraabdominal İnfeksiyonlar

Bakteriyoloji	%
• Aeroplar	17
• Anaeroplar	1
• Anaerop + Aerop	82

Polimikrobiyal

İntraabdominal İnfeksiyonlar

- Koliformlar
  - *Escherichia coli*
  - *Klebsiella* spp
  - *Proteus* spp
  - *Enterobacter* spp
- Streptokoklar
- Enterokoklar
- Anaerop bakteriler

İntraabdominal İnfeksiyonlar

Tedavi:

- Kaynak kontrolü
  - Cerrahi
  - Perkütan drenaj
- Antimikrobiyal
  - Mikrobiyolojik inceleme
  - Ampirik

Solomkin Clin Infect Dis 2010;50:133
Sartelli World J Emerg Surg 2013;8:3
Rhodes Crit Care Med 2017;45:486

İntraabdominal İnfeksiyonlar

- Ayrıca:
  - İnfeksiyonun yerleşimi ve tipi
    - Anaeroplar üst GİS için nispeten önemsiz
  - Cerrahi işlem yapılacak mı?
  - Bölgesel olarak Enterobacteriacea direnci
  - Hastanın toleransı (dayanma gücü)

Solomkin Clin Infect Dis 2010;50:133
Rhodes Crit Care Med 2017;45:486

İntraabdominal İnfeksiyonlar

Geniş Spektrumlu Tedavi Seçerken…

- Toplum kökenli x Hastane
- Dirençli bakteri riski?
  - Dirençli mikroorganizma yoğun olan yerde yaşama

Solomkin Clin Infect Dis 2010;50:133
Rhodes Crit Care Med 2017;45:486

İntraabdominal İnfeksiyonlar

Geniş Spektrumlu Tedavi Seçerken…

- Toplum kökenli x Hastane
- Dirençli bakteri riski?
  - Dirençli mikroorganizma yoğun olan yerde yaşama
- Prognoz kötü olabilir mi?
  - 70 yaş
  - Tedavinin başlanma zamanı >24 saat
  - Cerrahi gecikme
  - Komorbidite (KBY, Kc hast, malignansi)
  - İmmünkompromize hasta (Kötü kontrollü DM, nötropeni, ileri HIV vb)
  - Organ disfonksiyonu
  - Peritonun yaygın tutulumu
  - Düşük albumin
  - Beslenme bozukluğu

Solomkin Clin Infect Dis 2010;50:133
Rhodes Crit Care Med 2017;45:486

İntraabdominal İnfeksiyonlar

Toplum Kökenli İAİ (Safra yolları Hariç)

Tedavi	Hafif-orta riskli	Yüksek riskli ya da ciddi
Monoterapi	Sefoksitin, tigesiklin, ertapenem, moksifloksasin, tikarsilin-klavulanik asit	İmipenem, meropenem, doripenem, piperasilin-tazobaktam
Kombine terapi	Metronidazol + sefazolin, sefuroksim, seftriakson, sefotaksim, siprofloksasin, levofloksasin	Metronidazol + sefepim, seftazidim, siprofloksasin, levofloksasin

Kolesistitle Birlikte İAİ

Toplum kökenli hafif/orta kolesistit	Sefazolin, sefuroksim, seftriakson
Toplum kökenli ciddi kolesistit *ileri yaş, immünsüpresyon* Biliyo-enterik anastomoz	İmipenem, meropenem, doripenem, piperasilin-tazobaktam, siprofloksasin/levofloksasin + metronidazol, sefepim + metronidazol
Hastane kökenli kolesistit	İmipenem, meropenem, doripenem, piperasilin-tazobaktam, siprofloksasin/levofloksasin + metronidazol, sefepim + metronidazol + vankomisin

Solomkin Clin Infect Dis 2010;50:133
Sartelli World J Emerg Surg 2013;8:3
Rhodes Crit Care Med 2017;45:486

İntraabdominal İnfeksiyonlar

Yüksek Riskli Grupta Etken Hastane Kökenli mi?

- *P. aeruginosa*
- Enterobacteriacea
- Enterokoklar
- Anaeroplar

Monoterapi

- İmipenem
- Meropenem
- Doripenem
- Piperasilin-tazobaktam

Kombinasyon

- Sefepim
- Seftazidim

+ Metronidazol

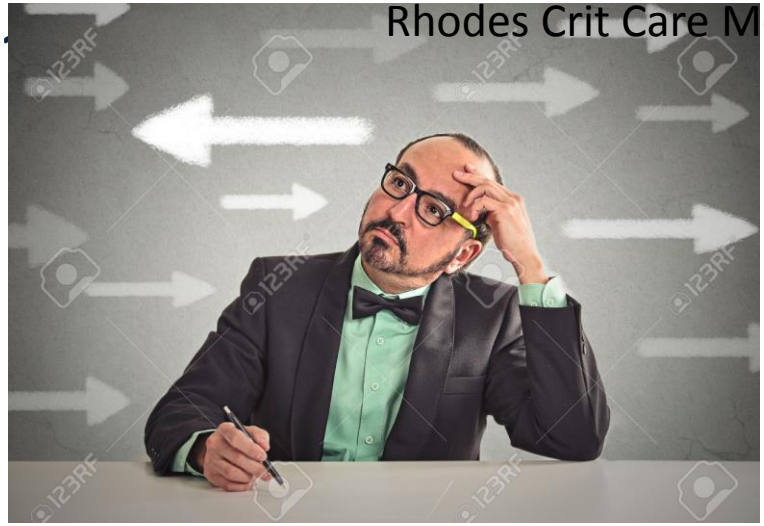
- VRE? Linezolid/Daptomisin
- MRSA? Vankomisin

Solomkin Clin Infect Dis 2010;50:133
Sartelli World J Emerg Surg 2013;8:3
Rhodes Crit Care Med 2017;45:486

İntraabdominal İnfeksiyonlar

- Tedavi başlanması
  - Muhtemel bakteriyel, fungal, hatta viral etkene
  - *Mümkün olan en erken dönemde*
- Tedavi süresi

Solomkin Clin Infect Dis 2010;50:133
Sartelli World J Emerg Surg 2013;8:3
Rhodes Crit Care Med 2017;45:486



İntraabdominal İnfeksiyonlar

- Tedavi süresi ?
  - IDSA Kılavuzu: 4-7 gün

Solomkin Clin Infect Dis 2010;50:133

  - Pratikte Karar: iyileşme süresi 7-14 gün
  - Gözlem: 10-14 gün

Riccio Surg Infect 2014;15:417
Guirao J Antimicrob Chemother 2013;68 Suppl2:ii37
Samuelsson Scand J Infect Dis 2012;44:820.

İntraabdominal İnfeksiyonlar

- Uzun Süreli Tedavi Gerekebilir:
  - Kaynak kontrolü yetersiz: Hastaya göre!
  - Ankomplike apandisit
    - Acil cerrahi gerekmeyen
    - 10 güne uzatın

Livingston JAMA 2015;313:2327

  - Enfekte materyalin drenajı için kateter yerleşmişse
    - Drenaj yeterince azalana kadar
    - En az 2 hafta

İntraabdominal İnfeksiyonlar

- Tedavi süresinin etkileyen faktör
  - Kaynak kontrolü

Solomkin Clin Infect Dis 2010;50:133
Sartelli World J Emerg Surg 2013;8:3
Rhodes Crit Care Med 2017;45:486
Schein World J Surg 2004;28:638

İntraabdominal İnfeksiyonlar

- Postoperatif iyileşme takibi
  - 65 intraabdominal sepsis

  Ateş, lökositoz : Enfeksiyon bulguları

  Antibiyotiğe devam
  - BK ≥ 10.000 /mm^3
  - Ateş > 37,6^oC
  - p <0,005

Lennard Ann Surg 1982;195:19

İntraabdominal İnfeksiyonlar

World J. Surg. 28, 638–645, 2004
DOI: 10.1007/s00268-004-7505-2

WORLD
Journal of
SURGERY

Editorial Update

Source Control for Surgical Infections

Moshe Schein, M.D.,[1] John Marshall, M.D.[2]

[1]Department of Surgery, Bronx Lebanon Hospital Center, 1650 Selwyn Avenue, 4th Floor, Suite 4F, Bronx, New York 10457, USA
[2]Department of Surgery, Toronto General Hospital, 200 Elizabeth Street, Toronto, Ontario, Canada

Published Online: June 8, 2004

Abstract. The concept of source control encompasses all of the physical interventions, surgical and otherwise, that are used to treat infection. Although source control is one of the most important aspects of the treatment of serious infection, it has received relatively little attention. It is the topic of this overview, which draws heavily on a book we edited recently: *Source Control: A Guide to the Management of Surgical Infection* (Springer-Verlag, 2002). The first section focuses on general considerations: historical perspective, scientific basis, and surgical principles of source control. The second section highlights specific considerations of source control in various situations.

early decades of the twentieth century [3]. Specific antimicrobial therapy did not become practical until World War II and the ensuing decades [4–6]. Successful modulation of the host response elicited by infection remains a largely unfulfilled dream, although recent promise has been shown by a variety of strategies [7, 8].

The surgical management of infection dates to antiquity. Evidence of trephination has been identified in skulls that are upward of 10,000 years old, and the management of abscesses and infected

İntraabdominal İnfeksiyonlar

BJS

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Original Article

Minimal antibiotic therapy after emergency abdominal surgery: A prospective study

Dr M. Schein ✉, A. Assalia, H. Bachus

First published: July 1994 Full publication history

DOI: 10.1002/bjs.1800810720 View/save citation

Cited by: 58 articles Citation tools

View issue TOC
Volume 81, Issue 7
July 1994
Pages 989–991

- Diffüz peritonitli 23 hasta
- 4 grup
  - Antibiyotiksiz
  - 24 st
  - 48 st
  - 72st-5 gün

emergency abdominal
ion was based on the
gree of the latter. A total of
groups: group 1 (60 patients),
24 h; group 3 (48),
72 h to 5 days. Three patients
er cent) and postoperative
topped according to the
ed a subhepatic abscess and
infection and operative
erative antibiotic policy to be

Schein Br J Surg 1994;372:1996

İntraabdominal İnfeksiyonlar

- Prospektif, randomize, kontrollü
  - 111 hasta
  - Ertapenem

	Kür	Eradikasyon
• 3 gün	%93	%95
• ≥5 gün	%90	%94

Basoli J Gastroenterol Surg 2008;12:592

İntraabdominal İnfeksiyonlar

- Retrospektif
  - Virginia Health System Records
  - 5561 genel cerrahi işlemi
  - 4470 hastada yüksek ateş veya lökositoz

  1. Toplam antibiyotik süresi
  2. Ateş ve lökositoz düzeltikten sonra ted süresi

  En azdan en fazla olana göre sıralamış

  4 Gruba ayrılarak karşılaştırılmış

  Sonuç: Kısa süre tedavi verilen grupta komplikasyon benzer veya daha az

Hedrick Surg Infect 2006;7:419

SURGICAL INFECTIONS
Volume 15, Number 4, 2014

DOI: 10.1089/sur.2012.077

Association of Excessive Duration of Antibiotic Therapy for Intra-Abdominal Infection with Subsequent Extra-Abdominal Infection and Death: A Study of 2,552 Consecutive Infections

Lin M. Riccio, Kimberley A. Popovsky, Tjasa Hranjec, Amani D. Politano, Laura H. Rosenberger, Kristin C. Tura, and Robert G. Sawyer

Abstract

Background: We hypothesized that a longer duration of antibiotic treatment for intra-abdominal infections (IAI) would be associated with an increased risk of extra-abdominal infections (EAI) and high mortality.
Methods: We reviewed all IAI occurring in a single institution between 1997 and 2010. The IAI were divided into two groups consisting of those with a subsequent EAI and those without; the data for each group were analyzed. Patients with EAI following IAI were matched in a 1:2 ratio with patients who did not develop EAI on the basis of their Acute Physiology and Chronic Health Evaluation (APACHE II) score ± 1 point. Statistical analyses were done with the Student *t*-test, χ^2 analysis, Wilcoxon rank sum test, and multi-variable analysis.
Results: We identified 2,552 IAI, of which 549 (21.5%) were followed by EAI. Those IAI that were followed by EAI were associated with a longer initial duration of antimicrobial therapy than were IAI without subsequent EAI (median 14 d [inter-quartile range (IQR) 10–22 d], vs. 10 d [IQR 6–15 d], respectively, $p < 0.01$), a higher APACHE II score (16.6 ± 0.3 vs. 11.2 ± 0.2 points, $p < 0.01$), and higher in-hospital mortality (17.1% vs. 5.4%, $p < 0.01$). The rate of EAI following IAI in patients treated initially with antibiotics for 0–7 d was 13.3%, vs. 25.1% in patients treated initially for >7 d ($p < 0.01$). A successful match was made of 469 patients with subsequent EAI to 938 patients without subsequent EAI, resulting in a mean APACHE II score of 15.2 for each group. After matching, IAI followed by EAI were associated with a longer duration of initial antimicrobial therapy than were IAI without subsequent EAI (median 14 d [9–22 d], vs. 11 d [7–16 d], respectively, $p < 0.01$), and with a higher in-hospital mortality (14.9% vs. 9.0%, respectively, $p < 0.01$). Logistic regression showed that days of antimicrobial therapy for IAI was an independent predictor of subsequent EAI ($p < 0.001$).
Conclusions: A longer duration of antibiotic therapy for IAI is associated with an increased risk of subsequent EAI and increased mortality.

İntraabdominal İnfeksiyonlar

Hipotez:

İAİ için uzun süreli antibiyotik tedavisi yeni İAİ oranını ve mortaliteyi artırıyor!?

- 1997- 2010: 2552 İAİ
- Yeniden İAİ 549 (%21,5)

	Yeni İAİ gelişmeyen	x	Yeni İAİ Gelişen	
Medyan	10 gün (10-22 g)		14 gün (6-15)	P<0,01
Mortalite	%9		%14,9	P<0,01

- Ortalama 14 gün daha uzun antibiyotik

Riccio Surg Infect 2013;15:417

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection

R.G. Sawyer, J.A. Claridge, A.B. Nathens, O.D. Rotstein, T.M. Duane, H.L. Evans, C.H. Cook, P.J. O'Neill, J.E. Mazuski, R. Askari, M.A. Wilson, L.M. Napolitano, N. Namias, P.R. Miller, E.P. Dellinger, C.M. Watson, R. Coimbra, D.L. Dent, S.F. Lowry,* C.S. Cocanour, M.A. West, K.L. Banton, W.G. Cheadle, P.A. Lipsett, C.A. Guidry, and K. Popovsky

İntraabdominal İnfeksiyonlar için Kısa Süreli Antimikrobiyal Tedavi Denemesi

* Deceased.

N Engl J Med 2015;372:1996-2005.
DOI: 10.1056/NEJMoa1411162

adequate source control to receive antibiotics until 2 days after the resolution of fever, leukocytosis, and ileus, with a maximum of 10 days of therapy (control group), or to receive a fixed course of antibiotics (experimental group) for 4±1 calendar days. The primary outcome was a composite of surgical-site infection, recurrent intraabdominal infection, or death within 30 days after the index source-control procedure, according to treatment group. Secondary outcomes included the duration of therapy and rates of subsequent infections.

İntraabdominal İnfeksiyonlar

- STOP-IT
  - Study To Optimize Peritoneal Infection Therapy
  - Komplike İAİ
  - Yeterli kaynak kontrolü
- Hipotez: Yeterli kaynak kontrolünden sonra sabit 4 gün antibiyotik tedavisi yeterlidir
- Geleneksel görüş: SIRS ile ilişkili anormallikler düzeldikten 2 gün sonrasına kadar verilmeli

Sawyer N Engl J Med 2015;372:1996

İntraabdominal İnfeksiyonlar

- Ağustos 2008-Ağustos 2013
- 518 hasta
- Antibiyotik gruplarına randomizasyon

1. Olgu grubu: Sabit süre: 4±1 gün
2. Kontrol grubu: SIRS bulgularının düzeldiği maks 10 günlük süre
   - Ateş, lökositoz, ileus

Sawyer N Engl J Med 2015;372:1996

İntraabdominal İnfeksiyonlar

Table 1. Baseline Demographic and Clinical Characteristics, According to Study Group.*

Variable	Control Group (N=260)	Experimental Group (N=258)
Age — yr	52.2±1.0	52.2±1.0
Male sex — no. (%)	145 (55.8)	144 (55.8)
Race or ethnic group — no. (%)†		
White	208 (80.0)	196 (76.0)
Black	43 (16.5)	51 (19.8)
Asian	5 (1.9)	6 (2.3)
American Indian or Alaskan Native	2 (0.8)	1 (0.4)
Hispanic — no. (%)	20 (7.7)	15 (5.8)
Other	2 (0.8)	4 (1.6)
Characteristics of index infection		
APACHE II score‡	9.9±0.4	10.3±0.4
Maximum white-cell count — per mm^3	15,600±0.4	17,100±0.7
Maximum body temperature — °C	37.8±0.1	37.7±0.1
Organ of origin — no. (%)		
Colon or rectum	80 (30.8)	97 (37.6)
Appendix	34 (13.1)	39 (15.1)
Small bowel	31 (11.9)	42 (16.3)
Source-control procedure — no. (%)		
Percutaneous drainage	86 (33.1)	86 (33.3)
Resection and anastomosis or closure	69 (26.5)	64 (24.8)
Surgical drainage only	55 (21.2)	54 (20.9)
Resection and proximal diversion	27 (10.4)	37 (14.3)
Simple closure	20 (7.7)	12 (4.7)
Surgical drainage and diversion	3 (1.2)	4 (1.6)

Sawyer N Engl J Med 2015;372:1996

İntraabdominal İnfeksiyonlar

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Sawyer N Engl J Med 2015;372:1996

İntraabdominal İnfeksiyonlar

- Birincil Sonlanım Noktası :
  - Cerrahi alan infeksiyonu
  - Tekrarlayan İAİ
  - Ölüm
- Olgu 56/257 % 21,8
- Kontrol 58/257 % 22,3
  - %95 CI, -7.0 ila -8.0; P0,92

Sawyer N Engl J Med 2015;372:1996

İntraabdominal İnfeksiyonlar

Secondary outcome	Control Group (N = 260)	Experimental Group (N = 257)	P Value
Surgical-site infection or recurrent intraabdominal infection with resistant pathogen — no. (%)	9 (3.5)	6 (2.3)	0.62
Site of extraabdominal infection — no. (%)			
Any site†	13 (5.0)	23 (8.9)	0.11
Urine	10 (3.8)	13 (5.1)	0.65
Blood	3 (1.2)	5 (1.9)	0.71
Lung	3 (1.2)	3 (1.2)	0.99
Area of skin other than surgical site	1 (0.4)	4 (1.6)	0.36
Vascular catheter	0 (0)	2 (0.8)	0.47
Clostridium difficile infection — no. (%)	3 (1.2)	5 (1.9)	0.71
Extraabdominal infection with resistant pathogen — no. (%)	6 (2.3)	2 (0.8)	0.29
Duration of outcome — days			
Antimicrobial therapy for index infection			<0.001
Median	8	4	
Interquartile range	5–10	4–5	
Antimicrobial-free days at 30 days			<0.001
Median	21	25	
Interquartile range	18–25	21–26	
Hospitalization after index procedure			0.48
Median	7	7	
Interquartile range	4–11	4–11	
Hospital-free days at 30 days			0.22
Median	23	22	
Interquartile range	18–26	16–26	

Sawyer N Engl J Med 2015;372:1996

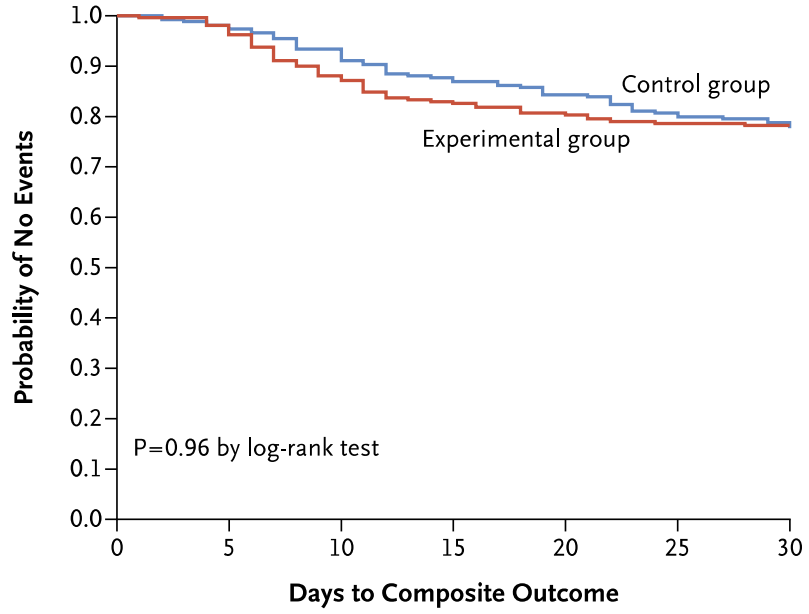
İntraabdominal İnfeksiyonlar

Table 2. Primary and Major Secondary Outcomes.*

Variable	Control Group (N=260)	Experimental Group (N=257)	P Value
Primary outcome: surgical-site infection, recurrent intraabdominal infection, or death — no. (%)	58 (22.3)	56 (21.8)	0.92
Surgical-site infection	23 (8.8)	17 (6.6)	0.43
Recurrent intraabdominal infection	36 (13.8)	40 (15.6)	0.67
Death	2 (0.8)	3 (1.2)	0.99
Time to event — no. of days after index source-control procedure			
Diagnosis of surgical-site infection	15.1±0.6	8.8±0.4	<0.001
Diagnosis of recurrent intraabdominal infection	15.1±0.5	10.8±0.4	<0.001
Death	19.0±1.0	18.5±0.5	0.66

Sawyer N Engl J Med 2015;372:1996

İntraabdominal İnfeksiyonlar



No. at Risk							
Control group	260	255	243	228	219	210	205
Experimental group	258	253	227	214	208	203	202

Figure 2. Kaplan–Meier Time-to-Event Curves for the Composite Primary Outcome, According to Treatment Group.

The composite primary outcome was surgical-site infection, recurrent intraabdominal infection, or death.

- Mortalite %1
- APACHE II 10

Sawyer N Engl J Med 2015;372:1996

İntraabdominal İnfeksiyonlar

CRP

- Ucuz
- Kolay
- Hızlı
- Nonspesifik
  - Cerrahi
  - Travma

Prokalsitonin

- Sepsis ayırımında iyi
- Pahalı
- Yaygın değil

- Tedaviye yanıtı değerlendirme?

Sartelli Surg Infect 2016;17:9

İntraabdominal İnfeksiyonlar

- 1996-2011 46 çalışma: Prokalsitonin
  - Pubmed ve Google Scholar
- 39 olumlu, 7 olumsuz
- Sepsiste antibiyotik deeskalasyonu veya kesilmesi
- 4 çalışma

Sridharan Surg Infect 2013;14:1

İntraabdominal İnfeksiyonlar

Study, year	Total no. of patients	PCT Arm			Control Arm			*p value (treatment duration)
		No. of patients	Treatment duration (d)	Mortality† n (%)	No. of patients	Treatment duration (d)	Mortality†, n (%)	
Nobre et al., 2007 [72][a]	68	31	6 (95% CI (days) 4–16)	5 (16%)	37	10 (95% CI 3,33) d	6 (16%)	=0.003
Hochreiter et al., 2009 [73][b]	110	57	5.9±1.7 d	15 (26%)	53	7.9±0.5 d	14 (26%)	<0.001
Schroeder et al., 2009 [74][c]	27	14	6.6±1.1 d	3 (21%)	13	8.3±0.7 d	3 (23%)	<0.001
Bouadma et al., 2010 [75][d]	621	307	14.3±9.1 d w/o ABx	65 (21%)	314	11.6±8.2 d w/o Abx	64 (20%)	<0.0001

Sridharan Surg Infect 2013;14:1

İntraabdominal İnfeksiyonlar

- Ekim 2006-Nisan 2007
- 27 ağır sepsis

Antibiyotik Süresi

- 14 Pct 6,6 ± 1 gün
- 13 kontrol 8,3 ±0,7 gün P<0,001

Schroeder Langenbeck Arch Surg 2009;14:221

İntraabdominal İnfeksiyonlar

- Ocak 2006 - Mart 2007
- 110 cerrahi yoğun bakım
  - Pnömoni
  - Peritonit
  - Yumuşak doku enf
  - Ürosepsis

Antibiyotik Süresi

- 57 Pct 5,9 ± 1,7 gün
- 13 kontrol 7,9 ± 0,5 gün P<0,001

Hochreiter Crit Care 2009;13:R83

İntraabdominal İnfeksiyonlar

Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial

Lila Bouadma, Charles-Edouard Luyt, Florence Tubach, Christophe Cracco, Antonio Alvarez, Carole Schwebel, Frédérique Schortgen, Sigismond Lasocki, Benoît Veber, Monique Dehoux, Maguy Bernard, Blandine Pasquet, Bernard Régnier, Christian Brun-Buisson, Jean Chastre, Michel Wolff,* for the PRORATA trial group†*

Summary

Background Reduced duration of antibiotic treatment might contain the emergence of multidrug-resistant bacteria in intensive care units. We aimed to establish the effectiveness of an algorithm based on the biomarker procalcitonin to reduce antibiotic exposure in this setting.

Methods In this multicentre, prospective, parallel-group, open-label trial, we used an independent, computer-generated randomisation sequence to randomly assign patients in a 1:1 ratio to procalcitonin (n=311 patients) or control (n=319) groups; investigators were masked to assignment before, but not after, randomisation. For the procalcitonin group, antibiotics were started or stopped based on predefined cut-off ranges of procalcitonin concentrations; the control group received antibiotics according to present guidelines. Drug selection and the final decision to start or stop antibiotics were at the discretion of the physician. Patients were expected to stay in the intensive care unit for more than 3 days, had suspected bacterial infections, and were aged 18 years or older. Primary endpoints were mortality at days 28 and 60 (non-inferiority analysis), and number of days without antibiotics by day 28 (superiority analysis). Analyses were by intention to treat. The margin of non-inferiority was 10%. This trial is registered with ClinicalTrials.gov, number NCT00472667.

Lancet 2010; 375: 463–74

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See Comment page 435

*Authors contributed equally

†Members listed at end of paper

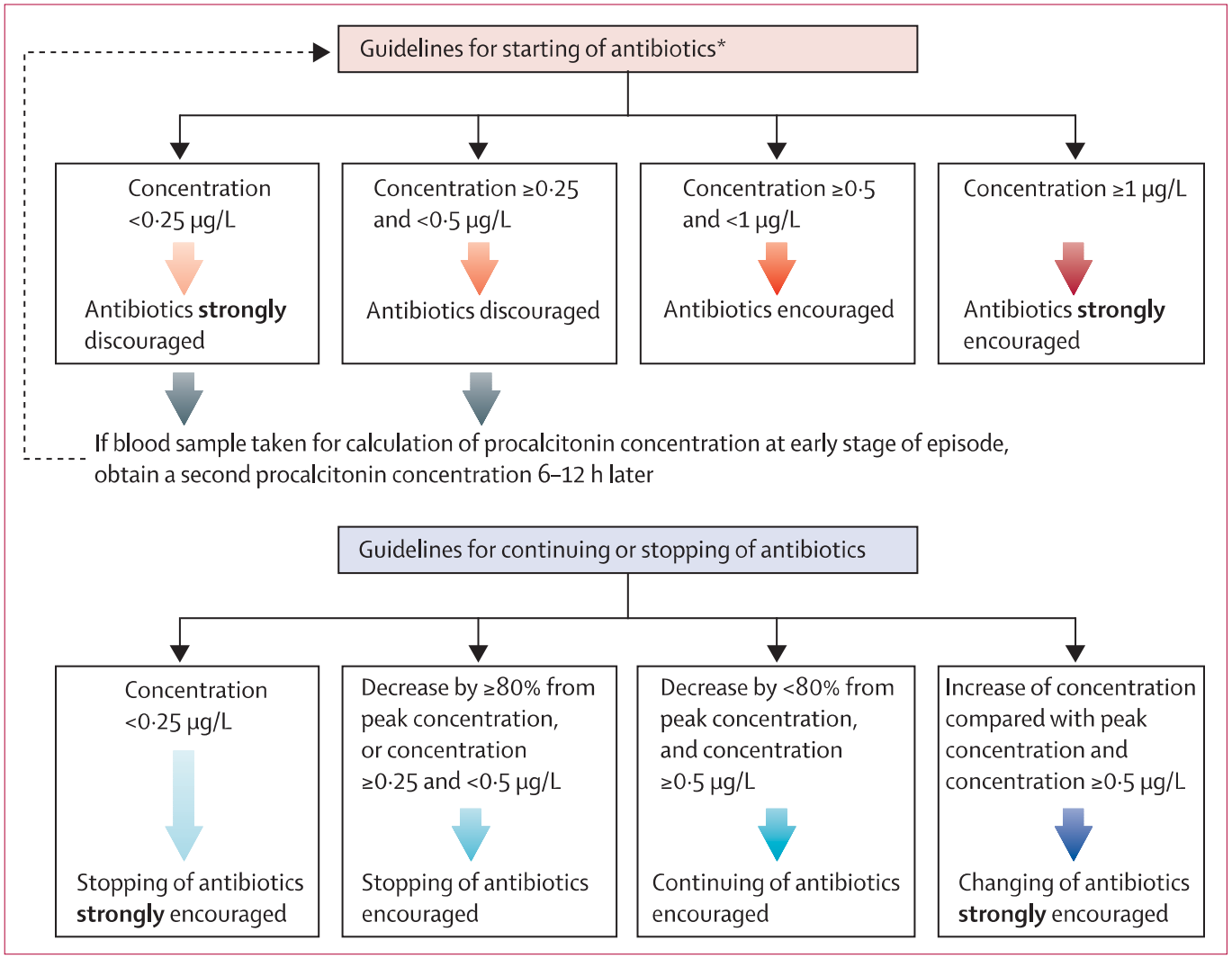
Service de Réanimation Médicale (L Bouadma MD, Prof B Régnier MD, Prof M Wolff MD), **Département d'Epidémiologie Biostatistique et Recherche Clinique** (F Tubach MD, B Pasquet MS), **Département d'Anesthésie et**

İntraabdominal İnfeksiyonlar

- PRORATA
- Procalcitonin to Reduce Antibiotic Treatments in Acutely Ill Patients
- Fransa, Haziran 2007-Mayıs 2008
- 5 Medikal, 2 Cerrahi YB

- Tedavi başlanmadan önce prokalsitonin bakılmış

İntraabdominal İnfeksiyonlar



İntraabdominal İnfeksiyonlar

	Procalcitonin group (n=307)	Control group (n=314)	Between-group absolute difference	p value
Primary endpoints				
28-day mortality*	65 (21·2%)	64 (20·4%)	0·8% (–4·6 to 6·2)	NA
60-day mortality*	92 (30·0%)	82 (26·1%)	3·8% (–2·1 to 9·7)	NA
Number of days without antibiotics	14·3 (9·1)	11·6 (8·2)	2·7 (1·4 to 4·1)	<0·0001
Secondary endpoints (days 1–28)				
Relapse	20 (6·5%)	16 (5·1%)	1·4% (–2·3 to 5·1)	0·45
Superinfection	106 (34·5%)	97 (30·9%)	3·6% (–3·8 to 11·0)	0·29
Number of days without mechanical ventilation	16·2 (11·1)	16·9 (10·9)	–0·7 (–2·4 to 1·1)	0·47
SOFA score				
Day 1	7·5 (4·4)	7·2 (4·4)	0·3 (–0·4 to 1·0)	0·39
Day 7	4·1 (4·2)	4·0 (4·2)	0·1 (–0·6 to 0·8)	0·73
Day 14	2·8 (3·5)	2·8 (3·6)	0 (–0·6 to 0·7)	0·87
Day 21	2·1 (3·3)	1·9 (3·1)	0·2 (–0·4 to 0·8)	0·52
Day 28	1·5 (3·0)	0·9 (2·4)	0·6 (0·0 to 1·1)	0·0370
Length of stay in ICU from inclusion (days)	15·9 (16·1)	14·4 (14·1)	1·5 (–0·9 to 3·9)	0·23
Length of stay in hospital from inclusion (days)	26·1 (19·3)	26·4 (18·3)	–0·3 (–3·2 to 2·7)	0·87
Multidrug-resistant bacteria†	55 (17·9%)	52 (16·6%)	1·3% (–4·6 to 7·2)	0·67
Days of antibiotic exposure per 1000 inpatient days	653	812	–159 (–185 to –131)	<0·0001
Duration of first episode of antibiotic treatment (number [%]; days [SD])				
Overall population	307 (100%); 6·1 (6·0)	314 (100%); 9·9 (7·1)	–3·8 (–4·8 to –2·7)	<0·0001
Community-acquired pneumonia	79 (26%); 5·5 (4·0)	101 (32%); 10·5 (6·4)	–5·0 (–6·6 to –3·4)	<0·0001
Ventilator-associated pneumonia	75 (24%); 7·3 (5·3)	66 (21%); 9·8 (5·7)	–2·4 (–4·0 to –0·8)	0·0029
Intra-abdominal infection	14 (5%); 8·1 (7·7)	20 (6%); 10·8 (6·7)	–2·7 (–7·7 to 2·4)	0·29
Urinary tract infection	24 (8%), 7·4 (6·3)	18 (6%), 14·5 (9·3)	–7·1 (–11·9 to –2·2)	0·0053
Infection with positive blood culture	55 (18%), 9·8 (7·7)	53 (17%), 12·8 (8·1)	–3·0 (–6·0 to 0·1)	0·06

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PLOS ONE

A Procalcitonin-Based Algorithm to Guide Antibiotic Therapy in Secondary Peritonitis following Emergency Surgery: A Prospective Study with Propensity Score Matching Analysis

Ting-Shuo Huang[1,2], Shie-Shian Huang[3], Yu-Chiau Shyu[4,5], Chun-Hui Lee[2], Shyh-Chuan Jwo[2], Pei-Jer Chen[1], Huang-Yang Chen[2]*

1 The Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, **2** Division of General Surgery, Department of Surgery, Chang Gung Memorial Hospital, Keelung Branch, Keelung, Taiwan, **3** Division of Infectious Diseases, Department of Medicine, Chang Gung Memorial Hospital, Keelung Branch, Keelung, Taiwan, **4** Institute of Biopharmaceutical Sciences, National Yang-Ming University, Taipei, Taiwan, **5** Department of Education and Research, Taipei City Hospital, Taipei, Taiwan

Abstract

Background: Procalcitonin (PCT)-based algorithms have been used to guide antibiotic therapy in several clinical settings. However, evidence supporting PCT-based algorithms for secondary peritonitis after emergency surgery is scanty. In this study, we aimed to investigate whether a PCT-based algorithm could safely reduce antibiotic exposure in this population.

Methods/Principal Findings: From April 2012 to March 2013, patients that had secondary peritonitis diagnosed at the emergency department and underwent emergency surgery were screened for eligibility. PCT levels were obtained pre-operatively, on post-operative days 1, 3, 5, and 7, and on subsequent days if needed. Antibiotics were discontinued if PCT was <1.0 ng/mL or decreased by 80% versus day 1, with resolution of clinical signs. Primary endpoints were time to discontinuation of intravenous antibiotics for the first episode and adverse events. Historical controls were retrieved for propensity score matching. After matching, 30 patients in the PCT group and 60 in the control were included for analysis. The median duration of antibiotic exposure in PCT group was 3.4 days (interquartile range [IQR] 2.2 days), while 6.1 days (IQR 3.2 days) in control ($p < 0.001$). The PCT algorithm significantly improves time to antibiotic discontinuation ($p < 0.001$, log-rank test). The rates of adverse events were comparable between 2 groups. Multivariate-adjusted extended Cox model demonstrated that the PCT-based algorithm was significantly associated with a 87% reduction in hazard of antibiotic exposure within 7 days (hazard ratio [HR] 0.13, 95% CI 0.07–0.21, $p < 0.001$), and a 68% reduction in hazard after 7 days (adjusted HR 0.32, 95% CI 0.11–0.99, $p = 0.047$). Advanced age, coexisting pulmonary diseases, and higher severity of illness were significantly associated with longer durations of antibiotic use.

Conclusions/Significance: The PCT-based algorithm safely reduces antibiotic exposure in this study. Further randomized trials are needed to confirm our findings and incorporate cost-effectiveness analysis.

Trial Registration: Australian New Zealand Clinical Trials Registry ACTRN12612000601831

İntraabdominal İnfeksiyonlar

- Acile başvuran sekonder peritonit
- Nisan 2012-Mart 2013

- Pct tetkik: Preop, 1,3,5,7

Pct değerine dayanarak antibiyotik kesilmiş

  - < 1ng/ml
  - 1. güne göre %80 ve üzerinde düştüyse

Huang PLoSOne 2014;9:e90539

İntraabdominal İnfeksiyonlar

Characteristics	PCT group		Control group		P value
	(n = 30)		(n = 60)		
Age, y *	70	(34.0)	67	(28.5)	0.811
Male sex, no. (%)	18	(60.0)	37	(61.7%)	0.878
Coexisting illnesses, no. (%)					
Cardiovascular disease	10	(33.3)	13	(21.7)	0.232
Pulmonary disease	4	(13.3)	13	(21.7)	0.405
Cerebrovascular disease	3	(10.0)	7	(11.7)	1
Renal dysfunction	6	(20.0)	10	(16.7)	0.772
Diabetes mellitus	9	(30.0)	16	(26.7)	0.739
Malignancy	4	(13.3)	8	(13.3)	1
Disease etiology, no. (%)					
Hollow organ perforation	15	(50.0)	30	(50.0)	1
Acute cholecystitis	3	(10.0)	6	(10.0)	
Acute cholangitis	3	(10.0)	6	(10.0)	
Ruptured appendicitis	5	(16.7)	10	(16.7)	
Bowel ischemia	4	(13.3)	8	(13.3)	
Laboratory findings					
Preoperative leukocyte count, cells/μL *	11850	(8525)	11900	(7000)	0.844
Severity scores					
Mannheim peritonitis index *	23	(5.75)	22	(6)	0.823
APACHE II ≥ 15, no. (%)	8	(26.7)	10	(16.7)	0.264
Morbidity, no. (%)					
Any adverse outcomes	11	(36.7)	16	(26.7)	0.329
Deep SSI/organ space SSI	3	(10.0)	5	(8.3)	1
Medical complications	7	(23.3)	10	(16.7)	0.446
Mortality, no. (%)	0	(0.00)	6	(10.0)	0.173
Antibiotics use					
Intravenous antibiotic use, d *	3.4	(2.2)	6.1	(3.2)	<0.001
Extended oral antibiotic use, no. (%)	1	(3.3)	20	(33.3)	0.001

Huang PLoSOne 2014;9:e90539

Jung et al. Critical Care 2013, 17:R255
http://ccforum.com/content/17/5/R255

CRITICAL CARE

RESEARCH Open Access

Procalcitonin biomarker kinetics fails to predict treatment response in perioperative abdominal infection with septic shock

Boris Jung[1,2], Nicolas Molinari[3], Mourad Nasri[1], Zied Hajjej[1], Gerald Chanques[1,2], Helene Jean-Pierre[4], Fabrizio Panaro[5] and Samir Jaber[1,2,6*]

Abstract

Introduction: Procalcitonin (PCT) biomarker is suggested to tailor antibiotic therapy in the medical intensive care unit (ICU) but studies in perioperative medicine are scarce. The aim of this study was to determine whether PCT reported thresholds are associated with the initial treatment response in perioperative septic shock secondary to intra-abdominal infection.

Methods: This single ICU, observational study included patients with perioperative septic shocks secondary to intra-abdominal infection. Demographics, PCT at days 0, 1, 3, 5, treatment response and outcome were collected. Treatment failure included death related to the initial infection, second source control treatment or a new onset intra-abdominal infection. The primary endpoint was to assess whether PCT thresholds (0.5 ng/ml or a drop from the peak of at least 80%) predict the initial treatment response.

Results: We included 101 consecutive cases. Initial treatment failed in 36 patients with a subsequent mortality of 75%. Upon admission, PCT was doubled when treatment ultimately failed (21.7 ng/ml ± 38.7 vs. 41.7 ng/ml ± 75.7; $P = 0.04$). Although 95% of the patients in whom PCT dropped down below 0.5 ng/ml responded to treatment, 50% of the patients in whom PCT remained above 0.5 ng/ml also responded successfully to treatment. Moreover, despite a PCT drop of at least 80%, 40% of patients had treatment failure.

Conclusions: In perioperative intra-abdominal infections with shock, PCT decrease to 0.5 ng/ml lacked sensitivity to predict treatment response and its decrease of at least 80% from its peak failed to accurately predict treatment response. Studies in perioperative severe infections are needed before using PCT to tailor antibiotic use in this population.

İntraabdominal İnfeksiyonlar

- Erişkin yoğun bakım
  - Abdominal septik şok
  - Postoperatif septik şok
- 114 hasta
- Ocak 2008 - Mart 2011

Antibiyotik kesme kararında öngörü?

1. Prokalsitonin eşik değeri 0,5 ng/ml
2. Prokalsitonin pik değere göre %80 düşme

Jung Crit Care 2013;17:R255

İntraabdominal İnfeksiyonlar

- Tedavi seçimi: IDSA kılavuzu
  - » Solomkin Clin Infect Dis 2010
- Başlangıç tedavisi başarısız 36 olgu (%32)
  - Relaparatomi %47
    - Relaparatomide ölüm %39

Jung Crit Care 2013;17:R255

Jung *et al. Critical Care* 2013, **17**:R255
http://ccforum.com/content/17/5/R255

CRITICAL CARE

RESEARCH Open Access

Procalcitonin biomarker kinetics fails to predict treatment response in perioperative abdominal infection with septic shock

Boris Jung[1,2], Nicolas Molinari[3], Mourad Nasri[1], Zied Hajjej[1], Gerald Chanques[1,2], Helene Jean-Pierre[4], Fabrizio Panaro[5] and Samir Jaber[1,2,6*]

Abstract

Prokalsitonin biyomarker kinetiği, septik şokta perioperatif abdominal enfeksiyonda tedavi cevabını öngörmede başarısız!

Results: We included 101 consecutive cases. Initial treatment failed in 36 patients with a subsequent mortality of 75%. Upon admission, PCT was doubled when treatment ultimately failed (21.7 ng/ml ± 38.7 vs. 41.7 ng/ml ± 75.7; $P = 0.04$). Although 95% of the patients in whom PCT dropped down below 0.5 ng/ml responded to treatment, 50% of the patients in whom PCT remained above 0.5 ng/ml also responded successfully to treatment. Moreover, despite a PCT drop of at least 80%, 40% of patients had treatment failure.

Conclusions: In perioperative intra-abdominal infections with shock, PCT decrease to 0.5 ng/ml lacked sensitivity to predict treatment response and its decrease of at least 80% from its peak failed to accurately predict treatment response. Studies in perioperative severe infections are needed before using PCT to tailor antibiotic use in this population.

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

Jean-Pierre Quenot[1,2], Charles-Edouard Luyt[3], Nicolas Roche[4], Martin Chalumeau[5,6], Pierre-Emmanuel Charles[1,7], Yann-Eric Claessens[8], Sigismond Lasocki[9], Jean-Pierre Bedos[10], Yves Péan[11], François Philippart[12], Stéphanie Ruiz[13], Christele Gras-Leguen[14], Anne-Marie Dupuy[15], Jérôme Pugin[16], Jean-Paul Stahl[17], Benoit Misset[12,18], Rémy Gauzit[19] and Christian Brun-Buisson[20,21*]

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

İntraabdominal İnfeksiyonlar

- Pct kılavuzluğunda antibiyotik kesilmesi
  - Karar verme ???
  - Ne zaman???
  - P
    - Kemik ve eklem infeksiyonları
    - Akut mediastinit
    - İntraserebral apse

Prokalsitonine dayanarak tedavi kesilmesi kararı için veriler henüz yeterli değil!

Quenot Ann Intensive Care 2013;3:21

Intensive Care Med (2017) 43:304–377
DOI 10.1007/s00134-017-4683-6

CONFERENCE REPORTS AND EXPERT PANEL

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

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

Prokalsitonin
Antibiyotik Tedavi Süresinin Kısaltılması ve Kesilmesi İçin

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).**

Rhodes Crit Care Med 2017;45:486

Prokalsitonin
Antibiyotik Tedavi Süresinin Kısaltılması ve Kesilmesi İçin

It is important to note that procalcitonin and all other biomarkers can provide only supportive and supplemental data to clinical assessment. Decisions on initiating, altering, or discontinuing antimicrobial therapy should never be made solely on the basis of changes in any biomarker, including procalcitonin.

Pct ve bütün diğer biyomarkırlar klinik değerlendirmeye destek ve tamamlayıcı olarak bilgi verebilirler. Antimikrobiyal tedaviyi başlama, değiştirme ve kesme kararı prokalsitonin de dahil olmak üzere, asla sadece biyomarkır değişimine göre verilmemelidir.

Rhodes Crit Care Med 2017;45:486

Teşekkür ederim.