Yoğun Bakımda İnvaziv Fungal Enfeksiyonlar
Riskli Hasta Grupları, Tanı, Skorlamalar ve Profilaksi

E. Ediz Tütüncü

EKMUD 2016
Sistemik Fungal Enfeksiyonlarda Tanı ve Tedavi
11 Mayıs 2016, Antalya

MAJOR ARTICLE

The Epidemiology and Attributable Outcomes of Candidemia in Adults and Children Hospitalized in the United States: A Propensity Analysis

Theoklis E. Zaoutis,[1,2,5] Jesse Argon,[1] Jaclyn Chu,[1,2] Jesse A. Berlin,[4,a] Thomas J. Walsh,[6] and Chris Feudtner[1,3]

[1]Pediatric Generalists Research Group, Division of General Pediatrics, and [2]Division of Infectious Diseases, The Children's Hospital of Philadelphia, [3]Leonard Davis Institute of Health Economics, University of Pennsylvania, [4]Department of Biostatistics and the Center for Clinical Epidemiology and Biostatistics, and [5]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; and [6]Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, Bethesda, Maryland

Table 3. Outcomes attributable to candidemia in the United States, 2000.

	Pediatric patients			Adult patients		
Variable	With candidemia (n = 1118)	Without candidemia (n = 2062)	Attributable increase (95% CI)	With candidemia (n = 8949)	Without candidemia (n = 17,267)	Attributable increase (95% CI)
Mortality, %	15.8	5.9	10.0 (6.2–13.8)	30.6	16.1	14.5 (12.1–16.9)
Length of stay, mean no. of days per patient	44.8	23.7	21.1 (14.4–27.8)	18.6	8.5	10.1 (8.9–11.3)
Total charges, mean US$ per patient	183,645	91,379	92,266 (65,058–119,474)	66,154	26,823	39,331 (33,60–45,602)

Zaoutis TE, Clin Infect Dis 2005;41:1232

MAJOR ARTICLE

The Epidemiology and Attributable Outcomes of Candidemia in Adults and Children Hospitalized in the United States: A Propensity Analysis

Theoklis E. Zaoutis,[1,2,5] Jesse Argon,[1] Jaclyn Chu,[1,2] Jesse A. Berlin,[4,a] Thomas J. Walsh,[6] and Chris Feudtner[1,3]

[1]Pediatric Generalists Research Group, Division of General Pediatrics, and [2]Division of Infectious Diseases, The Children's Hospital of Philadelphia, [3]Leonard Davis Institute of Health Economics, University of Pennsylvania, [4]Department of Biostatistics and the Center for Clinical Epidemiology and Biostatistics, and [5]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; and [6]Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, Bethesda, Maryland

Atfedilen mortalite

Yetişkinler %15-25

Çocuklar %10-15

Zaoutis TE, Clin Infect Dis 2005;41:1232

Eur J Clin Microbiol Infect Dis (2006) 25:419–425
DOI 10.1007/s10096-006-0159-2

REVIEW

Attributable mortality of candidemia: a systematic review of matched cohort and case-control studies

M. E. Falagas · K. E. Apostolou · V. D. Pappas

Atfedilen mortalite %5-71

Falagas ME, Eur J Clin Microbiol Infect Dis 2006;25:419

	Olgu sayısı	Mortalite
Çelebi S, 2000-2007	28	%42.8
Erdem I, 2004-2007	50	%56
Horasan EŞ, 2004-2009	118	%70
Koçak B, 2008	38	%58
Dizbay M, 2007	35	%65.7
Albayrak Y, 2011-2014	72	%69.4

Celebi S, Pediatr Int 2012:54;341

Erdem I, Med Princ Pract 2010;19:463

Horasan ES, Mycopathologia 2010;170:263

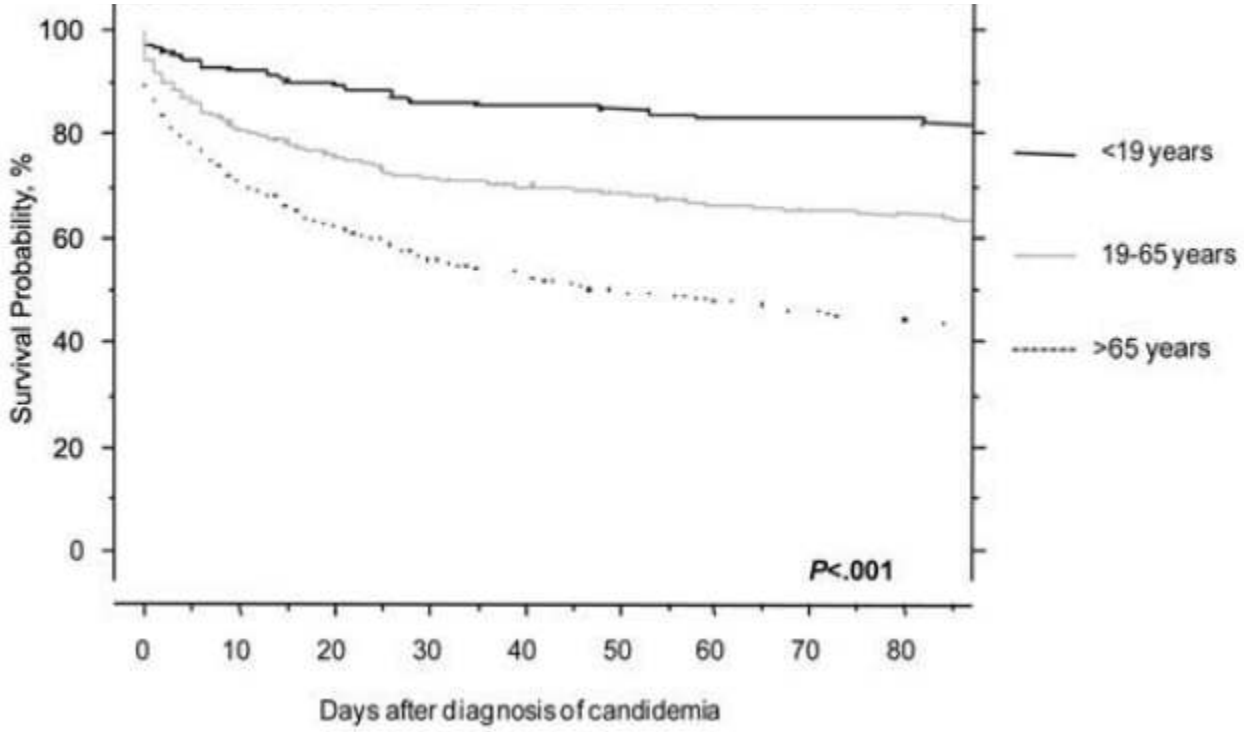
Yenigün Koçak B, Mikrobiyol Bul 2011;45:489

Dizbay M, Scand J Infect Dis. 2010;42:114

Epidemiology and Outcomes of Candidemia in 2019 Patients: Data from the Prospective Antifungal Therapy Alliance Registry

David L. Horn,[1] Dionissios Neofytos,[1,2] Elias J. Anaissie,[3] Jay A. Fishman,[4] William J. Steinbach,[5] Ali J. Olyaei,[6] Kieren A. Marr,[2] Michael A. Pfaller,[7] Chi-Hsing Chang,[8] and Karen M. Webster[9]

[1]Thomas Jefferson University Hospital, Philadelphia, Pennsylvania; [2]Johns Hopkins University School of Medicine, Baltimore, Maryland; [3]University of Arkansas for Medical Sciences, Little Rock; [4]Massachusetts General Hospital, Boston; [5]Duke University Medical Center, Durham, North Carolina; [6]Oregon Health Sciences University, Portland; [7]University of Iowa Health Care, Iowa City; and [8]Info-Spectrum, Markham, and [9]EBM Consulting, Mississauga, Ontario, Canada



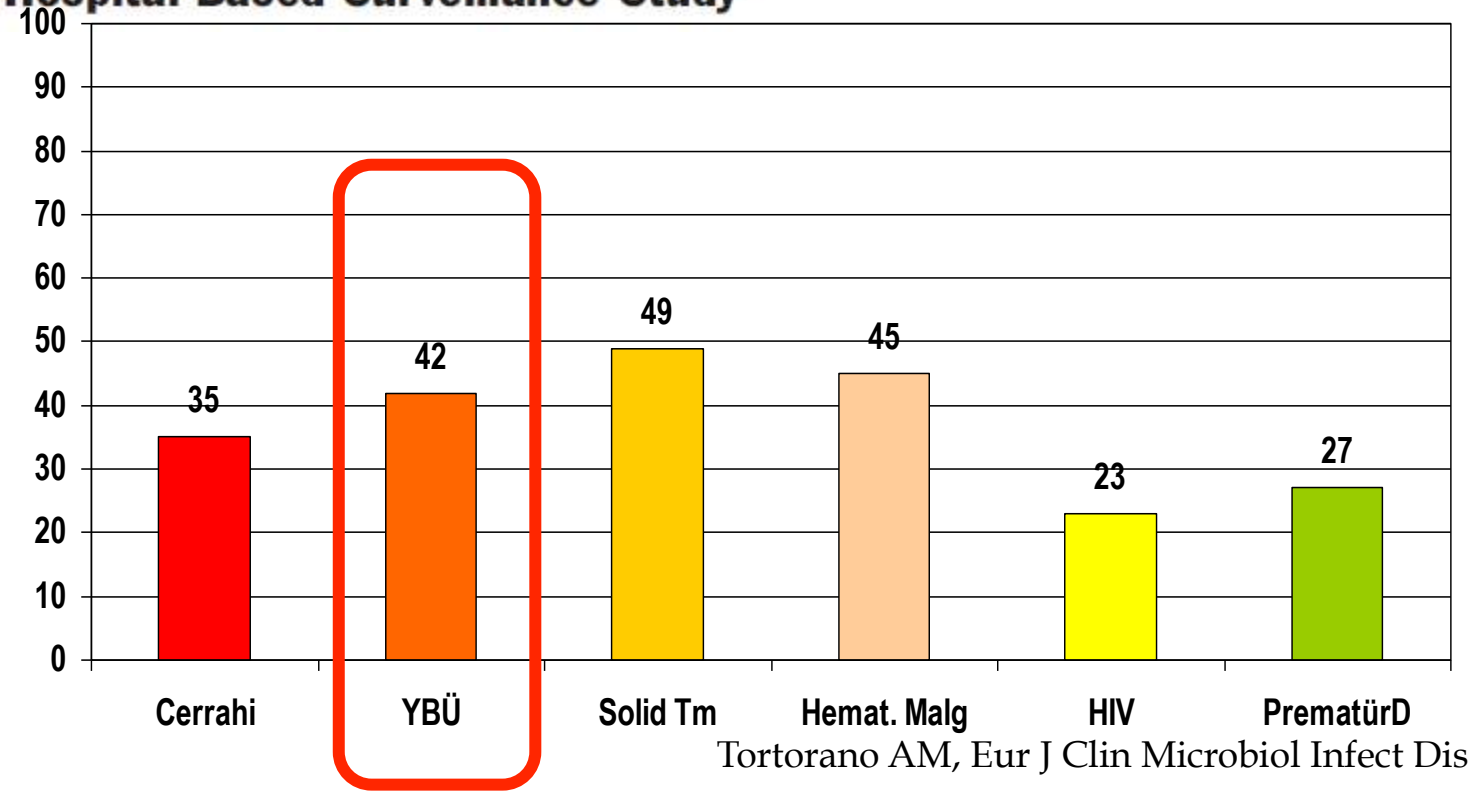
Horn DL, Clin Infect Dis 2009;48:1695

Eur J Clin Microbiol Infect Dis (2004) 23: 317–322
DOI 10.1007/s10096-004-1103-y

ARTICLE

A. M. Tortorano · J. Peman · H. Bernhardt ·
L. Klingspor · C. C. Kibbler · O. Faure · E. Biraghi ·
E. Canton · K. Zimmermann · S. Seaton · R. Grillot ·
the ECMM Working Group on Candidaemia

Epidemiology of Candidaemia in Europe: Results of 28-Month European Confederation of Medical Mycology (ECMM) Hospital-Based Surveillance Study

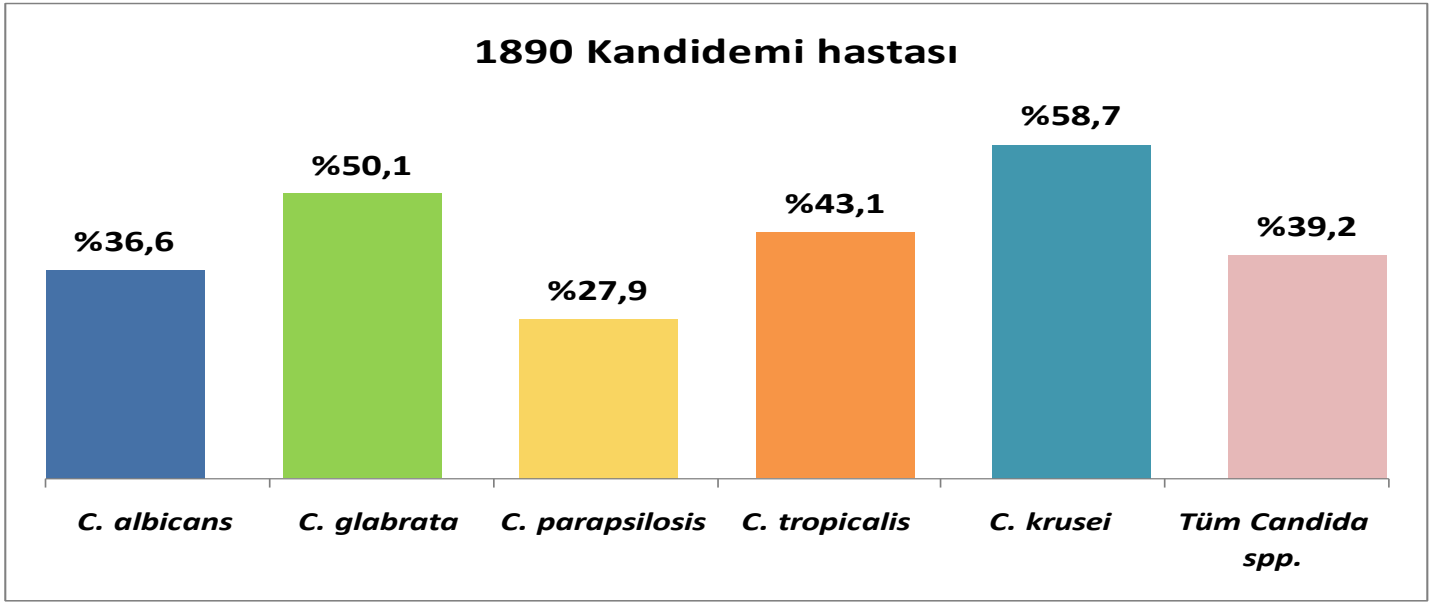


Tortorano AM, Eur J Clin Microbiol Infect Dis 2004;23:317

Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study

Hilmar Wisplinghoff,[1,2] Tammy Bischoff,[1] Sandra M. Tallent,[1] Harald Seifert,[2] Richard P. Wenzel,[1] and Michael B. Edmond[1]

[1]Department of Internal Medicine, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, Virginia; and [2]Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Germany



Wisplinghoff H, Clin Infect Dis 2004;39:309

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 2005, p. 3640–3645 Vol. 49, No. 9
0066-4804/05/$08.00+0 doi:10.1128/AAC.49.9.3640–3645.2005

Delaying the Empiric Treatment of *Candida* Bloodstream Infection until Positive Blood Culture Results Are Obtained: a Potential Risk Factor for Hospital Mortality

Matthew Morrell,[1] Victoria J. Fraser,[2] and Marin H. Kollef[1]*

Pulmonary and Critical Care Division[1] and Division of Infectious Diseases,[2] Washington University School of Medicine, St. Louis, Missouri 63110

Tek merkez, 157 olgu, 2001-2004

Antifungal tedavi başlama zamanı mortalite ilişkisi

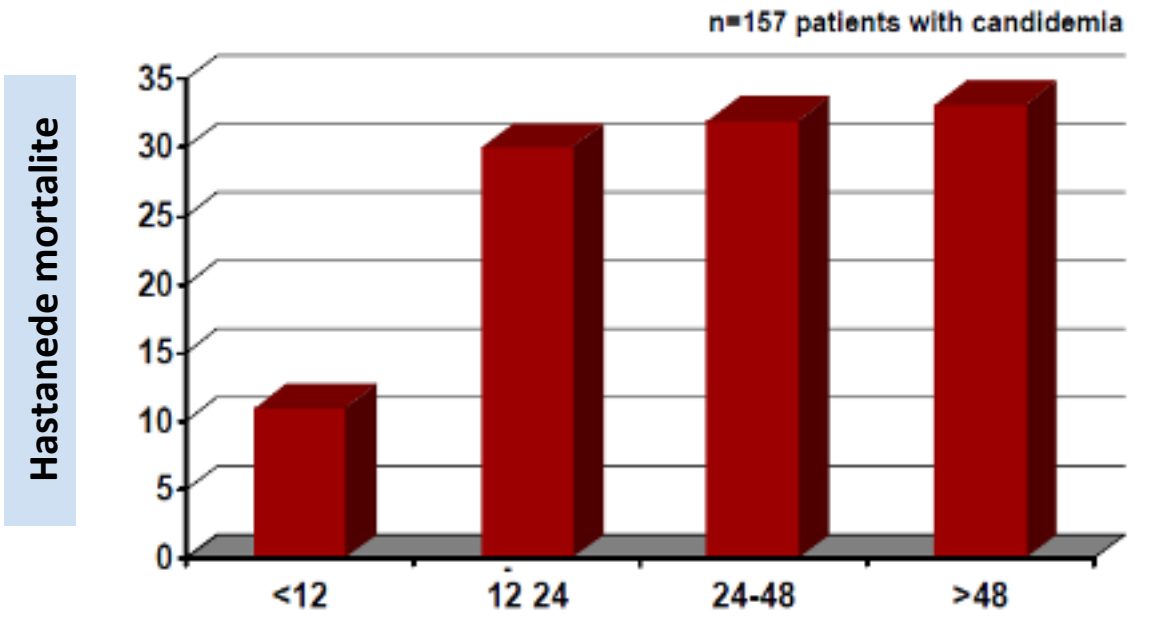
Morrell M, Antimicrob Agents Chemother 2005;49:3640

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 2005, p. 3640–3645 Vol. 49, No. 9
0066-4804/05/$08.00+0 doi:10.1128/AAC.49.9.3640–3645.2005

Delaying the Empiric Treatment of *Candida* Bloodstream Infection until Positive Blood Culture Results Are Obtained: a Potential Risk Factor for Hospital Mortality

Matthew Morrell,[1] Victoria J. Fraser,[2] and Marin H. Kollef[1]*

Pulmonary and Critical Care Division[1] and Division of Infectious Diseases,[2] Washington University School of Medicine, St. Louis, Missouri 63110



İlk pozitif kan kültürünün alınması ile antifungal tedavi başlanması arasında geçen zaman

Morrell M, Antimicrob Agents Chemother 2005;49:3640

MAJOR ARTICLE

Time to Initiation of Fluconazole Therapy Impacts Mortality in Patients with Candidemia: A Multi-Institutional Study

Kevin W. Garey,[1] Milind Rege,[1] Manjunath P. Pai,[2] Dana E. Mingo,[3] Katie J. Suda,[4] Robin S. Turpin,[5] and David T. Bearden[6]

[1]Department of Clinical Science and Administration, University of Houston College of Pharmacy, Houston, Texas; [2]University of New Mexico College of Pharmacy, Albuquerque; [3]Baptist Memorial Health Care and [4]Department of Pharmacy, University of Tennessee Health Science Center, Memphis; [5]Merck, West Point, Pennsylvania; and [6]Oregon State University College of Pharmacy, Portland

4 merkez, 230 olgu, 2001-2004

Flukonazol başlama zamanı mortalite ilişkisi

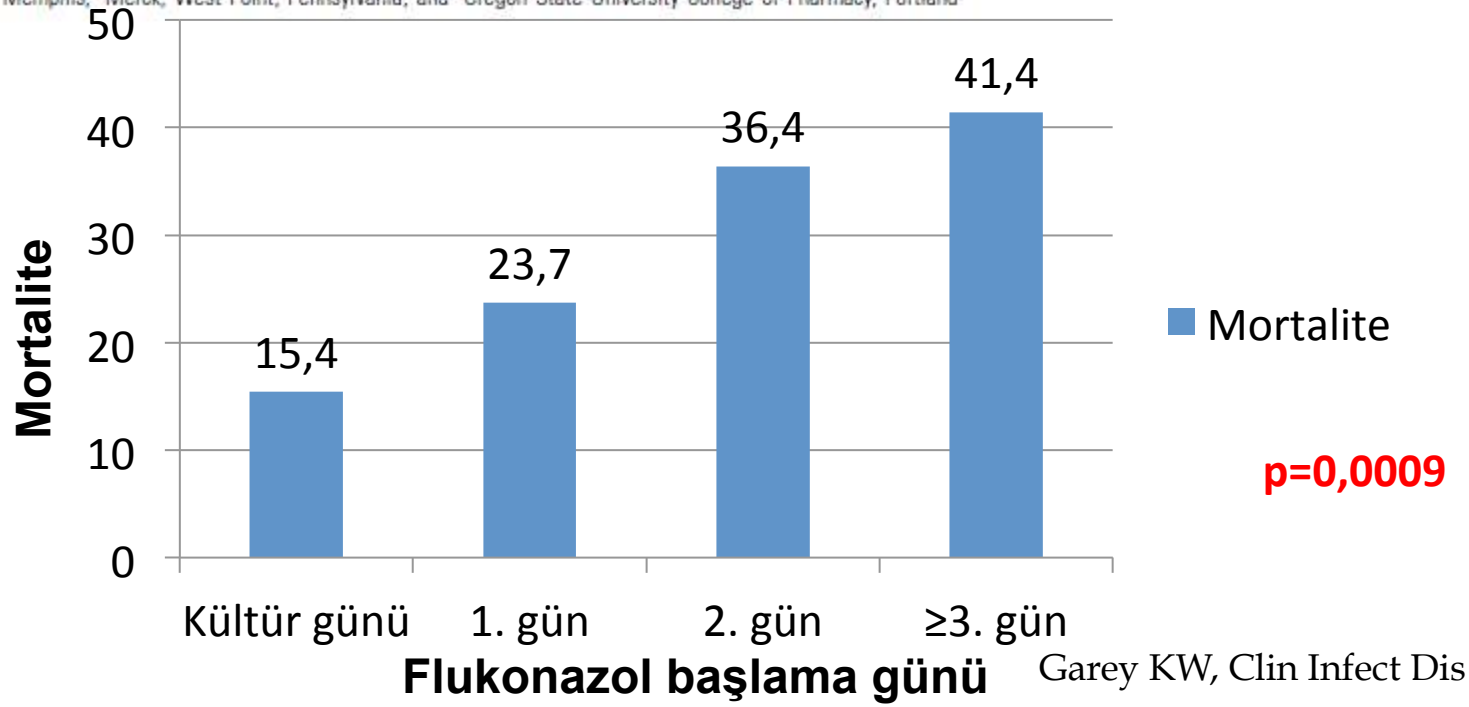
Garey KW, Clin Infect Dis 2006;43:25

MAJOR ARTICLE

Time to Initiation of Fluconazole Therapy Impacts Mortality in Patients with Candidemia: A Multi-Institutional Study

Kevin W. Garey,[1] Milind Rege,[1] Manjunath P. Pai,[2] Dana E. Mingo,[3] Katie J. Suda,[4] Robin S. Turpin,[5] and David T. Bearden[6]

[1]Department of Clinical Science and Administration, University of Houston College of Pharmacy, Houston, Texas; [2]University of New Mexico College of Pharmacy, Albuquerque; [3]Baptist Memorial Health Care and [4]Department of Pharmacy, University of Tennessee Health Science Center, Memphis; [5]Merck, West Point, Pennsylvania; and [6]Oregon State University College of Pharmacy, Portland



Garey KW, Clin Infect Dis 2006;43:25

Journal of Antimicrobial Chemotherapy (2007) **60**, 613–618
doi:10.1093/jac/dkm212
Advance Access publication 18 June 2007

JAC

Adequacy of empirical antifungal therapy and effect on outcome among patients with invasive *Candida* species infections

Michael D. Parkins[1], Deana M. Sabuda[1], Sameer Elsayed[2–4] and Kevin B. Laupland[1–3,5,6]*

[1]*Department of Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;*
[2]*Department of Pathology and Laboratory Medicine, Calgary Health Region and University of Calgary, Calgary,*

Kohort 199 olgu, 1999-2004

165/199 (%83) antifungal tedavi

64/199 (%32) ampirik antifungal tedavi

Parkins MD, J Antimicrob Chemother 2007;60:613

Journal of Antimicrobial Chemotherapy (2007) **60**, 613–618
doi:10.1093/jac/dkm212
Advance Access publication 18 June 2007

JAC

Adequacy of empirical antifungal therapy and effect on outcome among patients with invasive *Candida* species infections

Michael D. Parkins[1], Deana M. Sabuda[1], Sameer Elsayed[2–4] and Kevin B. Laupland[1–3,5,6]*

[1]*Department of Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;*
[2]*Department of Pathology and Laboratory Medicine, Calgary Health Region and University of Calgary, Calgary,*

64/199 (%32) ampirik antifungal tedavi

%80 uygun %20 uygunsuz

Parkins MD, J Antimicrob Chemother 2007;60:613

Journal of Antimicrobial Chemotherapy (2007) **60**, 613–618
doi:10.1093/jac/dkm212
Advance Access publication 18 June 2007

JAC

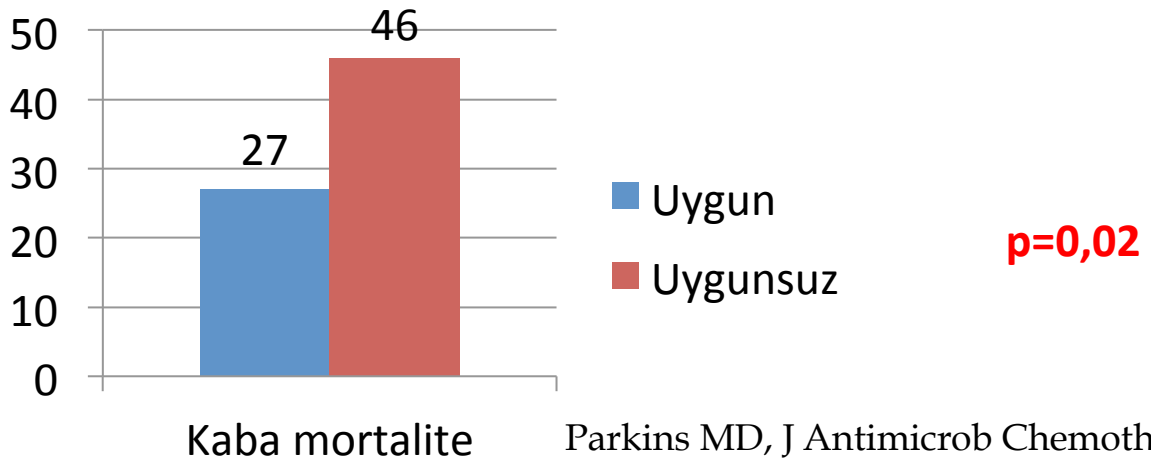
Adequacy of empirical antifungal therapy and effect on outcome among patients with invasive *Candida* species infections

Michael D. Parkins[1], Deana M. Sabuda[1], Sameer Elsayed[2–4] and Kevin B. Laupland[1–3,5,6]*

[1]*Department of Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;*
[2]*Department of Pathology and Laboratory Medicine, Calgary Health Region and University of Calgary, Calgary,*

64/199 (%32) ampirik antifungal tedavi

%80 uygun %20 uygunsuz



p=0,02

Parkins MD, J Antimicrob Chemother 2007;60:613

J Antimicrob Chemother 2012; **67**: 707–714
doi:10.1093/jac/dkr511 Advance Access publication 18 December 2011

Journal of Antimicrobial Chemotherapy

Timing of susceptibility-based antifungal drug administration in patients with *Candida* bloodstream infection: correlation with outcomes

Shellee A. Grim[1,2*], Karen Berger[1†], Christine Teng[3], Sandeep Gupta[4], Jennifer E. Layden[2], William M. Janda[5] and Nina M. Clark[2]

[1]*Department of Pharmacy Practice, University of Illinois at Chicago, 833 S. Wood Street Room 164 (M/C 886), Chicago, IL 60612, USA;*
[2]*Section of Infectious Diseases, Department of Internal Medicine, University of Illinois at Chicago, 808 S. Wood Street Room 888 (M/C*

Tek merkez, 446 olgu, 2001-2009

Grim SA, J Antimicrob Chemother 2012;67:707

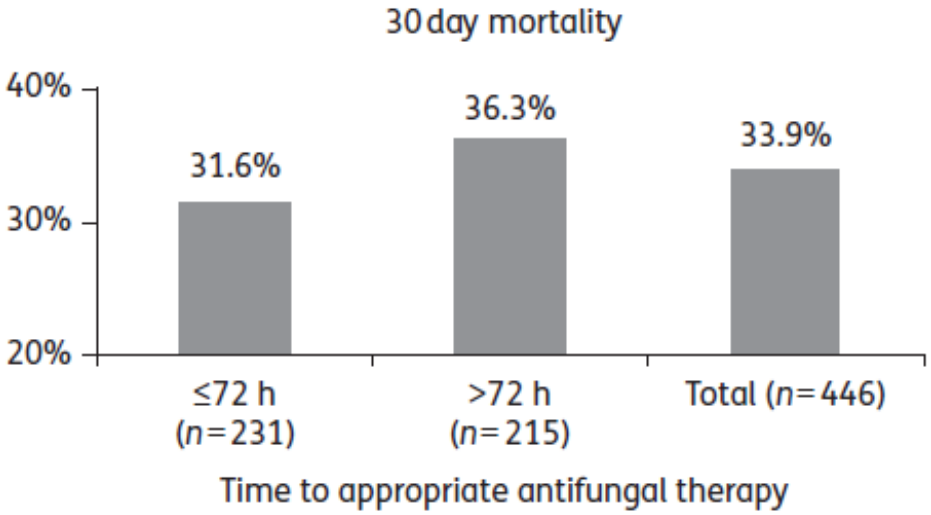
J Antimicrob Chemother 2012; **67**: 707–714
doi:10.1093/jac/dkr511 Advance Access publication 18 December 2011

Journal of Antimicrobial Chemotherapy

Timing of susceptibility-based antifungal drug administration in patients with *Candida* bloodstream infection: correlation with outcomes

Shellee A. Grim[1,2*], Karen Berger[1†], Christine Teng[3], Sandeep Gupta[4], Jennifer E. Layden[2], William M. Janda[5] and Nina M. Clark[2]

[1]*Department of Pharmacy Practice, University of Illinois at Chicago, 833 S. Wood Street Room 164 (M/C 886), Chicago, IL 60612, USA;*
[2]*Section of Infectious Diseases, Department of Internal Medicine, University of Illinois at Chicago, 808 S. Wood Street Room 888 (M/C*



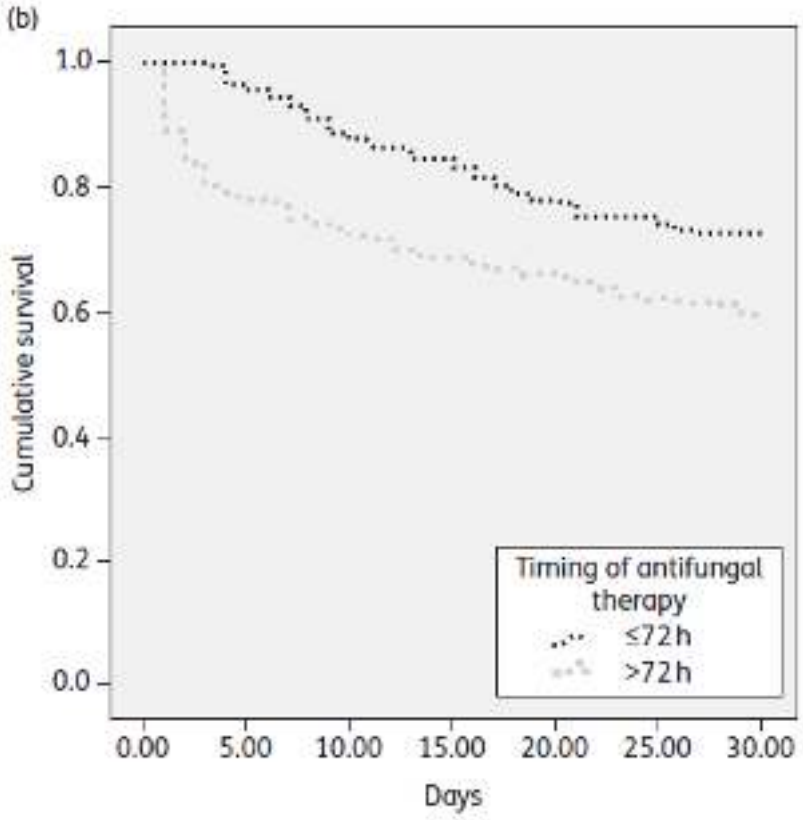
p=0,11

Grim SA, J Antimicrob Chemother 2012;67:707

J Antimicrob Chemother 2012; **67**: 707–714
doi:10.1093/jac/dkr511 Advance Access publication 18 December 2011

Journal of Antimicrobial Chemotherapy

Timing of susceptibility-based antifungal drug administration in patients with *Candida* bloodstream infection: correlation with outcomes



p=0,001

nicrob Chemother 2012;67:707

Etkin antifungal tedaviye başlanma zamanı mortalitenin en önemli belirleyicilerinden birisidir.

Erken başlanması,

Uygun ilacın seçilmesi,

Yeterli süre verilmesi

5N1K

Ne?

Kandidemi

5N1K

Ne?

Nerede?

YBÜ

Cerrahi, travma, yanık, yenidoğan YBÜ

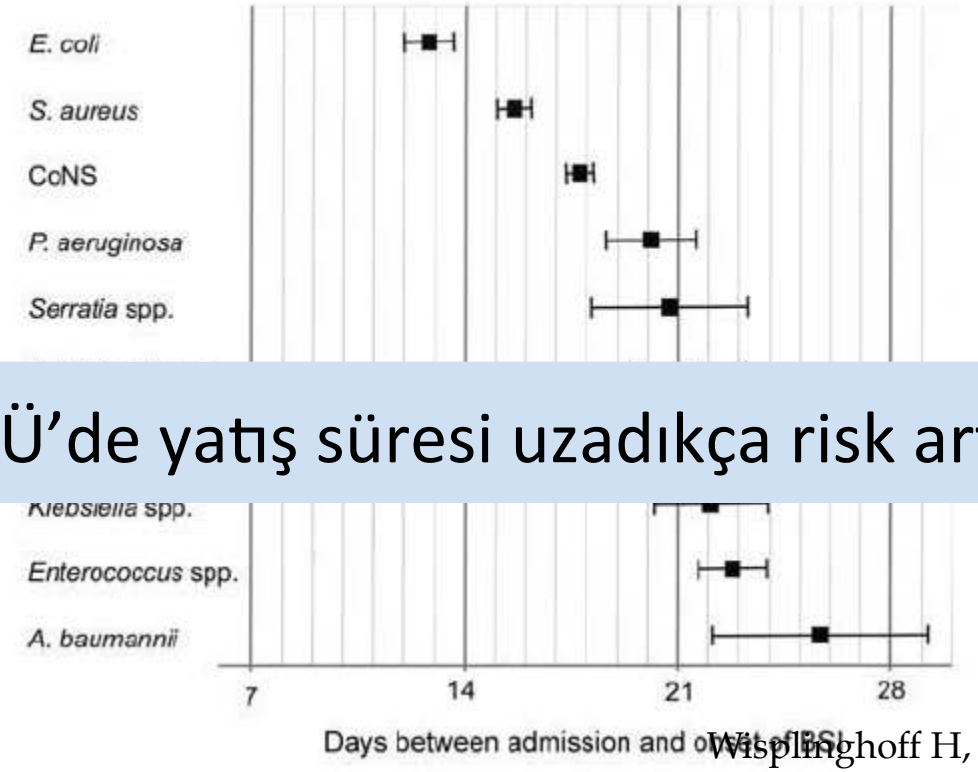
5N1K

- Ne?
- Nerede?
- Ne zaman?

Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study

Hilmar Wisplinghoff,[1,2] Tammy Bischoff,[1] Sandra M. Tallent,[1] Harald Seifert,[2] Richard P. Wenzel,[1] and Michael B. Edmond[1]

[1]Department of Internal Medicine, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, Virginia; and [2]Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Germany



YBÜ'de yatış süresi uzadıkça risk artar

Wisplinghoff H, Clin Infect Dis 2004;39:309

5N1K

- Ne?
- Nerede?
- Ne zaman?
- Nasıl?

GİS mukozasından penetrasyon

İntravasküler kateterler

Total parenteral nütrisyon

Lokalize odak

5N1K

- Ne?
- Nerede?
- Ne zaman?
- Nasıl?
- Neden?

YBÜ yatak sayısı ve erişiminin artması,

İnvaziv araç kullanımındaki artış

HSCT ve SOT olgularında artış,

Yeni kemoterapötik ve immünmodülatör ilaçlar

Paramythiotou E, Molecules 2014;19:1085

5N1K

- Ne?
- Nerede?
- Ne zaman?
- Nasıl?
- Neden?
- Kim?

Muskett *et al. Critical Care* 2011, **15**:R287
http://ccforum.com/content/15/6/R287

CRITICAL CARE

RESEARCH Open Access

Risk factors for invasive fungal disease in critically ill adult patients: a systematic review

Hannah Muskett[1], Jason Shahin[1], Gavin Eyres[1], Sheila Harvey[1], Kathy Rowan[1,2] and David Harrison[1,3*]

Table 2 Risk factors and adjusted effect estimates

Risk factors	Studies	OR (95% CI)	P-values
Surgery			
General abdominal surgery	Agvald-Ohman *et al*, 2008 [28]	60.7 (7.3 to infinity)	0.0013
Any surgery	Blumberg *et al*, 2001 [29]	7.3 (1 to 53.8)	0.05
Elective surgery	Jordà-Marcos *et al*, 2007 [26]*	2.75 (1.17 to 6.45)	0.02
Surgery on ICU admission	León *et al*, 2006 [27]*	2.71 (1.45 to 5.06)	< 0.001
Gastrointestinal procedure	Chow *et al*, 2008 [30]	2.24 (1.49 to 3.38)β	< 0.001β
Major pre-ICU operation	Chow *et al*, 2008 [30]	2.12 (1.14 to 3.97)β	0.02β
Major operation during ICU stay	Chow *et al*, 2008 [30]	1.26α	0.04α
Multiple surgical procedures	McKinnon *et al*, 2001 [32]	NR	≤ 0.05
Total parenteral nutrition			
Total parenteral nutrition duration/days at risk	Chow *et al*, 2008 [30]	11 (5.52 to 21.7)α	< 0.01α
		2.87 (1.4 to 5.9)β	< 0.01β
Total parenteral nutrition	Jordà-Marcos *et al*, 2007 [26]*	3.89 (1.73 to 8.78)	0.001
Total parenteral nutrition	Blumberg *et al*, 2001 [29]	3.6 (1.8 to 7.5)	< 0.001
Total parenteral nutrition	León *et al*, 2006 [27]*	2.48 (1.16 to 5.31)	< 0.001
Total parenteral nutrition	Borzotta & Beardsley, 1999 [34]	NR	< 0.001
Fungal Colonisation			
Digestive focus	Ibáñez-Nolla *et al*, 2004 [31]	20.24 (6.11 to 67.03)	< 0.001
Colonisation index ≥ 0.5	Agvald-Ohman *et al*, 2008 [28]	19.1 (2.38 to 435)	0.017
Non-*Candida albicans* at screening	Ibáñez-Nolla *et al*, 2004 [31]	11.68 (1.93 to 70.63)	0.007
Respiratory focus	Ibáñez-Nolla *et al*, 2004 [31]	6.55 (1.25 to 34.3)	0.026
Candida colonisation	Jordà-Marcos *et al*, 2007 [26]*	4.12 (1.82 to 9.33)	0.001
Candida colonisation	León *et al*, 2006 [27]*	3.04 (1.45 to 6.39)	< 0.001
Candida species corrected colonisation index	Pittet *et al*, 1994 [33]	4.01 (2.16 to 7.45)	< 0.001
Renal replacement therapy			
Haemodialysis duration/days at risk	Chow *et al*, 2008 [30]	3.84 (1.75 to 8.4)α	< 0.001α
		6.2 (2.67 to 14.4)β	< 0.0001β
New-onset haemodialysis	Paphitou *et al*, 2005 [35]	5.4 (2.5 to 11.8)	0.029
Haemofiltration	Jordà-Marcos *et al*, 2007 [26]*	1.96 (1.06 to 3.62)	0.032
Infection/sepsis			
Hospital acquired	Michalopoulos *et al*, 2003 [36]	9.4 (2.5 to 48.3)	< 0.001
Severe sepsis	León *et al*, 2006 [27]*	7.68 (4.14 to 14.22)	< 0.001
Enteric bacteraemia	Chow *et al*, 2008 [30]	3.45 (1.38 to 8.63)α	< 0.01α
		3.43 (1.39 to 8.48)β	< 0.01β
Mechanical ventilation			
Mechanical ventilation > 10 days	Michalopoulos *et al*, 2003 [36]	28.2 (3.6 to 119.5)	< 0.001
Mechanical ventilation after day 3	McKinnon *et al*, 2001 [32]	NR	≤ 0.05
Diabetes			
Diabetes	Paphitou *et al*, 2005 [35]	2.8 (1.6 to 4.7)	0.053
Diabetes	Michalopoulos *et al*, 2003 [36]	2.4 (1.3 to 13.5)	< 001
APACHE II or APACHE III score			
APACHE II score	Pittet *et al*, 1994 [33]	1.03 (1.01 to 1.05)	0.007
APACHE III score	Ibáñez-Nolla *et al*, 2004 [31]	1.03 (1.00 to 1.06)	0.004
Cardiopulmonary bypass time > 120 min	Michalopoulos *et al*, 2003 [36]	8.1 (2.9 to 23.6)	< 001
Acute renal failure	Blumberg *et al*, 2001 [29]	4.2 (2.1 to 8.3)	< 0.001
Broad spectrum antibiotics	Paphitou *et al*, 2005 [35]	3.0(1.8 to 5.0)	0.028
Red blood cell transfusion	Chow *et al*, 2008 [30]	1.97 (0.98 to 3.99)α	0.06α
		2.72 (1.33 to 5.58)β	< 0.01β
Antifungal medication	Blumberg *et al*, 2001 [29]	0.3 (0.1 to 0.6)	< 0.001
Central venous catheters	McKinnon *et al*, 2001 [32]	NR	≤ 0.05
Diarrhoea	McKinnon *et al*, 2001 [32]	NR	≤ 0.05
Peripheral catheter use	McKinnon *et al*, 2001 [32]	NR	≤ 0.05

Muskett H, Crit Care 2011;15:R287

CRITICAL CARE

Cerrahi girişim, özellikle abdominal cerrahi

Total parenteral nütrisyon

Fungal kolonizasyon

ABY, hemodiyaliz gereksinimi

Mekanik ventilasyon >10 gün

Yüksek APACHE skoru

Table 2 Risk fact

Risk factors							
Surgery							< 0.001[a]
General abdominal surgery	Agvald-Ohman *et al*, 2008 [28]	60.7 (7.3 to infinity)	0.0013	New-onset haemodialysis	Paphitou *et al*, 2005 [35]	5.4 (2.5 to 11.8)	0.029
Any surgery							0.032
Elective surgery							
Surgery on ICU a							< 0.001
Gastrointestinal p							< 0.001
Major pre-ICU op							< 0.01[a]
Major operation o							< 0.01[b]
Multiple surgical procedures	McKinnon *et al*, 2001 [32]	NR	< 0.05	Mechanical ventilation			< 0.001
Total parenteral nutrit							< 0.001
Total parenteral nutrit							≤ 0.05
Total parenteral r							0.053
Total parenteral r							< 0.01
Total parenteral nutrition							
Total parenteral nutrition							0.007
Fungal Colonisation							0.004
Digestive focus							< 0.01
Colonisation index ≥							< 0.001
Non-*Candida albicans*							0.028
Respiratory focus							0.06[a]
Candida colonisation	Jarda-Marcos *et al*, 2007 [36][a]	4.12 (1.82 to 9.33)	0.001			2.72 (1.33 to 5.58)[b]	< 0.01[b]
Candida colonisation	León *et al*, 2006 [27][a]	3.04 (1.45 to 6.39)	< 0.001	Antifungal medication	Blumberg *et al*, 2001 [29]	0.3 (0.1 to 0.6)	< 0.001
Candida species corrected colonisation index	Pittet *et al*, 1994 [33]	4.01 (2.16 to 7.45)	< 0.001	Central venous catheters	McKinnon *et al*, 2001 [32]	NR	≤ 0.05
				Diarrhoea	McKinnon *et al*, 2001 [32]	NR	≤ 0.05
				Peripheral catheter use	McKinnon *et al*, 2001 [32]	NR	≤ 0.05

Muskett H, Crit Care 2011;15:R287

CRITICAL CARE

Geniş spektrumlu antibiyotik tedavisi

Santral kateter varlığı

Uzamış YBÜ izlemi

Diyabet

İleri yaş

Yanık >%50, major travma

İmmün süpresyon, nötropeni

Table 2 Risk fact

Risk factors						
Surgery						
General abdominal surgery	Agvald-Ohman *et al*, 2008 [28]	60.7 (7.3 to Infinity)	0.0013	New-onset haemodialysis	Papastou *et al*, 2005 [33]	5.4 (2.3 to 11.8)
Any surgery						
Elective surgery						
Surgery on ICU ad						
Gastrointestinal pr						
Major pre-ICU ope						
Major operation d						
Multiple surgical procedures	McKinnon *et al*, 2001 [32]	NR	≤ 0.05	Mechanical ventilation		
Total parenteral nutritio						
Total parenteral nutriti						
Total parenteral n						
Total parenteral n						
Total parenteral nu						
Total parenteral nutrition	Borzotta & Beardsley, 1999 [36]	NR	< 0.001	APACHE II score	Pittet *et al*, 1994 [31]	1.03 (1.01 to 1.05)
Fungal Colonisation						
Digestive focus						
Colonisation index ≥ 0						
Non-*Candida albicans*						
Respiratory focus						
Candida colonisation						
Candida colonisation	León *et al*, 2006 [27]	3.04 (1.45 to 6.39)	< 0.001	Antifungal medication	Blumberg *et al*, 2001 [29]	0.3 (0.1 to 0.6)
Candida species c						

< 0.001	
< 0.0001	
0.029	
0.032	
< 0.001	
< 0.001	
< 0.01	
< 0.01	
< 0.001	
≤ 0.05	
0.053	
< 0.01	
0.007	
0.004	
< 0.01	
< 0.001	
0.028	
0.06	
< 0.01	
< 0.001	
≤ 0.05	
≤ 0.05	
≤ 0.05	

İnvaziv kandida enfeksiyonlarında tanısal güçlükler vardır.

- Klinik bulgular / Anamnez / Fizik inceleme

- Direkt mikroskopi / Histopatolojik inceleme

- Kültür

- Serolojik / Moleküler yöntemler

- Radyoloji

ORIGINAL ARTICLE

High incidence of Candida parapsilosis candidaemia in non-neutropenic critically ill patients: Epidemiology and antifungal susceptibility

MURAT DIZBAY[1], ISIL FIDAN[2], AYSE KALKANCI[2], NURAN SARI[1], BURCE YALCIN[2], SEMRA KUSTIMUR[2] & DILEK ARMAN[1]

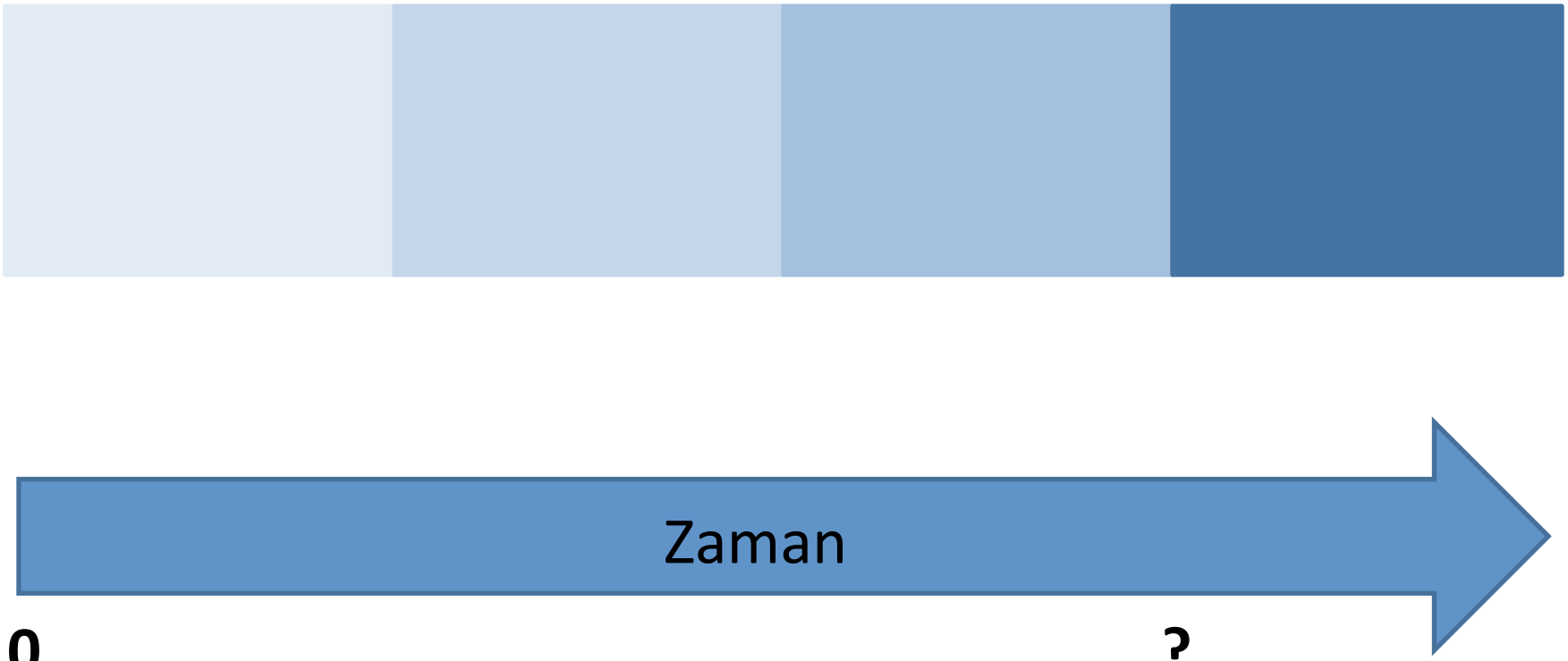
From the [1]Department of Clinical Microbiology and Infectious Diseases, and [2]Department of Microbiology, Gazi University School of Medicine, Besevler, Ankara, Turkey

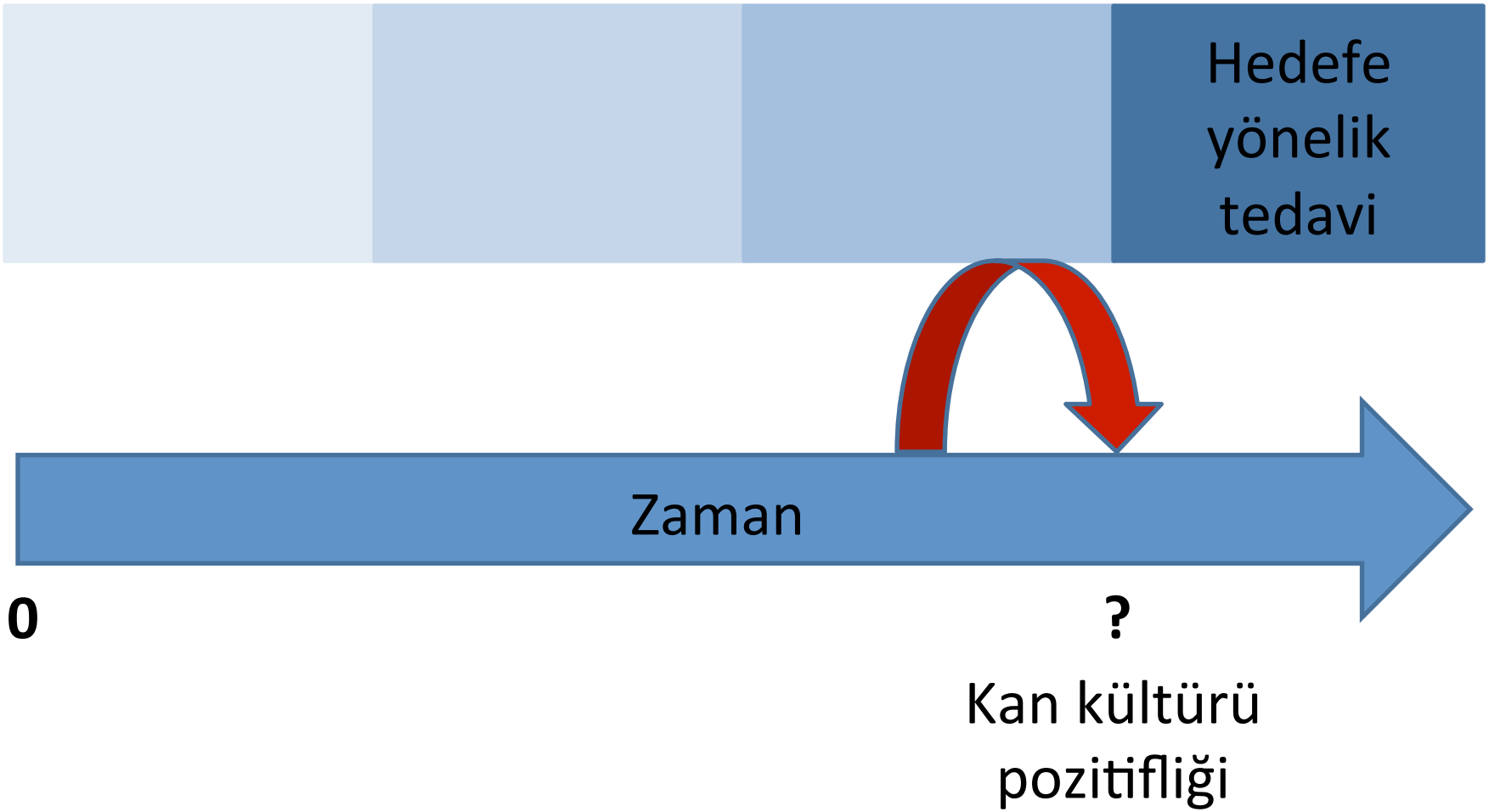
35 kandidemi olgusu,
30 günlük mortalite 23/35 (%65,7)

Ölen hastaların %41,2'sinde kan kültüründe üreme hasta öldükten sonra saptandı…

72 kandidemi olgusu,
30 günlük mortalite 50/72 (%69,4)

9 hastada kan kültüründe üreme hasta öldükten sonra saptandı…


Zaman
0
?
Kan kültürü
pozitifliği


Hedefe yönelik tedavi
Zaman
0
?
Kan kültürü pozitifliği

Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America

Peter G. Pappas,[1] Carol A. Kauffman,[2] David Andes,[4] Daniel K. Benjamin, Jr.,[5] Thierry F. Calandra,[11] John E. Edwards, Jr.,[6] Scott G. Filler,[6] John F. Fisher,[7] Bart-Jan Kullberg,[12] Luis Ostrosky-Zeichner,[8] Annette C. Reboli,[9] John H. Rex,[13] Thomas J. Walsh,[10] and Jack D. Sobel[3]

Table 2. Summary of recommendations for the treatment of candidiasis.

Condition or treatment group	Therapy		
	Primary	Alternative	Comments
Candidemia			
Nonneutropenic adults	Fluconazole 800-mg (12-mg/kg) loading dose, then 400 mg (6 mg/kg) daily or an echinocandin[a] (A-I). For species-specific recommendations, see text.	LFAmB 3–5 mg/kg daily; or AmB-d 0.5–1 mg/kg daily; or voriconazole 400 mg (6 mg/kg) bid for 2 doses, then 200 mg (3 mg/kg) bid (A-I)	Choose an echinocandin for moderately severe to severe illness and for patients with recent azole exposure. Transition to fluconazole after initial echinocandin is appropriate in many cases. Remove all intravascular catheters, if possible. Treat 14 days after first negative blood culture result and resolution of signs and symptoms associated with candidemia. Ophthalmological examination recommended for all patients.

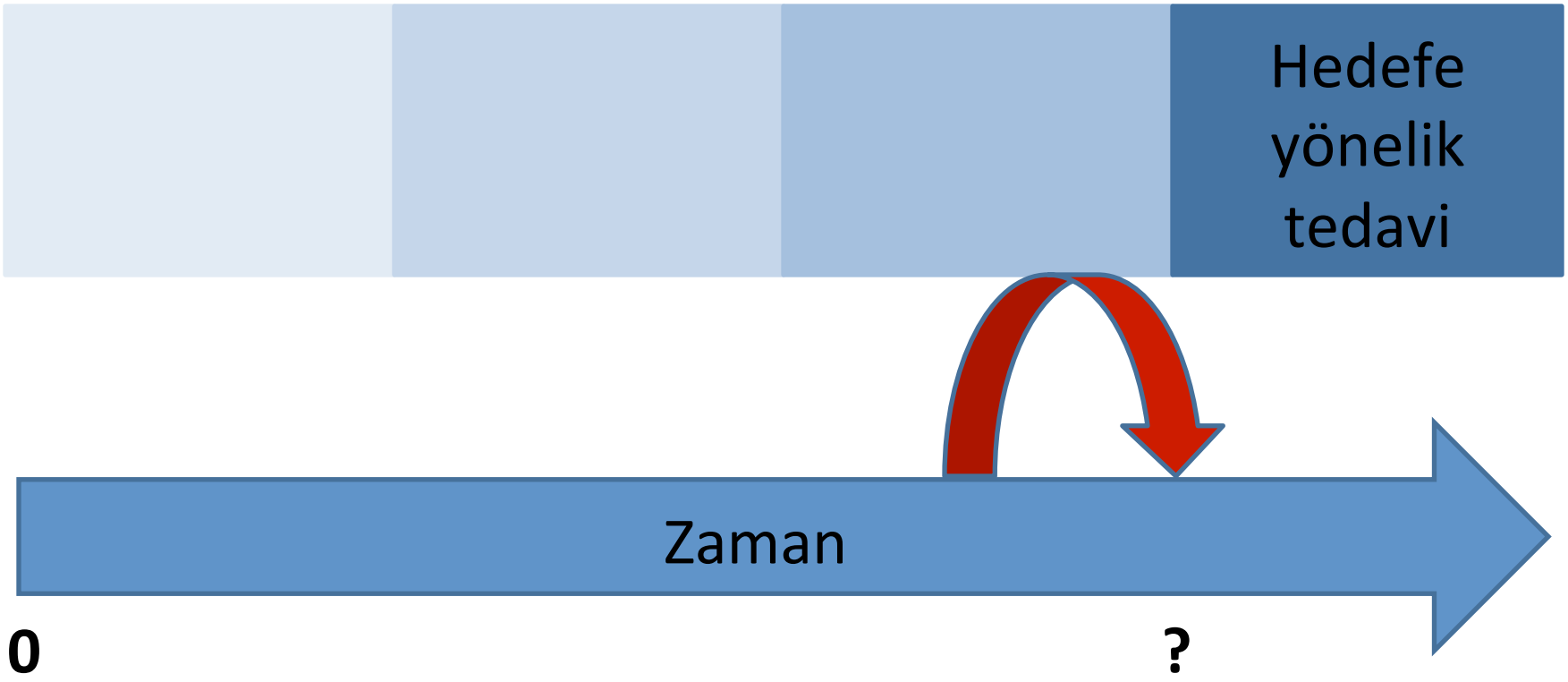
Pappas PG, Clin Infect Dis 2009;48:503

TABLE 5. Recommendations on initial targeted treatment of candidaemia and invasive candidiasis in adult patients

Intervention	SoR	QoE	References	Comment
Anidulafungin 200/100 mg	A	I	[64]	Consider local epidemiology (*Candida parapsilosis*, *Candida krusei*), less drug–drug interactions than caspofungin
Caspofungin 70/50 mg	A	I	[67] [55] [63]	Consider local epidemiology (*C. parapsilosis*)
Micafungin 100 mg	A	I	[61] [63]	Consider local epidemiology (*C. parapsilosis*), less drug–drug interactions than caspofungin, consider EMA warning label
Amphotericin B liposomal 3 mg/kg	B	I	[61] [62]	Similar efficacy as micafungin, higher renal toxicity than micafungin
Voriconazole 6/3 mg/kg/day[a,b]	B	I	[43] [78] [77]	Limited spectrum compared to echinocandins, drug–drug interactions, limitation of IV formulation in renal impairment, consider therapeutic drug monitoring
Fluconazole 400–800 mg[a]	C	I	[165] [53] [74] [54] [64] [76] [75] [73] [72]	Limited spectrum, inferiority to anidulafungin (especially in the subgroup with high APACHE scores), may be better than echinocandins against *C. parapsilosis*
Amphotericin B lipid complex 5 mg/kg	C	II_a	[57] [58]	
Amphotericin B deoxycholate 0.7–1.0 mg/kg	D	I	[50] [51] [165] [53] [54] [55]	Substantial renal and infusion-related toxicity
Amphotericin B deoxycholate plus fluconazole	D	I	[74]	Efficacious, but increased risk of toxicity in ICU patients No survival benefit
Amphotericin B deoxycholate plus 5-fluorocytosine	D	II	[75]	
Efungumab plus lipid-associated amphotericin B	D	II	[166]	
Amphotericin B colloidal dispersion	D	II_a	[60]	
Itraconazole	D	II_a	[76]	
Posaconazole	D	III	No reference found	

EMA, European Medicines Agency.
Comparative clinical trials did not prove a survival benefit of one treatment over another. Primary intention of treating candidaemia is clearing the blood stream.
[a]Not all experts agreed, SoR results from a majority vote.
[b]The licensed maintenance dosing is 4 mg/kg/day.

Cornely OA, Clin Microbiol Infect 2012;18(S7):19


Hedefe yönelik tedavi
Zaman
0
?
Kan kültürü pozitifliği

Kan kültürü pozitifliği

Kan kültürlerinin duyarlılığı düşüktür

Sonuçlanması zaman alıcıdır

İnvazif kandidiyazis otopsi çalışmalarında kan kültürü performansı			
Referans	**Hasta Sayısı**	**Altta Yatan Hastalık**	**Duyarlılık**
Louria (1962)	19	Hematolojik maligniteler, solid tümörler, dahili ve cerrahi durumlar	%42
Bodey (1966)	61	Akut lösemi	%25
Taschdijan (1969)	17	Maligniteler ve diğer dahili durumlar	%47
Hart (1969)	16	Hematolojik maligniteler, solid tümörler, transplantlar, dahili ve cerrahi durumlar	%44
Bernhardt (1972)	14	Transplant ve cerrahi durumlar	%36
Gaines (1973)	26	Hematolojik maligniteler, solid tümörler, dahili ve cerrahi durumlar	%54
Myerowitz (1977)	39	Hematolojik maligniteler, solid tümörler, dahili ve cerrahi durumlar	%44
Ness (1989)	7	Hematolojik maligniteler ve KİT hastaları	%71
Singer (1977)	16	Hematolojik maligniteler	%31
Berenguer (1993)	37	Çoğunlukla hematolojik maligniteler ve solid tümörler	%43
Van Burik (1998)	62	KİT hastaları	%52
Kami (2002)	91	Hematolojik maligniteler	%21
Thorn (2010)	10	Hematolojik maligniteler, gastrointestinal hastalıklar, transplantlar, prematürite	%50

Clancy CJ, Clin Infect Dis 2013;56:1285

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: diagnostic procedures

M. Cuenca-Estrella[1†], P. E. Verweij[2†], M. C. Arendrup[3†], S. Arikan-Akdagli[4†], J. Bille[5†], J. P. Donnelly[2†], H. E. Jensen[6†], C. Lass-Flörl[7†], M. D. Richardson[8†], M. Akova[9], M. Bassetti[10], T. Calandra[11], E. Castagnola[12], O. A. Cornely[13], J. Garbino[14], A. H. Groll[15], R. Herbrecht[16], W. W. Hope[17], B. J. Kullberg[2], O. Lortholary[18,19], W. Meersseman[20], G. Petrikkos[21], E. Roilides[22], C. Viscoli[23] and A. J. Ullmann[24] for the ESCMID Fungal Infection Study Group (EFISG)

1) *Servicio de Micología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain,* 2) *Department of Medical Microbiology, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands,* 3) *Unit of Mycology, Department of Microbiological Surveillance and Research, Statens Serum Institut, Copenhagen, Denmark,* 4) *Department of Medical Microbiology, Hacettepe University School of Medicine, Ankara, Turkey,* 5) *Institute of Microbiology, University of Lausanne and University Hospital Center, Lausanne, Switzerland,* 6) *University of Copenhagen, Frederiksberg, Denmark,* 7) *Divi-*

Kan kültürü alınmasına dair tüm önerilerin uygun biçimde yerine getirildiği durumlarda dahi, duyarlılık %50-75 dolayındadır.

Cuenca-Estrella M, Clin Microbiol Infect 2012;18(S7):9

Kandidemide kan kültürü

Hangi miktarda?

Tek seferde 3 set kan kültürü alınması önerilir (2-4).

Hastanın yaşına göre alınacak toplam kan miktarı değişir:

I. Yetişkinlerde 40-60 ml
II. <2 kg çocuklarda 2-4 ml
III. 2-12 kg çocuklarda 6 ml
IV. 12-36 kg çocuklarda 20 ml

Nereden?

Kültürler, farklı bölgelerden, art arda alınmalıdır.

Önerilen teknik damardan venöz kan alınmasıdır.

Nasıl?

Bir set, 30 dk içerisinde alınmış toplam 60 ml kan (yetişkinlerde) içermelidir.

Alınan örnek, her birine 10 ml'lik miktar olacak şekilde toplam 3 aerob, 3 anaerob şişeye aktarılmalıdır.

Hangi sıklıkta?

Kandidemi şüphesi varlığında, her gün örnek alınması önerilir.

İnkübasyon periyodu en az 5 gün olmalıdır.

Kan kültürü performansı çok iyi değildir ve bir erken tanı tekniği olarak kabul edilemez.

Clancy CJ, Clin Infect Dis 2013;56:1285

JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 2003, p. 4714–4717 Vol. 41, No. 10
0095-1137/03/$08.00+0 DOI: 10.1128/JCM.41.10.4714–4717.2003

Detection of Simulated Candidemia by the BACTEC 9240 System with Plus Aerobic/F and Anaerobic/F Blood Culture Bottles

Lynn L. Horvath,* Duane R. Hospenthal, Clinton K. Murray, and David P. Dooley

Department of Medicine, Brooke Army Medical Center, Fort Sam Houston, Texas

TABLE 3. Incubation time to growth detection by the BACTEC 9240 using Aerobic Plus/F and Anaerobic Plus/F blood culture bottles

Species (total no.	Mean time to growth detection (h) (avg ± SD)	
C. parapsilosis (3)	25.01 ± 0.51 (3)	ND
C. guilliermondii (2)	21.34 ± 0.53 (2)	ND
C. kefyr (2)	14.19 (2)	ND
C. firmetaria (1)	35.19 (1)	ND
C. rugosa (1)	ND	ND

[a] ND, no growth detected by BACTEC 9240 automated system.

Candida türüne göre üreme süresi farklılık gösterir,
En az 5 gün inkübasyon önerilir.

Horvath LL, J Clin Microbiol 2003;41:4714


Hedefe yönelik tedavi
Hedefe yönelik tedavi "gecikmiş tedavi"dir
0
pozitifliği

ESCMID PUBLICATIONS 10.1111/1469-0691.12039

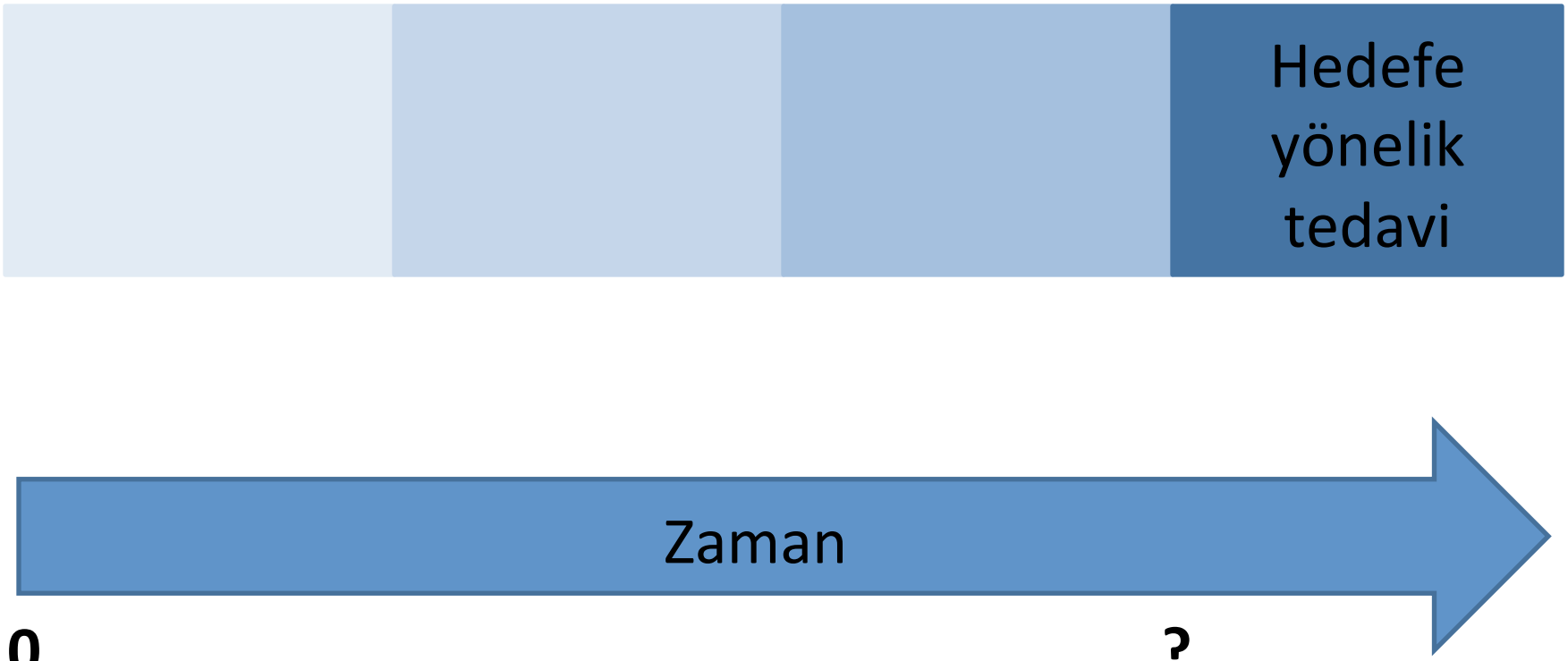
ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

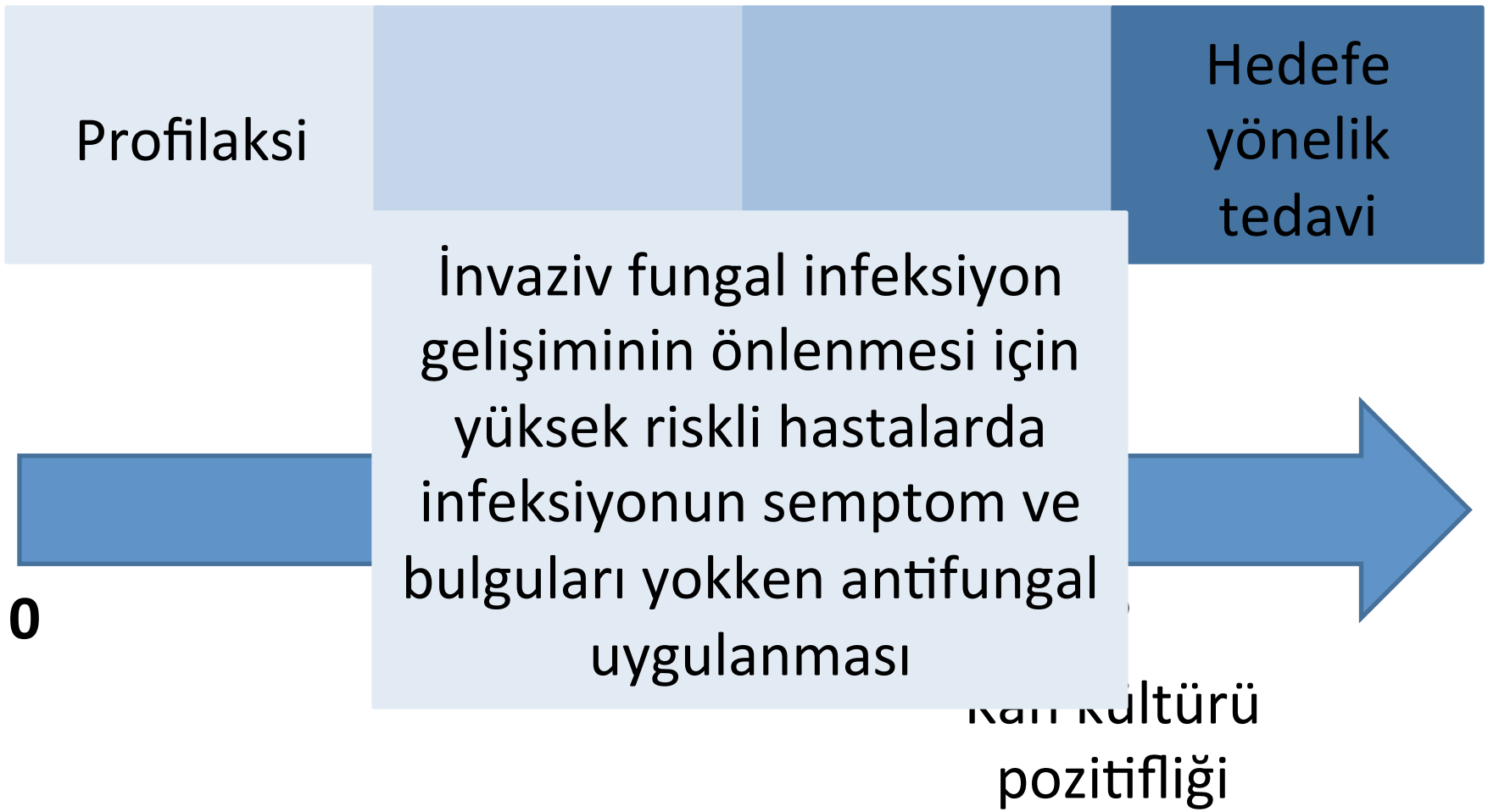
O. A. Cornely[1†], M. Bassetti[2†], T. Calandra[3†], J. Garbino[4†], B. J. Kullberg[5†], O. Lortholary[6,7†], W. Meersseman[8†], M. Akova[9], M. C. Arendrup[10], S. Arikan-Akdagli[11], J. Bille[3], E. Castagnola[12], M. Cuenca-Estrella[13], J. P. Donnelly[5], A. H. Groll[4], R. Herbrecht[15], W. W. Hope[16], H. E. Jensen[17], C. Lass-Flörl[18], G. Petrikkos[19], M. D. Richardson[20], E. Roilides[21], P. E. Verweij[5], C. Viscoli[22] and A. J. Ullmann[23] for the ESCMID Fungal Infection Study Group (EFISG)

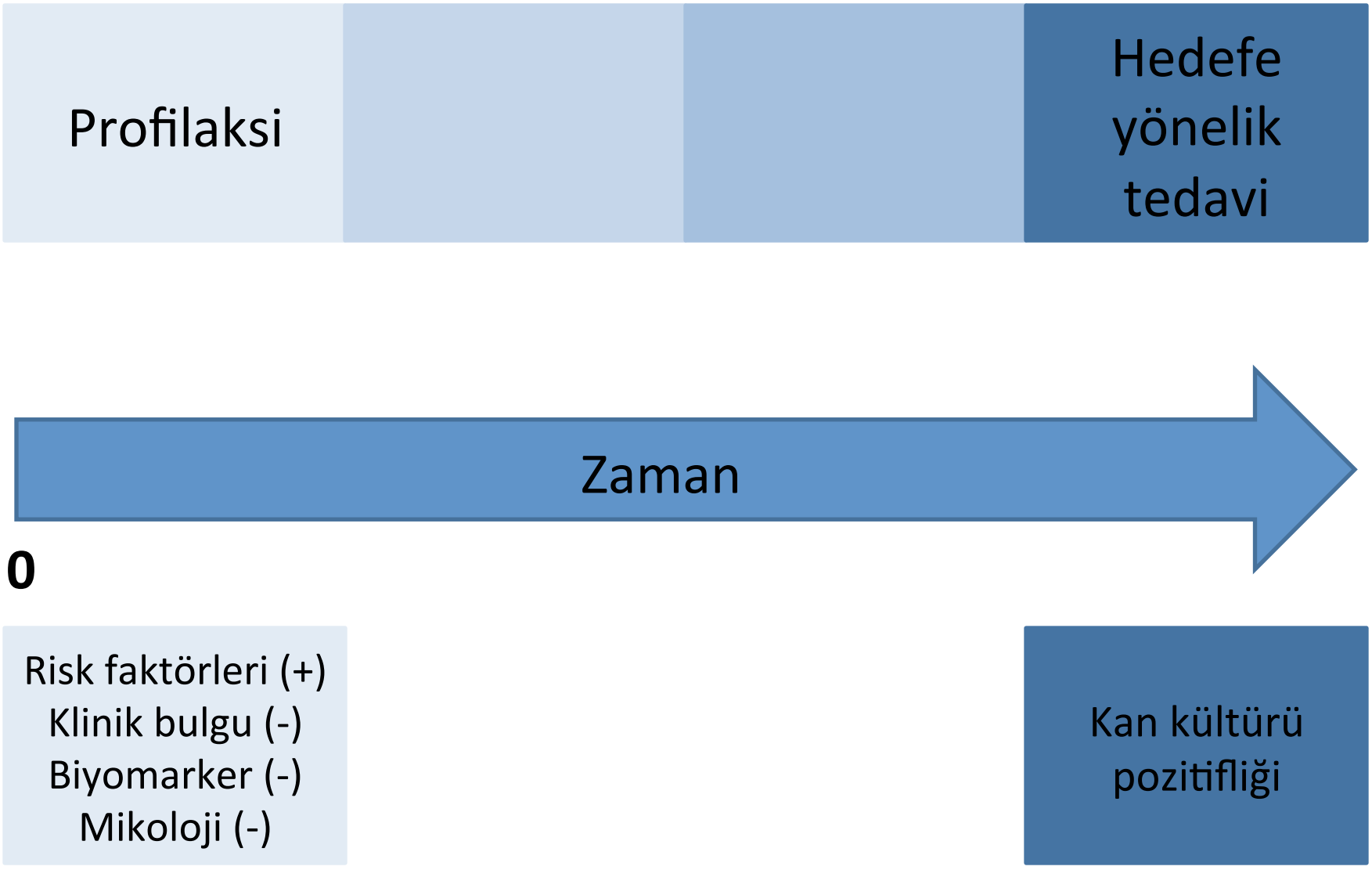
İnvaziv kandidiyazın ve erken tedavi yaklaşımlarından fayda görecek hastaların öngörülebilmesi için iyi tanımlanmış bir yöntem yok,

Antifungal tedavinin başlanması için optimal zamanın belirlenmesi güçtür.

Cornely OA, Clin Microbiol Infect 2012;18(S7):19


Hedefe yönelik tedavi
Zaman
0
?
Kan kültürü pozitifliği


Profilaksi
Hedefe yönelik tedavi
İnvaziv fungal infeksiyon gelişiminin önlenmesi için yüksek riskli hastalarda infeksiyonun semptom ve bulguları yokken antifungal uygulanması
0
pozitifliği


Profilaksi
Hedefe yönelik tedavi
Zaman
0
Risk faktörleri (+)
Klinik bulgu (-)
Biyomarker (-)
Mikoloji (-)
Kan kültürü pozitifliği

ANNALS OF SURGERY
Vol. 233, No. 4, 542–548

Double-Blind Placebo-Controlled Trial of Fluconazole to Prevent Candidal Infections in Critically Ill Surgical Patients

Robert K. Pelz, MD,*‖ Craig W. Hendrix, MD*‡‖ Sandra M. Swoboda, RN, MS,† Marie Diener-West, PhD,‡ William G. Merz, PhD,§ Janet Hammond, MD,* and Pamela A. Lipsett, MD,†¶

Tek merkez, YBÜ yatışı ≥3 gün olan 260 cerrahi olgu

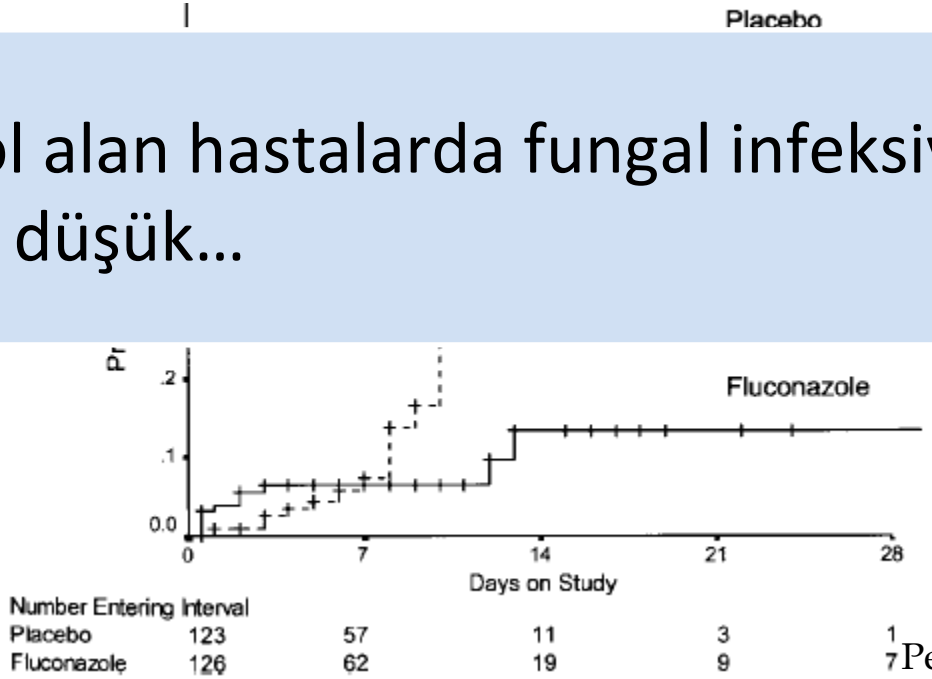
Pelz RK, Ann Surg 2001;233:542

ANNALS OF SURGERY
Vol. 233, No. 4, 542–548

Double-Blind Placebo-Controlled Trial of Fluconazole to Prevent Candidal Infections in Critically Ill Surgical Patients

Robert K. Pelz, MD,*‖ Craig W. Hendrix, MD*‡‖ Sandra M. Swoboda, RN, MS,† Marie Diener-West, PhD,‡ William G. Merz, PhD,§ Janet Hammond, MD,* and Pamela A. Lipsett, MD,†¶

Flukonazol alan hastalarda fungal infeksiyon riski %55 daha düşük…



Pelz RK, Ann Surg 2001;233:542

Journal of Antimicrobial Chemotherapy (2006) 57, 628–638
doi:10.1093/jac/dki491
Advance Access publication 3 February 2006

JAC

Antifungal agents for preventing fungal infections in non-neutropenic critically ill and surgical patients: systematic review and meta-analysis of randomized clinical trials

E. Geoffrey Playford[1,2]*, Angela C. Webster[3,4], Tania C. Sorrell[2,5] and Jonathan C. Craig[3,4]

[1]*Infection Management Services, Princess Alexandra Hospital, Brisbane, Queensland 4102, Australia;* [2]*Department of Medicine, University of Sydney, Sydney, NSW 2006, Australia;* [3]*School of Public Health, University of Sydney, Sydney, NSW 2006, Australia;* [4]*Cochrane Renal Group, Centre for Kidney Research, Children's Hospital at Westmead, NSW 2145, Australia;* [5]*Centre for Infectious Diseases and Microbiology, University of Sydney (Western Clinical School), Westmead, NSW 2145, Australia*

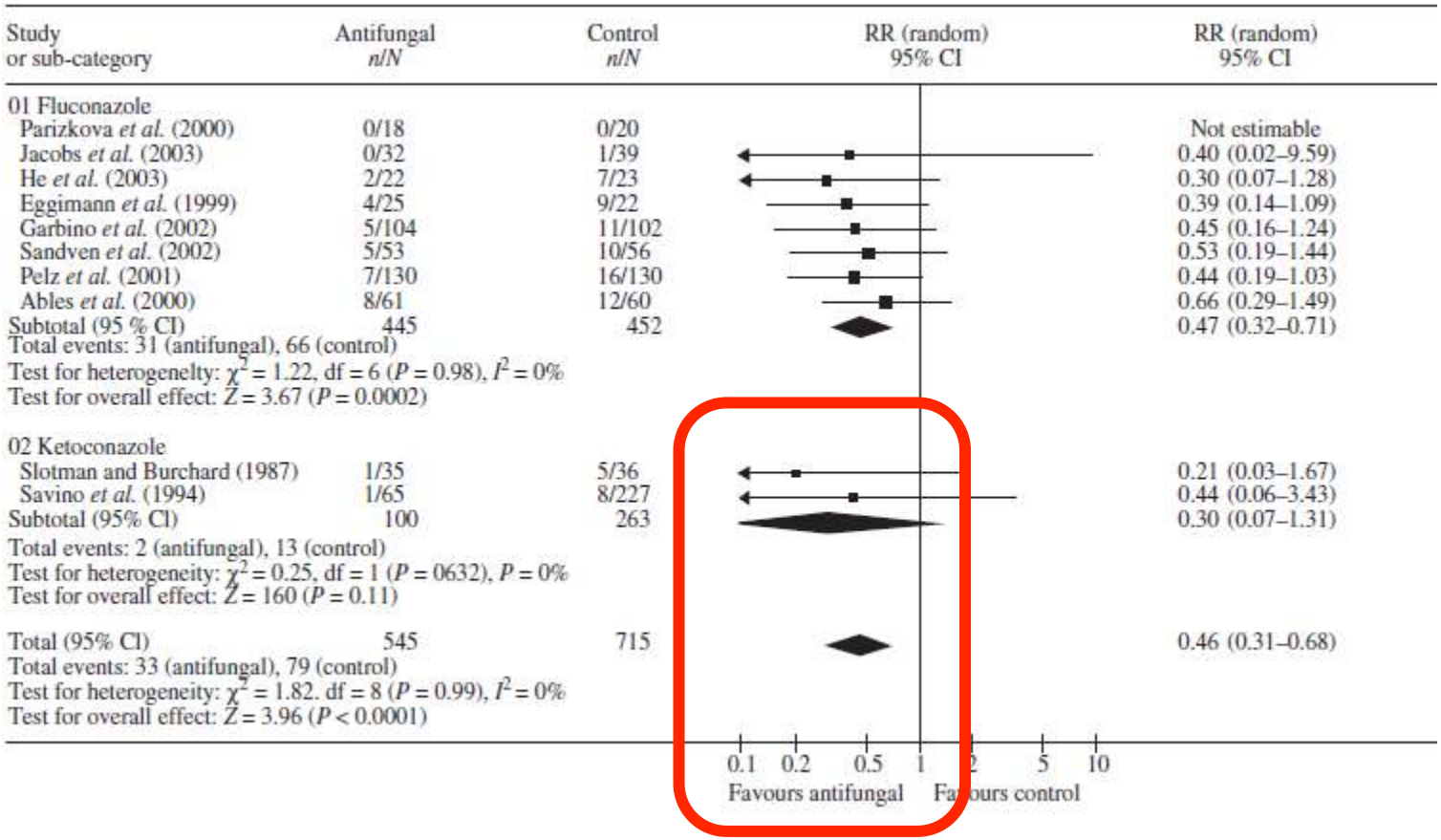
12 RCT, 1606 hasta

Playford EG, J Antimicrob Chemother 2006;57:628

Journal of Antimicrobial Chemotherapy (2006) 57, 628–638
doi:10.1093/jac/dki491
Advance Access publication 3 February 2006

JAC

Antifungal agents for preventing fungal infections in non-neutropenic critically ill and surgical patients: systematic review and meta-analysis of randomized clinical trials



Playford EG, J Antimicrob Chemother 2006;57:628

Prophylaxis, empirical and preemptive treatment of invasive candidiasis

Elliott Geoffrey Playford[a,b], Jeff Lipman[c,d] and Tania C. Sorrell[e,f]

[a]Infection Management Services, Princess Alexandra Hospital, [b]Centre for Clinical Research, University of Queensland, [c]Department of Intensive Care, Royal Brisbane and Women's Hospital, [d]Burns Trauma Critical Care Research Centre, University of Queensland, Brisbane, Queensland, [e]Centre for Infectious Diseases and Microbiology and Westmead Millennium Institute, Westmead and [f]Sydney Medical School, University of Sydney, Sydney, Australia

Correspondence to Dr Geoffrey Playford, Infection Management Services, Princess Alexandra Hospital,

Purpose of review

Invasive candidiasis remains an important infection for ICU patients, associated with poor clinical outcomes. It has been increasingly recognized that the traditional paradigm of culture-directed antifungal treatment is unsatisfactory, and that earlier antifungal intervention strategies, such as prophylaxis, preemptive therapy, and empiric therapy, are required to improve patient outcomes. The purpose of this review is to summarize the recent supportive evidence for such strategies and to highlight the current challenges in their implementation.

"Yüksek riskli" hastaların tanımlanması sorunludur…

Playford EG, Curr Opin Crit Care 2010;16:470

Prophylaxis, empirical and preemptive treatment of invasive candidiasis

Elliott Geoffrey Playford[a,b], Jeff Lipman[c,d] and Tania C. Sorrell[e,f]

[a]Infection Management Services, Princess Alexandra Hospital, [b]Centre for Clinical Research, University of Queensland, [c]Department of Intensive Care, Royal Brisbane and Women's Hospital, [d]Burns Trauma Critical Care Research Centre, University of Queensland, Brisbane, Queensland, [e]Centre for Infectious Diseases and Microbiology and Westmead Millennium Institute, Westmead and [f]Sydney Medical School, University of Sydney, Sydney, Australia

Correspondence to Dr Geoffrey Playford, Infection Management Services, Princess Alexandra Hospital,

Purpose of review

Invasive candidiasis remains an important infection for ICU patients, associated with poor clinical outcomes. It has been increasingly recognized that the traditional paradigm of culture-directed antifungal treatment is unsatisfactory, and that earlier antifungal intervention strategies, such as prophylaxis, preemptive therapy, and empiric therapy, are required to improve patient outcomes. The purpose of this review is to summarize the recent supportive evidence for such strategies and to highlight the current challenges in their implementation.

"Seçilmemiş" YBÜ'lerinde invaziv kandidiyaz insidansı %1-2

Bir infeksiyonun önlenmesi için 100-200 hastaya profilaksi verilmesi gerek…

Playford EG, Curr Opin Crit Care 2010;16:470

Antifungal direnç gelişimi için seçici bir baskı oluşturmak,

Yan etkiler,

Artmış maliyet

ESCMID PUBLICATIONS 10.1111/1469-0691.12039

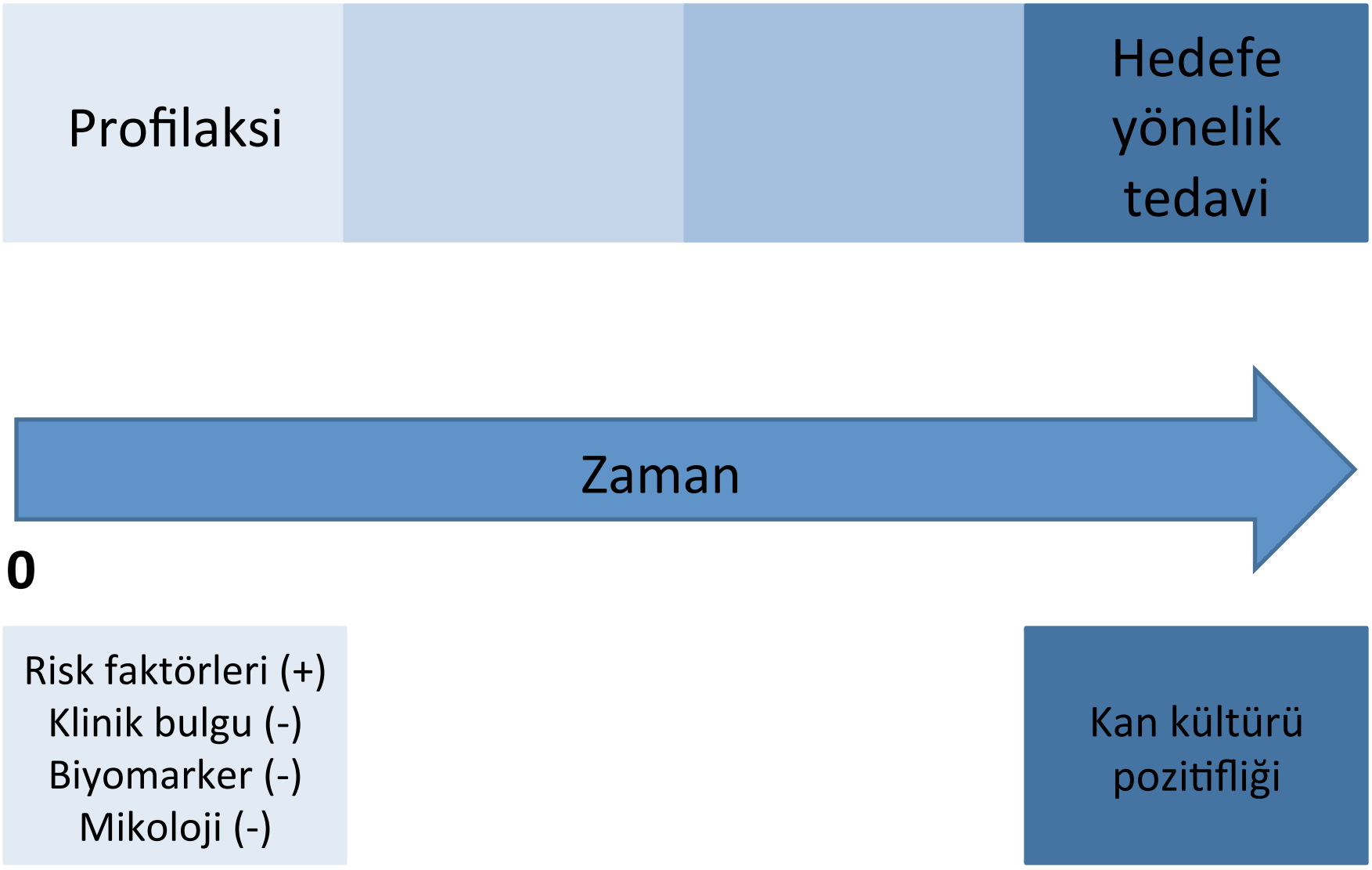
ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

O. A. Cornely[1†], M. Bassetti[2†], T. Calandra[3†], J. Garbino[4†], B. J. Kullberg[5†], O. Lortholary[6,7†], W. Meersseman[8†], M. Akova[9], M. C. Arendrup[10], S. Arikan-Akdagli[11], J. Bille[3], E. Castagnola[12], M. Cuenca-Estrella[13], J. P. Donnelly[5], A. H. Groll[4], R. Herbrecht[15], W. W. Hope[16], H. E. Jensen[17], C. Lass-Flörl[18], G. Petrikkos[19], M. D. Richardson[20], E. Roilides[21], P. E. Verweij[5], C. Viscoli[22] and A. J. Ullmann[23] for the ESCMID Fungal Infection Study Group (EFISG)

Abdominal cerrahi VE rekürren gastrointestinal perforasyonu ya da anastamoz kaçağı olan hastalar (BI)

Critically ill surgical patients with an expected length of ICU stay ≥3 day	To delay the time to fungal infection	Fluconazole 400 mg/day	C	I	[10]	Placebo *N* = 260
Ventilated for 48 h and expected to be ventilated for another ≥72 h	To prevent invasive candidiasis/candidaemia	Fluconazole 100 mg/day	C	I	[162]	Placebo *N* = 204 SDD used
Ventilated, hospitalized for ≥3 day, received antibiotics, CVC, and ≥1 of: parenteral nutrition, dialysis, major surgery, pancreatitis, systemic steroids, immunosuppression	To prevent invasive candidiasis/candidaemia	Caspofungin 50 mg/day	C	II_a	[5]	Placebo *N* = 186 EORTC/MSG criteria used
Surgical ICU patients	To prevent invasive candidiasis/candidaemia	Ketoconazole 200 mg/day	D	I	[22]	Placebo *N* = 57
Critically ill patients with risk factors for invasive candidiasis/candidaemia	To prevent invasive candidiasis/candidaemia	Itraconazole 400 mg/day	D	I	[21]	Open *N* = 147
Surgical ICU with catabolism	To prevent invasive candidiasis/candidaemia	Nystatin 4 Mio IU/day	D	I	[20]	Placebo *N* = 46

Cornely OA, Clin Microbiol Infect 2012;18(S7):19


Profilaksi
Hedefe yönelik tedavi
Zaman
0
Risk faktörleri (+)
Klinik bulgu (-)
Biyomarker (-)
Mikoloji (-)
Kan kültürü pozitifliği

Profilaksi	Pre-emptif tedavi	Ampirik tedavi	Hedefe yönelik tedavi

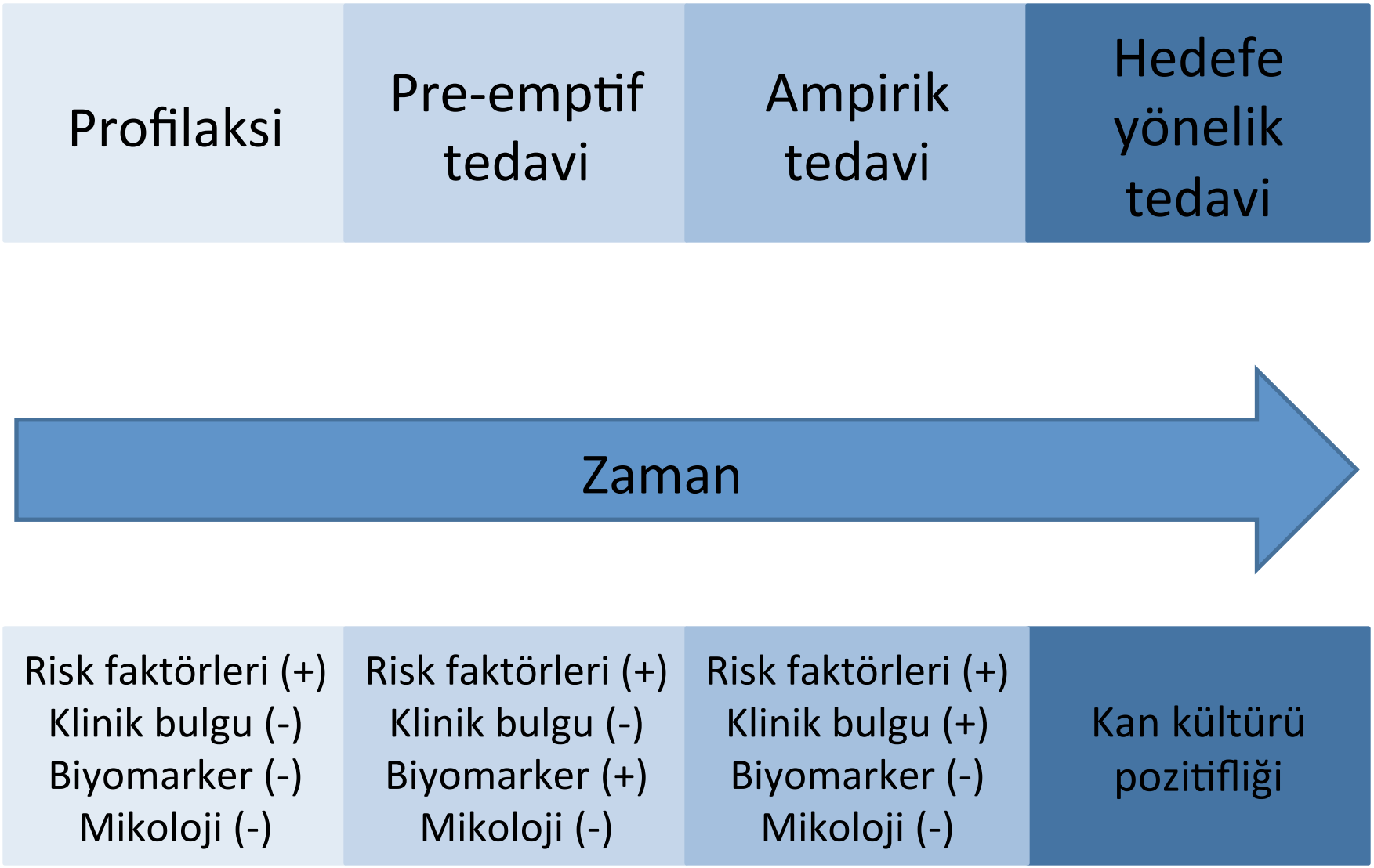
İnfeksiyon riskini gösteren bir ya da birkaç biyolojik göstergeye dayanarak tedavi başlanması

Mikrobiyolojik doğrulama olmaksızın inflamatuvar yanıt sendromu klinik bulguları olan hastalara tedavi başlanması

0

Biyomarker (-)
Mikoloji (-)

pozitifliği


Profilaksi
Pre-emptif tedavi
Ampirik tedavi
Hedefe yönelik tedavi
Zaman
Risk faktörleri (+)
Klinik bulgu (-)
Biyomarker (-)
Mikoloji (-)
Risk faktörleri (+)
Klinik bulgu (-)
Biyomarker (+)
Mikoloji (-)
Risk faktörleri (+)
Klinik bulgu (+)
Biyomarker (-)
Mikoloji (-)
Kan kültürü pozitifliği

Ampirik tedavi

Mikrobiyolojik doğrulama olmaksızın inflamatuvar yanıt sendromu klinik bulguları olan hastalara tedavi başlanması

Journal of Antimicrobial Chemotherapy (2007) **60**, 613–618
doi:10.1093/jac/dkm212
Advance Access publication 18 June 2007

JAC

Adequacy of empirical antifungal therapy and effect on outcome among patients with invasive *Candida* species infections

Michael D. Parkins[1], Deana M. Sabuda[1], Sameer Elsayed[2–4] and Kevin B. Laupland[1–3,5,6]*

[1]*Department of Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;* [2]*Department of Pathology and Laboratory Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;* [3]*The Center for Anti-Microbial Resistance, Calgary Health Region, University of Calgary and Calgary Laboratory Services, Calgary, Alberta, Canada;* [4]*Division of Microbiology, Calgary Laboratory Services, Calgary, Alberta, Canada;* [5]*Department of Critical Care Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;* [6]*Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada*

Tek merkez, 207 kandidemi olgusu

%32 ampirik tedavi

Parkins MD, J Antimicrob Chemother 2007;60:613

Journal of Antimicrobial Chemotherapy (2007) **60**, 613–618
doi:10.1093/jac/dkm212
Advance Access publication 18 June 2007

JAC

Adequacy of empirical antifungal therapy and effect on outcome among patients with invasive *Candida* species infections

Michael D. Parkins[1], Deana M. Sabuda[1], Sameer Elsayed[2–4] and Kevin B. Laupland[1–3,5,6]*

[1]*Department of Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;* [2]*Department of Pathology and Laboratory Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;* [3]*The Center for Anti-Microbial Resistance, Calgary Health Region, University of Calgary and Calgary Laboratory Services, Calgary, Alberta, Canada;* [4]*Division of Microbiology, Calgary Laboratory Services, Calgary, Alberta, Canada;* [5]*Department of Critical Care Medicine, Calgary Health Region and University of Calgary, Calgary, Alberta, Canada;* [6]*Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada*

Uygun ampirik tedavi alanlar ile almayanlarda kaba mortalite %27 vs %46 (p=0.02)

Parkins MD, J Antimicrob Chemother 2007;60:613

P47

Empirical antifungal treatment in the critically ill patients: how does it impact on the outcome?

R Bruyère, C Vigneron, J Quenot, M Hamet, F Dalle, S Prin, PE Charles
University Hospital, Dijon, France

Critical Care 2012, **16(Suppl 1):**P47 (doi: 10.1186/cc10654)

Ampirik antifungal tedavi alan hastalarda klinik düzelme, kanıtlanmış invaziv kandidiyazı olan olgulara göre anlamlı olarak daha yüksektir (p=0.032)

Bruyere R, Crit Care 2012;16(S1):P47

Prophylaxis, empirical and preemptive treatment of invasive candidiasis

Elliott Geoffrey Playford[a,b], Jeff Lipman[c,d] and Tania C. Sorrell[e,f]

[a]Infection Management Services, Princess Alexandra Hospital, [b]Centre for Clinical Research, University of Queensland, [c]Department of Intensive Care, Royal Brisbane and Women's Hospital, [d]Burns Trauma Critical Care Research Centre, University of Queensland, Brisbane, Queensland, [e]Centre for Infectious Diseases and Microbiology and Westmead Millennium Institute, Westmead and [f]Sydney Medical School, University of Sydney, Sydney, Australia

Correspondence to Dr Geoffrey Playford, Infection Management Services, Princess Alexandra Hospital,

Purpose of review

Invasive candidiasis remains an important infection for ICU patients, associated with poor clinical outcomes. It has been increasingly recognized that the traditional paradigm of culture-directed antifungal treatment is unsatisfactory, and that earlier antifungal intervention strategies, such as prophylaxis, preemptive therapy, and empiric therapy, are required to improve patient outcomes. The purpose of this review is to summarize the recent supportive evidence for such strategies and to highlight the current challenges in their implementation.

Bu yaklaşımın temel sorunu, invaziv kandidiyaz ile fungal olmayan diğer infektif ve noninfektif süreçlerin klinik bulgularının örtüşmesidir.

Playford EG, Curr Opin Crit Care 2010;16:470

Annals of Internal Medicine | ARTICLE

Empirical Fluconazole versus Placebo for Intensive Care Unit Patients

A Randomized Trial

Mindy G. Schuster, MD; John E. Edwards Jr., MD; Jack D. Sobel, MD; Rabih O. Darouiche, MD; Adolf W. Karchmer, MD; Susan Hadley, MD; Gus Slotman, MD; Helene Panzer, PhD; Pinaki Biswas, PhD; and John H. Rex, MD

Background: Invasive infection with *Candida* species is an important cause of morbidity and mortality in intensive care unit (ICU) patients. Optimal preventive strategies have not been clearly defined.

Objective: To see whether empirical fluconazole improves clinical outcomes more than placebo in adult ICU patients at high risk for invasive candidiasis.

Results: Only 44 of 122 (36%) fluconazole recipients and 48 of 127 (38%) placebo recipients had a successful outcome (relative risk, 0.95 [95% CI, 0.69 to 1.32; $P = 0.78$]). The main reason for failure was lack of resolution of fever (51% for fluconazole and 57% for placebo). Documented invasive candidiasis occurred in 5% of fluconazole recipients and 9% of placebo recipients (relative risk, 0.57 [CI, 0.22 to 1.49]). Seven (5%) fluconazole recipients and 10 (7%) placebo recipients had adverse events resulting in discontin-

Çok merkezli, RCT,
Antibakteriyellere refrakter ateşi olan 270 olgu
APACHE II>16

Flukonazol vs plasebo

Schuster MG, Ann Intern Med 2008;149:83

Annals of Internal Medicine | ARTICLE

Empirical Fluconazole versus Placebo for Intensive Care Unit Patients

A Randomized Trial

Mindy G. Schuster, MD; John E. Edwards Jr., MD; Jack D. Sobel, MD; Rabih O. Darouiche, MD; Adolf W. Karchmer, MD; Susan Hadley, MD; Gus Slotman, MD; Helene Panzer, PhD; Pinaki Biswas, PhD; and John H. Rex, MD

Background: Invasive infection with *Candida* species is an important cause of morbidity and mortality in intensive care unit (ICU) patients. Optimal preventive strategies have not been clearly defined.

Objective: To see whether empirical fluconazole improves clinical outcomes more than placebo in adult ICU patients at high risk for invasive candidiasis.

Results: Only 44 of 122 (36%) fluconazole recipients and 48 of 127 (38%) placebo recipients had a successful outcome (relative risk, 0.95 [95% CI, 0.69 to 1.32; $P = 0.78$]). The main reason for failure was lack of resolution of fever (51% for fluconazole and 57% for placebo). Documented invasive candidiasis occurred in 5% of fluconazole recipients and 9% of placebo recipients (relative risk, 0.57 [CI, 0.22 to 1.49]). Seven (5%) fluconazole recipients and 10 (7%) placebo recipients had adverse events resulting in discontin-

Tedavi başarısı açısından iki grup arasında fark yok.

Schuster MG, Ann Intern Med 2008;149:83

Annals of Internal Medicine | ARTICLE

Empirical Fluconazole versus Placebo for Intensive Care Unit Patients

A Randomized Trial

Mindy G. Schuster, MD; John E. Edwards Jr., MD; Jack D. Sobel, MD; Rabih O. Darouiche, MD; Adolf W. Karchmer, MD; Susan Hadley, MD; Gus Slotman, MD; Helene Panzer, PhD; Pinaki Biswas, PhD; and John H. Rex, MD

Background: Invasive infection with *Candida* species is an important cause of morbidity and mortality in intensive care unit (ICU) patients. Optimal preventive strategies have not been clearly defined.

Objective: To see whether empirical fluconazole improves clinical outcomes more than placebo in adult ICU patients at high risk for invasive candidiasis.

Results: Only 44 of 122 (36%) fluconazole recipients and 48 of 127 (38%) placebo recipients had a successful outcome (relative risk, 0.95 [95% CI, 0.69 to 1.32; $P = 0.78$]). The main reason for failure was lack of resolution of fever (51% for fluconazole and 57% for placebo). Documented invasive candidiasis occurred in 5% of fluconazole recipients and 9% of placebo recipients (relative risk, 0.57 [CI, 0.22 to 1.49]). Seven (5%) fluconazole recipients and 10 (7%) placebo recipients had adverse events resulting in discontin-

Sadece nonspesifik klinik özelliklere dayanarak ampirik antifungal tedavi başlanmasının yararı tartışmalıdır.

Schuster MG, Ann Intern Med 2008;149:83

ESCMID PUBLICATIONS 10.1111/1469-0691.12039

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

O. A. Cornely[1†], M. Bassetti[2†], T. Calandra[3†], J. Garbino[4†], B. J. Kullberg[5†], O. Lortholary[6,7†], W. Meersseman[8†], M. Akova[9], M. C. Arendrup[10], S. Arikan-Akdagli[11], J. Bille[3], E. Castagnola[12], M. Cuenca-Estrella[13], J. P. Donnelly[5], A. H. Groll[4], R. Herbrecht[15], W. W. Hope[16], H. E. Jensen[17], C. Lass-Flörl[18], G. Petrikkos[19], M. D. Richardson[20], E. Roilides[21], P. E. Verweij[5], C. Viscoli[22] and A. J. Ullmann[23] for the ESCMID Fungal Infection Study Group (EFISG)

TABLE 4. Recommendations on fever-driven and diagnosis-driven therapy of candidaemia and invasive candidiasis

Population	Intention	Intervention	SoR	QoE	References
Adult ICU patients with fever despite broad-spectrum antibiotics and APACHE II > 16	To resolve fever	Fluconazole 800 mg/day	D	I	[30]
					[32] [36] [34] [33]
Any patient with *Candida* isolated from a blood culture	To cure invasive candidiasis	Antifungal treatment	A	II	[46] [47] [48] [49]

Ampirik tedavi mortalitenin azalmasını sağlayabilir ancak antifungal tedavinin başlanması kararının neye göre verileceği belirsizdir (CII).

Cornely OA, Clin Microbiol Infect 2012;18(S7):19

Pre-emptif tedavi

İnfeksiyon riskini gösteren bir ya da birkaç biyolojik göstergeye dayanarak tedavi başlanması

Serolojik yöntemler

Kolonizasyon temelli risk değerlendirmesi

Skorlama yöntemleri ile risk değerlendirmesi

JOURNAL OF CLINICAL MICROBIOLOGY, Dec. 2005, p. 5957–5962 Vol. 43, No. 12
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.12.5957–5962.2005

Evaluation of a (1→3)-β-D-Glucan Assay for Diagnosis of Invasive Fungal Infections

Jerry W. Pickering,[1]* Howard W. Sant,[1] Catherine A. P. Bowles,[1,2] William L. Roberts,[1,2] and Gail L. Woods[1,2]

Associated Regional and University Pathologists, Inc. (ARUP), Institute for Clinical and Experimental Pathology, Salt Lake City, Utah 84108,[1] and Department of Pathology, University of Utah School of Medicine, Salt Lake City, Utah 84108[2]

Duyarlılık %93,3, özgüllük %77,2
PPV %51.9, NPV %97,8

Pickering JW, J Clin Microbiol 2005;43:5957

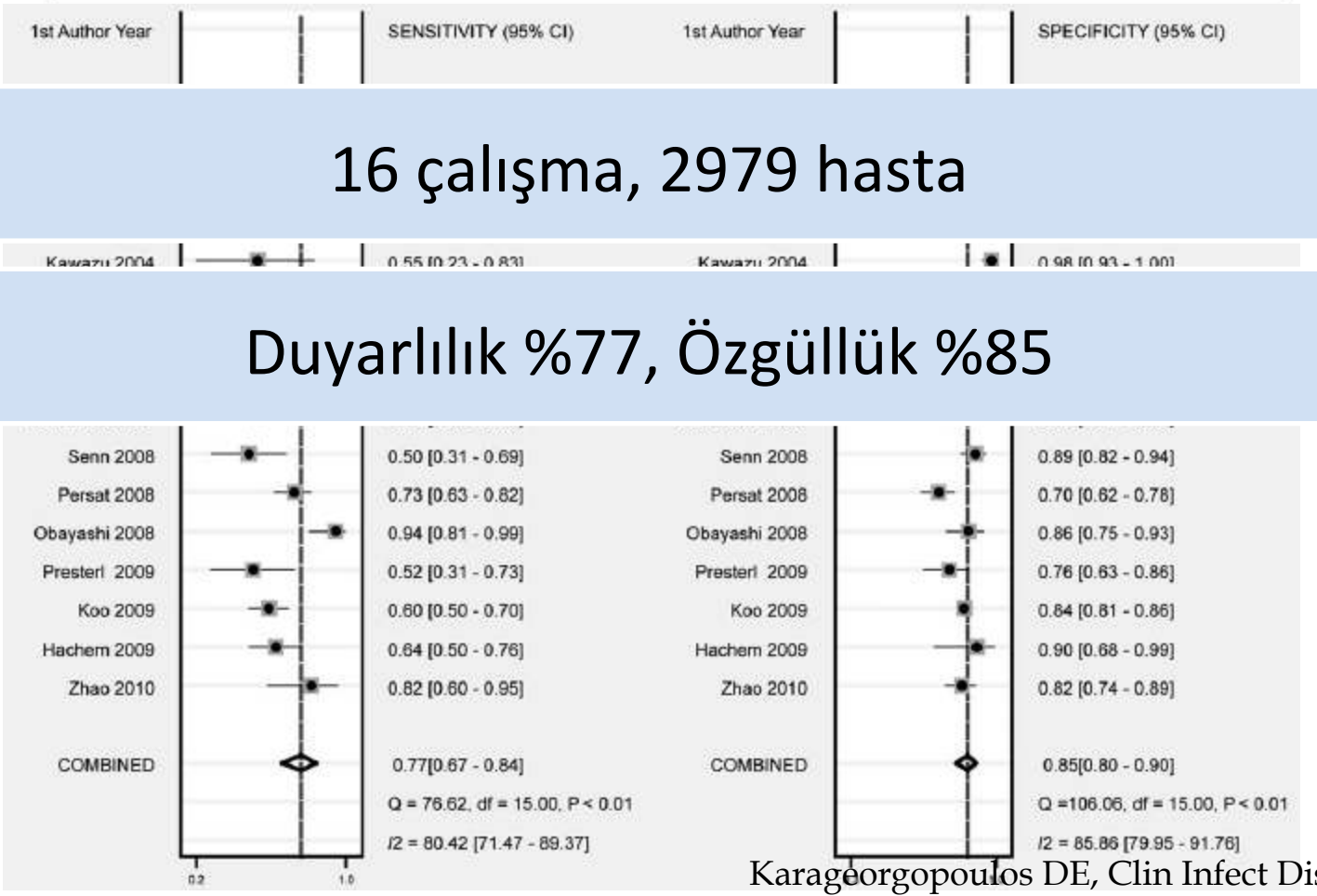
β-D-Glucan Assay for the Diagnosis of Invasive Fungal Infections: A Meta-analysis

Drosos E. Karageorgopoulos,[1,2] Evridiki K. Vouloumanou,[1] Fotinie Ntziora,[1,2] Argyris Michalopoulos,[1,3] Petros I. Rafailidis,[1,4] and Matthew E. Falagas[1,4,5]

[1]Alfa Institute of Biomedical Sciences; [2]Department of Medicine, Laikon General Hospital, and [3]Intensive Care Unit and [4]Department of Medicine, Henry Dunant Hospital, Athens, Greece; and [5]Department of Medicine, Tufts University School of Medicine, Boston, Massachusetts

16 çalışma, 2979 hasta

Duyarlılık %77, Özgüllük %85



Karageorgopoulos DE, Clin Infect Dis 2011;52:750

OPEN ACCESS Freely available online

PLoS one

β-D-glucan Surveillance with Preemptive Anidulafungin for Invasive Candidiasis in Intensive Care Unit Patients: A Randomized Pilot Study

Kimberly E. Hanson[1]*, Christopher D. Pfeiffer[2], Erika D. Lease[3], Alfred H. Balch[4], Aimee K. Zaas[3], John R. Perfect[3], Barbara D. Alexander[3]*

1 Departments of Medicine and Pathology, University of Utah, Salt Lake City, Utah, United States of America, **2** Department of Medicine, Oregon Health Sciences University, Portland, Oregon, United States of America, **3** Department of Medicine, Duke University, Durham, North Carolina, United States of America, **4** Department of

64 hasta,
BDG düzeyleri invaziv kandidiyazı olan hastalarda daha yüksek (117 pg/ml vs 28 pg/ml, $p<0.001$)

2 ardışık BDG>80 pg/ml
duyarlılık %100, özgüllük %75
ppv %30, npv %100

Hanson KE, PLoS One 2012;7:e42282

(1-3) β-D-Glukan testinin özgüllüğü düşüktür.

– Kan/kan ürünleri transfüzyonu,
– Albümin kullanımı,
– İmmunglobulin kullanımı,
– Hemodiyaliz / selülöz membran kullanımı,
– Gram pozitif kan dolaşımı infeksiyonları,
– Beta-laktam antibiyotikler,
– Cerrahi tamponlar ve gazlı bez kullanımı

yalancı pozitif sonuçlarla ilişkili

ESCMID PUBLICATIONS 10.1111/1469-0691.12039

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

O. A. Cornely[1†], M. Bassetti[2†], T. Calandra[3†], J. Garbino[4†], B. J. Kullberg[5†], O. Lortholary[6,7†], W. Meersseman[8†], M. Akova[9], M. C. Arendrup[10], S. Arikan-Akdagli[11], J. Bille[3], E. Castagnola[12], M. Cuenca-Estrella[13], J. P. Donnelly[5], A. H. Groll[4], R. Herbrecht[15], W. W. Hope[16], H. E. Jensen[17], C. Lass-Flörl[18], G. Petrikkos[19], M. D. Richardson[20], E. Roilides[21], P. E. Verweij[5], C. Viscoli[22] and A. J. Ullmann[23] for the ESCMID Fungal Infection Study Group (EFISG)

İnvaziv kandidiyazı güvenilir biçimde doğrulamamakla birlikte yüksek NPV nedeniyle dışlamak için kullanılabilir.

Cut-off 80 pg/ml

YBÜ hastalarında haftada iki kez 1-3 BDG izlemi önerilmektedir.

Cornely OA, Clin Microbiol Infect 2012;18(S7):19

JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2011, p. 58–61 Vol. 49, No. 1
0095-1137/11/$12.00 doi:10.1128/JCM.01240-10

Prospective Survey of (1→3)-β-D-Glucan and Its Relationship to Invasive Candidiasis in the Surgical Intensive Care Unit Setting▽

John F. Mohr,[1] Charles Sims,[1] Victor Paetznick,[1] Jose Rodriguez,[1] Malcolm A. Finkelman,[2] John H. Rex,[1,3] and Luis Ostrosky-Zeichner[1]*

Division of Infectious Diseases and Center for the Study of Emerging and Re-emerging Pathogens, University of Texas Health Science Center, Houston, Texas[1]; Associates of Cape Cod, Falmouth, Massachusetts[2]; and Astra Zeneca, Macclesfield, United Kingdom[3]

1-3 β-D-Glukan testinin invaziv infeksiyon gelişen hastalarda kan kültüründe üremeden 6 gün önce pozitifleştiği belirlenmiştir.

Mohr JF, J Clin Microbiol 2011;49:58

MAJOR ARTICLE

(1,3)-β-D-Glucan as a Prognostic Marker of Treatment Response in Invasive Candidiasis

Siraya Jaijakul,[1] Jose A. Vazquez,[2] Robert N. Swanson,[3] and Luis Ostrosky-Zeichner[1]

[1]University of Texas Health Science Center at Houston; [2]Henry Ford Hospital, Detroit, Michigan; and [3]Pfizer, Inc, New York, New York

Tedavi sırasında BDG düzeylerinde düşüş, tedavi başarısı ile ilişkilidir.

Jaijakul S, Clin Infect Dis 2012;55:521

JCM
Journals.ASM.org

LETTER TO THE EDITOR

Why Should We Monitor (1-3)-β-D-Glucan Levels during Invasive Candidiasis? Just Ask Your Ophthalmologist!

Gennaro De Pascale,[a] Brunella Posteraro,[b] Salvatore Lucio Cutuli,[a] Anselmo Caricato,[a] Domenico Lepore,[c] Mario Tumbarello,[d] Mariano Alberto Pennisi,[a] Maurizio Sanguinetti,[e] Massimo Antonelli[a]

Department of Intensive Care and Anesthesiology, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy[a]; Institute of Hygiene, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy[b]; Department of Ophthalmology, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy[c]; Institute of Infectious Diseases, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy[d]; Institute of Microbiology, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy[e]

Tedavi ile BDG düzeylerinde düşüş gerçekleşmemesi, residüel / metastatik fungal odağı akla getirmelidir.

De Pascale G, J Clin Microbiol 2013;51:1645

Mikulska *et al. Critical Care* 2010, **14**:R222
http://ccforum.com/content/14/6/R222

CRITICAL CARE

RESEARCH Open Access

The use of mannan antigen and anti-mannan antibodies in the diagnosis of invasive candidiasis: recommendations from the Third European Conference on Infections in Leukemia

Małgorzata Mikulska[1*], Thierry Calandra[2], Maurizio Sanguinetti[3], Daniel Poulain[4], Claudio Viscoli[5], the Third European Conference on Infections in Leukemia Group

14 çalışma, 453 hasta

Mn Ag >0,5 ng/ml
Anti-Mn >10 U/ml

Mikulska M, Crit Care 2010;14:R222

Mikulska *et al. Critical Care* 2010, **14**:R222
http://ccforum.com/content/14/6/R222

CRITICAL CARE

RESEARCH Open Access

The use of mannan antigen and anti-mannan antibodies in the diagnosis of invasive candidiasis: recommendations from the Third European Conference on Infections in Leukemia

Małgorzata Mikulska[1*], Thierry Calandra[2], Maurizio Sanguinetti[3], Daniel Poulain[4], Claudio Viscoli[5], the Third European Conference on Infections in Leukemia Group

Kombine Mn/A-Mn testi
duyarlılık %83, özgüllük %86

Kan kültürlerinden ortalama 6 gün önce pozitifleşiyor.

Mikulska M, Crit Care 2010;14:R222

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: diagnostic procedures

M. Cuenca-Estrella[1†], P. E. Verweij[2†], M. C. Arendrup[3†], S. Arikan-Akdagli[4†], J. Bille[5†], J. P. Donnelly[2†], H. E. Jensen[6†], C. Lass-Flörl[7†], M. D. Richardson[8†], M. Akova[9], M. Bassetti[10], T. Calandra[11], E. Castagnola[12], O. A. Cornely[13], J. Garbino[14], A. H. Groll[15], R. Herbrecht[16], W. W. Hope[17], B. J. Kullberg[2], O. Lortholary[18,19], W. Meersseman[20], G. Petrikkos[21], E. Roilides[22], C. Viscoli[23] and A. J. Ullmann[24] for the ESCMID Fungal Infection Study Group (EFISG)

1) *Servicio de Micología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain,* 2) *Department of Medical Microbiology, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands,* 3) *Unit of Mycology, Department of Microbiological Surveillance and Research, Statens Serum Institut, Copenhagen, Denmark,* 4) *Department of Medical Microbiology, Hacettepe University School of Medicine, Ankara, Turkey,* 5) *Institute of Microbiology, University of Lausanne and University Hospital Center, Lausanne, Switzerland,* 6) *University of Copenhagen, Frederiksberg, Denmark,* 7) *Divi-*

TABLE 2. Summary of recommendations by *Candida* disease, specimen and test evaluated

Disease		Test	Recommendation	Level of evidence
Cand				
Invasi				
		In-house PCR	No recommendation	No data
	Tissue and sterile body fluids	Direct microscopy and histopathology	Essential investigation	NA
		Culture	Essential investigation	NA
		Immuno-histochemistry	No recommendation	No data
		Tissue PCR	No recommendation	No data
		In situ hybridization	No recommendation	No data

BDG ve Mn/A-Mn testleri, gereksiz profilaktik ya da ampirik antifungal kullanımını önlenme stratejisi olarak kullanılabilir.

Cuenca-Estrella M, Clin Microbiol Infect 2012;18(S7):9

JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2011, p. 665–670 Vol. 49, No. 2
0095-1137/11/$12.00 doi:10.1128/JCM.01602-10

PCR Diagnosis of Invasive Candidiasis: Systematic Review and Meta-Analysis▽†

Tomer Avni,[1]* Leonard Leibovici,[1] and Mical Paul[2]

Medicine E[1] and Unit of Infectious Diseases,[2] Rabin Medical Center, Beilinson Hospital and Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

54 çalışma, 4694 hasta

Kandidemili olgularda D/Ö: %100

Şüpheli olgularda duyarlılık %95, özgüllük %92

Tam kan örneklerinden PCR incelemesinin, kandidiyazın erken tanısında yeri vardır.

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: diagnostic procedures

M. Cuenca-Estrella[1†], P. E. Verweij[2†], M. C. Arendrup[3†], S. Arikan-Akdagli[4†], J. Bille[5†], J. P. Donnelly[2†], H. E. Jensen[6†], C. Lass-Flörl[7†], M. D. Richardson[8†], M. Akova[9], M. Bassetti[10], T. Calandra[11], E. Castagnola[12], O. A. Cornely[13], J. Garbino[14], A. H. Groll[15], R. Herbrecht[16], W. W. Hope[17], B. J. Kullberg[2], O. Lortholary[18,19], W. Meersseman[20], G. Petrikkos[21], E. Roilides[22], C. Viscoli[23] and A. J. Ullmann[24] for the ESCMID Fungal Infection Study Group (EFISG)

1) *Servicio de Micología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain,* 2) *Department of Medical Microbiology, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands,* 3) *Unit of Mycology, Department of Microbiological Surveillance and Research, Statens Serum Institut, Copenhagen, Denmark,* 4) *Department of Medical Microbiology, Hacettepe University School of Medicine, Ankara, Turkey,* 5) *Institute of Microbiology, University of Lausanne and University Hospital Center, Lausanne, Switzerland,* 6) *University of Copenhagen, Frederiksberg, Denmark,* 7) *Divi-*

TABLE 2. Summary of recommendations by *Candida* disease, specimen and test evaluated

Disease	Specimen	Test	Recommendation	Level of evidence
Candidaemia	Blood	Blood culture	Essential investigation[a]	NA
	Serum	Mannan/anti-mannan	Recommended	II
		B-D-glucan	Recommended	II
Invasi				
		Septifast PCR kit	No recommendation	No data
		In-house PCR	No recommendation	No data
	Tissue and sterile body fluids	Direct microscopy and histopathology	Essential investigation	NA
		Culture	Essential investigation	NA
		Immuno-histochemistry	No recommendation	No data
		Tissue PCR	No recommendation	No data
		In situ hybridization	No recommendation	No data

Öneride bulunulamaz.

Cuenca-Estrella M, Clin Microbiol Infect 2012;18(S7):9

Pre-emptif tedavi

İnfeksiyon riskini gösteren bir ya da birkaç biyolojik göstergeye dayanarak tedavi başlanması

Serolojik yöntemler

Kolonizasyon temelli risk değerlendirmesi

Eggimann et al. Annals of Intensive Care 2011, 1:37
http://www.annalsofintensivecare.com/content/1/1/37

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Diagnosis of invasive candidiasis in the ICU

Philippe Eggimann[1*], Jacques Bille[2] and Oscar Marchetti[3]

Kolonizasyon temelli risk değerlendirmesi, kolonizasyon dinamiklerinin periyodik olarak izlenmesi ile risk altındaki hastaların öngörülmesi için kullanılır.

Eggimann P, Ann Inten Care 2011;1:37

Usefulness of the "*Candida* score" for discriminating between *Candida* colonization and invasive candidiasis in non-neutropenic critically ill patients: A prospective multicenter study

Cristóbal León, MD; Sergio Ruiz-Santana, MD, PhD; Pedro Saavedra, PhD; Beatriz Galván, MD; Armando Blanco, MD; Carmen Castro, MD; Carina Balasini, MD; Aránzazu Utande-Vázquez, MD; Francisco J. González de Molina, MD; Miguel A. Blasco-Navalproto, MD; Maria J. López, MD; Pierre Emmanuel Charles, MD, PhD; Estrella Martín, PhD; María Adela Hernández-Viera, MD; on behalf of the Cava Study Group

Table 2. Incidences of invasive candidiasis/*Candida* species colonization during the study

	Week			
	2	3	4	5
Patients (n)	1107	652	378	252
New cases of invasive candidiasis	33	16	3	6
Incidence rate of invasive candidiasis (95% CI)	2.98 (1.97–3.98)	2.56 (1.32–3.80)	0.86 (0–1.82)	2.61 (0.55–4.67)
Accumulated cases of invasive candidiasis	33	49	52	58
New cases of *Candida* species colonization	734	75	18	7
Accumulated cases of *Candida* species colonization	734	809	827	834

Leon C, Crit Care Med 2009;37:1624

ANNALS OF SURGERY
Vol. 220, No. 6, 751–758

Candida Colonization and Subsequent Infections in Critically Ill Surgical Patients

Didier Pittet, M.D., M.S.,* Michel Monod, Ph.D.,‡ Peter M. Suter, M.D., F.C.C.P., F.C.C.M.,†
Edgar Frenk, M.D.,‡ and Raymond Auckenthaler, M.D.*

Kandida Kolonizasyon İndeksi

Farklı bölgelerden alınan kültürlerden *Candida spp.* kolonizasyonu olan bölge sayısının alınan kültür sayısına oranı

Pittet D, Ann Surgery 1994;220:751

ANNALS OF SURGERY
Vol. 220, No. 6, 751–758

Candida Colonization and Subsequent Infections in Critically Ill Surgical Patients

Didier Pittet, M.D., M.S.,* Michel Monod, Ph.D.,‡ Peter M. Suter, M.D., F.C.C.P., F.C.C.M.,†
Edgar Frenk, M.D.,‡ and Raymond Auckenthaler, M.D.*

Kandida Düzeltilmiş Kolonizasyon İndeksi

Farklı bölgelerden alınan kültürlerden yüksek derecede *Candida spp.* kolonizasyonu olan bölge sayısının alınan kültür sayısına oranı

Pittet D, Ann Surgery 1994;220:751

ANNALS OF SURGERY
Vol. 220, No. 6, 751–758

Candida Colonization and Subsequent Infections in Critically Ill Surgical Patients

Didier Pittet, M.D., M.S.,* Michel Monod, Ph.D.,‡ Peter M. Suter, M.D., F.C.C.P., F.C.C.M.,†
Edgar Frenk, M.D.,‡ and Raymond Auckenthaler, M.D.*

From the Division of Infectious Diseases and Laboratory of Clinical Microbiology and the Division of Surgical Intensive Care,† University Hospital of Geneva, Geneva, Switzerland; and the Department of Dermatology,‡ Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland*

Eşik değer

Kandida Kolonizasyon İndeksi ≥0,5

Kandida Düzeltilmiş Kolonizasyon İndeksi ≥0,4

Pittet D, Ann Surgery 1994;220:751

ANNALS OF SURGERY
Vol. 220, No. 6, 751–758

Candida Colonization and Subsequent Infections in Critically Ill Surgical Patients

Didier Pittet, M.D., M.S.,* Michel Monod, Ph.D.,‡ Peter M. Suter, M.D., F.C.C.P., F.C.C.M.,†
Edgar Frenk, M.D.,‡ and Raymond Auckenthaler, M.D.*

Eşlik eden diğer risk faktörleri ile birlikte değerlendirildiğinde, kolonizasyonun derecesi invaziv kandidiyaz gelişimini öngörmede başarılıdır.

More than two sites	73	56	50	77
Three sites or more	45	72	50	68
Candida colonization index	100	69	66	100
Candida corrected colonization index	100	100	100	100

Pittet D, Ann Surgery 1994;220:751

Eggimann et al. Annals of Intensive Care 2011, 1:37
http://www.annalsofintensivecare.com/content/1/1/37

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Diagnosis of invasive candidiasis in the ICU

Philippe Eggimann[1*], Jacques Bille[2] and Oscar Marchetti[3]

Kolonizasyon indeksi erken antifungal tedaviden fayda görecek kritik hastaların belirlenmesinde yararlı olmakla birlikte, rutin sürveyans kültürleri gerektirmesi nedeniyle çok emek yoğun, pahalı ve rutin kullanım için güçtür.

Eggimann P, Ann Inten Care 2011;1:37

Pre-emptif tedavi

İnfeksiyon riskini gösteren bir ya da birkaç biyolojik göstergeye dayanarak tedavi başlanması

Serolojik yöntemler

Kolonizasyon temelli risk değerlendirmesi

Skorlama yöntemleri ile risk değerlendirmesi

Eggimann et al. Annals of Intensive Care 2011, 1:37
http://www.annalsofintensivecare.com/content/1/1/37

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Diagnosis of invasive candidiasis in the ICU

Philippe Eggimann[1*], Jacques Bille[2] and Oscar Marchetti[3]

Klinik risk faktörleri ile birlikte *Candida spp.* kolonizasyonuna dair bilginin biraraya getirilmesi ile skorlama sistemleri ya da "predictive rules" "öngörü kuralları" tanımlanmıştır.

Eggimann P, Ann Inten Care 2011;1:37

A bedside scoring system ("Candida score") for early antifungal treatment in nonneutropenic critically ill patients with *Candida* colonization*

Cristóbal León, MD; Sergio Ruiz-Santana, MD, PhD; Pedro Saavedra, PhD; Benito Almirante, MD, PhD; Juan Nolla-Salas, MD, PhD; Francisco Álvarez-Lerma, MD, PhD; José Garnacho-Montero, MD; María Ángeles León, MD, PhD; EPCAN Study Group

Kandida Skoru

- Ağır sepsis 2 puan
- Cerrahi 1 puan
- TPN 1 puan
- Multifokal *Candida* kolonizasyonu 1 puan

Leon C, Crit Care Med 2006;34:730

A bedside scoring system ("Candida score") for early antifungal treatment in nonneutropenic critically ill patients with *Candida* colonization*

Cristóbal León, MD; Sergio Ruiz-Santana, MD, PhD; Pedro Saavedra, PhD; Benito Almirante, MD, PhD; Juan Nolla-Salas, MD, PhD; Francisco Álvarez-Lerma, MD, PhD; José Garnacho-Montero, MD; María Ángeles León, MD, PhD; EPCAN Study Group

Eşik değer ≥2,5

duyarlılık %81, özgüllük %74

ppv %16, npv %98

Leon C, Crit Care Med 2006;34:730

Usefulness of the "*Candida* score" for discriminating between *Candida* colonization and invasive candidiasis in non-neutropenic critically ill patients: A prospective multicenter study

Cristóbal León, MD; Sergio Ruiz-Santana, MD, PhD; Pedro Saavedra, PhD; Beatriz Galván, MD; Armando Blanco, MD; Carmen Castro, MD; Carina Balasini, MD; Aránzazu Utande-Vázquez, MD; Francisco J. González de Molina, MD; Miguel A. Blasco-Navalproto, MD; Maria J. López, MD; Pierre Emmanuel Charles, MD, PhD; Estrella Martín, PhD; María Adela Hernández-Viera, MD; on behalf of the Cava Study Group

Table 4. Rates of invasive candidiasis according to the *Candida* score

Cutoff Value	Incidence Rate (%) (95% CI)	Relative Risk (95% CI)
<3	2.3 (1.1–3.5)	1
3	8.5 (4.2–12.7)	3.7 (1.8–7.7)
4	16.8 (9.7–23.9)	7.3 (3.7–14.5)
5	23.6 (12.4–34.9)	10.3 (5.0–21.0)

Leon C, Crit Care Med 2009;37:1624

Usefulness of the "*Candida* score" for discriminating between *Candida* colonization and invasive candidiasis in non-neutropenic critically ill patients: A prospective multicenter study

Cristóbal León, MD; Sergio Ruiz-Santana, MD, PhD; Pedro Saavedra, PhD; Beatriz Galván, MD; Armando Blanco, MD; Carmen Castro, MD; Carina Balasini, MD; Aránzazu Utande-Vázquez, MD; Francisco J. González de Molina, MD; Miguel A. Blasco-Navalproto, MD; Maria J. López, MD; Pierre Emmanuel Charles, MD, PhD; Estrella Martín, PhD; María Adela Hernández-Viera, MD; on behalf of the Cava Study Group

Table 5. *Candida* score vs. colonization index discriminatory power

	Candida Score ≥3 (95% CI)	Colonization Index ≥0.5 (95% CI)
Area under ROC curve	0.774 (0.715–0.832)	0.633 (0.557–0.709)
Sensitivity	77.6 (66.9–88.3)	72.4 (60.9–83.9)
Specificity	66.2 (63.0–69.4)	47.4 (44.0–50.8)
Predictive positive value	13.8 (10.0–17.5)	8.7 (6.2–11.3)
Predictive negative value	97.7 (96.4–98.9)	96.1 (94.2–98.0)
Relative risk for invasive candidiasis	5.98 (3.28–10.92)	2.24 (1.28–3.93)

Leon C, Crit Care Med 2009;37:1624

Usefulness of the "*Candida* score" for discriminating between *Candida* colonization and invasive candidiasis in non-neutropenic critically ill patients: A prospective multicenter study

Cristóbal León, MD; Sergio Ruiz-Santana, MD, PhD; Pedro Saavedra, PhD; Beatriz Galván, MD; Armando Blanco, MD; Carmen Castro, MD; Carina Balasini, MD; Aránzazu Utande-Vázquez, MD; Francisco J. González de Molina, MD; Miguel A. Blasco-Navalproto, MD; Maria J. López, MD; Pierre Emmanuel Charles, MD, PhD; Estrella Martín, PhD; María Adela Hernández-Viera, MD; on behalf of the Cava Study Group

Candida skorunun günlük pratikte uygulanması, YBÜ'de gereksiz antifungal kullanımını önemli ölçüde azaltacak bir yaklaşımdır.

Leon C, Crit Care Med 2009;37:1624

Eur J Clin Microbiol Infect Dis (2007) 26:271–276
DOI 10.1007/s10096-007-0270-z

CONCISE ARTICLE

Multicenter retrospective development and validation of a clinical prediction rule for nosocomial invasive candidiasis in the intensive care setting

L. Ostrosky-Zeichner · C. Sable · J. Sobel ·

Öngörü kuralı

- en az dört gündür YBÜ'de izlenen hastada,
  - son üç gün içinde sistemik antibiyotik kullanımı ya da SVK varlığı VE en az ikisi;
    - son üç gün içinde TPN, diyaliz,
    - son yedi gün içinde major cerrahi, pankreatit, immünsüpresif steroid ya da kullanımı

Eur J Clin Microbiol Infect Dis (2007) 26:271–276
DOI 10.1007/s10096-007-0270-z

CONCISE ARTICLE

Multicenter retrospective development and validation of a clinical prediction rule for nosocomial invasive candidiasis in the intensive care setting

L. Ostrosky-Zeichner · C. Sable · J. Sobel ·
B. D. Alexander · G. Donowitz · V. Kan ·
C. A. Kauffman · D. Kett · R. A. Larsen · V. Morrison ·
M. Nucci · P. G. Pappas · M. E. Bradley · S. Major ·
L. Zimmer · D. Wallace · W. E. Dismukes · J. H. Rex

duyarlılık %34, özgüllük %90
ppv %10, npv %97

Ostrosky-Zeichner L, Eur J Clin Microbiol Infect Dis 2007;26:271

Table 2 Post-hoc performance of selected predictive rules on the complete population analyzed

Rule[a] (*n*=2,890)	Rule description	No. of patients selected by rule (% of total)	No. of cases selected by rule (% of total)	Infection rate among IC patients	
				Not selected by rule (%)	Selected by rule (%)
1 (*n*=2,889)	Any antibiotic use (day 1–3) AND CVC (day 1–3)	1,801 (62.3)	78 (88.6)	0.9	4.3
2 (*n*=2,879)	Any antibiotic use (day 1–3) AND CVC (day 1–3) AND at least one of the following additional risk factors: any surgery (day −7–0); immunosuppressive use (day −7–0); pancreatitis (day −7–0); TPN (day 1–3); any dialysis (day 1–3); steroid use (day −7–3)	916 (31.8)	58 (65.9)	1.5	6.3
3 (*n*=2,859)	Any antibiotic use (day 1–3) OR CVC (day 1–3) AND at least two of the following additional risk factors: any surgery (day −7–0); immunosuppressive use (day −7–0); pancreatitis (day −7–0); TPN (day 1–3); any dialysis (day 1–3); steroid use (day −7–3)	303 (10.6)	30 (34.1)	2.3	9.9

Ostrosky-Zeichner L, Eur J Clin Microbiol Infect Dis 2007;26:271

mycoses
Diagnosis, Therapy and Prophylaxis of Fungal Diseases

Original article

Improvement of a clinical prediction rule for clinical trials on prophylaxis for invasive candidiasis in the intensive care unit

Luis Ostrosky-Zeichner,[1] Peter G. Pappas,[2] Shmuel Shoham,[3] Annette Reboli,[4] Michelle A. Barron,[5]

Öngörü kuralı

- en az dört gündür YBÜ'de izlenen hastada,
  - ≥48 saat mekanik ventilasyon VE antibiyotik kullanımı VE SVK varlığı VE en az biri;
    - üç gün içinde TPN, diyaliz
    - son yedi gün içinde major cerrahi, pankreatit, steroid ya da immünsüpresif kullanımı

Ostrosky-Zeichner L, Mycoses 2009;54:46

mycoses
Diagnosis, Therapy and Prophylaxis of Fungal Diseases

Original article

Improvement of a clinical prediction rule for clinical trials on prophylaxis for invasive candidiasis in the intensive care unit

Luis Ostrosky-Zeichner,[1] Peter G. Pappas,[2] Shmuel Shoham,[3] Annette Reboli,[4] Michelle A. Barron,[5] Charles Sims,[1] Craig Wood[6] and Jack D. Sobel[7]

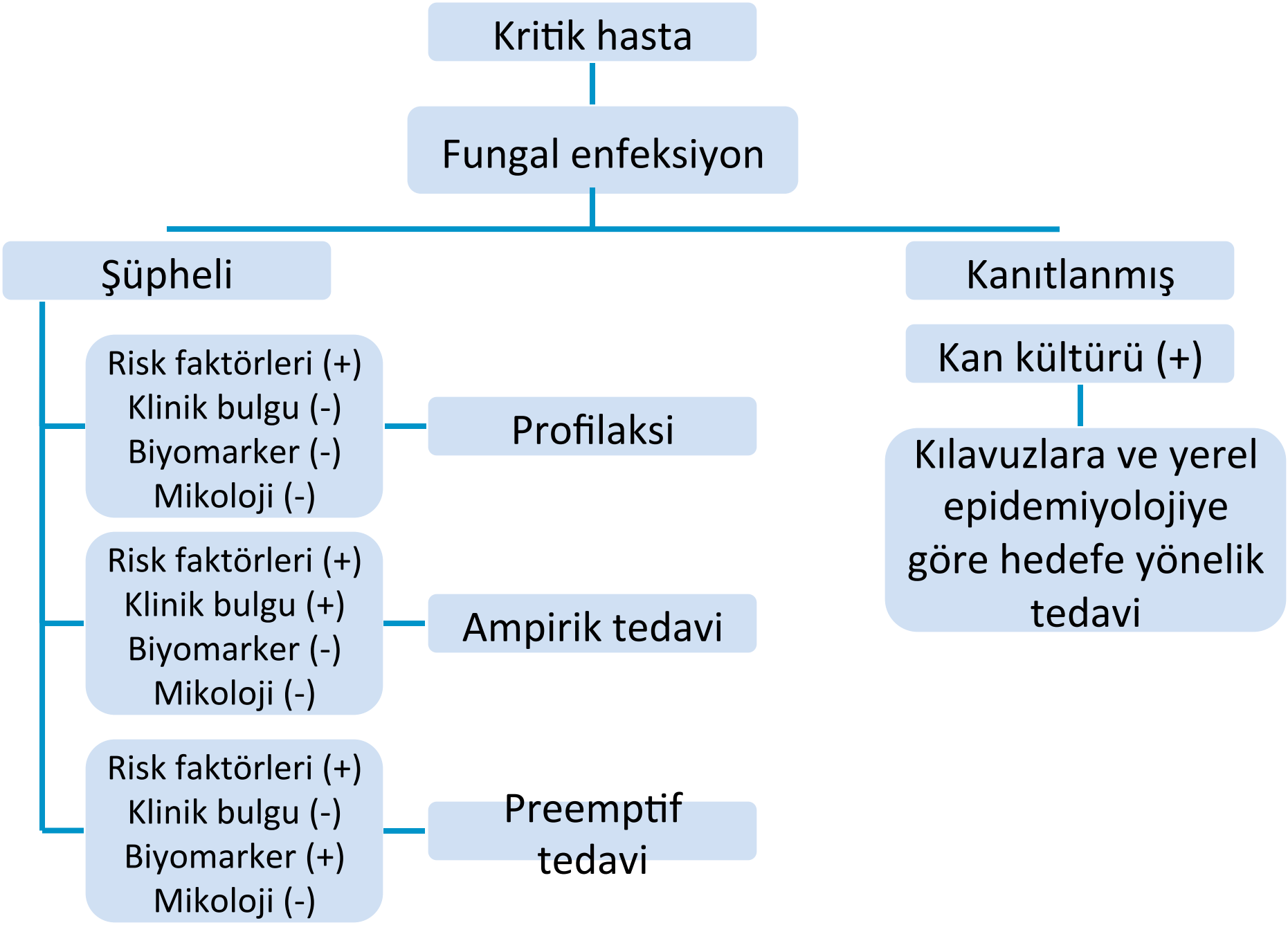
[1]University of Texas Medical School at Houston, Houston, TX, USA, [2]University of Alabama at Birmingham, Birmingham, AL, USA, [3]Washington Hospital Center, Washington, DC, USA, [4]University of Medicine and Dentistry of New Jersey/Robert Wood Johnson Medical School, Camden, NJ, USA, [5]University of Colorado Denver, Denver, CO, USA, [6]Merck & Co., West Point, PA, USA and [7]Wayne State University School of Medicine, Detroit, MI, USA

duyarlılık %50, özgüllük %83
ppv %10, npv %97

Ostrosky-Zeichner L, Mycoses 2009;54:46

Table 1 Definitions and diagnostic performance of the original and proposed clinical prediction rules for invasive candidiasis (IC) in the intensive care unit (ICU) setting.

Rule	Patients who stay in the ICU for at least 4 days and:	Sensitivity	Specificity	PPV	NPV	Accuracy	% population selected by rule	% cases of IC captured	Incidence (%) of IC in that do not meet rule	Incidence (%) of IC in that meet rule
Original rule	Any antibiotic use, D 1–3 OR CVC, D 1–3 AND at least two of the following additional risk factors: Any surgery, D −7–0 Immunosuppressive use, D −7–0 Pancreatitis, D −7–0 TPN, D 1–3 Any dialysis, D 1–3 Steroid use, D −7–3	0.27	0.93	0.13	0.97	0.90	8	27	2.9	13.3
A	Have been mechanically ventilated for at least 48 h AND stayed in the unit for at least another 72 h	0.90	0.40	0.05	0.99	0.42	61	91	0.9	5.5
B	Any antibiotic use, D 1–3 AND CVC, D 1–3	0.95	0.37	0.05	0.99	0.39	63	95	0.5	5.5
C	Have been mechanically ventilated for at least 48 h AND Any antibiotic use, D 1–3 AND CVC, D 1–3	0.86	0.56	0.07	0.99	0.57	45	86	0.9	7.0
D	Have been mechanically ventilated for at least 48 h AND Antibacterial antibiotic use, D 1–3 AND CVC, D 1–3 AND at least one of the following additional risk factors: Any surgery, D −7–0 Immunosuppressive use, D −7–0 Pancreatitis, D −7–0 TPN, D 1–3 Any dialysis, D 1–3 Steroid use, D −7–0	0.50	0.83	0.10	0.97	0.8	18	50	2.3	10.1


Kritik hasta
Fungal enfeksiyon
Şüpheli
Kanıtlanmış
Risk faktörleri (+)
Klinik bulgu (-)
Biyomarker (-)
Mikoloji (-)
Profilaksi
Risk faktörleri (+)
Klinik bulgu (+)
Biyomarker (-)
Mikoloji (-)
Ampirik tedavi
Risk faktörleri (+)
Klinik bulgu (-)
Biyomarker (+)
Mikoloji (-)
Preemptif tedavi
Kan kültürü (+)
Kılavuzlara ve yerel epidemiyolojiye göre hedefe yönelik tedavi

Eggimann et al. Annals of Intensive Care 2011, 1:37
http://www.annalsofintensivecare.com/content/1/1/37

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Diagnosis of invasive candidiasis in the ICU

Philippe Eggimann[1*], Jacques Bille[2] and Oscar Marchetti[3]

Önemli bir risk faktörü olarak tanımlanmış olmasına karşın, kolonizasyon ampirik antifungal tedavi başlanması için yeterli bir gerekçe oluşturmaz.

Biyomarkerlara dair sonuçlar henüz araştırma aşamasındadır ve pek çok merkezde erişilebilir değildir.

Eggimann P, Ann Inten Care 2011;1:37

Eggimann et al. Annals of Intensive Care 2011, 1:37
http://www.annalsofintensivecare.com/content/1/1/37

Annals of Intensive Care
a SpringerOpen Journal

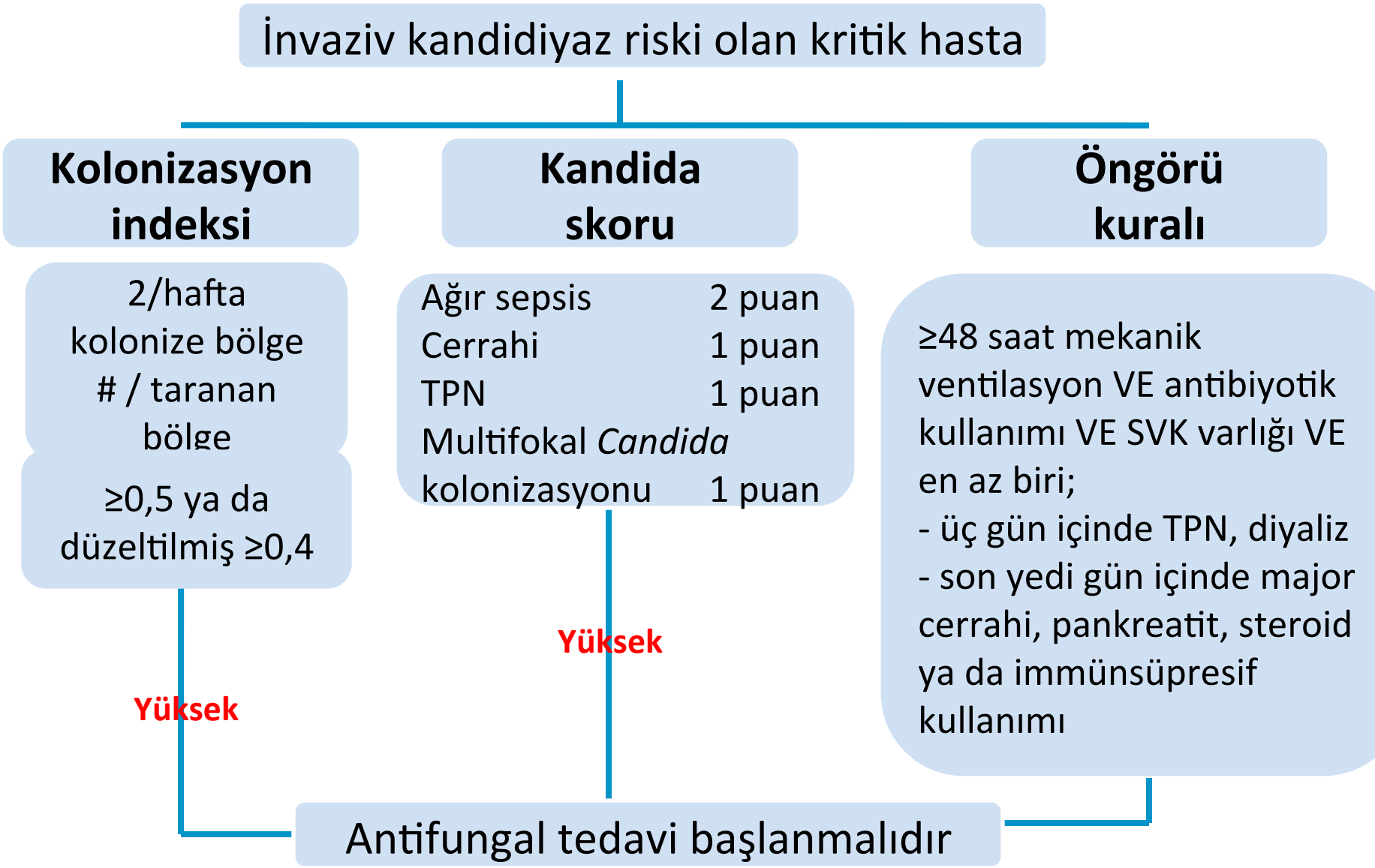
REVIEW Open Access

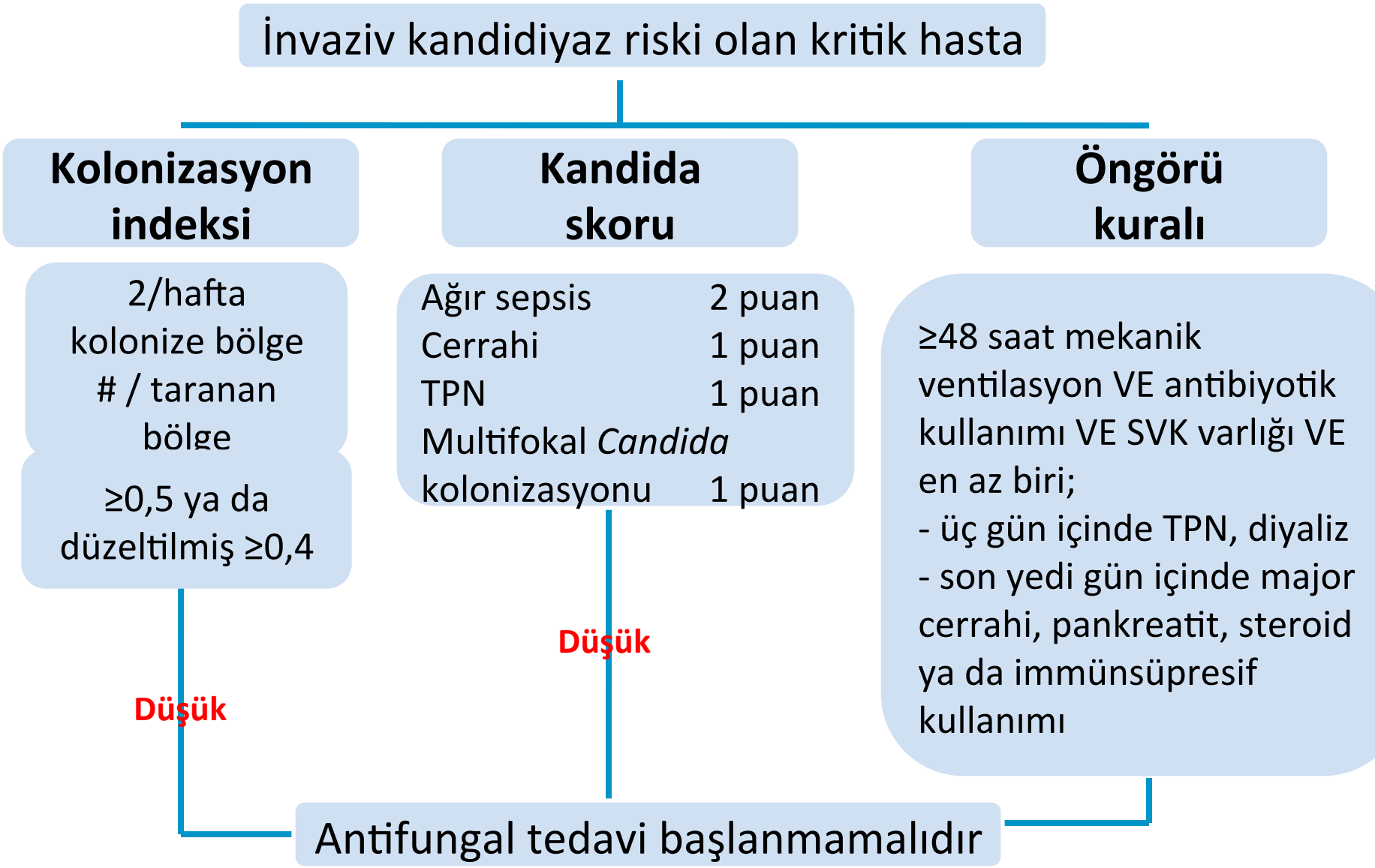
Diagnosis of invasive candidiasis in the ICU

Philippe Eggimann[1*], Jacques Bille[2] and Oscar Marchetti[3]

Klinisyenler erken antifungal tedaviden fayda görecek kritik YBÜ hastalarının belirlenmesinde risk faktörleriyle kolonizasyon dinamiklerini birlikte dikkate almalıdır.

Eggimann P, Ann Inten Care 2011;1:37


İnvaziv kandidiyaz riski olan kritik hasta
Kolonizasyon indeksi
Kandida skoru
Öngörü kuralı
2/hafta kolonize bölge # / taranan bölge
≥0,5 ya da düzeltilmiş ≥0,4
Ağır sepsis 2 puan
Cerrahi 1 puan
TPN 1 puan
Multifokal Candida kolonizasyonu 1 puan
≥48 saat mekanik ventilasyon VE antibiyotik kullanımı VE SVK varlığı VE en az biri;
- üç gün içinde TPN, diyaliz
- son yedi gün içinde major cerrahi, pankreatit, steroid ya da immünsüpresif kullanımı
Yüksek
Yüksek
Antifungal tedavi başlanmalıdır


İnvaziv kandidiyaz riski olan kritik hasta
Kolonizasyon indeksi
Kandida skoru
Öngörü kuralı
2/hafta kolonize bölge # / taranan bölge
≥0,5 ya da düzeltilmiş ≥0,4
Ağır sepsis 2 puan
Cerrahi 1 puan
TPN 1 puan
Multifokal Candida kolonizasyonu 1 puan
≥48 saat mekanik ventilasyon VE antibiyotik kullanımı VE SVK varlığı VE en az biri;
- üç gün içinde TPN, diyaliz
- son yedi gün içinde major cerrahi, pankreatit, steroid ya da immünsüpresif kullanımı
Düşük
Düşük
Antifungal tedavi başlanmamalıdır