İnvaziv Kandidiyazis Tanı Yöntemleri

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Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

İnvaziv Kandidiyazis

Candida türleri invaziv mantar enfeksiyonlarının en sık nedenidir

Tüm invaziv mikozların %70-90'ını oluşturur

Günümüzde yoğun bakımda yatan ve immünsüprese hasta sayısında artışla ilişkili olarak kandida enfeksiyonları artmaktadır

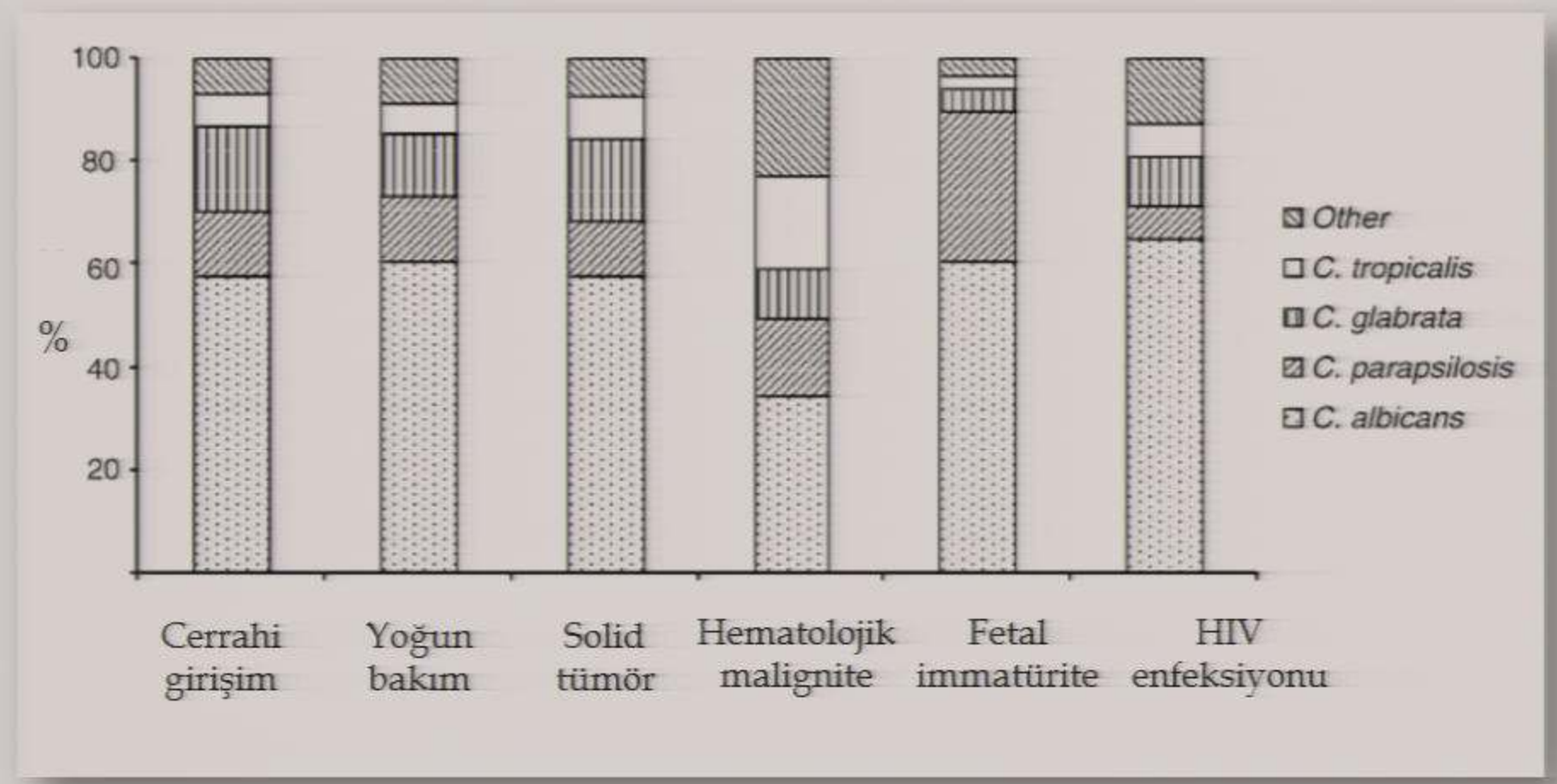
- Yoğun bakım ünitelerinde prevalans 6.9 /1000 hasta günü

Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.
Pfaller MA, et al. Clin Microbiol Rev 2007; 20: 133-63.
Kett DH, et al. Crit Care Med 2011; 39: 665–70

Kandidemili hastalarda altta yatan patoloji/tıbbi hizmet

	%
Cerrahi girişim	**48.2**
Yoğun bakım	**40.2**
Solid tümör	22.5
Steroid kullanımı	17.4
Hematolojik malignite	12.3
Prematüre doğum	6.0
HIV enfeksiyonu	3.0
Yanık	1.4

Tortorano AM, et al. Int J Antimicrob Agents 2006; 27:359-66.



Tortorano AM, et al. Int J Antimicrob Agents 2006; 27:359-66.

İnvaziv Kandidiyazis

Klinik önemleri ve yüksek mortalitelerine rağmen fungal enfeksiyonların tanısı hala zor ve sorunludur

Klinik bulgular etkene özgül değildir ve kolonizasyonun invaziv hastalıktan ayırt edilmesi kolay olmamaktadır

Fungal enfeksiyonlarda tedavinin zamanlaması mortalite üzerine önemli bir etkiye sahiptir

Erken ve uygun tedaviye başlamak için mevcut tanı araçları optimal kullanılmalıdır

Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.

İnvaziv Kandidiyazis

- Kandidemi
- Dissemine kandidemi (akut, kronik)
- Endokardit
- Menenjit
- Endoftalmi
- diğer derin organ tutulumları dahil şiddetli ve invaziv hastalıkları kapsayan terimdir

Pappas PG. Infect Dis Clin N Am 2006;20(3):485-506.

Kandidemi

- Herhangi bir kandida türünün kanda bulunması

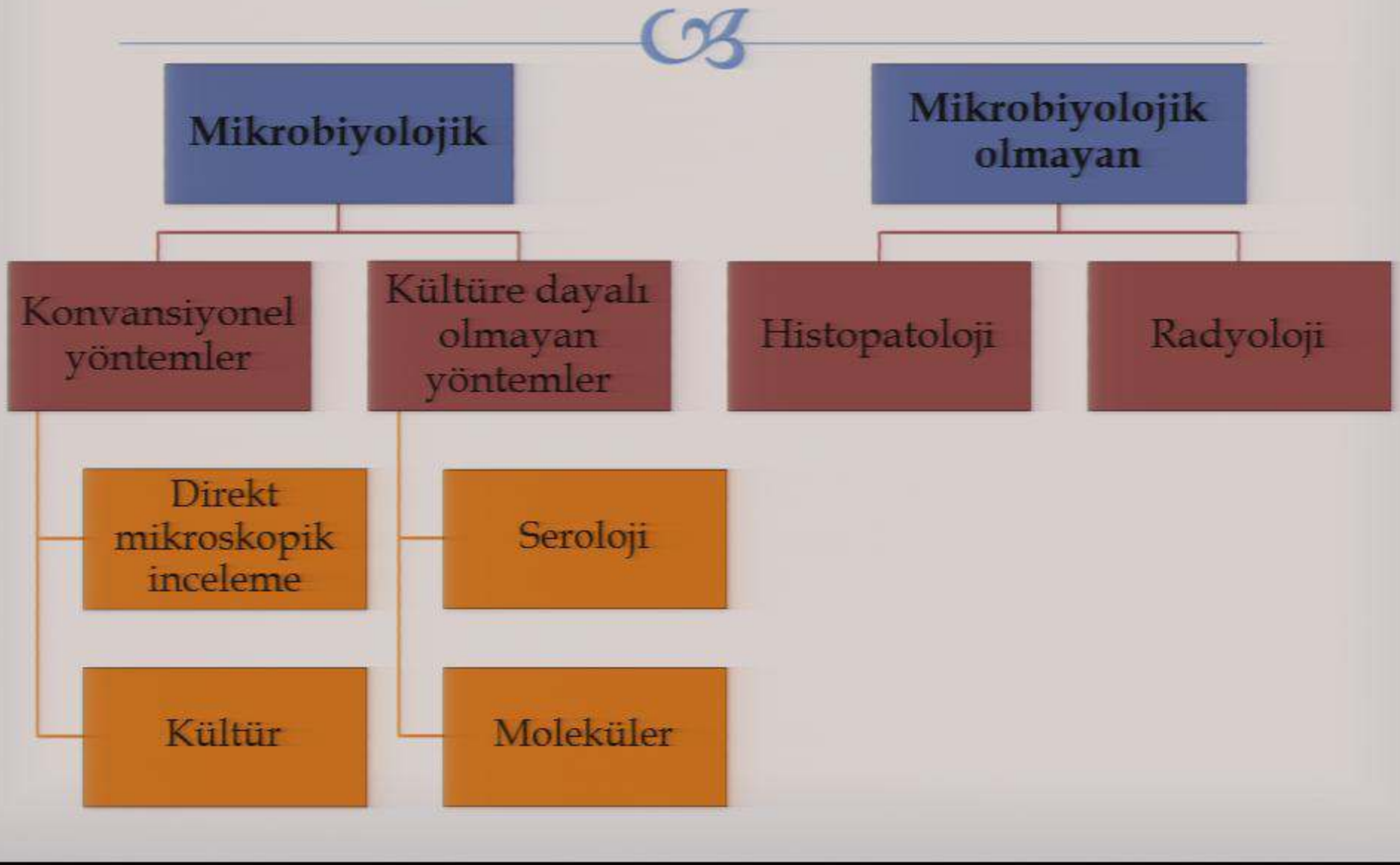
Kan dolaşımı enfeksiyonları arasında 4. sırada

Atfedilen mortalite % 47

Her bir epizodun ek maliyeti 40.000 dolar

Pappas PG. Infect Dis Clin N Am 2006;20(3):485-506.

İnvaziv Kandidiyazis Tanı



İnvaziv Kandidiyazis Tanı

Kan Kültürü

	Örnek	Test	Öneri
Kandidemi	Kan	Kan kültürü	**Temel inceleme**
İnvaziv kandidiyaz	Kan	Kan kültürü	**Temel inceleme**
Kronik dissemine kandidiyaz	Kan	Kan kültürü	**Temel inceleme**

ESCMID guideline for the diagnosis and management of Candida diseases 2012

Kan Kültürü

Kandidemi tanısı için **altın standart**

Duyarlılığı düşük

- %50-75
- Nötropenik hastalarda ve antifungal tedavi altında duyarlılık düşük

Modern otomatik kan kültür sistemleri ve lizis santrifüjleme yöntemi ile duyarlılık artırılabilir

Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.

Kan Kültürü

Kan kültürü sayısı

- 30 dakikalık süre içinde 3 (2-4)

Toplam volüm

- 40-60 mL

Sıklık

- Kandidemi şüphesi devam ettiği sürece günlük

İnkübasyon süresi

- En az 5 gün

Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.

Kan Kültürü

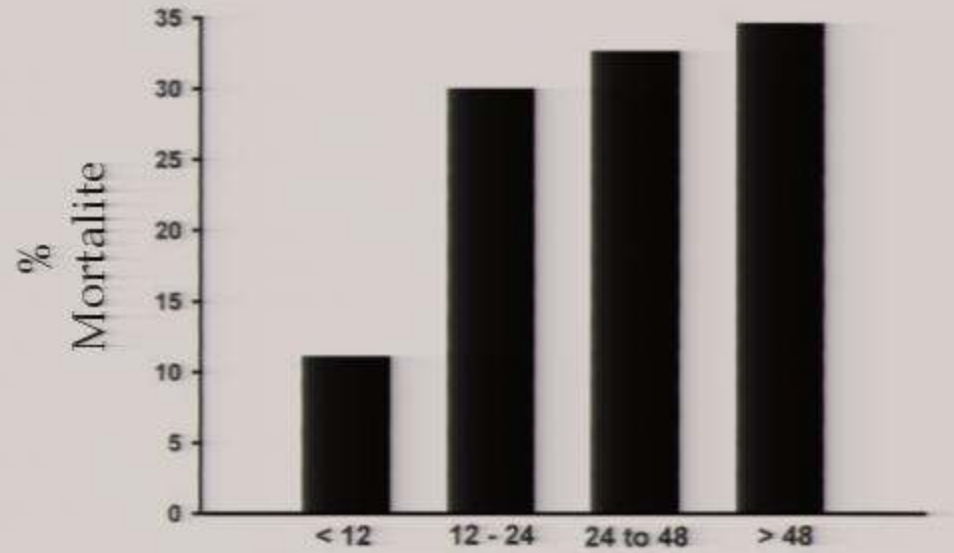
Tek kan kültüründe *Candida* türlerinin üremesi invaziv enfeksiyon lehine anlamlı

Katater varlığında kateterden alınan kan kültürü, eşzamanlı periferik kan kültüründen önce pozitif olduğunda kateter ilişkili enfeksiyon düşünülmeli

Arendrup MC. Bone Marrow Transplant 2012;47):1030-45.

Kan Kültürü

- Pozitif kan kültürü sonuçları elde edilinceye kadar tedaviyi geciktirmek mortaliteyi artırmakta



Morrell M, et al. Antimicrob Agents Chemother 2005 49: 3640-5.

Kan Kültürü

Kan kültüründe üreme olguların %41.2'sinde hasta öldükten sonra

Yoğun bakım hastalarının en az üçte birinde kan kültürleri negatif

Kronik dissemine kandidiyazis nadiren kan kültürü ile tespit edilir

Bu nedenle kan kültürü erken tanı yöntemi olarak kabul edilemez

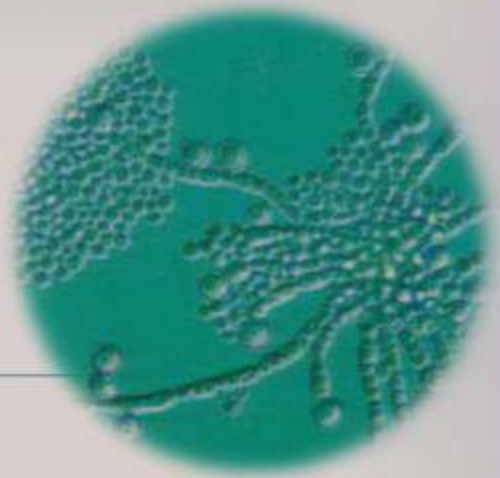
Dizbay M. Scand J Infect Dis 201042(2):114-20.
Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.

Direkt mikroskopi, histopatoloji, kültür

	Örnek	Test	Öneri
İnvaziv kandidiyaz	Doku ve steril vücut sıvıları	Direkt mikroskopi ve histopatoloji	**Temel inceleme**
		Kültür	**Temel inceleme**
Kronik dissemine kandidiyaz	Doku ve steril vücut sıvıları	Direkt mikroskopi ve histopatoloji	**Temel inceleme**
		Kültür	**Temel inceleme**

ESCMID guideline for the diagnosis and management of Candida diseases 2012

Direkt mikroskopi, histopatoloji, kültür



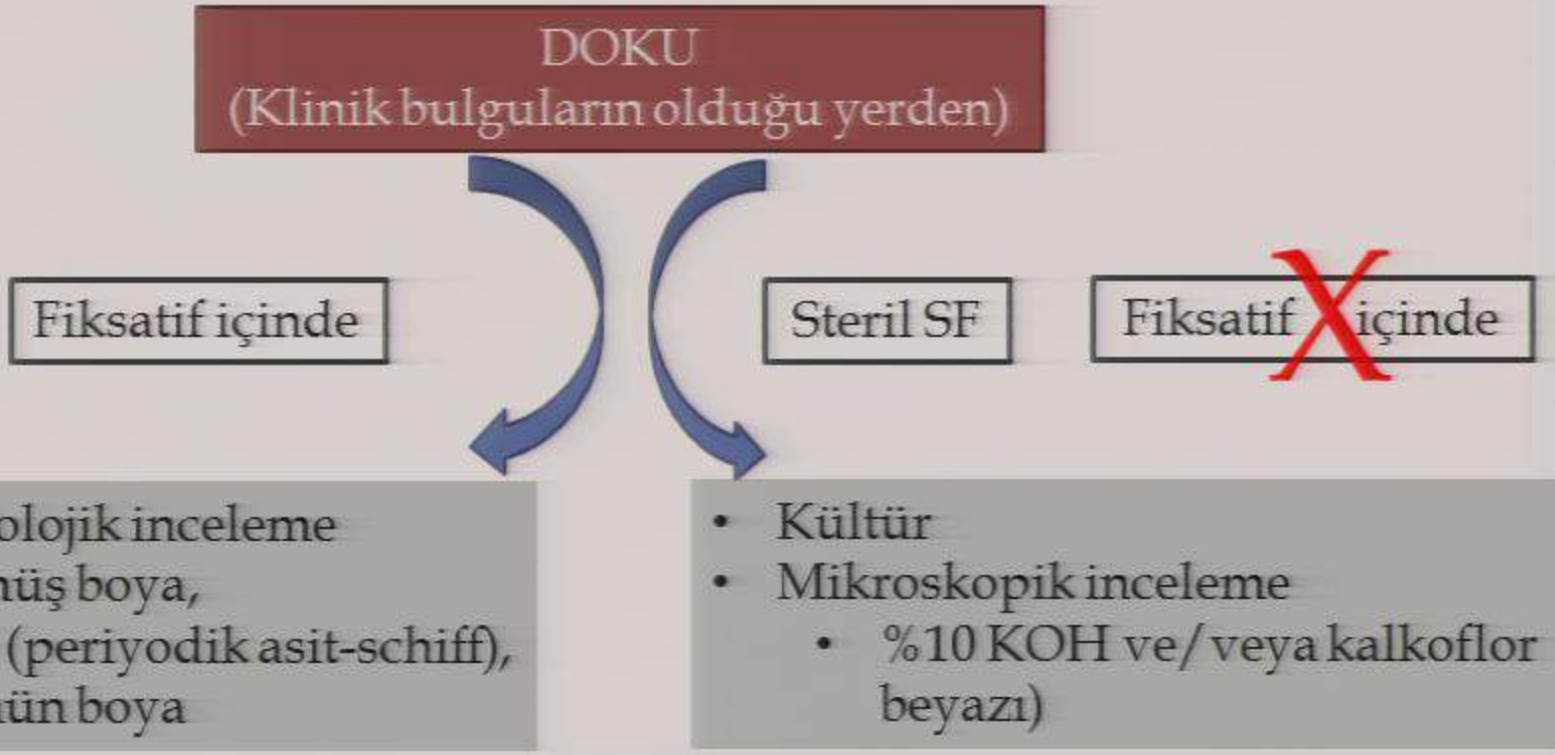
İnvaziv kandidiyaz tanısı için önemli ancak duyarlılık düşük

Bu yöntemler, derin doku örnekleri elde edilebildiğinde kullanışlı

- Ancak birçok hastada bu örnekler elde edilemez

Direkt mikroskopi, histopatoloji, kültür

- Doku örnekleri ve steril vücut sıvıları aseptik koşullarda alınmalı ve derhal laboratuvara taşınmalıdır



Kültür

- Örneğin hemen incelenmesi mümkün değilse, 4-5°C'de saklanmalıdır
- Bazı türlerin kültürde 5-14 günde ürediği dikkate alınmalıdır
- Steril doku veya vücut sıvılarından maya izolasyonu genellikle derin yerleşimli enfeksiyona işaret eder
- Kültürün negatif olması kandida enfeksiyonunu dışlamaz
- İzolatların tür düzeyinde tanımlanması gereklidir

Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.

EORTC tanı

- Kanıtlanmış invaziv fungal enfeksiyon diyebilmek için etkenin görülmesi şarttır

Mikrobiyolojik kriterler

Mukoza dışı alanların biyopsi/iğne aspirasyonunda maya veya psödohif gösterilmesi

Normalde steril olan, ancak klinik veya radyolojik olarak enfeksiyon ile uyumlu anormal bir bölgeden alınan kültürden maya üretilmesi

Uyumlu klinik bulgu ve belirti olanlarda kan kültüründen *Candida* ve diğer mayaların üretilmesi

De Pauw B, et al. Clin Infect Dis 2008;46:1813–21.

Kültür

Avantajları

Dezavantajları

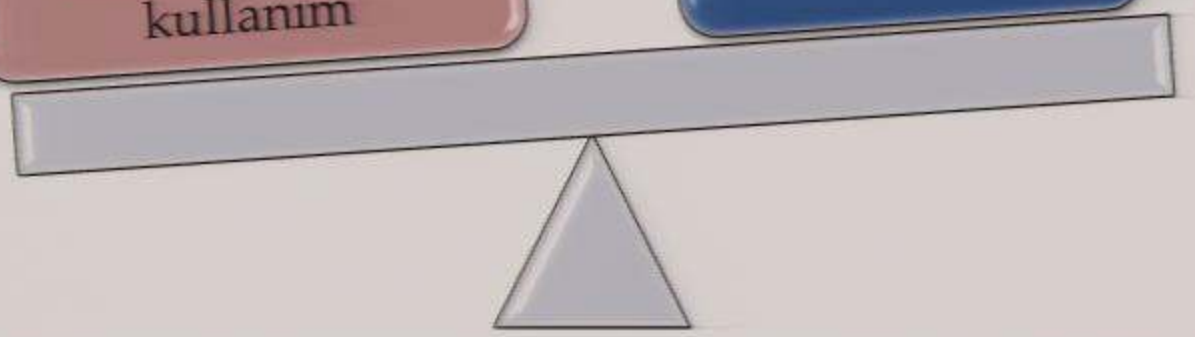
Antifungal duyarlılık çalışmalarına olanak sağlar

Cins ve tür düzeyinde tanımlamayı sağlar

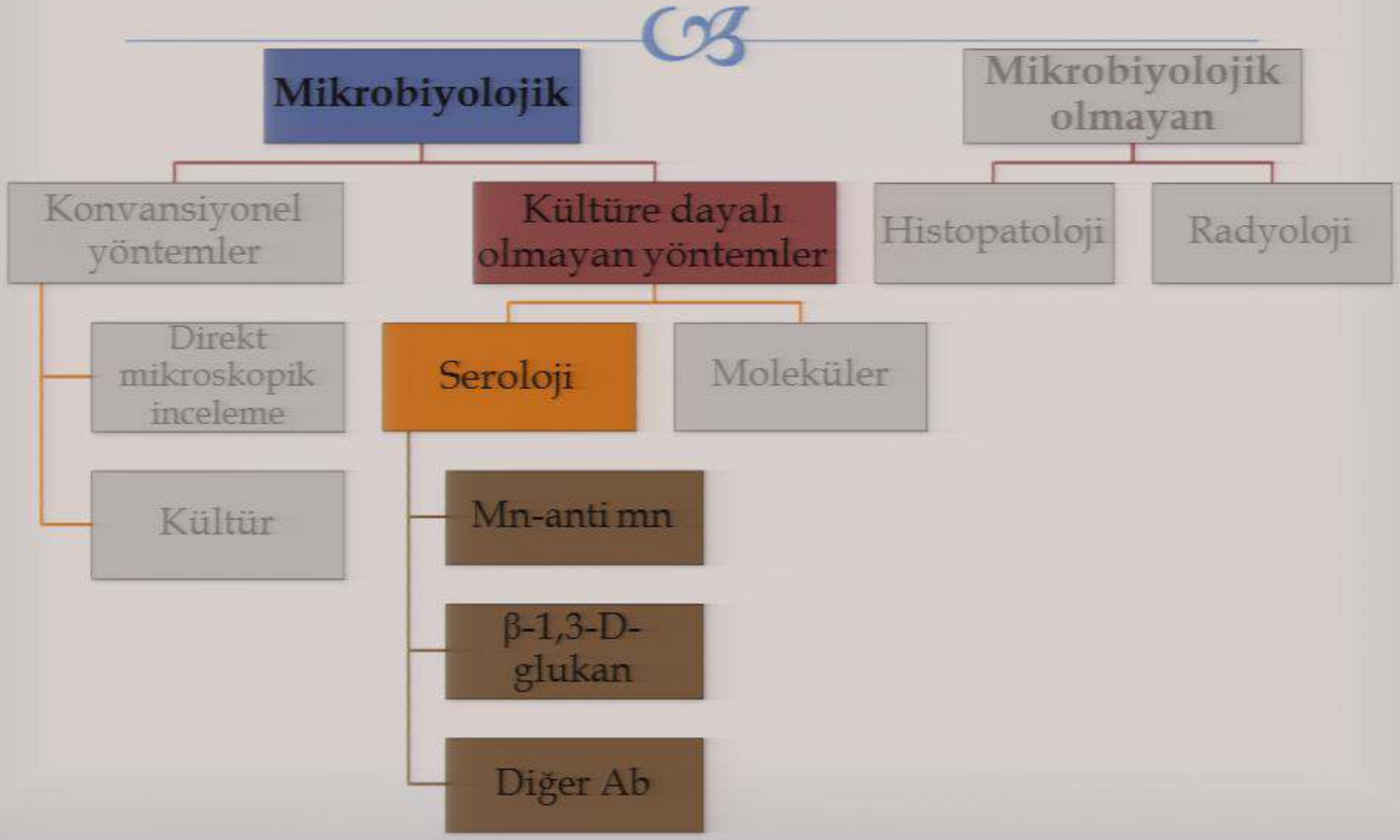
Serumda ve diğer klinik örneklerde kullanım

Zaman gerektirir

Düşük duyarlılık



İnvaziv Kandidiyazis Tanı



Mannan – Anti-mannan

	Örnek	Test	Öneri	Kanıt düzeyi
Kandidemi	Serum	Mannan/anti-mannan	Önerilir	**II**
İnvaziv kandidiyaz	Serum	Mannan/anti-mannan	Öneri yok	**Veri yok**
Kronik dissemine kandidiyaz	Serum	Mannan/anti-mannan	Önerilir	**II**

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	Örnek	Test	Kanıt düzeyi
Kandidemi	Serum	Mannan/anti-mannan	**C II**
Kronik dissemine kandidiyaz	Serum	Mannan/anti-mannan	**B III**

ECIL 2009

Mannan – Anti-mannan

Mannan *Candida* hücre duvarının bileşeni olan bir polisakkarit

Mannan Ag ve anti-mannan antikorlarının birlikte saptanması, serumda *Candida* türlerinin spesifik tespiti için kabul edilen bir yöntemdir

Seri ölçüm yapılması gerekir

Yapılan bir çok çalışmada %80 duyarlılık ve %85 özgüllük oranları ile kandidemi tanısında etkinliği kanıtlanmıştır

Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.

Mannan – Anti-mannan

Kan kültürlerinden ortalama **6 gün önce** pozitif olması enfeksiyonun erken tespitine olanak sağlar

Testin negatif prediktif değerinin (>%85) yüksek olması enfeksiyonu ekarte etmek için kullanılmasını sağlar

- Yoğun bakım ortamlarında antifungal ajanların gereksiz kullanımını azaltır

Cuenca-Estrella M, et all. Clin Microbiol Infect. 2012;7:9-18.

Mannan – Anti-mannan

Testin duyarlılığı *Candida* türlerine göre farklılık gösterir

- ***C.albicans, C. glabrata*** ve ***C. tropicalis'*** te duyarlılık yüksek
- ***C. parapsilosis, C. krusei*** ve ***C. kefyr'*** de düşük

	Mannan – Anti-mannan Duyarlılık
C.albicans	**%100**
C. glabrata	**%83**
C. tropicalis	**%80**
C. parapsilosis	%40
C. krusei	%50

Sendid B, et al. J Med Microbiol 2002;51(5):433-42.

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

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

14 çalışmanın değerlendirildiği metaanaliz

- 453 hasta, 767 kontrol

45 kandidemili hastanın %73'ünde kültür sonuçlarına göre;

- Mannan Ag testi **6 gün önce**
- Mannan Ab testi **7 gün önce** pozitif tespit edilmiş

	Mannan Ab	Mannan Ag	Kombine Mn-Anti-Mn
Duyarlılık	%58	%59	%83
Özgüllük	%93	%83	%86

Available online at www.sciencedirect.com
SCIENCE DIRECT
ELSEVIER
Diagnostic Microbiology and Infectious Disease 51 (2005) 95–101
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

Mycology

Early diagnosis of invasive candidiasis with mannan antigenemia and antimannan antibodies☆

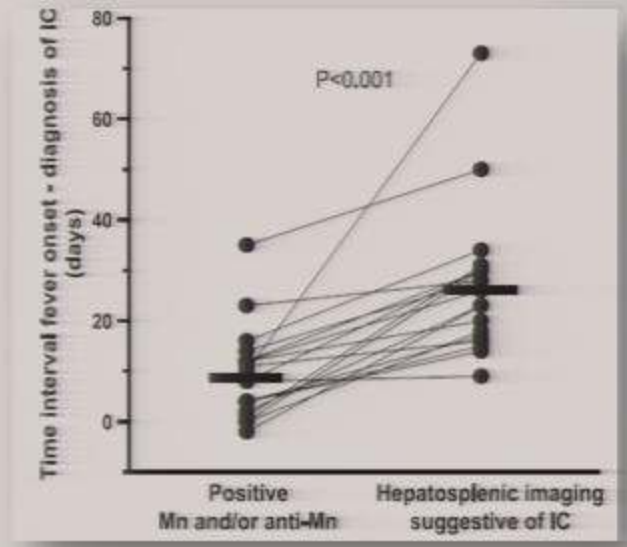
Maura Prella[a], Jacques Bille[b], Mauro Pugnale[c], Bertrand Duvoisin[c], Matthias Cavassini[a,b], Thierry Calandra[a], Oscar Marchetti[a,*]

[a]Infectious Diseases Service, Department of Internal Medicine, Centre Hospitalier Universitaire Vaudois, CH-1011 Lausanne, Switzerland
[b]Institute of Microbiology, Centre Hospitalier Universitaire Vaudois, CH-1011 Lausanne, Switzerland
[c]Diagnostic Radiology Service, Centre Hospitalier Universitaire Vaudois, CH-1011 Lausanne, Switzerland

Received 1 June 2004; accepted 31 August 2004

28 invaziv kandida enfeksiyonu, 25 kontrol

- 21 Hepatosplenik kandidiyazisli hasta
  - 18'inde (%86) karaciğer veya dalak lezyonlarının radyolojik tespitinden ortalama **16 gün önce** Mannan Ag veya Mannan Ab pozitif saptanmış



JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2004, p. 867–870 Vol. 42, No. 2
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.2.867–870.2004

Detection of the *Candida* Antigen Mannan in Cerebrospinal Fluid Specimens from Patients Suspected of Having *Candida* Meningitis

Frans M. Verduyn Lunel,[1] Andreas Voss,[2,3] Ed J. Kuijper,[4] L. B. S. Gelinck,[5] Peter M. Hoogerbrugge,[6] K. L. Liem,[7] Bart Jan Kullberg,[3,8] and Paul E. Verweij[2,3]*

Department of Medical Microbiology and Infectious Diseases, Canisius-Wilhelmina Hospital,[1] and Departments of Medical Microbiology,[2] Pediatric Oncology,[6] Neonatal Intensive Care,[7] and General Internal Medicine,[8] Nijmegen University Center for Infectious Diseases,[3] University Medical Center Nijmegen, Nijmegen, and Departments of Medical Microbiology[4] and Infectious Diseases,[5] Center of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands

Candida menenjit tanısı alan 5 hasta değerlendirilmiş

4'ünde BOS'ta mannan Ag pozitif saptanmış

Mannan – Anti-mannan

β-1,3-D-glukan

	Örnek	Test	Öneri	Kanıt düzeyi
Kandidemi	Serum	B-D-glukan	Önerilir	II
İnvaziv kandidiyaz	Serum	B-D-glukan	Önerilir	II
Kronik dissemine kandidiyaz	Serum	B-D-glukan	Önerilir	II

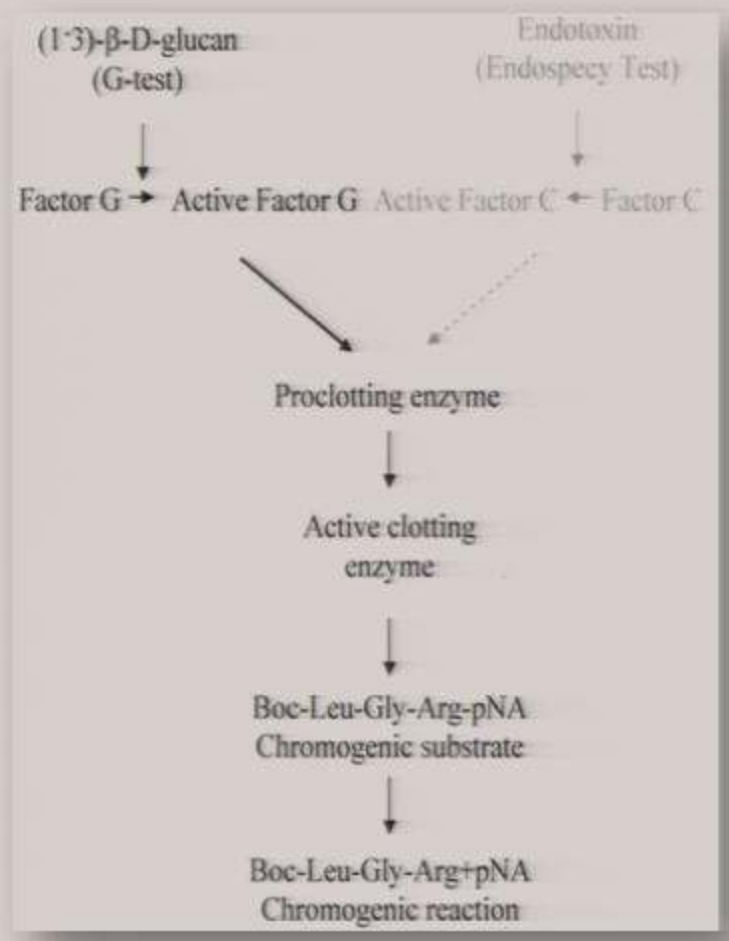
ESCMID guideline for the diagnosis and management of Candida diseases 2012

Hematoloji hastalarında «BII»

ECIL 2009

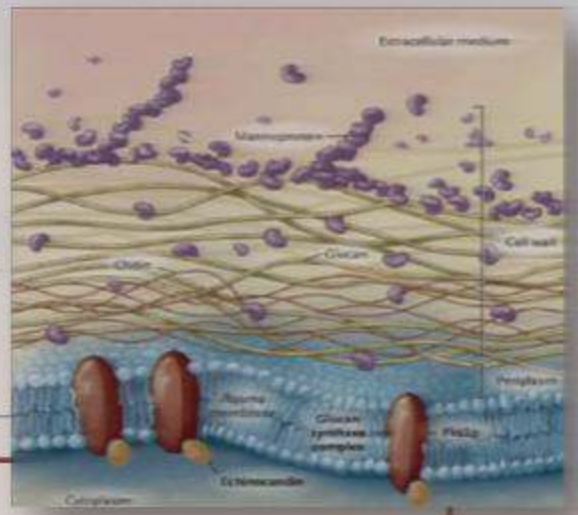
β-1,3-D-glukan

Test at nalı yengeçten izole edilen koagülasyon faktörünün β-1,3-D-glukan ile temas ettiğinde kimyasal reaksiyon vermesi temeline dayanır



Ellepola ANB, Morrison CJ. J Microbiol. 2005; 43: 65-84.

β-1,3-D-glukan



Candida türleri ve diğer mantarların hücre duvarı bileşenidir (*Cryptococcus* ve *Zygomycetes* dışında)

Candida'nın saptanması için faydalı ancak birçok mantar türünde bulunduğu için *Candida*'ya spesifik değildir

Panfungal tanı yöntemi olarak kabul edilmektedir

De Pauw B, et al. Clin Infect Dis 2008;46:1813–21.
Cuenca-Estrella M, et al. Clin Microbiol Infect 2012;18(Suppl 7):9–18.

β-1,3-D-glukan

Serumdaki glukan tespiti için piyasada çeşitli teknikler vardır

- Fungitell-Glucatell test (80pg/ml)
- Fungitec-G-Test MK (30pg/ml)
- Fungitec G-Test (20pg/ml)
- Wako β -Glucan (11pg/ml)

Avrupa ve Amerika'da, en çok kullanılan Fungitell'dir

Cut-off değerinin 80 pg/mL olduğu çalışmalarda

- Duyarlılığı >% 65,
- Özgüllük oranı >% 80,
- Negatif prediktif değeri >% 85

Kan kültürüyle birlikte kullanıldığında duyarlılığı %79

Koo S, et al. Clin Infect Dis 2009; 49: 1650–1659.
Nguyen MH, et al. Clin Infect Dis 2012;54:1240-8.

β-1,3-D-glukan

2008 yılında EORTC / MSG (Avrupa Kanser Araştırma ve Tedavi Organizasyonu/Mikoz Çalışma Grubu)

2012 yılında ESCMID (Avrupa Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Derneği)

β-1,3-D-glukanı invaziv fungal enfeksiyonlar için tanı kriterlerine dahil etmiştir

De Pauw B, et al. Clin Infect Dis 2008;46:1813–21.
Cuenca-Estrella M, et al. Clin Microbiol Infect 2012;18(Suppl 7):9–18.

Clinical Infectious Diseases 2004; 39:199–205

MAJOR ARTICLE

β-D-Glucan as a Diagnostic Adjunct for Invasive Fungal Infections: Validation, Cutoff Development, and Performance in Patients with Acute Myelogenous Leukemia and Myelodysplastic Syndrome

Zekaver Odabasi,[1] Gloria Mattiuzzi,[2] Elihu Estey,[2] Hagop Kantarjian,[2] Fumihiro Saeki,[3] Richard J. Ridge,[3] Paul A. Ketchum,[3] Malcolm A. Finkelman,[3] John H. Rex,[1,4] and Luis Ostrosky-Zeichner[1]

[1]Laboratory of Medical Mycology, University of Texas–Houston Medical School, and [2]The University of Texas M.D. Anderson Cancer Center, Houston, Texas; and [3]Associates of Cape Cod, Falmouth, Massachusetts

283 hematolojik maligniteli hasta

Kanıtlanmış veya olası invaziv fungal enfeksiyonu olan hastalarda en az 1 serum örneği ile klinik tanıdan ortalama **10 gün önce** pozitiflik

Table 3. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of (1→3)-β-D-glucan (BG) detection in subjects with an invasive fungal infection (IFI), by EORTC-MSG diagnostic certainty category, who had 1–3 serum specimens positive for BG.

No. of BG-positive serum samples	Proven or probable IFI				Proven, probable, or possible IFI			
	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Sensitivity, %	Specificity, %	PPV, %	NPV, %
1 specimen	100	90	43	100	70	96	79	93
≥2 sequential specimens	65	96	57	97	38	99	87	87
≥3 sequential specimens	60	99	80	96	28	100	100	85

β-1,3-D-glukan

Test klinik tanıdan **4-14 gün önce** tanı koymayı sağlar

Haftada iki kez seri ölçüm tavsiye edilir

- İki ardışık test pozitif olduğunda optimal sonuç elde edilir

Enfeksiyonu ekarte etmede çok yararlıdır

Tissot F, et al. Am J Respir Crit Care Med 2013;188:1100–9.
Hanson KE, et al. PLoS One. 2012;7:e42282.

MAJOR ARTICLE

Clinical Infectious Diseases 2009; 49:1650–9

Diagnostic Performance of the (1→3)-β-D-Glucan Assay for Invasive Fungal Disease

Sophia Koo,[1,2,3] Julie M. Bryar,[1,4] John H. Page,[4] Lindsey R. Baden,[1,2,3] and Francisco M. Marty[1,2,3]

[1]Brigham and Women's Hospital, [2]Dana-Farber Cancer Institute, [3]Harvard Medical School, and [4]Harvard School of Public Health, Boston, Massachusetts

871 hastanın 1308 örneği değerlendirilmiş

- Duyarlılık %64
- Özgüllük %84

Hematolojik malignitesi olan veya KİT hastalarında duyarlılık daha düşük

Albümin, IVIG kullanan, hemodiyalize giren hastalarda yalancı pozitiflik

β-1,3-D-glukan

Yalancı pozitiflik

- Albümin, immünglobulin kullanımı
- Sellüloz membranlar ile hemodiyaliz
- Pamuk bandaj
- Glukan-kontamine kan toplama tüpleri
- Özellikle *Streptococcus pneumoniae* gibi gram-pozitif organizmalarla olan bakteremi
- Piperasilin tazobaktam, amoksisilin-klavulanat gibi antibiyotikler
- Gıdalar: tahıl, soya fasulyesi, mantar

Schuetz AN. Clin Lab Med 2013; 33:505–525.

Clinical Infectious Diseases 2012;54(5):633–43

MAJOR ARTICLE

β-Glucan Antigenemia Assay for the Diagnosis of Invasive Fungal Infections in Patients With Hematological Malignancies: A Systematic Review and Meta-Analysis of Cohort Studies From the Third European Conference on Infections in Leukemia (ECIL-3)

Frédéric Lamoth,[1,a] Mario Cruciani,[2,a] Carlo Mengoli,[3] Elio Castagnola,[4] Olivier Lortholary,[5,6,7] Malcolm Richardson,[8] and Oscar Marchetti,[1] on behalf of the Third European Conference on Infections in Leukemia (ECIL-3)

[1]Infectious Diseases Service, Department of Medicine, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Switzerland; [2]Center of Community Medicine and Infectious Diseases Service, San Bonifacio Hospital, Verona; [3]Department of Histology, Microbiology and Medical Biotechnology, University of Padova; [4]Infectious Diseases Unit, Department of Hematology and Oncology, G. Gaslini Childrens' Hospital, Genova, Italy; [5]Université Paris Descartes, Service des Maladies Infectieuses et Tropicales, Hôpital Necker Enfants Malades, Centre d'Infectiologie Necker-Pasteur, Paris, [6]Institut Pasteur, Centre National de Référence Mycologie et Antifongiques, Unité de Mycologie Moléculaire, Paris, [7]CNRS URA3012, Paris, France; and [8]Mycology Reference Centre, Education and Research Centre, University Hospital of South Manchester (Wythenshawe Hospital), School of Translational Medicine, Manchester Academic Health Science Centre, University of Manchester, United Kingdom

6 kohort çalışmayı içeren metaanaliz

1771 hasta, 414 invaziv fungal enfeksiyon

Kanıtlanmış veya olası invaziv fungal enfeksiyonda testin tanısal performansı 2 ardışık pozitif test sonucu ile daha iyi

- Duyarlılık % 49.6
- Özgüllük % 98.9
- PPD % 83.5
- NPD % 94.6

Sonuç

- İki ardışık pozitiflik yüksek özgüllük, PPD ve NPD sahip
- Ancak duyarlılık düşük olduğu için testin klinik, patolojik ve mikrobiyolojik bulgular ile kombine edilmesi gerekmektedir

REVIEW ARTICLE

Clinical Infectious Diseases 2011;52(6):750–770

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 çalışmanın verilerinin değerlendirildiği meta-analiz

- Duyarlılık % 76,8
- Özgüllük % 85,3

Sonuç

- Uygun ortamda uygulanır ve sınırlamaları dikkate alınarak yorumlanırsa klinik pratikte yararlı olabilir

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Nov. 2008, p. 4121–4129 Vol. 52, No. 11
0066-4804/08/$08.00+0 doi:10.1128/AAC.00674-08

Cerebrospinal Fluid and Plasma (1→3)-β-D-Glucan as Surrogate Markers for Detection and Monitoring of Therapeutic Response in Experimental Hematogenous *Candida* Meningoencephalitis▽

Ruta Petraitiene,[1,2] Vidmantas Petraitis,[1,2] William W. Hope,[1] Diana Mickiene,[1,2] Amy M. Kelaher,[1] Heidi A. Murray,[1] Christine Mya-San,[1] Johanna E. Hughes,[1] Margaret P. Cotton,[1] John Bacher,[3] and Thomas J. Walsh[1]*

Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, Bethesda,[1] Laboratory Animal Sciences Program, SAIC-Frederick, Inc., Frederick,[2] and Surgery Service, Division of Veterinary Resources, Office of Research Services, Bethesda,[3] Maryland

Candida meningoensefalitli nötropenik olmayan tavşanlar üzerinde yapılan çalışma

BOS β-1,3-D-glukan düzeyi plazma düzeyinden yüksek bulunmuş ve terapötik yanıtla korele sonuçlar elde edilmiş

Candida meningoensefaliti tanısında ve tedavi yanıtını izlemede faydalı olabileceği sonucuna varılmış

β-1,3-D-glukan

Avantajları	Dezavantajları
Antifungal tedavinin testin duyarlılığı üzerinde etkisi yok	Hematolojik hastalarda daha az duyarlılık
Haftada 2 kez ölçülmesi uygun bir tarama stratejisi	Olumlu sonuçlar için eşik değeri kullanılan teste bağlı
2 saat içinde sonuç	Yanlış pozitif sonuçlar, metodolojik kaygılar
Yüksek özgüllük	Pan fungal test

Diğer antikorlar

	Örnek	Test	Öneri	Kanıt düzeyi
Kandidemi	Serum	Diğer antikorlar	Öneri yok	**Veri yok**

ESCMID guideline for the diagnosis and management of Candida diseases 2012

Diğer antikorlar

Antikor belirleme kitleri değerlendirme aşamasındadır ve klinik doğrulukları konusunda sınırlı veri vardır

Candida albicans germ tüp antikor testi

- Hematolojik malignite, kemik iliği nakli veya yoğun bakım hastalarında yapılan sınırlı klinik çalışmalarda
  - Duyarlılığı %77-89,
  - Özgüllüğü %91-100 olarak saptanmıştır

Peman J, et al. BMC Infect Dis 2011;11:60.
Martinez M, et al. American Society for Microbiology, Washington DC, p 48

Pemán et al. BMC Infectious Diseases 2011, 11:60
http://www.biomedcentral.com/1471-2334/11/60

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Clinical factors associated with a *Candida albicans* Germ Tube Antibody positive test in Intensive Care Unit patients

Javier Pemán[1*], Rafael Zaragoza[2], Guillermo Quindós[3], Miriam Alkorta[4], María S Cuétara[5], Juan J Camarena[6], Paula Ramírez[7], María J Giménez[1], Estrella Martín-Mazuelos[8], María J Linares-Sicilia[9], José Pontón[3], the study group Candida albicans Germ Tube Antibody Detection in Critically Ill Patients (CAGTAUCI)

Prospektif, çok merkezli çalışma

53 non-nötropenik yoğun bakım hastası

- 22 (%41.5) hastada *Candida albicans* germ tüp antikor testi pozitif
  - Hiçbirinde kan kültürü pozitifliği yok

Sonuç

- *Candida albicans* germ tüp antikor tespiti yoğun bakım hastalarında invaziv kandidiyazis tanısı için önemli olabilir

Candida albicans germ tüp antikor testi

Avantajları

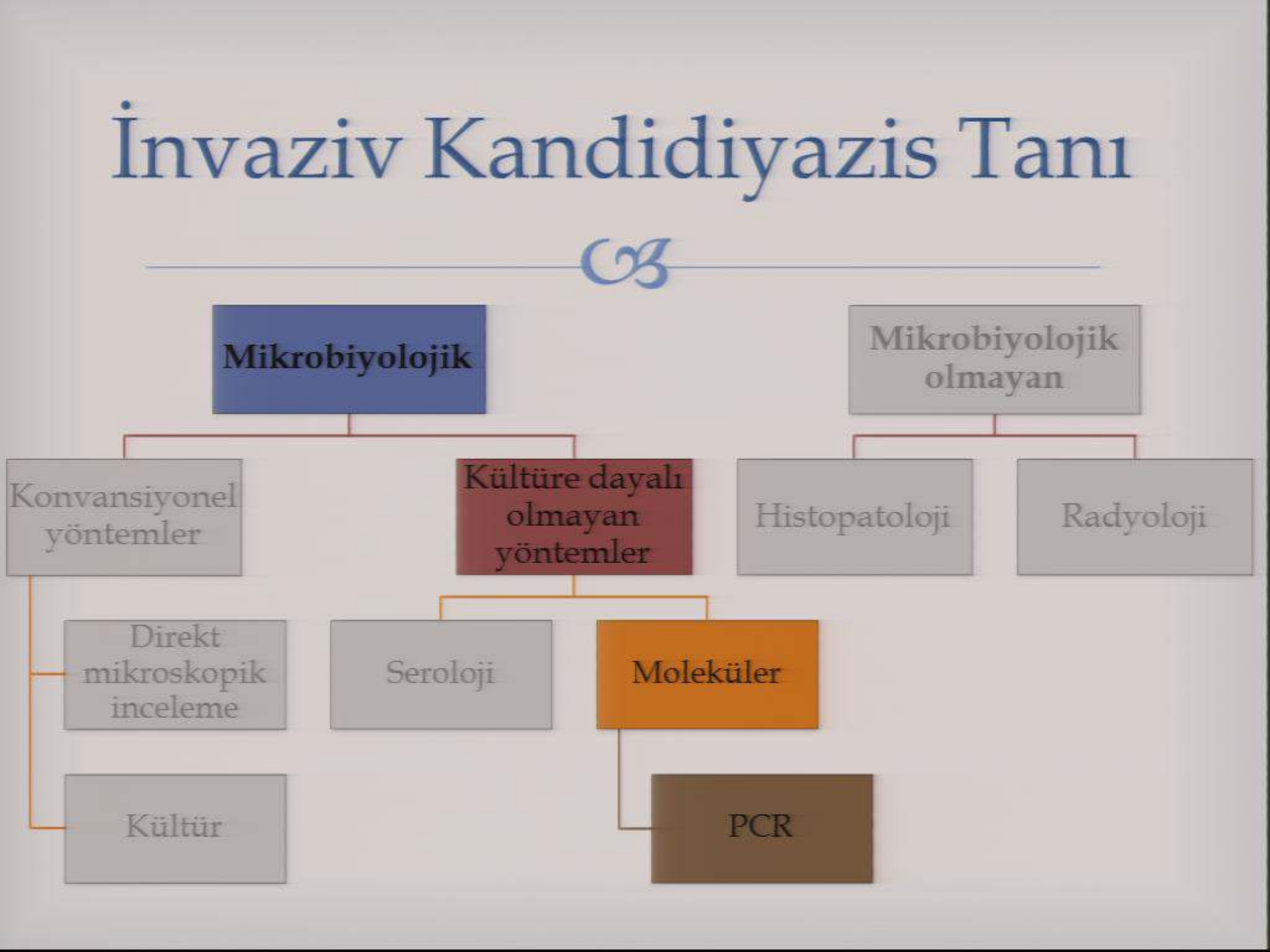
Dezavantajları

Yüksek özgüllük

Tanı ve tedaviyi izleme

Sınırlı deneyim

İnvaziv Kandidiyazis Tanı



Polimeraz Zincir Reaksiyonu

	Örnek	Test	Öneri	Kanıt düzeyi
Kandidemi	Serum	Septifast PCR kit	Öneri yok	**Veri yok**
		In-house PCR	Öneri yok	**Veri yok**
İnvaziv kandidiyaz	Serum	Septifast PCR kit	Öneri yok	**Veri yok**
		In-house PCR	Öneri yok	**Veri yok**
Kronik dissemine kandidiyaz	Serum	Septifast PCR kit	Öneri yok	**Veri yok**
		In-house PCR	Öneri yok	**Veri yok**

ESCMID guideline for the diagnosis and management of Candida diseases 2012

PCR

PCR ile DNA tespiti, enfeksiyonun hızlı tanısına yardımcı olmak amacıyla geliştirilmiştir

Pozitif PCR sonuçları kolonizasyon-enfeksiyon ayrımını yapamamaktadır

Maliyet ve teknik donanım yaygın kullanım için engel oluşturmaktadır

1000'den fazla hastayı içeren çok sayıda çalışma yayınlanmıştır

Lau A, et al. J Clin Microbiol. 2007; 45: 380–5.
Lau A, et al. J Clin Microbiol. 2010; 48: 811–6.
McMullan R, et al. Clin Infect Dis. 2008; 46: 890–6.
Wellinghausen N, et al. J Med Microbiol. 2009; 58: 1106–11.
Avni T, et al. J Clin Microbiol. 2011; 49: 665–70.

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 hastanın değerlendirildiği metaanaliz

Şüpheli, olası veya kanıtlanmış invaziv kandidiyazisli 963 hasta

Kandidemili hastalarda

- Duyarlılık %95
- Özgüllük %92

Olası veya kanıtlanmış invaziv kandidiyazisli hastalarda,

- PCR'ın duyarlılığı %85 (78-91),
- Kan kültürünün %38 (29-46) olarak bulunmuş

JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 2010, p. 811–816 Vol. 48, No. 3
0095-1137/10/$12.00 doi:10.1128/JCM.01650-09

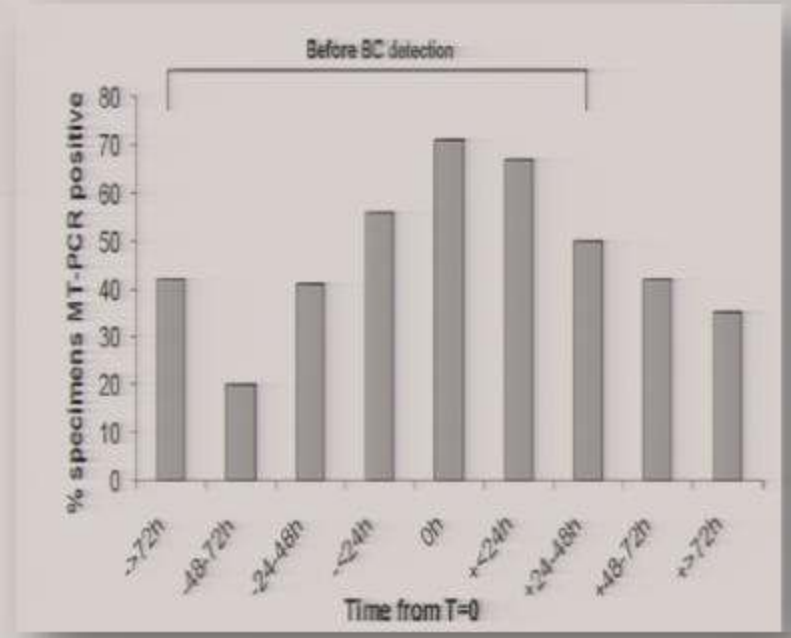
Comparison of Whole Blood, Serum, and Plasma for Early Detection of Candidemia by Multiplex-Tandem PCR▽

Anna Lau,[1,2] Catriona Halliday,[1,3] Sharon C.-A. Chen,[1,3] E. Geoffrey Playford,[4] Keith Stanley,[5] and Tania C. Sorrell[1,2]*

Centre for Infectious Diseases and Microbiology,[1] Westmead Millennium Institute,[2] and Centre for Infectious Diseases and Microbiology Laboratory Services, Institute of Clinical Pathology and Medical Research, Sydney West Area Health Service,[3] Westmead, NSW, Princess Alexandra Hospital, Brisbane, QLD,[4] and AusDiagnostics Pty. Ltd., Alexandria, NSW,[5] Australia

Kandidemili 109 hasta, 255 örnek

- Duyarlılık %75
- Özgüllük %97
- PPD %95
- NPD %85
- Ortalama 2.2 (0.5-8 gün) günde tespit



PCR

PCR bazlı tekniklerin klinik faydası ile ilgili öneri yapılmadan önce sonuçları ve uyumu değerlendirilmelidir

***Candida* DNA'nın doğrudan moleküler tespiti henüz standardize edilmemiştir**

PCR'ın değeri belirsizliğini korumaktadır

PCR


Avantajları
Dezavantajları
Serumda ve diğer klinik örneklerde kullanım
Standardize değil
Yüksek özgüllük
Kolonizasyonla enfeksiyonun ayırt edilememesi

SONUÇ

Kültür ve mikroskobik inceleme bütün kılavuzlarda önerilmekte

Serolojik testlerin yeri ancak destekleyici nitelikte

PCR testleri için ise henüz öneri yok

İnvaziv kandidiyaz güncel tedavi önerileri

Dr. Bilgin ARDA
Ege Üniversitesi Tıp Fakültesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

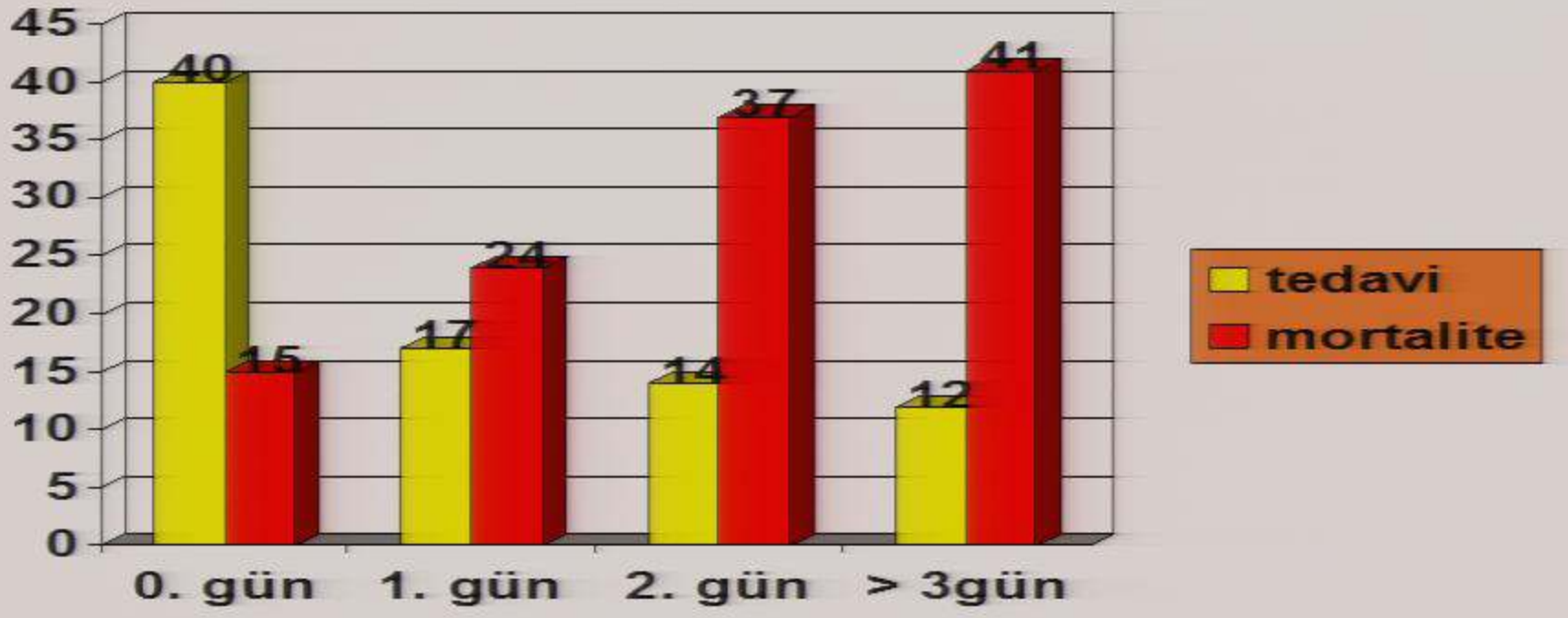
İnvaziv kandida infeksiyonlarının tedavisi

İki ana ilke

İnvaziv kandida infeksiyonlarının tedavisi

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]



İnvaziv kandidoz tedavi yaklaşımları

Paramythiotou E, et al. *Molecules* 2014; 19: 1085-1119

İnvaziv kandidoz tedavi yaklaşımları

- Profilaksi
- Preemptif tedavi
- Ampirik tedavi
- Hedeflenmiş tedavi

İnvaziv kandidoz tedavi yaklaşımları

Paramythiotou E, et al. *Molecules* 2014; 19: 1085-1119

İnvaziv kandidoz tedavi yaklaşımları

Risk faktörü	(+)
Biyomarker	(-)
Kinik bulgu	(-)
Mikoloji	(-)

Profilaksi

Paramythiotou E, et al. *Molecules* 2014; 19: 1085-1119

İnvaziv kandidoz tedavi yaklaşımları

Risk faktörü	(+)
Biyomarker	(-)
Kinik bulgu	(-)
Mikoloji	(-)

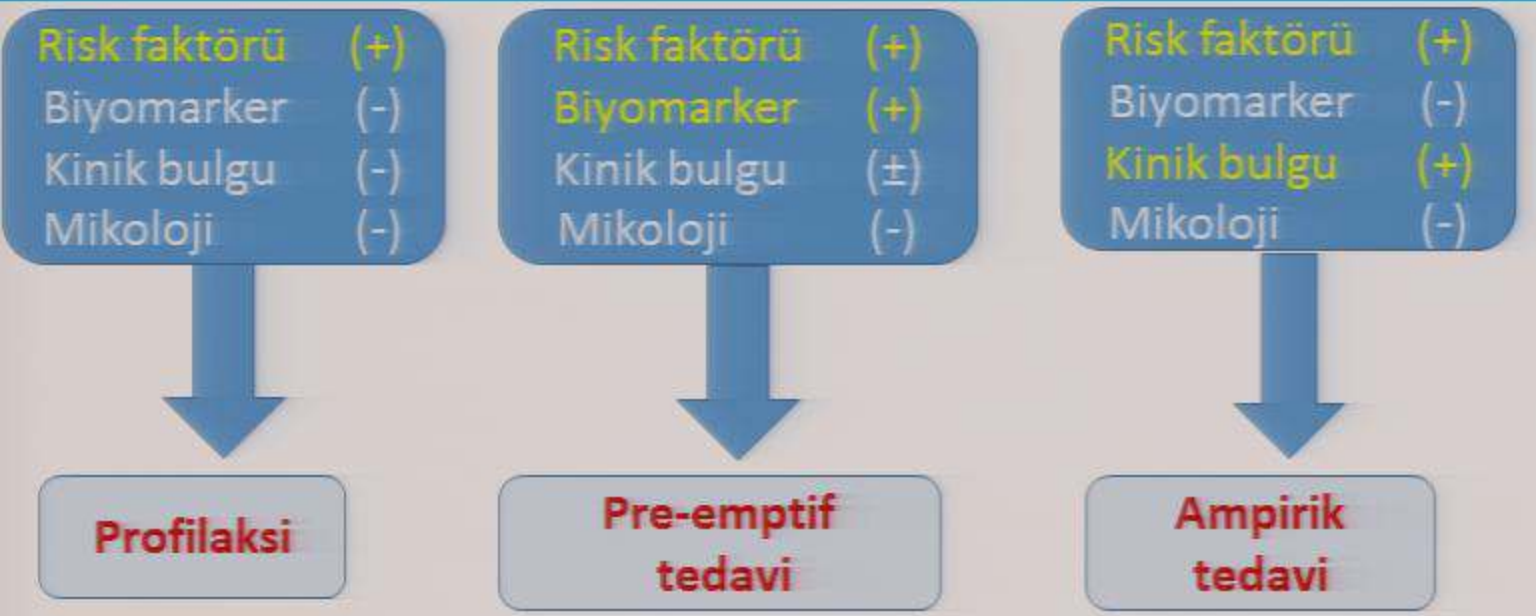
Profilaksi

Risk faktörü	(+)
Biyomarker	(+)
Kinik bulgu	(±)
Mikoloji	(-)

Pre-emptif tedavi

Paramythiotou E, et al. *Molecules* 2014; 19: 1085-1119

İnvaziv kandidoz tedavi yaklaşımları



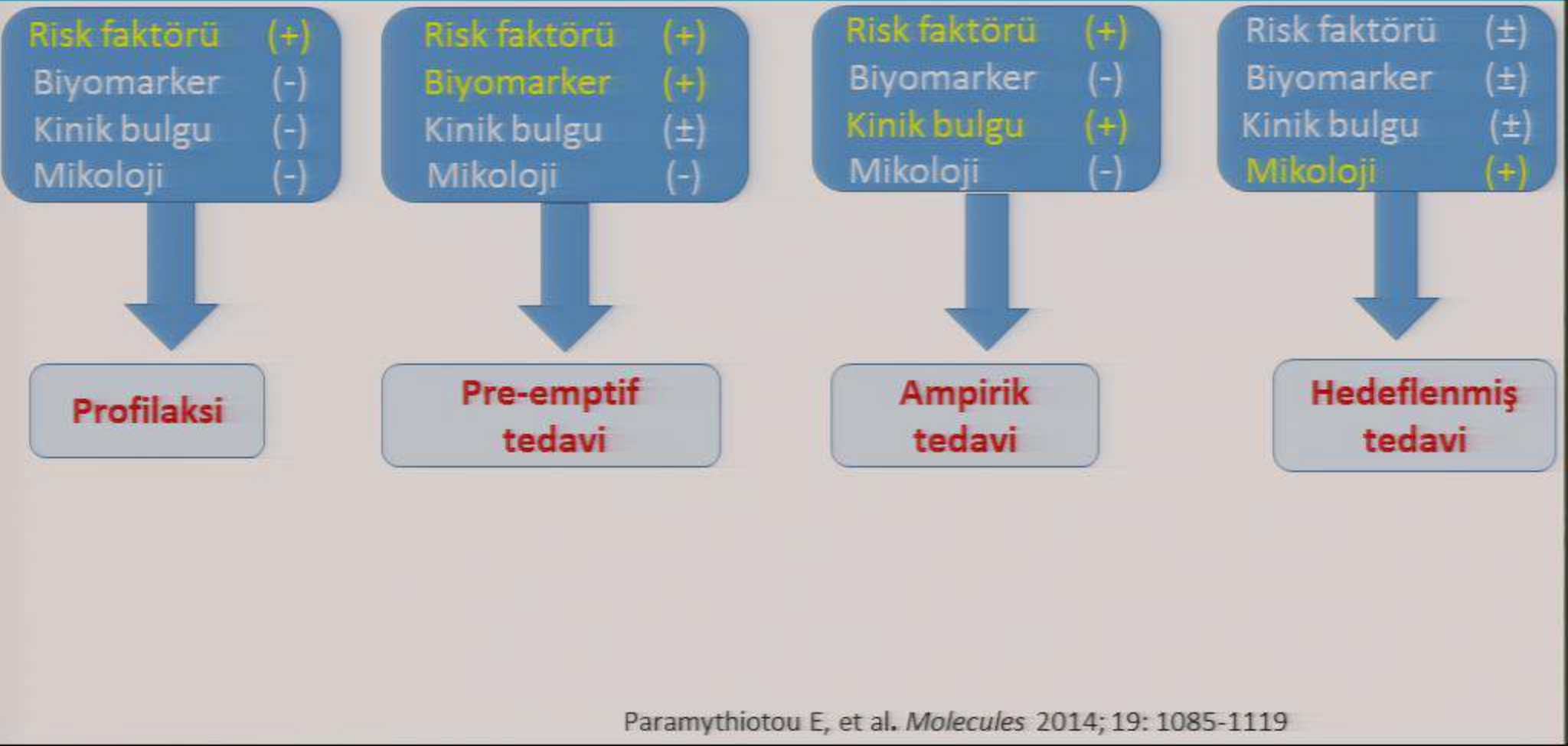
Paramythiotou E, et al. *Molecules* 2014; 19: 1085-1119

Profilaksi

- Flukonazol 400 mg/gün
  - Kandidemi insidansının yüksek olduğu üniteler
  - Yüksek riskli hastalar (SVK, TPN, GI cerrahi, kandida kolonizasyonu)
  - İnvaziv kandidoz riskini azaltır, ancak uzun dönem sağkalıma etkisi yok
  - Direnç artışı veya *Candida* türlerinde majör değişiklikle ilişkili değil

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

İnvaziv kandidoz tedavi yaklaşımları



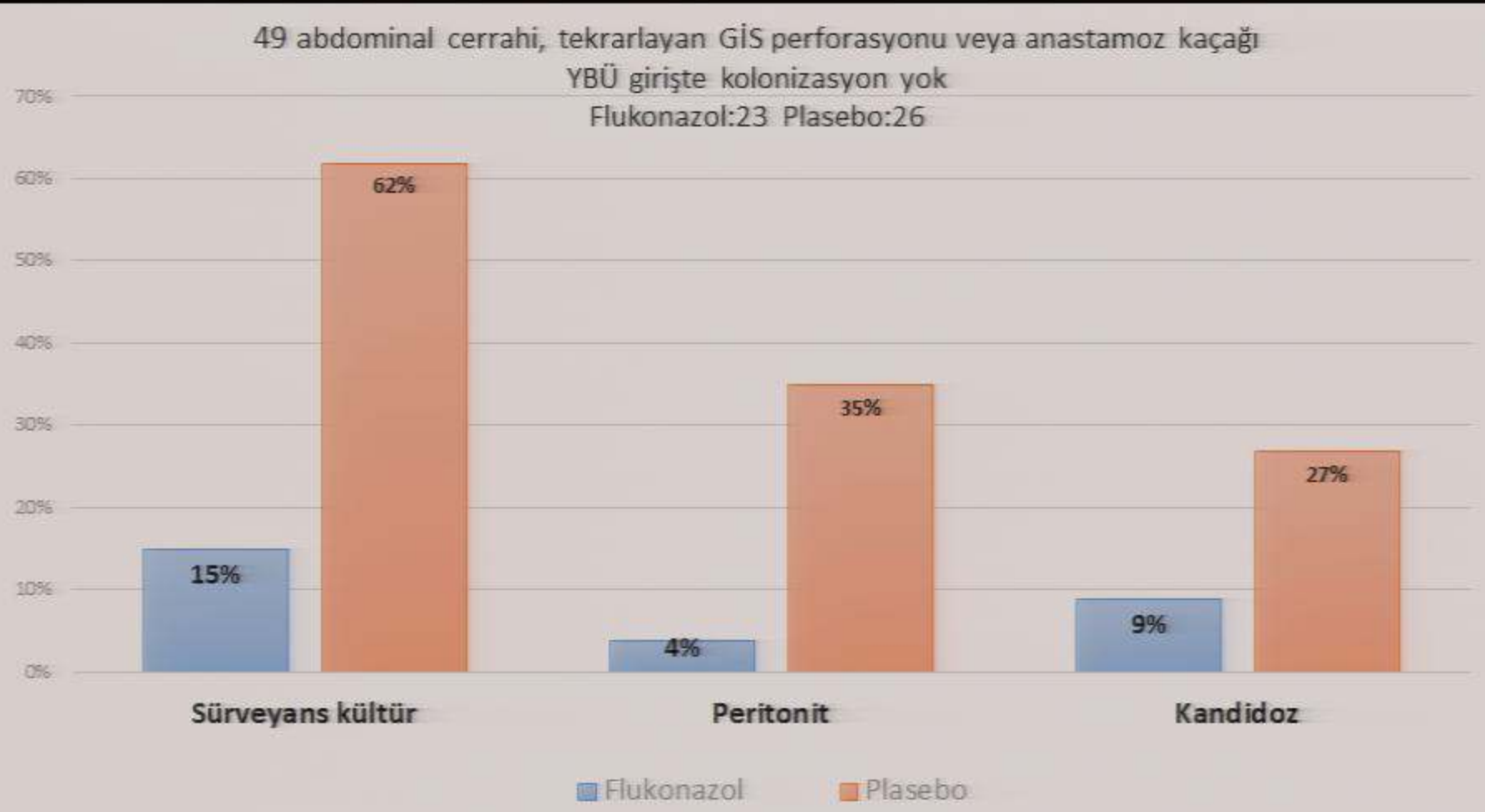
Paramythiotou E, et al. *Molecules* 2014; 19: 1085-1119

Profilaksi

- Flukonazol 400 mg/gün
  - Kandidemi insidansının yüksek olduğu üniteler
  - Yüksek riskli hastalar (SVK, TPN, GI cerrahi, kandida kolonizasyonu)
  - İnvaziv kandidoz riskini azaltır, ancak uzun dönem sağkalıma etkisi yok
  - Direnç artışı veya *Candida* türlerinde majör değişiklikle ilişkili değil

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Hasta grubu	Amaç	İlaç	Ö	K	
Abdominal cerrahi ve tekrarlayan GİS perforasyonu veya anastamoz kaçağı	İntraabdominal *Candida* infeksiyonundan koruma	Fluconazole 400 mg/day	B	I	Placebo *N* = 43
		Caspofungin 70/50 mg/day	C	II_u	Single arm *N* = 19
YBÜ ≥3 gün kalması beklenen cerrahi kritik hasta	Fungal infeksiyon gelişim zamanını geciktirmek	Fluconazole 400 mg/day	C	I	Placebo *N* = 260
48 saatir MV desteğinde olup ≥72 saat daha MV desteği sürmesi beklenen hasta	İnvasiv kandidoz/kandidemiden korunma	Fluconazole 100 mg/day	C	I	Placebo *N* = 204 SDD used
MV, hastanede ≥3 gün, AB, CVC, ve ≥1: parenteral nutrisyon, diyaliz, major cerrahi, pancreatit, sistemik steroit, immunsupresyon		Caspofungin 50 mg/day	C	II_a	Placebo *N* = 186 EORTC/MSG criteria used
Cerrahi YBÜ hastası		Ketoconazole 200 mg/day	D	I	Placebo *N* = 57
İnvasiv kandidoz/kandidemi risk faktörü olan YBÜ hastası		Itraconazole 400 mg/day	D	I	Open *N* = 147
Cerrahi katabolik YBÜ hastası		Nystatin 4 Mio IU/day	D	I	Placebo *N* = 46


49 abdominal cerrahi, tekrarlayan GİS perforasyonu veya anastamoz kaçağı
YBÜ girişte kolonizasyon yok
Flukonazol:23 Plasebo:26
70%
60%
50%
40%
30%
20%
10%
0%
62%
35%
27%
15%
4%
9%
Sürveyans kültür
Peritonit
Kandidoz
Flukonazol
Plasebo

Profilaksi

- Yakın zamanda abdominal cerrahi geçiren ve tekrarlayan gastrointestinal perforasyonları olan veya anastomoz kaçağı olan hastalar için flukonazol 400 mg/gün (kanıt düzeyi BI)

ESCMID. *Clin Microbiol Infect* 2012;18 (Suppl. 7): 19–37

Ampirik

- Retrospektif, kontrol grubu olmayan çalışmalar
- Ampirik AF tedavi alıp, sonrasında duyarlı etken saptanalarda mortalite düşük
- Ampirik AF tedavi toplam mortaliteyi düşürebilir
- Sadece ateş, AF tedavi için yeterli mi ?

ESCMID. *Clin Microbiol Infect* 2012;18 (Suppl. 7): 19–37

Ampirik tedavi - Nötropenik olmayan hasta
(invaziv kandidozdan şüphelenildiğinde)

YBÜ hastasında ampirik antifungal tedavi,

- İnvaziv kandida infeksiyonu için risk faktörlerinin varlığında, ateşi açıklayacak başka bir neden yoksa, kandida serolojisi pozitifse ve kolonizasyon durumuna göre dikkate alınmalıdır (BIII)

Ampirik tedavi, kandidemi tedavisi gibidir

- Flukonazol
- Caspofungin
- Anidulafungin
- Vorikonazol
- Amfoterisin B (Alternatif)

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Ampirik

Hasta grubu	Amaç	İlaç	Ö	K
YBÜ hastası, geniş spektrumlu ab yanıt vermeyen ateş, APACHE II >16 270 hasta	Ateşin düşmesi	Fluconazol 800 mg/gün	D	I
YBÜ hastası, yüksek ateş	Mortaliteyi düşürmek	Fluconazol veya ekinokandin	C	II

ESCMID. *Clin Microbiol Infect* 2012;18 (Suppl. 7): 19–37

Preemtif

- **Beta –D- glukan testi:** Duyarlılık >%65, özgüllük >%80
  - Yalancı pozitiflik: Bakteriyemi ile birliktelik, hemofiltrasyon, albumin, immünoglobulin kullanımı, gazlı bez, çeşitli antibiyotikler (TMT-SMX, ertapenem, sefepim, kolistin,…)
- **Mannan antijeni ve anti-mannan antikoru:** Duyarlılık %80, özgüllük %85
- **Polimeraz zincir reaksiyonu:** Duyarlılık ve özgüllüğü >%85

ESCMID. *Clin Microbiol Infect* 2012;18 (Suppl. 7): 19–37

Posteraro et al. Critical Care 2011, 15:R249
http://ccforum.com/content/15/5/R249

CRITICAL CARE

RESEARCH Open Access

Early diagnosis of candidemia in intensive care unit patients with sepsis: a prospective comparison of (1→3)-β-D-glucan assay, *Candida* score, and colonization index

Brunella Posteraro[1], Gennaro De Pascale[2], Mario Tumbarello[3*], Riccardo Torelli[1], Mariano Alberto Pennisi[2], Giuseppe Bello[2], Riccardo Maviglia[2], Giovanni Fadda[1], Maurizio Sanguinetti[1] and Massimo Antonelli[2]

	Duyarlılık %	Özgüllük %	PPD %	NPD %
BG eşik değer 80 pg/ml	92.9	93.7	72.2	98.7
Kandida skoru ≥3	85.7	88.6	57.1	97.2
Kolonizasyon indeksi ≥0.5	64.3	69.6	27.3	91.7
BG + kandida skoru	100	83.5	51.8	100

Preemtif

Hasta grubu	Amaç	İlaç	Ö	K
YB hastası, pozitif (1,3)-β-d-glucan test	Erken tanı, tedavi, kür	Herhangi bir antifungal	C	II_u

ESCMID. *Clin Microbiol Infect* 2012;18 (Suppl. 7): 19–37

Clinical Infectious Diseases Advance Access published February 27, 2014

MAJOR ARTICLE

MSG-01: A Randomized, Double-Blind, Placebo-Controlled Trial of Caspofungin Prophylaxis Followed by Preemptive Therapy for Invasive Candidiasis in High-Risk Adults in the Critical Care Setting

Luis Ostrosky-Zeichner,[1] Shmuel Shoham,[2] Jose Vazquez,[3] Annette Reboli,[4] Robert Betts,[5] Michelle A. Barron,[6] Mindy Schuster,[7] Marc A. Judson,[8] Sanjay G. Revankar,[9] Juan Pablo Caeiro,[10] Julie E. Mangino,[11] David Mushatt,[12] Roger Bedimo,[13] Alison Freifeld,[14] Minh Hong Nguyen,[15] Carol A. Kauffman,[16] William E. Dismukes,[17] Andrew O. Westfall, Jeanna Beth Deerman,[17] Craig Wood,[19] Jack D. Sobel,[9] and Peter G. Pappas[17]

Table 1. Definitions of Proven and Probable Invasive Candidiasis

Definition	Parameters
Proven invasive candidiasis	Blood culture that yields *Candida* spp OR histopathologic or cytopathologic examination of a needle aspiration or biopsy specimen from a normally sterile site excluding mucous membranes showing yeast cells OR recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly [<24 h] placed drain) from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process.
Probable invasive candidiasis	Serum BG levels >80 pg/mL in 2 consecutive samples AND 1 of the following: 1. Temperature >38°C or <36°C. 2. Hypotension defined as systolic BP <90 mm Hg or a significant drop (40 mm Hg) in BP from baseline. 3. WBC count >12 000 cells/μL.

Clinical Infectious Diseases Advance Access published February 27, 2014

MAJOR ARTICLE

Yüksek olası invaziv kandidoz

Ardışık iki örnekte serum BG seviyesi >80 pg/mL olması ve aşağıdakilerden biri

1. Ateş >38^{0}C veya <36^{0}C
2. Hipotansiyon (sistolik kan basıncı <90 mmHg veya bazalden ≥40 mm Hg azalması
3. BK > 12000 hücre/ µ. L

rapy
ults

. Barron,[5]
vid Mushatt,[12]
drew O. Westfall,

Proven invasive candidiasis	Blood culture that yields *Candida* spp OR histopathologic or cytopathologic examination of a needle aspiration or biopsy specimen from a normally sterile site excluding mucous membranes showing yeast cells OR recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly [<24 h] placed drain) from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process.

Serum BG levels >80 pg/mL in 2 consecutive samples AND 1 of the following:

1. Temperature >38°C or <36°C.
2. Hypotension defined as systolic BP <90 mm Hg or a significant drop (40 mm Hg) in BP from baseline.
3. WBC count >12 000 cells/µL.

Kesin invaziv kandidoz

- Kan kültüründe *Candida* spp. üremesi veya
- Muköz membranlar dışında normalde steril bölgeden alınan biyopsi veya aspirasyon materyalinin histopatolojik incelemesinde maya görülmesi veya
- Klinik veya radyolojik olarak enfeksiyonla uyumlu normalde steril bölgeden steril olarak alınan örnekte *Candida* spp. üremesi (<24 saat içinde takılmış dren dahil)

Ostrosky-Zeichner L, et al. Clin Infect Dis 2014 (baskıda

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

- Nötropenik olmayan YBÜ hastasında kandidemi tedavisi
- Nötropenik hastada kandidemi tedavisi
- Nötropenik olmayan hastada empirik tedavi
- Nötropenik hastada empirik tedavi
- Diğer invaziv kandida infeksiyonlarında tedavi
- YBÜ hastasında antifungal profilaksi

Kandidemi tedavi – Nötropenik olmayan hasta

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik olmayan hasta

Flukonazol (AI)
Caspofungin (AI)
Anidulafungin (AI)
Vorikonazol (AI)*

Kritik hasta
Azol öyküsü

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik olmayan hasta

Flukonazol (AI)
Caspofungin (AI)
Anidulafungin (AI)
Vorikonazol (AI)*

Kritik hasta
Azol öyküsü

(-) Flukonazol (AIII)

(+) Ekinokandin (Caspo, Anidula) (AIII)

İzolat duyarlıysa ve hasta klinik olarak stabilse flukonazole geç (AII)

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik olmayan hasta

Flukonazol (AI)
Caspofungin (AI)
Anidulafungin (AI)
Vorikonazol (AI)*

Kritik hasta
Azol öyküsü

(-) Flukonazol (AIII)

(+) Ekinokandin (Caspo, Anidula) (AIII)

İzolat duyarlıysa ve hasta klinik olarak stabilse flukonazole geç (AII)

C. glabrata → Ekinokandin (BIII)
C. parapsilosis → Flukonazol (BIII)

Klinik düzelme var, kontrol kültürlerde üreme yoksa başlangıç tedavisine devam (BIII)

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik olmayan hasta

Flukonazol (AI)
Caspofungin (AI)
Anidulafungin (AI)
Vorikonazol (AI)*

Kritik hasta
Azol öyküsü

(-) Flukonazol (AIII)

(+) Ekinokandin (Caspo, Anidula) (AIII)

İzolat duyarlıysa ve hasta klinik olarak stabilse flukonazole geç (AII)

C. glabrata → Ekinokandin (BIII)
C. parapsilosis → Flukonazol (BIII)

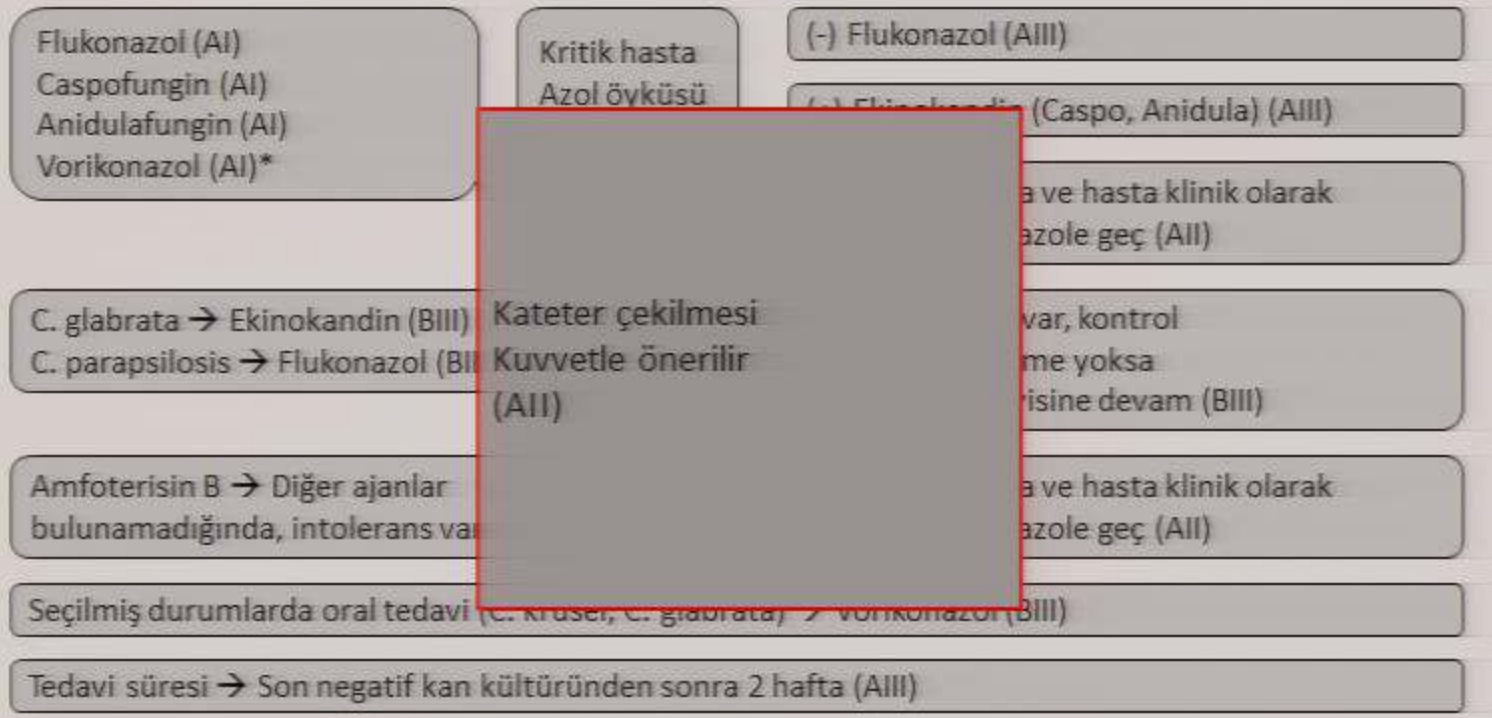
Klinik düzelme var, kontrol kültürlerde üreme yoksa başlangıç tedavisine devam (BIII)

Amfoterisin B → Diğer ajanlar bulunamadığında, intolerans varsa (AI)

İzolat duyarlıysa ve hasta klinik olarak stabilse flukonazole geç (AII)

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik olmayan hasta



IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik hasta

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik hasta

Caspofungin (AII)
Anidulafungin (AIII)
L- Amfoterisin B (AII)

Önerilen Tedavi

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik hasta

Caspofungin (AII) Anidulafungin (AIII) L- Amfoterisin B (AII)	Önerilen Tedavi
Flukonazol (AI) Vorikonazol (AI)*	Kritik olmayan hasta, Azol öyküsü yok *Aspergillus kapsanmak isteniyorsa

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik hasta

Caspofungin (AII)
Anidulafungin (AIII)
L- Amfoterisin B (AII)

Önerilen Tedavi

Flukonazol (AI)
Vorikonazol (AI)*

Kritik olmayan hasta, Azol öyküsü yok
*Aspergillus kapsanmak isteniyorsa

C. glabrata → Ekinokandin (BIII)
LAB etkili ancak toksisitesi yüksek (BIII)

C. parapsilosis → Flukonazol (BIII)
L-amfoterisin B (BIII)

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik hasta

Caspofungin (AII)
Anidulafungin (AIII)
L- Amfoterisin B (AII)

Önerilen Tedavi

Flukonazol (AI)
Vorikonazol (AI)*

Kritik olmayan hasta, Azol öyküsü yok
*Aspergillus kapsanmak isteniyorsa

C. glabrata → Ekinokandin (BIII)
LAB etkili ancak toksisitesi yüksek (BIII)

C. parapsilosis → Flukonazol (BIII)
L-amfoterisin B (BIII)

Klinik düzelme var, kontrol kültürlerinde üreme yoksa başlangıç tedavisine devam (BIII)

C. krusei → Ekinokandin, L-Amfoterisin B veya Vorikonazol (BIII)

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik hasta

Caspofungin (AII)
Anidulafungin (AIII)
L- Amfoterisin B (AII)

Önerilen Tedavi

Flukonazol (AI)
Vorikonazol (AI)*

Kritik olmayan hasta, Azol öyküsü yok
*Aspergillus kapsanmak isteniyorsa

C. glabrata → Ekinokandin (BIII)
LAB etkili ancak toksisitesi yüksek (BIII)

C. parapsilosis → Flukonazol (BIII)
L-amfoterisin B (BIII)

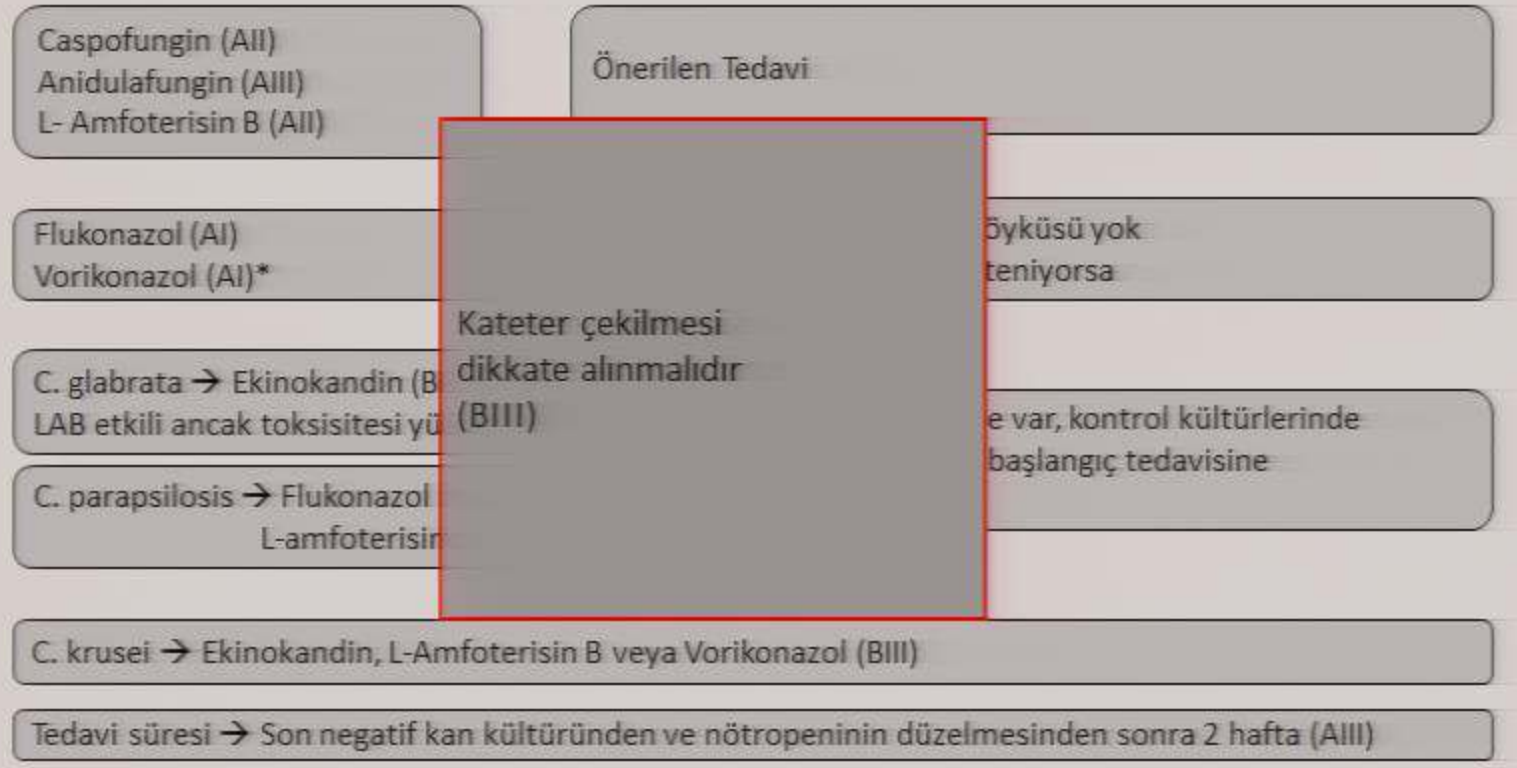
Klinik düzelme var, kontrol kültürlerinde üreme yoksa başlangıç tedavisine devam (BIII)

C. krusei → Ekinokandin, L-Amfoterisin B veya Vorikonazol (BIII)

Tedavi süresi → Son negatif kan kültüründen ve nötropeninin düzelmesinden sonra 2 hafta (AIII)

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidemi tedavi – Nötropenik hasta



IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Klinik tablo	Primer	Alternatif	Yorum
Asemptomatik İYE	Tedavi edilmez	-	Düşük doğum ağ. bebekler, nötropeni, ürolojik girişim
Semptomatik sistit	FL, 2 hf	K-AB	K-AB ile mesane yıkaması, dirençli suşlarla gelişen refrakter inf.da
Pyelonefrit	FL, 2 hf	K-AB	Dissemine kandidiyaza sekonder ise kandidemi gibi tedavi edilir
Vulvovajinal	Topikal, FL 150 mg tek doz	-	Rekürren inf.da FL 150 mg/hf, 6 ay
Osteomyelit	FL, 6-12 ay. LAB birkaç hafta, sonra FL ile devam	Ekinokandin birkaç hf, FL ile devam (6-12 ay)	Sıklıkla cerrahi debridman gerekir
Septik artrit	FL, 6 hf. LAB 2 hf, sonra FL ile devam	Ekinokandin birkaç hf, FL ile devam (6-12 ay)	Bütün olgularda cerrahi debridman gerekir
Protez infeksiyonu	FL, LAB veya ekinokandin 6 hf.	-	Protez çıkarılmalıdır, aksi taktirde FL ile kronik supresyon

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Kandidüri

- Kandidüri kandidemi ile ilişkili olabilir
- Kandidemik hastaların %46-68'inde kandidüri saptanmış.

Bross J, et al. Am J Med 1989;87:614-620
Charles PE, et al. Intensive Care Med 2003;29:2162-2169

- Kandidürili hastaların %4.3'ünde kandidemi saptanmış.

Jain M, Dogra V, et al. Indian J Pathol Microbiol. 2011 Jul-Sep;54(3):552-5.

- Üriner tıkanıklık kandidemi riskini artırır

Toya SP, et al. *Journal of Hospital Infection* 2007; 66: 201-206

Kandidüri

- Asemptomatik kandidüride kandidemi risk faktörlerini değerlendir.
- Düşük doğum ağırlıklı yenidoğan, nötropenik ve ürolojik cerrahi uygulanacak hastalarda tedavi et
- İdrar kültürünü tekrar ederek kontaminasyonu dışla
- Kolonizasyon indeksini değerlendir

Klinik tablo	Primer	Alternatif	Yorum
SSS kandidozu	LAB ± Flusitozin başlangıçta birkaç hafta, sonra FL ile semptomlara düzelene kadar devam		Ventriküler kateter varsa çıkarılmalıdır
Candida endoftalmiti	K-AB, FL 4-6 hf	LAB, VO, Ekinokandin	Tanı için vitreal aspirasyon
Endokardit	K-AB, LAB, Ekinokandin	Stabil hastada etken duyarlıysa ve kan kültürleri negatifleşmişse FL'e geçilir	Kapak replasmanı kuvvetle önerilir. Prostetik kapak değişmemişse ömür boyu supresyon tedavisi
Solunum örn.den Candida izolasyonu	**Tedavi önerilmez**	-	**Tedavi için histopatolojik kanıt gereklidir**
Orofarengeal kandidoz	Nistatin süsp., FL	ITR, VO, K-AB, POS, Ekinokandin	7-14 gün süre ile
Özofageal kandidoz	FL, Ekinokandin, K-AB	ITR, VO, POS	14-21 gün süre ile

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Klinik tablo	Primer	Alternatif	Yorum
SSS kandidozu	LAB ± Flusitozin başlangıçta birkaç hafta, sonra FL ile semptomlara düzelene kadar devam		Ventriküler kateter varsa çıkarılmalıdır
Candida endoftalmiti	Kandidemisi olan bütün hastalar tedavinin erken döneminde en az bir kez endoftalmit açısından değerlendirilmelidir (AII)		
Endokardit	K-AB, LAB, Ekinokandin	Stabil hastada etken duyarlıysa ve kan kültürleri negatifleşmişse FL'e geçilir	Kapak replasmanı kuvvetle önerilir. Prostetik kapak değişmemişse ömür boyu supresyon tedavisi
Solunum örn.den Candida izolasyonu	**Tedavi önerilmez**	-	**Tedavi için histopatolojik kanıt gereklidir**
Orofarengeal kandidoz	Nistatin süsp., FL	ITR, VO, K-AB, POS, Ekinokandin	7-14 gün süre ile
Özofageal kandidoz	FL, Ekinokandin, K-AB	ITR, VO, POS	14-21 gün süre ile

IDSA 2009 Kandidiyaz Tedavi Kılavuzu

Solunum örnekleri: Kandida

- Akciğer apsesi: Kandidemiye sekonder (febril nötropeni..)
- Genellikle kolonizasyon
- 232 YBÜ hastası, 135 (%58) histopatolojik pnömoni
- 77 olgunun son iki hafta içinde solunum örneğinde *Candida* spp.
- Histopatolojik kandida pnömonisi: 0

Meersseman W Intensive Care Med. 2009 Sep;35(9):1526-31

Significance of the isolation of Candida species from airway samples in critically ill patients: a prospective, autopsy study.

Olgu 1

- 68 y E
- Yakınma: sağ yan ağrısı, ateş yüksekliği
- Özgeçmiş: DM-10 yıldır, KBY-3 yıldır

  sigara- 60 paket yıl

  alkol- 40 yıl günde 3 duble(3 yıldır içmiyor)

  2011 de alkole bağlı karaciğer sirozu nedeniyle karaciğer tx

İlaçlar: Certican (everolimus) 0.25 mg 2x1

Soygeçmiş: özellik yok

Fizik muayene

Genel durumu orta-kötü

Ateş 40°, TA:180/100mmHg, Kalp hızı: 120/dk

Bilinç konfü

Bilateral solunum sesleri kaba

Taşikardik

Batında hassasiyet yok

Pretibial ödem yok

Laboratuvar

Üre	H	181	mg/dL
Kreatinin	H	5.54	mg/dL
Sodyum	L	134	mEq/L
Potasyum		4.3	mEq/L
Klorür		106	mEq/L
Kalsiyum	L	7.9	mg/dL
Magnezyum		1.9	mg/dL
Protrombin Zamanı (süre)		14.4	sn
Protrombin Zamanı (aktivite)	L	75	%
INR		1.2	
APTZ		30.4	sn
CRP	H	41.02	mg/dL

Laboratuvar

SGOT(AST)	H	530	U/L
SGPT(ALT)	H	371	U/L
Alkalen Fosfataz		113	U/L
GGT		16	U/L
Total Protein		6.5	g/dL
Albümin	L	2.9	g/dL
Total Bilirubin		0.52	mg/dL
Direkt Bilirubin	H	0.36	mg/dL
LDH	H	723	U/L
CK	H	9392	IU/L
CK-MB	H	139	U/L
Miyoglobin		>3000	ng/mL

- Lökosit:15.400/mm, %85 PNL
- İzleminde konfüzyonunun artması ve livedo retikülaris gelişmesi üzerine alınan kontrol AKG de laktat 1.8 HCO_3:14 pH:7.30 olması üzerine hemodiyalize alındı
- Gram (-) sepsis düşünülerek meropenem başlandı
- Ateş yanıtı alınamadı
- Alınan idrar ve kan kültüründe *Candida albicans* üredi

1. Candida albicans

Antibiyogram Adı	1
Amfoterisin B	S
Flukonazol	S
İtrakonazol	S
Vorikonazol	S
Kaspofungin	S
Posakonazol	S

Maya mantarı üredi.

Kandida türleri	Risk faktörleri
Tüm Kandida türleri	İnvaziv cerrahi işlemler (özl. GIS cerrahisi) Santral venöz kateter Total Parenteral Nutrisyon Nötropeni İmmün baskılayıcı tedavi (1) Diabetes mellitus (2) Ağır pankreatit

Mayr A, et al. *Clin Microbiol Infect* 2011; 17 (Suppl. 1): 1–12
Mikulska M, et al. *Expert Rev Anti Infect Ther* 2012; 8(8): 755-65.

Kandida türleri	Risk faktörleri
Tüm Kandida türleri	Yoğun bakımda uzun yatış süresi
	Geniş spektrumlu antibiyotik kullanımı
	Kanser kemoterapisi, transplantasyon
	H2 reseptör blokörü kullanımı (3)
	Prematüre yenidoğan
	Renal yetmezlik/hemodiyaliz (4)
	Mukozal kandida kolonizasyonu
	Bakteriyel enfeksiyon

Mayr A, et al. *Clin Microbiol Infect* 2011; 17 (Suppl. 1): 1–12
Mikulska M, et al. *Expert Rev Anti Infect Ther* 2012; 8(8): 755-65.

Nötropenik olmayan kandidemili hastalarda tedavi (IDSA)

Pappas PG, et al. *Clin Infect Dis* 2009; 48:503–35

Nötropenik olmayan kandidemili hastalarda tedavi (IDSA)

- Erişkin hastalar:
  - Flukonazol-AI
  - Ekinokandin-AI
- Yakın zamanda azol grubu antifungal alan, orta veya ağır hastalığı olanlarda, yaşlılar, DM, kanserli hastalarda:
  - Ekinokandin-AIII

Pappas PG, et al. *Clin Infect Dis* 2009; 48:503–35

Nötropenik olmayan kandidemili hastalarda tedavi (IDSA)

- Erişkin hastalar:
  - Flukonazol-AI
  - Ekinokandin-AI
- Yakın zamanda azol grubu antifungal alan, orta veya ağır hastalığı olanlarda, yaşlılar, DM, kanserli hastalarda:
  - Ekinokandin-AIII
- Kritik olmayan hasta ve azol kullanımı olmayanlarda
  - Flukonazol-AIII

Pappas PG, et al. *Clin Infect Dis* 2009; 48:503–35

Nötropenik olmayan kandidemili hastalarda tedavi (ESCMID 2012)

- Anidulafungin 200/100 mg (A I)
- Caspofungin 70/50 mg (A I)
- Mikafungin 100 mg (A I)
- Liposomal Amfoterisin B 3 mg/kg (B I)
- Vorikonazol 6/3 mg/kg/gün (B I)
- Flukonazol 400–800 mg (C)

	Anidulafungin	Caspofungin	Mikafungin	
Karşılaşma ilacı	Flukonazol	Amphotericin B deoksikolat	Caspofungin	Liposomal amphoterisin B
n	127 / 118	109 / 115	247 / 247	191 / 188
Non albicans (%)	36 / 41	64.4 / 45.9	62.4 / 58.9	54.5 / 60.6
Genel tedavi başarısı iv (%)	75.6 / 60.2 [p = 0.01]	73.4 / 61.7 [p = n.s.]	74.1 / 69.6 [p = n.s.]	76.4 / 72.3 [p = n.s.]
Genel tedavi başarısı (%)	74.0 / 56.8 [p < 0.02]	72.5 / 61.7	74.1 / 69.6	74.9 / 70.2
2 haftalık izlem	64.6 / 49.2	63.6 / 53.8	Veri yok	54.5/ 50.5
6 haftalık izlem	55.9 / 44.1	56.6 /47.5	Veri yok	46.6 / 42.6
Mortalite	22.8 / 31.4	34.2 / 30.4	40 / 40	29.0 / 26.4

İlaç etkileşimi

Caspofungin	Micafungin	Anidulafungin
o Cyclosporine o Tacrolimus o Rifampicin o Efavirenz o Nevirapine o Dexamethasone o Phenytoin o Carbamazepine	CYP3A yolunu kullanan ilaçlarla düşük düzeyde etkileşim	Bilinen ilaç etkileşimi yok

George Dimopoulos et al. How to select an antifungal agent in critically ill patients☆Journal of Critical Care (2013) 28, 717–727

Tedavi-izlem

- Andilofungin 100mg/gün başlandı
- 24 saat içinde ateş yanıtı alındı
- İdrar çıkışı progresif azaldı
- KBY, son dönem böbrek yetmezliği olarak kabul edildi
- Kalıcı hemodiyaliz katateri takıldı
- Rutin hemodiyalize başlandı

Kontrol kan kültürleri ne zaman alınmalı?

- ESCMID; Günde en az bir tane
- IDSA; Her gün veya gün aşırı

Tedavi-izlem

- Ateş kontrolü sağlandıktan sonra 5 .günde tekrar ateşi oldu
- Andilofungin başlandıktan sonra düşen CRP tekrar arttı
- Batın BT: Sol üreter taşı, sol böbrekte pelvikaliksiyel sistemde dilatasyon, sol pyelonefrit
- Mantar sepsisi
  - Kaynak: idrar, pyelonefrit?

Tedavi-izlem

- Hastaya sistoskopi planlandı
- Yanıt alınamazsa, son dönem böbrek yetmezliği ve rutin hemodiyaliz hastası olan olguya nativ nefrektomi planlandı
- Alınan kültürlerde *Candida* üremesi devam etmesi üzerine lipozomal amfoterisin B ye geçildi

- Göz dibi: normal

- Ekokardiyografi: normal

Tedavi-izlem

- Retrograd sistografi taş kırma - pürülan
- İdrar kültürü: Candida albicans
- Kan kültürü takibi
  - VRE
- Tedavi Daptomisin iv eklendi

- Kontrol kan kültürlerinde Candida üremesi olmadı
- KCFT düzeldi, KBY (hemodiyaliz hastası)
- Flukonazol iv/oral (14 gün)

De-eskalasyon

- Nötropenik olmayan hastalarda klinik stabil olunca veya *C. albicans* veya flukonazole duyarlı Candida türü ürerse, ekinokandinden flukonazole geçilmesi

Guarascio AJ, et al. *Int J Clin Pharm* 2013; 35:145–148

De-eskalasyon

- Hastanın oral tedaviyi tolere edebilmesi
- En az 24 saattir ateşi olmaması
- Kan kültürleri negatifleşmesi
- Klinik iyileşme olması
- Diyare, kusma veya ileus olmaması
- İzol edilen kandidanın *C. glabrata* veya *C. krusei* olmaması ve flukonazole duyarlı olması

Ardışık oral tedavi

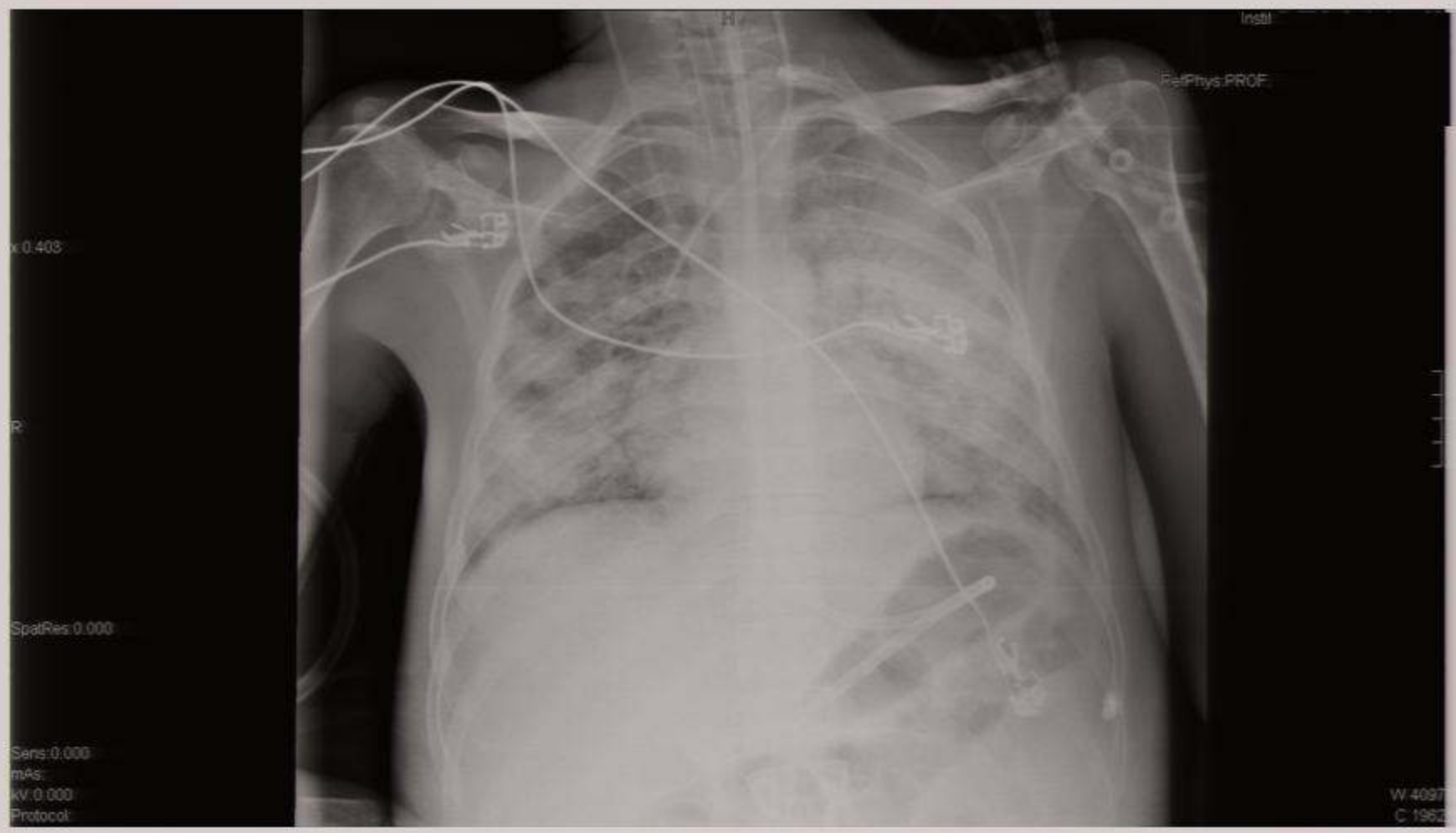
- Hasta stabil ve oral ilaca duyarlı ise;
  - ESCMID 10 günlük tedavi sonrası
  - IDSA 3-5 gün tedavi sonrası
  - Alman klavuzu: Hastanın klinik bulgularının düzelmesi, Kan kültürlerinin negatifleşmesi ve maya duyarlı ise 4-10 gün sonra

Ruhnke M, et al. Mycoses 2011;54:279–310.

Olgu 2

- 17 y, Erkek, 60 kg
- 1 yaşında ansefalosel tanısıyla opere
- Ventrikülоperitoneal şant
- 7 kez revizyon operasyonu
- 20.11.2013 E4M5 bilinç skoru ile beyin cerrahisi kliniğine yatırılmış
- 1 ay sonra entube MV ----anestezi YBÜ

- Beyin cerrahisinde aldığı ted
  - Vankomisin (14. gün)
  - Meropemnem (5. gün)
- An YBÜ APACHEII: 5 mortalite:%5,8
- Ateş:38,8 TA:120/80 N: 90
- Lökosit:9600 CRP:9,9 PCT:46 üre:20 kreatinin0,26 KCFT:N Diğerleri :N
- İnotrop (-)
- Enfeksiyon bulguları
- Akciğer gr:
- Solunum sekresyonları: Artmış, pürülan


R
Instit
RefPhys:PROF
x 0.403
R
SpatRes:0.000
Sens:0.000
mAs:
kV:0.000
Protocol:
W 4097
C 1962

YBÜ 2. gün

Periferik kan kültürü: *Enterococcus faecium*		**Periferik kan kültürü: *Acinetobacter baumannii***	
Penisilin	R	Meropenem	R
Gentamisin	R	İmipenem	R
Streptomisin	R	Sefo/sulbaktam	R
Vankomisin	S	Levofloksasin	R
Teikoplanin	S	Netilmisin	S
Linezolid	S	Kolistin	S
Tigesiklin	S	Tigesiklin	S

Tedavi

- Kolistin 1X300mg, 2x150mg iv
- Netilmisin 1X400mg
- Linezolit 2x600mg iv

YBÜ 3. gün

Periferik kan kültürü: ***Candida tropicalis***	
Flukonazol	S
İtrakonazol	S
Vorikonazol	S
Amfoterisin B	S
Kaspofungin	S
Anidulofungin	S

Invasive Fungal Infections in the ICU: How to Approach, How to Treat *Molecules* **2014**, *19*, 1085-1119

Elisabeth Paramythiotou *, Frantzeska Frantzeskaki, Aikaterini Flevari, Apostolos Armaganidis and George Dimopoulos

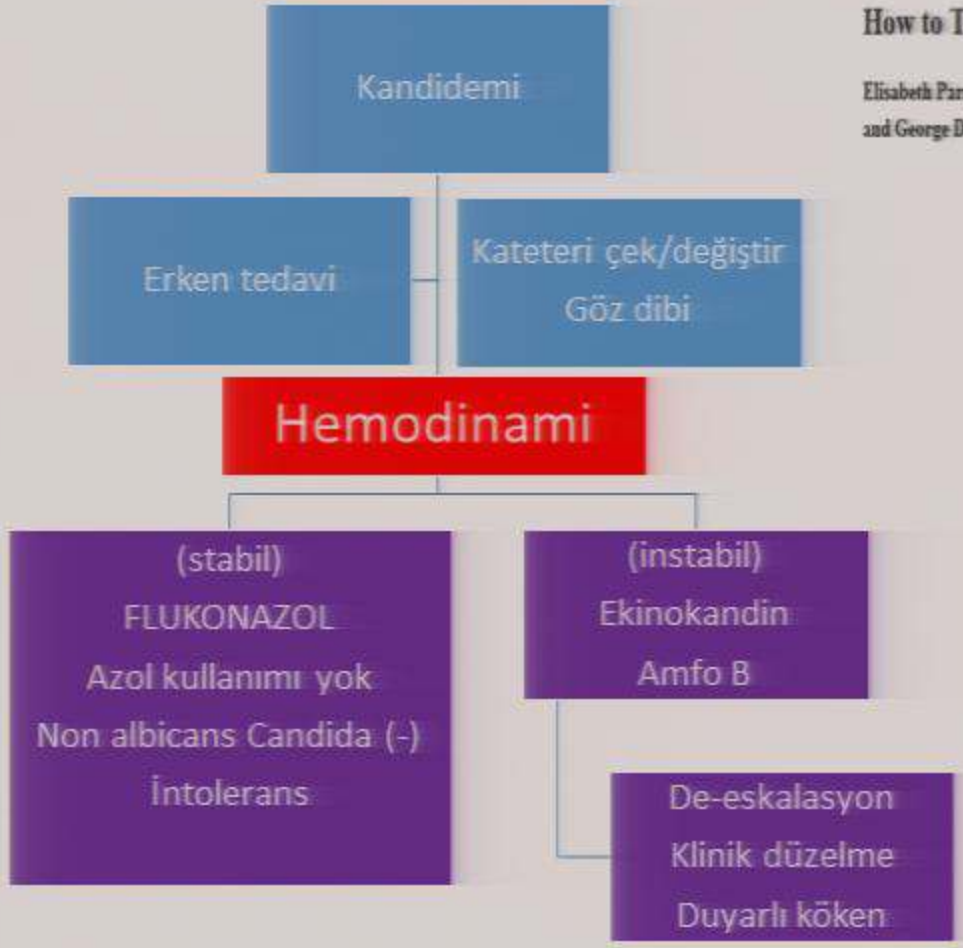


Table 7. Suggested treatment of documented candidaemia/invasive candidiasis in non-neutropenic patients according to different guidelines.

Society	First line	Alternative I	Alternative II
IDSA [114]	Fluconazole -stable patient, azole naïve Echinocandins -severe sepsis -recent azole exposure	AmB or lipid formulations of AmB (intolerance to others or limited availability)	Voriconazole
ESCMID [151]	Echinocandins	LipAmB, voriconazole	fluconazole, lcAmB
European Expert Opinion [152]	Fluconazole - stable patient - susceptible isolate Echinocandins - severe sepsis - micafungin last choice	lipidformulations of amphotericin B	
Canadian clinical practice guidelines for invasive candidiasis in adults [150]	Fluconazole -stable patient, azole naïve -unstable patient with *C.parapsilosis* Echinocandins -stable or unstable patient -recent azole exposure -avoid in *C.parapsilosis*	LipAmB or AmB	
Joint recommendations of the German speaking mycological society [154]	Fluconazole -stable patient -susceptible isolate Echinocandins -critically ill septic patient	Lip AmB -critically ill, septic patients voriconazole	

Tedavi / Mortalite

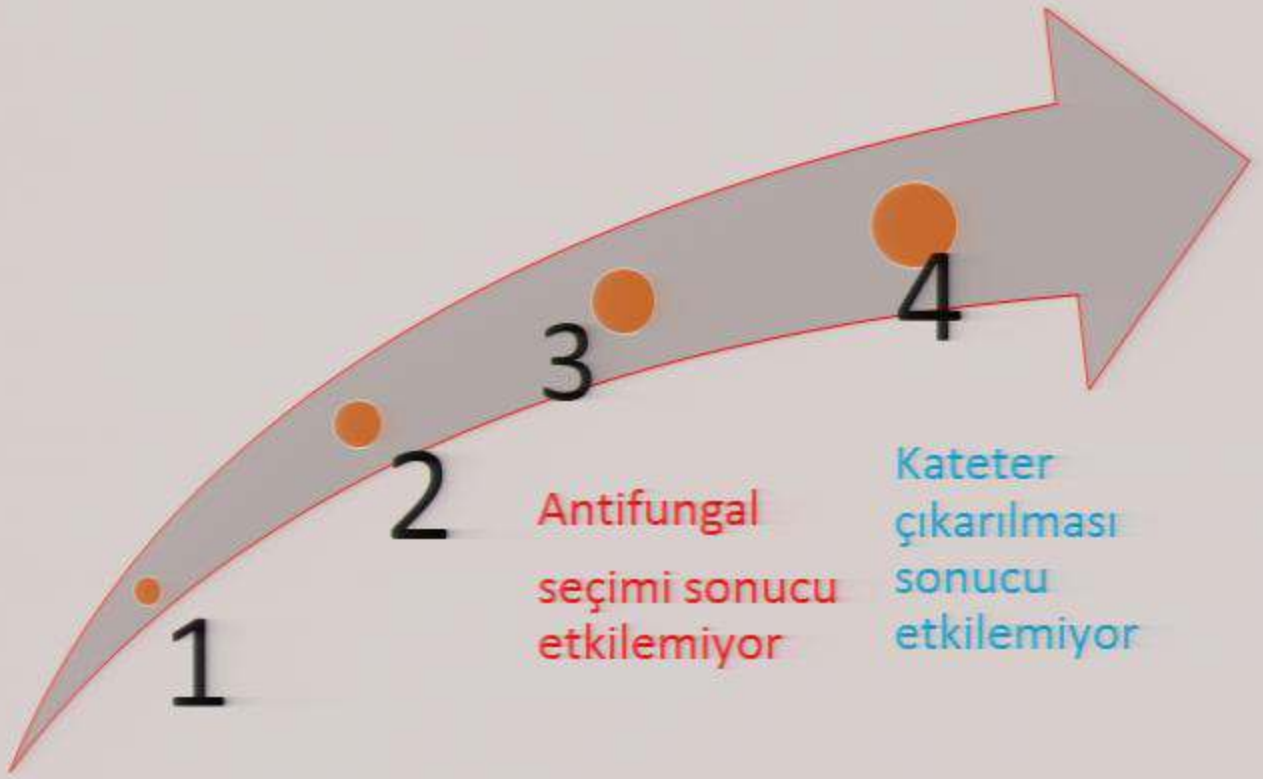
Ekinokandin	%27
Diğer	%36

Clinical Infectious Diseases Advance Access published March 14, 2012

Kateter / Mortalite

Çıkarılan	%28
Çıkarılmayan	%41

Clinical Infectious Diseases Advance Access published March 14, 2012



APACHE II (0-11) (12-23) (24-35) (36-47)

Clinical Infectious Diseases Advance Access published March 14, 2012

APACHE II

	Hasta Sayısı	Tedavide Geçikme YOK Mortalite %	Tedavide ≥ 12 st Geçikme VAR Mortalite
APACHE II ≤ 15	90	0.0	23.5
APACHE II ≥ 15	67	25.0	46.0

Hollenbach E. Mycoses 2008;51(Suppl 2):25

Tedavi

- Flukonazol 12mg/kg-gün
  6mg/kg-gün

Ekokardiyografi

7 gün flukonazol tedavisi altında

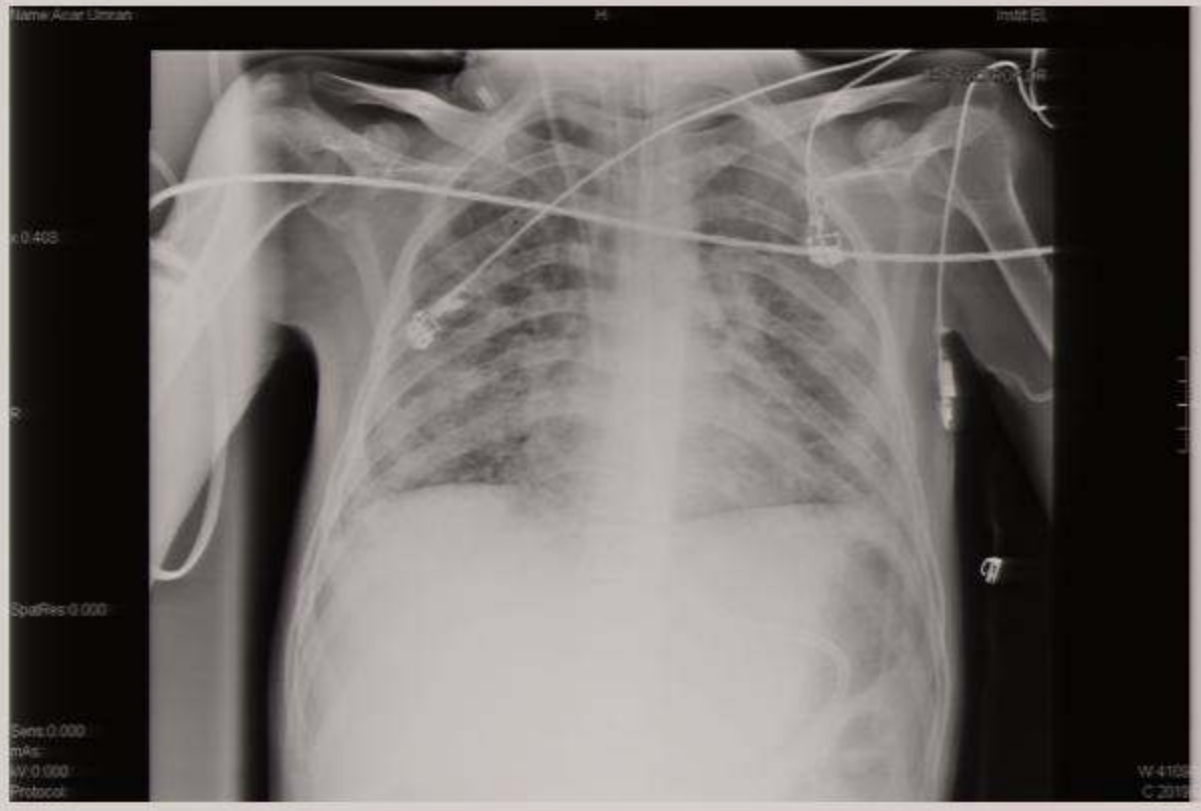
- Vegetasyon: triküsbt kapakta 1x1,4 cm hareketli, ekojen kitle

- Ateş 38,7
- Lökosit:13,800
- CRP:19
- PCT:2,6
- KCFT:N
- Böbrek :N

Infection type	Suggested treatment
Pyelonephritis	fluconazole 3–6 mg/kg/d (14 days) **or** AmB 0.3–0.6 mg/kg/d for 1–7 days
Urinary fungus ball	Surgical removal recommended fluconazole 3–6 mg/kg/d **or** AmB 0.5–0.7 mg/kg/d
Candida osteomyelitis	fluconazole 6 mg/kg/d (6–12months) **or** LipAmB 3–5 mg/kg/d (weeks), then fluconazole for 6–12 months
Septic arthritis	fluconazole 6 mg/kg/d (6 weeks) **or** LipAmB 3–5 mg/kg/d (weeks) then fluconazole
CNS infection	LipAmB 3–5 mg/kg (±5FTC 25mg/kg/qid) several weeks, then fluconazole (6–12 mg/kg/d) daily **or** fluconazole 400–800 mg/d in LipAmB intolerance
Endocarditis	LipAmB 3–5 mg/kg (±5FTC 25mg/kg qid) **or** AmB 0.6–1 mg/kg/d (±5FTC 25 mg/kg) **or** an echinocandin
Suppurative thrombophlebitis	LipAmB 3–5 mg/kg/d **or** fluconazole 400–800 mg d **or** an echinocandins
Endophthalmitis	AmB 0.7–1 mg/kg plus 5FTC **or** fluconazole 6–12 mg/kg/d **or** LipAmB 3–5 mg/kg/d **or** voriconazole 6 mg/kg/12 h, then 3 mg/kg/12 h **or** echinocandins

- Anidulofungin 200/100 mg
- 2 haftalık tedavi-- alınan kan ve BOS kültürleri (-)
- EKO kontrol (-)
- Şant çekildi (VP şanta geçildi)

20.gün



- Kranial kateter sürüntüsü
  - Pseudomonas + Acinetobacter
  - Tienam + Tigesiklin

- Şant revizyonu: VA-----VP

- Acinetobacter, Pseudomonas :3 hafta
- Anidulofungin 4 hafta, Flukonazol 2 hafta

- Kontrol kültürler ve klinik stabil, ateş yok

- VP şant değişimi sonrası, cerrahi kranial defekt, yara yeri enfeksiyonu, SSS + peritonit septik şok, ex. (şant değişiminden 1 ay sonra, yatışının 3. ayı)

BOS + Periton

ESBL(+)

	Enterobacter aerogenes	Proteus mirabilis
Antibiyogram Adı	1	2
Ampisilin	R	R
Amoksisilin/klavulanik asit	R	R
Piperasilin/tazobaktam	S	S
Sefuroksim aksetil	S	R
Seftriakson	S	I
Sefepim	S	I
İmipenem	I	R
Amikasin	S	S
Gentamisin	S	R
Siprofloksasin	S	S
Trimetoprim/sulfametoksazol	S	S
Meropenem		S
Ertapenem		

Kandida enfeksionlarının tedavisinde

- Hastanın klinik tablosu
- Hastanın daha önce antifungal alıp almadığı
- İnfekte eden etkenin olası türü
- Lokal epidemiyoloji
- Organ disfonksiyonunun varlığı
- İlaç toksisitesi
- İlaç etkileşimleri
- Yan etkiler
- Santral sinir sistemi, kadiyak kapak ve/veya visseral organ tutulumunun kanıtı

Teşekkür ederim

“Kandida salgını var ise...”

Doç. Dr. Zeliha KOÇAK TUFAN

Yıldırım Beyazıt Üniversitesi Tıp Fakültesi
Ankara Atatürk Eğitim ve Araştırma Hastanesi
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği
drztufan@yahoo.com

SO WHAT CAN I DO SOMETIMES...

İNVAZİV CANDİDA ENFEKSİYONU...

Mortalite %29-%76

Atfedilen mortalite %49

Kett DH, et al. Crit Care Med 2011
Vincent JL, et al. JAMA 2009


TÜRKİYE
EFES
TÜRKİYE
EFES

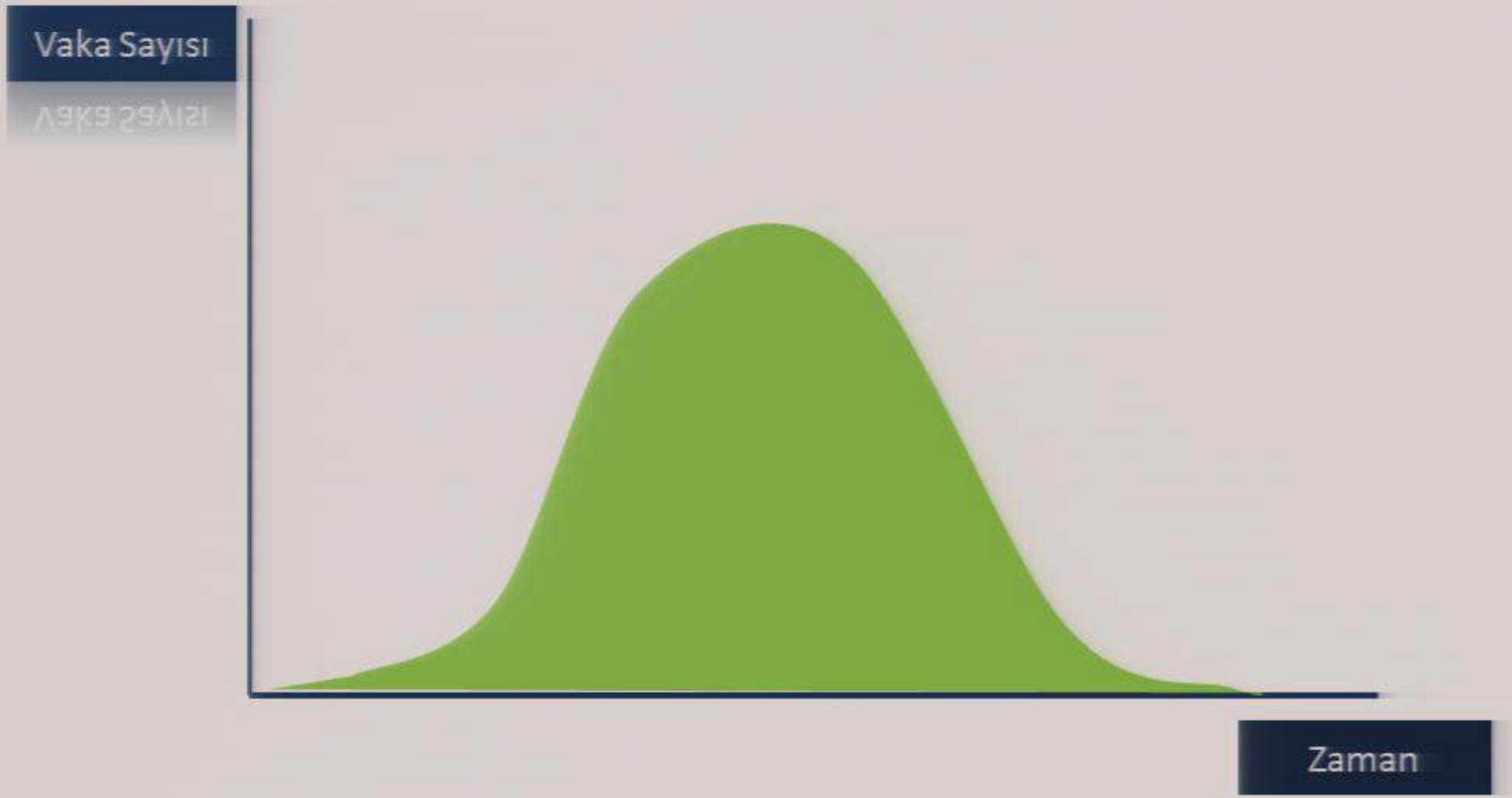
Salgın İnceleme

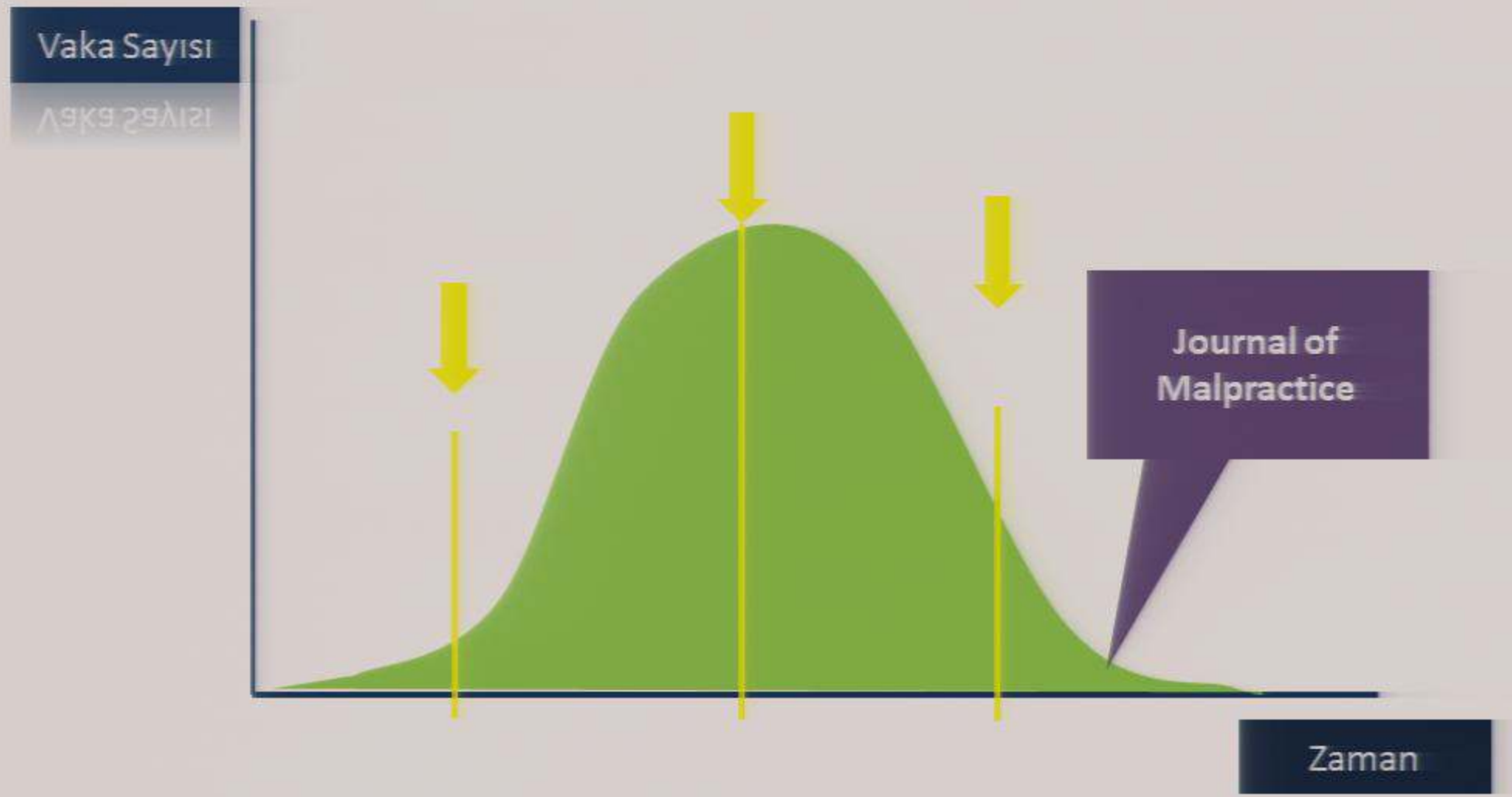
Ön inceleme ve tanımlayıcı çalışma (quick and dirty)

- Hazırlık
- **Salgın varlığının gösterilmesi**
- **Acil enfeksiyon kontrol önlemlerinin alınması**
- **Olgu tanımı**
- Olgu listesi
- **Tanımlayıcı epidemiyolojik incelemeler**

Esas inceleme ve karşılaştırmalı çalışma

- Hipotez oluşturma
- Hipotezin kanıtlanması
- Ek araştırmalar


Vaka Sayısı
Zaman


Vaka Sayısı
Journal of Malpractice
Zaman

Kandida salgını var ise...

KAYNAK ARAŞTIRILMASI (HASTA, ÇEVRE, SAĞLIK PERSONELİ KULLANILAN ÜRÜNLER...)

ÜNİTENİN VE HASTALARIN RİSK FAKTÖRLERİNİN DEĞERLENDİRİLMESİ

KAYNAK KONTROLÜ

UZUN DÖNEM HASTA TAKİBİ

Olgu Tanımı

An Italian consensus for invasive candidiasis management (ITALIC)

L. Scudeller et al

Infection (2014) 42:263–279

"Invasive candidiasis (IC)", indicating both deep-seated Candida infection and candidaemia

Proven IC: **cultural evidence** of Candida or evidence of **yeast cells or hyphae or pseudohyphae at histology** or at direct examination, in a normally sterile tissue or organ, i.e. excluding urine, sputum, fluids from bronchoalveolar lavage, mucous membrane swabs and specimens from skin sites.

Probable IC: concomitant presence of **an underlying disease** predisposing to IC, **adequate risk factors** with/out signs of active infection, with at least one **positive antigen test** (e.g. BDG, mannan/antimannan).

Possible IC: concomitant presence of an **underlying disease** predisposing to IC, **adequate risk factors** , with signs of active infection, but without any microbiological confirmation.

Candida bloodstream infections in intensive care units: Analysis of the extended prevalence of infection in intensive care unit study*

Daniel H. Kett, MD; Elie Azoulay, MD, PhD; Pablo M. Echeverria, MD; Jean-Louis Vincent, MD, PhD, FCCM; and for the Extended Prevalence of Infection in the ICU Study (EPIC II) Group of Investigators

Table 4. Baseline patient characteristics and outcomes grouped by bloodstream infection

	Candida BSI (n = 61)	Gram-Positive BSI (n = 420)	Gram-Negative BSI (n = 264)	Combination BSI (n = 38)
Patient characteristics				
Age, yrs (mean [IQR])	61 [46–71]	62 [48.5–72]	63 [47.5–72]	60.5 [46–69]
Male sex (no., %)	36 (59)	267 (63.7)	154 (58.3)	52 (59.1)
SAPS II score (mean [IQR])	38 [31–50]	37 [29–49.5]	37.5 [29.5–52]	38.5 [27–52]
SOFA total score (mean [IQR])	9 [6–13]	7 [5–10]	7 [4–10]	7.5 [5–12]
Prior days in ICU (mean [IQR])	14 [5–25]	8 [3–20]	10 [2–23]	11.5 [4–24]
Pre-existing conditions				
COPD (no., %)	8 (13.1)	52 (12.4)	44 (16.7)	11 (12.5)
Solid organ cancer (no., %)	15 (24.6)	40 (9.5)[a]	28 (10.6)[a]	13 (14.8)
Heart failure (no., %)	1 (1.6)	48 (11.4)	24 (9.1)	6 (6.8)
Diabetes mellitus (no., %)	4 (6.6)	49 (11.7)	36 (13.6)	9 (10.2)
Chronic renal failure (no., %)	6 (9.8)	46 (11)	33 (12.5)	6 (6.8)
Cirrhosis (no., %)	1 (1.6)	19 (4.5)	5 (1.9)	5 (5.7)
Hematologic cancer (no., %)	2 (3.3)	19 (4.5)	14 (5.3)	4 (4.5)
ICU-related interventions				
Mechanical ventilation (no., %)	44 (72.1)	307 (73.1)	175 (66.5)	64 (72.7)
Vasopressor use (no., %)	23 (37.7)	148 (35.2)	94 (35.6)	35 (39.8)
Hemodialysis/filtration (no., %)	17 (27.9)	67 (16)	55 (20.9)	16 (18.2)
Venous catheter (no., %)	54 (88.5)	361 (86.2)	227 (86)	79 (89.8)
Right heart catheter (no., %)	1 (1.6)	11 (2.6)	6 (2.3)	1 (1.1)
Arterial catheter (no., %)	39 (63.9)	269 (64.4)	173 (65.5)	64 (72.7)
Outcomes				
ICU mortality (no., %)	26 (42.6)	101 (25.3)	75 (29.1)	27 (31.4)
Hospital mortality (no., %)	26 (42.6)	135 (33.8)	91 (35.3)	33 (38.4)
ICU LOS (median [IQR])	33 [18–44]	20 [9–43]	21 [8–46]	24.5 [11–49]
Hospital LOS (median [IQR])	39 [26–62]	35 [17–62]	37 [17–66]	37 [23–69]

BSI, bloodstream infection; IQR, interquartile range; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; LOS, length of stay.

[a]$p < .05$ for differences between *Candida* BSIs and both Gram-positive and Gram-negative BSIs.

Risk faktörleri…

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14414 hasta
1265 YBU
76 ülke

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14414 hasta
1265 YBU
76 ülke

Yatış süresi (median)
Candida spp **33 gün**
Gr + **20 gün**
Gr - **21 gün**

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14414 hasta
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76 ülke

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Candida spp **33 gün**
Gr + **20 gün**
Gr - **21 gün**

Mortalite
kandidemi %43
Gr + bakteremi %25
Gr – bakteremi %29

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14414 hasta
1265 YBU
76 ülke

KDI
Kandidemi prevelansı
6.9 kandidemi/1000hasta

Yatış süresi (median)
Candida spp 33 gün
Gr + 20 gün
Gr - 21 gün

Mortalite
kandidemi %43
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14414 hasta
1265 YBU
76 ülke

KDI
Kandidemi prevelansı
6.9 kandidemi/1000hasta

61 hasta sadece kandidemi
38 hasta bakteremi+ kandidemi

Yatış süresi (median)
Candida spp **33 gün**
Gr + **20 gün**
Gr - **21 gün**

Mortalite
kandidemi %43
Gr + bakteremi %25
Gr – bakteremi %29

Diekema D, Diagn Mirobiol Infect Dis 2012
Morace G, Minerva Anest 2010
Wisplinghoff H, Clin Infcet Dis 2004
Morgan J, Infect Control Hosp Epidem 2005

Geniş spektrumlu antibiyotik kullanımı

Nozokomiyal Kandidemi Risk Faktörleri

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Cerrahi işlemler... İnvaziv alet kullanımı...

Diekema D, Diagn Mirobiol Infect Dis 2012
Morace G, Minerva Anest 2010
Wisplinghoff H, Clin Infcet Dis 2004
Morgan J, Infect Control Hosp Epidem 2005

Risk Faktörleri

Kandidemi öncesi aldığı antibiyotik sayısı;
Kan dışı alanlardan *Candida* spp. üretilmesi;
hemodiyaliz öyküsü;
Hickman kateter öyküsü;
Gastrointestinal-abdominal cerrahi;
YBU'da kalış süresi

Peritonit
Akut pankreatit
Nötropeni
Kemoterapi almış kanser hastaları

Chahoud J, Int J Antimicrob Agents 2013
Eggiman P, Lancet Infect Dis 2003
Hobson RP J Hosp Infect 2003
Nuskett H, Crit Care 2011

Corrected Candida colonisation index

A corrected Candida colonisation index C0.4 is an important risk factor for IC, but in many clinical settings, other stratification tools should be preferred owing to their greater simplicity of use

Ostrosky-Zeichner prediction rule

The Ostrosky-Zeichner prediction rule (based on risk factors in asymptomatic ICU patients) is probably best applied to exclude patients not at risk (rather than to identify those at risk) of developing IC, due to its low positive predictive value and high negative predictive value.

Candida score

The Candida score (based on clinical symptoms and signs of severe sepsis/septic shock) can be used as a tool for predicting the likelihood of actually having IC in symptomatic ICU patients, but it is probably best applied to identify patients without (rather than those with) IC, due to its low positive predictive value and high negative predictive value.

ITALIC Study

Molecules **2014**, *19*, 1085-1119; doi:10.3390/molecules19011085

OPEN ACCESS

molecules

ISSN 1420-3049

www.mdpi.com/journal/molecules

Review

Invasive Fungal Infections in the ICU: How to Approach, How to Treat

Elisabeth Paramythiotou *, Frantzeska Frantzeskaki, Aikaterini Flevari, Apostolos Armaganidis and George Dimopoulos

Table 2. Factors leading to *Candida albicans* invasive infections in ICU patients [53–56].

Prolonged ICU stay
Treatment with corticosteroids
Diabetes mellitus
Advanced age
Central venous catheter
Gastrointestinal surgery
Total parenteral nutrition
Prolonged antimicrobial use
Pancreatitis
Immunosuppressive agents
Chemotherapy
High disease severity score (APACHE II > 20)
Neutropenia
Renal replacement therapy
Malnutrition
Multiple site colonisation
Burns over 50% of body sites
Major trauma

Molecules **2014**, *19*, 1085-1119; doi:10.3390/molecules19011085

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High disease severity score (APACHE II > 20)
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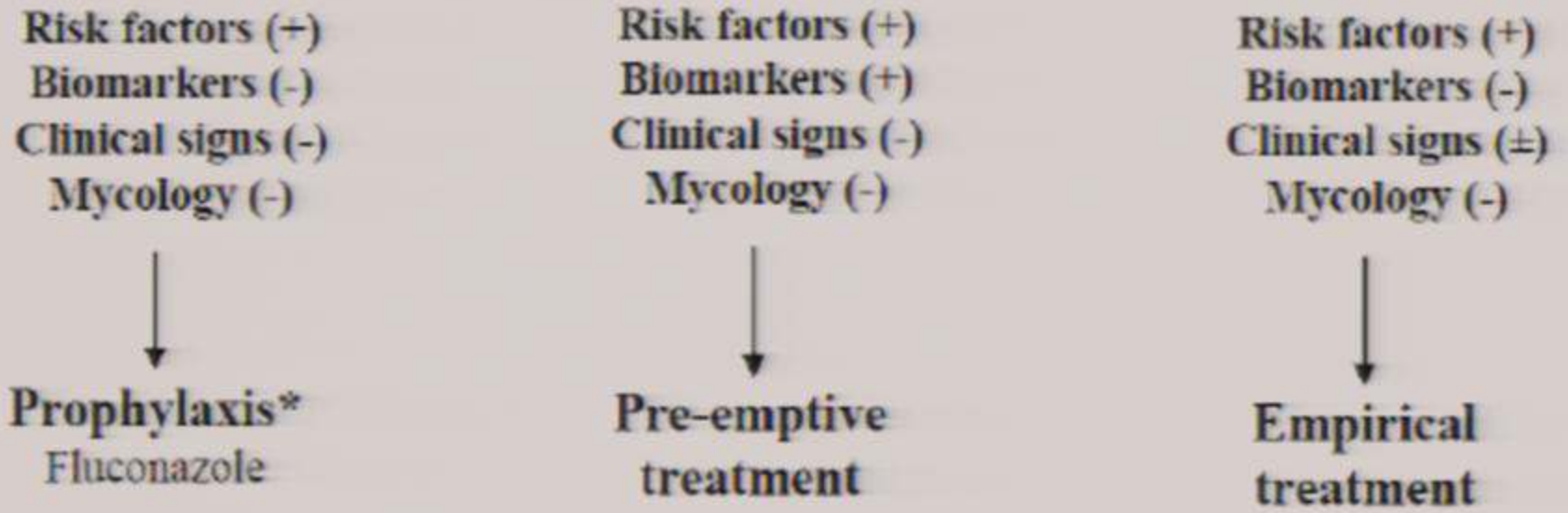
Renal replacement therapy
Malnutrition
Multiple site colonisation
Burns over 50% of body sites
Major trauma

Molecules **2014**, *19*

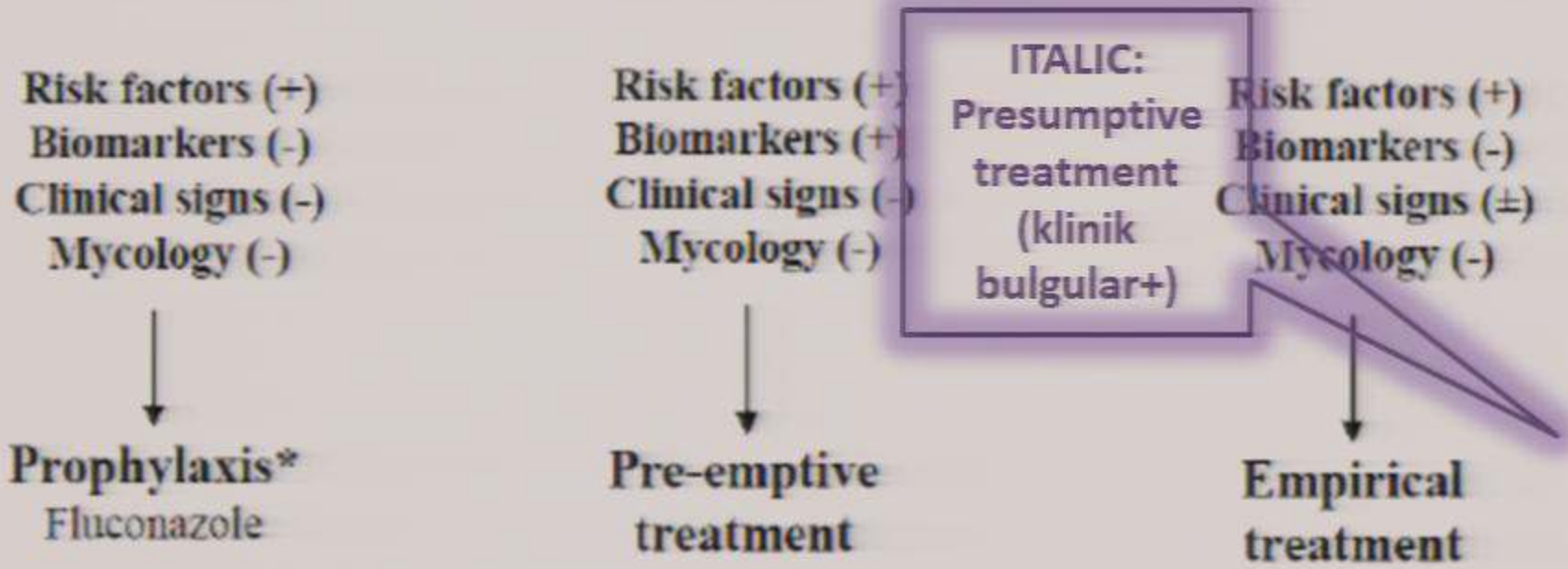
Figure 2. Types of treatment for suspected candidiasis in the critically ill.



* Prophylaxis is specific ICU population.

Molecules **2014**, *19*

Figure 2. Types of treatment for suspected candidiasis in the critically ill.



* Prophylaxis is specific ICU population.

Molecules **2014**, *19*

ITALIC Study

Treatment strategy	Certainty of diagnosis	Risk factors (including multi-site colonisation)	Clinical signs	Biomarkers	Microbiological diagnosis
Prophylaxis	Not applicable	+	−	Not applicable	Not applicable
Pre-emptive	Probable	+	−	+[a]	−
Empirical	Possible	+	+	−/not available	−/not available
Presumptive	Probable	+/−	+	+	−/not available
Targeted	Proven	+/−	+/−[a]	+/−/not available	+

ITALIC Study

Kaynak Araştırılması

Yang et al. BMC Infectious Diseases 2013, 13:10
http://www.biomedcentral.com/1471-2334/13/10

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

A risk factor analysis of healthcare-associated fungal infections in an intensive care unit: a retrospective cohort study

Su-Pen Yang[1,4], Yin-Yin Chen[2,5], Han-Shui Hsu[3,4], Fu-Der Wang[1,6], Liang-yu Chen[6,7] and Chang-Phone Fung[1,4*]

Methods: Surveillance fungal cultures were obtained from "sterile" objects, antiseptic solutions, environment of infected patients and hands of medical personnel. Risk factors for comparison included age, gender, admission service, and total length of stay in the ICU, Acute Physiology and Chronic Health Evaluation (APACHE) II scores at admission to the ICU, main diagnosis on ICU admission, use of invasive devices, receipt of hemodialysis, total parenteral nutrition (TPN) use, history of antibiotic therapy before HAI or during ICU stay in no HAI group, and ICU discharge status (ie, dead or alive). Univariable analysis followed by multiple logistic regression analysis was performed to identify the independent risk factors for ICU fungal HAIs and ICU mortality.

International Journal of Antimicrobial Agents 43 (2014) 78–81

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Short Communication

Nosocomial bloodstream infections due to *Candida* spp. in the USA: species distribution, clinical features and antifungal susceptibilities

Hilmar Wisplinghoff[a,b], Jenny Ebbers[a], Lea Geurtz[a], Danuta Stefanik[a], Yvette Major[b], Michael B. Edmond[b], Richard P. Wenzel[b], Harald Seifert[a,*]

[a] Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Goldenfelsstrasse 19-21, 50935 Cologne, Germany
[b] Division of Infectious Diseases, Department of Internal Medicine, Virginia Commonwealth University, Medical Center Box 980019, Richmond, VA 23298-0019, USA

52 merkez
Prospektif çalışma
1998-2006
1218 kandidemi atağı

Altta yatan hastalık:

Gastrointestinal %20.1

Pulmoner %13.0

Kaynak

IV kateter %19
İdrar yolu %8
kaynak belirlenememiş %61

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

C. albicans %50.7
C. parapsilosis %17.4
C.glabrata %16.7
C. tropicalis %10.2

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

C. albicans %50.7
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Flukonazol **direnci**

C. albicans %0.8
C.glabrata %100
C. parapsilosis %2.9
C.tropicalis %4.9

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

C. albicans %50.7
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Flukonazol **direnci**
C. albicans %0.8
C.glabrata %100
C. parapsilosis %2.9
C.tropicalis %4.9

Vorikanazol **direnci**
C.albicans %0.6
C. krusei %5
C. parapsilosis %7.6
C. tropicalis %9.8

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

C. albicans %50.7
C. parapsilosis %17.4
C.glabrata %16.7
C. tropicalis %10.2

Flukonazol **direnci**
C. albicans %0.8
C.glabrata %100
C. parapsilosis %2.9
C.tropicalis %4.9

Vorikanazol **direnci**
C.albicans %0.6
C. krusei %5
C. parapsilosis %7.6
C. tropicalis %9.8

%16 *C. glabrata*'da
MIC>2mg/L

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

C. albicans %50.7
C. parapsilosis %17.4
C.glabrata %16.7
C. tropicalis %10.2

Flukonazol **direnci**
C. albicans %0.8
C.glabrata %100
C. parapsilosis %2.9
C.tropicalis %4.9

Ekinokandinlere duyarlılık
.....
C. glabrata %38
kaspofungin S

Vorikanazol **direnci**
C.albicans %0.6
C. krusei %5
C. parapsilosis %7.6
C. tropicalis %9.8

%16 *C. glabrata*'da
MIC>2mg/L

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

Species	No. (%)
Candida albicans	611 (50.7)
Candida parapsilosis	210 (17.4)
Candida glabrata	201 (16.7)
Candida tropicalis	123 (10.2)
Candida lusitaniae	25 (2.1)
Candida krusei	19 (1.6)
Debaryomyces spp.	6 (0.5)
Candida famata	2 (0.2)
Cryptococcus neoformans	2 (0.2)
Trichosporon asahii	2 (0.2)
Candida dubliniensis	1 (0.1)
Candida guilliermondii	1 (0.1)
Candida rugosa	1 (0.1)
Candida sake	1 (0.1)
Saccharomyces cerevisiae	1 (0.1)

Yaşlı *candida* KDI ampirik tdv ekinokandin ilk?

C. glabrata- KDI

10 yaş daha yaşlılarda

6 gün daha fazla yatanlarda ($p<0.001$)

Gastrointestinal ($p=0.02$) ve renal hastalıklar ($p=0.06$) daha sık

C. parapsilosis

11 yaş daha gençlerde ($p<0.001$)

ÜSİ kaynaklı KDI diğerlerine göre daha sık ($p=0.022$)

Risk faktörleri

Belirgin fark yok

C. parapsilosis ve *C. glabrata*' da ventilatör destek daha sık

Mortalite %38

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

Origin of bloodstream infection (BSI) due to *Candida* spp.

Origin	No. (%) of patients with monomicrobial *Candida* BSI						*P*-value
	All (*n* = 1206)	*C. albicans* (*n* = 611)	*C. glabrata* (*n* = 201)	*C. parapsilosis* (*n* = 210)	*C. tropicalis* (*n* = 123)	Other species (*n* = 61)	
Gastrointestinal tract	30 (2.5)	12 (2.0)	8 (4.0)	3 (1.4)	5 (4.1)	2 (3.3)	N/S
Intravenous device	230 (19.1)	109 (17.8)	38 (18.9)	43 (20.5)	25 (20.3)	15 (24.6)	N/S
Respiratory tract	56 (4.6)	33 (5.4)	8 (4.0)	8 (3.8)	4 (3.3)	3 (4.9)	N/S
Other	30 (2.5)	11 (1.8)	10 (5.0)	6 (2.9)	2 (1.6)	1 (1.6)	N/D
Unknown	737 (61.1)	376 (61.5)	113 (56.2)	137 (65.2)	78 (63.4)	33 (54.1)	N/S
Urinary tract	97 (8.0)	57 (9.3)	18 (9.0)	9 (4.3) *	8 (6.5)	5 (8.2)	0.022
Wound infection	26 (2.2)	13 (2.1)	6 (3.0)	4 (1.9)	1 (0.8)	2 (3.3)	N/S

H. Wisplinghoff et al. / International Journal of Antimicrobial Agents 43 (2014) 78–81

Among the echinocandins, micafungin was slightly more active than anidulafungin and caspofungin for all *Candida* spp., except *C. parapsilosis* where caspofungin was the most active echinocandin. Confirming previous data, *C. parapsilosis* isolates were less susceptible to echinocandins than other *Candida* spp. Using the new species-specific CBPs, a considerable number of *C. glabrata* and *C. krusei* isolates were tested non-susceptible to caspofungin, whereas only four *C. glabrata* isolates (2%) and no *C. krusei* were non-susceptible to anidulafungin and micafungin. The high number of *C. glabrata* isolates non-susceptible to caspofungin in this study (62.9%), whilst not consistent with clinical experience, compares with other recent studies [2,16]. In a population-based study of 670

European Review for Medical and Pharmacological Sciences 2014; 18: 661-674

Candidemia in intensive care unit: a nationwide prospective observational survey (GISIA-3 study) and review of the European literature from 2000 through 2013

M.T. MONTAGNA[1], G. LOVERO[1], E. BORGHI[2], G. AMATO[3], S. ANDREONI[4], L. CAMPION[5], G. LO CASCIO[6], G. LOMBARDI[7], F. LUZZARO[8], E. MANSO[9], M. MUSSAP[10], P. PECILE[11], S. PERIN[12], E. TANGORRA[13], M. TRONCI[14], R. IATTA[15], G. MORACE[2]

15 merkez
2000-2013

462 Kandidemi atağı
C. albicans %49.4
C. parapsilosis %26
C. glabrata %10

Mortalite NAC %47
C. albicans %32

Risk faktörleri
NAC..parenteral nutrisyon
C. albicans... gastrik cerrahi

Montagna M, Europ Rev Med Pharm Sci2014

Table I. Characteristics of ICU patients with candidemia, Italy 2007-2008.

Characteristics[#]	Total n. 462	*C. albicans* n. 228 (49.4)[§]	*C. non-albicans* n. 234 (50.6)[§]
Age			
18-50	202 (43.7)	110 (48.2)	92 (39.3)
51-99	260 (56.3)	118 (51.8)	142 (60.7)
Male	281 (60.8)	139 (61.0)	142 (60.7)
Admission service			
Medical	191 (41.3)	87 (38.2)	104 (44.4)
Surgery*	210 (45.5)	116 (50.9)	94 (40.2)
Trauma	61 (13.2)	25 (11.0)	36 (15.4)
Central venous catheterization	412 (89.2)	209 (91.7)	203 (86.7)
Antibacterial therapy	282 (61.0)	145 (63.6)	137 (58.5)
Total parenteral nutrition*	254 (55.0)	113 (49.6)	141 (60.2)
Diabetes mellitus	44 (9.5)	26 (11.4)	18 (7.7)
Solid neoplastic tumor	28 (6.1)	10 (4.4)	18 (7.7)
Corticotherapy	26 (5.6)	9 (3.9)	17 (7.3)
Burns	21 (4.5)	9 (3.9)	12 (5.1)
Hematological malignancy	19 (4.1)	5 (2.2)	14 (6.0)

[#]More than one factor may be present in a single case; *Statistically significant *p*-value (< 0.05); [§]Numbers in parentheses, percent.

Table II. Distribution of *Candida* spp. from bloodstream infections in ICU patients, Europe 2000-2013.

Author		Nawrot et al. 2013[29]	Costa-de-Oliveira et al. 2008[34]	Almirante et al. 2005[18]	Pemàn et al. 2012[35]	Gürcüoglu et al. 2010[25]
Country/Period of design observation		**Polish** 2006-2007	**Portugal** 2004	**Spain** 2002-2003	**Spain** 2009-2010	**Turkey** 2002-2007 (original period 1996-2007)
Study design/setting		Retrospective laboratory based study/20 hospital - ? ICU and wards	Prospective observational study/single university hospital - ? ICU and wards	Prospective population-based study/14 hospital - ? ICU and wards	Prospective population-based study/44 tertiary hospital - ? ICU and wards	Retrospective observational study/single tertiary-care hospital-multidisciplinary ICU
% of isolates	No. Isolates[a]	98	33	115	469	76
	C. albicans	61.2	48.5	51.3	49.0	55.3
	C. parapsilosis	15.3	18.2	27.0	28.8	23.7
	C. glabrata	12.2	9.1	6.1	9.6	2.6
	C. tropicalis	3.1	21.2	8.7	8.7	10.5
	C. krusei	1.0	—	3.5	1.3	2.6
	C. kefyr	—	—	—	—	2.6
	C. dubliniensis	—	—	—	—	—
	C. famata	—	—	—	—	—
	C. guilliermondii	—	—	—	—	—
	C. intermedia	—	—	—	—	—
	C. lipolytica	—	—	—	—	—
	C. lusitaniae	—	—	—	—	—
	C. norvegensis	—	—	—	—	—
	C. sake	—	—	—	—	—
	C. utilis	—	—	—	—	—
	Candida spp[b]	7.1	3.0	3.5	2.8	2.6

Table continue on the next page

Table II. Distribution of *Candida* spp. from bloodstream infections in ICU patients, Europe 2000-2013.

Author		Horasan et al. 2010	Dizbay et al. 2010[36]	Das et al. 2011[23]
Country/Period of design observation		**Turkey** 2004-2009	**Turkey** 2007	**UK** 2005-2008
Study design/setting		Retrospective cohort study/single university hospital - medical-surgical, ICU	Prospective laboratory-based study/single tertiary hospital – surgical, anesthesiology, internal, medicine, neurology ICU[c]	Prospective observational study/single tertiary hospital - ? ICU and wards
% of isolates	No. Isolates[a]	118[d]	35	55
	C. albicans	18.6	22.9	52.7
	C. parapsilosis	66.1	77.1	16.4
	C. glabrata	2.5	—	21.8
	C. tropicalis	12.7	—	—
	C. krusei	—	—	—
	C. kefyr	—	—	—
	C. dubliniensis	—	—	—
	C. famata	—	—	—
	C. guilliermondii	—	—	—
	C. intermedia	—	—	—
	C. lipolytica	—	—	—
	C. lusitaniae	—	—	—
	C. norvegensis	—	—	—
	C. sake	—	—	—
	C. utilis	—	—	—
	Candida spp[b]	—	—	9.1

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%61 erkek
%56 hasta 51 yaşın üstünde
412 hastada SVK
249 SVK'lı hastadan SVK kültürü
196 (%79) kateter kaynaklı
%46 cerrahi işlem, bunların %54'ü GIS cerrahisi %23 kardiak cerrahi

Montagna M, Europ Rev Med Pharm Sci2014

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NAC... parenteral nutrisyon %60
C. albicans..... %50

Montagna M, Europ Rev Med Pharm Sci2014

%61 erkek
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NAC... parenteral nutrisyon %60
C. albicans..... %50

Cerrahi hastalarında
C. albicans, NAC'dan daha sık
%51 vs %40

Montagna M, Europ Rev Med Pharm Sci2014

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NAC... parenteral nutrisyon %60
C. albicans..... %50

Cerrahi hastalarında
C. albicans, NAC'dan daha sık
%51 vs %40

Sonlanım 201 hastada belirtilmiş
%39'u kandidemi başladıktan sonra 1 ay içinde ölmüş

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Yang et al. BMC Infectious Diseases 2013, 13:10
http://www.biomedcentral.com/1471-2334/13/10

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

A risk factor analysis of healthcare-associated fungal infections in an intensive care unit: a retrospective cohort study

Su-Pen Yang[1,4], Yin-Yin Chen[2,5], Han-Shui Hsu[3,4], Fu-Der Wang[1,6], Liang-yu Chen[6,7] and Chang-Phone Fung[1,4*]

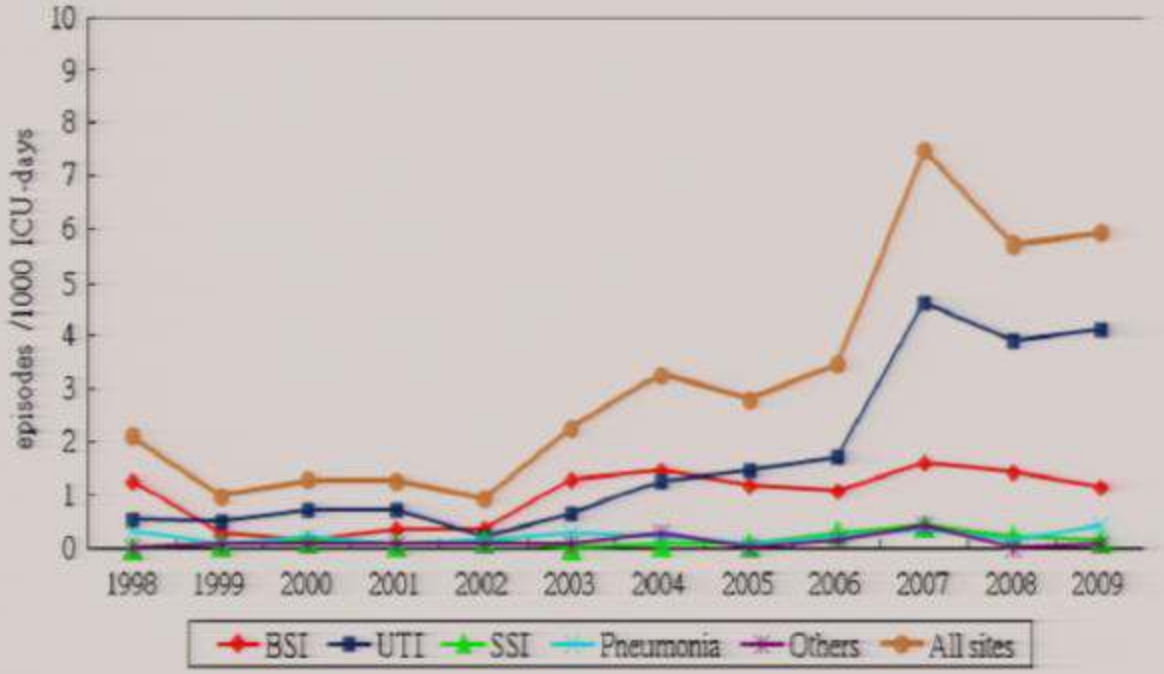

Figure 1 Trend for incidence of ICU fungal healthcare-associated infections from blood stream infection (BSI), urinary tract infection (UTI), surgical site infection (SSI), pneumonia, other sites and all sites.

Table 1 Demographic characteristics, univariable analysis between patients with ICU fungal HAIs and patients without ICU HAIs

Variables	No HAI n = 1674(%)	Fungal HAI n = 186(%)	*p* value
Age, years mean ± SD,	67.5 ± 18.0	71.6 ± 16.0	0.001
APACHE II score, mean ± SD	22.5 ± 7.6	24.7 ± 7.0	<0.001
ICU stay before infection, mean ± SD	6.9 ± 5.7	9.8 ± 7.1	<0.001
Length of ICU stay, mean ± SD	6.9 ± 5.7	20.9 ± 14.7	<0.001
Total parenteral nutrition use before infection, days, mean ± SD	6.9 ± 6.7	19.2 ± 1.7	<0.001
Total parenteral nutrition use (yes)	44(2.6)	36(19.4)	<0.001
Gender (male)	1192(71.2)	131(70.4)	0.865
Service (surgical)	643(38.4)	105(56.5)	<0.001
Main diagnosis(yes)			
Neoplasms	356(21.3)	40(21.5)	0.939
Digestive system	334(20.0)	54(29.0)	0.003
Respiratory system	272(16.2)	21(11.3)	0.078
Genitourinary system	174(10.4)	14(7.5)	0.218
Sepsis	51(3.0)	13(69.9)	0.005
7days before fungal infection with antibiotic therapy	1042(62.2)	141(75.8)	<0.001
Mortality in ICU	305 (18.2)	56 (30.1)	<0.001
Invasive procedures (yes)			
Central venous catheter	1550(92.6)	178(95.7)	<0.001
Mechanical ventilator	1139(68.0)	148(79.6)	0.001
Urinary catheter	854(51.0)	123(66.1)	<0.001
Wound drainage	1550(92.6)	178(95.7)	<0.001
Hemodialysis	417(24.9)	65(34.9)	0.003

SD, Standard deviation; *APACHE*, Acute Physiology and Chronic Health Evaluation; *ICU*, intensive care unit; *HAI*, healthcare-associated infection.

Table 2 Logistic regression analysis of risk factors for fungal infection

Variables	Urinary tract infection		Blood stream infection		Pneumonia		Surgical site infection		All infection sites	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age (>65 years)	0.90	0.54-1.50	0.70	0.30-1.34	1.45	0.58-3.62	0.58	0.23-1.48	0.94	0.64-1.40
Gender (male)	0.78	0.48-1.27	0.77	0.41-1.45	1.78	0.69-4.62	1.03	0.38-2.79	0.95	0.65-1.40
Service (surgical)	1.52	0.92-2.51	1.62	0.81-3.23	3.46*	1.44-8.28	11.79*	2.49-55.74	1.89*	1.27-2.80
APACHE II score	1.01	0.98-1.04	1.06*	1.02-1.11	1.03	0.97-1.09	0.99	0.93-1.06	1.01	0.99-1.04
ICU stay before infection(days)	0.98	0.95-1.01	1.00	0.97-1.03	1.01	0.99-1.03	0.99	0.95-1.04	1.00	0.98-1.02
antibiotic therapy	0.82	0.47-1.42	0.64	0.31-1.32	0.60	0.23-1.60	1.42	0.52-3.87	0.87	0.57-1.31
TPN	3.51*	1.69-7.31	8.47*	4.07-17.63	8.07*	3.24-20.13	8.82*	3.27-23.81	4.83*	2.80-8.34
Neoplasms	0.88	0.46-1.69	0.81	0.33-1.98	1.13	0.36-3.51	1.59	0.44-5.79	0.96	0.57-1.61
Respiratory system	0.90	0.43-1.88	0.60	0.18-2.03	1.06	0.26-4.33	—	—	0.79	0.42-1.47
Digestive system	1.03	0.53-2.01	1.21	0.51-2.88	1.84	0.60-5.60	2.61	0.78-8.72	1.32	0.80-2.19
Genitourinary system	0.76	0.32-1.81	1.00	0.32-3.11	1.20	0.30-4.79	—	—	0.72	0.36-1.44
Sepsis	1.60	0.56-4.57	5.26*	1.70-16.27	3.18	0.53-18.98	2.89	0.22-37.77	2.71*	1.24-5.92
Central line	2.63	0.61-11.24	0.90	0.20-3.99	0.51	0.11-2.46	6.80	—	1.21	0.50-2.92
Mechanical ventilator	2.85*	1.73-4.69	1.71	0.89-3.26	1.67	0.76-3.69	1.45	0.53-3.98	2.05*	1.40-2.99
Hemodialysis	0.70	0.36-1.37	0.72	0.29-1.80	1.67	0.62-4.47	3.08	0.87-10.81	1.21	0.74-1.98
Foley catheter	1.64*	1.01-2.67	1.02	0.56-1.88	2.00	0.92-4.35	0.92	0.37-2.33	1.52*	1.06-2.20
Wound drainage	0.76	0.29-2.02	1.52	0.56-4.12	0.15	0.02-1.43	1.01	0.29-3.55	0.96	0.49-1.88

OR, Odds Ratio; *CI*, Confidence interval; *APACHE*, Acute Physiology and Chronic Health Evaluation; TPN, Total Parenteral Nutrition

Olgu formunun oluşturulması

CARING FOR THE
CRITICALLY ILL PATIENT

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

Table 1. Basic Characteristics of Adult Patients in the EPIC II Study

Characteristic	No. (%)			P Value
	All Patients (n = 13 796)[a]	Not Infected (n = 6709)[b]	Infected (n = 7087)[c]	
Age, mean (95% CI), y	60.7 (60.4-61.0)	60.5 (60.1-60.9)	60.9 (60.5-61.3)	.21
Men	8587 (62.3)	4130 (61.7)	4457 (63.0)	.12
Severity score on study day, mean (95% CI)[d]				
SAPS II	35.1 (34.9-35.4)	31.3 (30.9-31.6)	38.7 (38.4-39.1)	<.001
SOFA	6.3 (6.2-6.4)	5.2 (5.1-5.3)	7.2 (7.1-7.3)	<.001
Type of admission				
Elective surgery	3209 (23.3)	2297 (34.4)	912 (12.9)	<.001
Medical	3878 (28.2)	1584 (23.7)	2294 (32.4)	
Emergency surgery	5298 (38.5)	2070 (31.0)	3228 (45.6)	
Trauma	1365 (9.9)	725 (10.9)	640 (9.0)	
Reason for ICU admission				
Respiratory	3091 (22.4)	845 (12.6)	2246 (31.7)	<.001
Cardiovascular	3041 (22.0)	1541 (23.0)	1500 (21.2)	
Surveillance/monitoring	2592 (18.8)	1968 (29.3)	624 (8.8)	
Neurologic	2010 (14.6)	994 (14.8)	1016 (14.3)	
Digestive/liver	1306 (9.5)	478 (7.1)	828 (11.7)	
Trauma	1119 (8.1)	593 (8.8)	526 (7.4)	
Renal	324 (2.3)	119 (1.8)	205 (2.9)	
Other[e]	313 (2.3)	171 (2.5)	142 (2.0)	

Source of admission				
Operating room/recovery	3510 (25.7)	2178 (32.9)	1332 (18.9)	<.001
ED/ambulance	4010 (29.3)	1980 (29.9)	2030 (28.8)	
Hospital floor	3789 (27.7)	1503 (22.7)	2286 (32.5)	
Other hospital	1921 (14.1)	751 (11.3)	1170 (16.6)	
Other	435 (3.2)	212 (3.2)	223 (3.2)	
Comorbid conditions				
COPD	2303 (16.7)	872 (13.0)	1431 (20.2)	<.001
Cancer	2086 (15.1)	975 (14.5)	1111 (15.7)	.06
Heart failure[f]	1342 (9.7)	604 (9.0)	738 (10.4)	.005
Diabetes mellitus	1336 (9.7)	605 (9.0)	731 (10.3)	.01
Chronic renal failure	1250 (9.1)	494 (7.4)	756 (10.7)	<.001
Immunosuppression	587 (4.3)	176 (2.6)	411 (5.8)	<.001
Cirrhosis	460 (3.3)	195 (2.9)	265 (3.7)	.006
Hematologic cancer	282 (2.0)	73 (1.1)	209 (2.9)	<.001
HIV	96 (0.7)	18 (0.3)	78 (1.1)	<.001
No. of comorbid conditions				
0	6686 (48.5)	3629 (54.1)	3060 (43.2)	<.001
1	4434 (32.1)	2076 (30.9)	2358 (33.3)	
2	1829 (13.3)	719 (10.7)	1110 (15.7)	
3	626 (4.5)	227 (3.4)	399 (5.6)	
>3	218 (1.6)	58 (0.9)	160 (2.3)	
Treatment on admission				
Mechanical ventilation	7694 (56.2)	2932 (44.1)	4762 (67.5)	<.001
Hemodialysis/hemofiltration	1247 (9.1)	322 (4.8)	925 (13.1)	<.001

ONLAR NE YAPMIŞ?

SALGIN ÖRNEKLERİ

Scandinavian Journal of Infectious Diseases, 2014; 46: 361–367

informa
healthcare

ORIGINAL ARTICLE

Parenteral nutrition-associated bloodstream infection in an Australian teaching hospital—An 8-year retrospective study of over 11,000 PN-days

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From the [1]Infection Management Services, Princess Alexandra Hospital, Woolloongabba, Brisbane, [2]Microbiology Department, Royal Brisbane and Women's Hospital, Herston, [3]Pharmacy Department, Princess Alexandra Hospital, Woolloongabba, Brisbane, and [4]School of Medicine, The University of Queensland, Brisbane, Queensland, Australia

Table IV. Univariate Cox regression analysis of risk factors for parenteral nutrition-associated BSI.[a]

	BSI, *n* (%)	No BSI, *n* (%)	HR (95% CI)	*p*-Value
PN episodes	106	674		
Male	63 (59.4)	405 (60.1)	1.00 (0.68–1.49)	0.99
Age, y	62 (47–72)	58 (46–70)	1.01 (1.00–1.02)	0.17
BMI, kg/m^2 (n = 572)	22.5 (19.7–27.7)	23.5 (20.0–27.4)	1.02 (0.99–1.05)	0.20
Solid organ malignancy	37 (34.9)	225 (33.4)	1.35 (0.91–2.01)	0.14
Haematological malignancy	14 (13.2)	73 (10.8)	1.51 (0.86–2.67)	0.15
Neutropenia	10 (9.4)	51 (7.6)	0.93 (0.47–1.83)	0.84
Surgery	72 (67.9)	458 (68.0)	1.02 (0.82–1.26)	0.89
ICU admission	40 (38.1)	218 (32.5)	1.59 (1.07–2.37)	0.023
Albumin, g/l				
Normal (>35)	6 (5.7)	86 (12.8)	1	0.004
Low (25–35)	41 (38.7)	318 (47.2)	2.25 (1.04–4.89)	
Very low (<25)	59 (55.7)	270 (40.1)	3.46 (1.58–7.57)	
Creatinine, µmol/l	65.5 (53–90)	69 (53–89)	1.00 (1.00–1.00)	0.76
Diabetes	16 (15.1)	88 (13.1)	1.21 (0.68–2.14)	0.52
Hyperglycemia	71 (67.0)	301 (44.7)	1.72 (1.16–2.55)	0.007
Insulin infusion	34 (32.1)	95 (14.1)	2.07 (1.38–3.13)	<0.001
Charlson score (n = 664)	2 (1–3)	2 (0–3)	1.14 (1.03–1.25)	0.008

BSI, bloodstream infection; HR, hazard ratio; CI, confidence interval; PN, parenteral nutrition; BMI, body mass index; ICU, intensive care unit; IQR, interquartile range.

[a]Results are *n* (%), or median (IQR).

Retrospektif kohort çalışma 2002-2009

Retrospektif
kohort çalışma
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780 PN kullanımı
120 KDI
İnsidans 10/1000 PN günü

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En sık etken *Candida*!

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Mortalite PN ilişkili KDI'de
PN ilişkisiz olanlara göre
2 kat yüksek (%17.9 vs %8.3)
OR2.4

Düşük albümin düzeyi ve iv insülin ihtiyacı PN ilişkili KDI için bağımsız risk faktörleri

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Worldwide Database for Nosocomial Outbreaks
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tatus

he current release provides most features and access to nearly all data. However, parts of Outbreak Database are still under reconstruction. We are currently adding new Outbreak Articles nd improving both the data quality and the website. E.g., we are adding more documentation.

ontact

you have any further questions or comments please do not hesitate to contact the Outbreak Database team.

Journal of Clinical Microbiology

Four-Year Persistence of a Single *Candida albicans* Genotype Causing Bloodstream Infections in a Surgical Ward Proven by Multilocus Sequence Typing

Maria Anna Viviani, Massimo Cogliati, Maria Carmela Esposto, Anna Prigitano and Anna Maria Tortorano

J. Clin. Microbiol. 2006, 44(1):218. DOI: 10.1128/JCM.44.1.218-221.2006.

J Clin Microbiol. (44 / 2006) [p. 218 to 221]

1. Candida albicans
PCR fingerprinting and Multilocus sequence typing (MLST) was applied. PCR analysis revealed that 13 isolates of the 8 patients had genotype B. MLST analysis showed that 8 of the 13 isolates with genotype B had the same Ia allelic profile, while the others had sequence types closely related to the Ia profile.

Type	Description
Sources	
Drug	Contamination of the parenteral nutrition fluids by a health care worker involved in the preparation of the parenteral nutrition bags was possibly the source of the outbreak.
Transmissions	
Invasive technique	Transmission occurred possibly via contaminated parenteral nutrition fluids.
Risk Factors	
Drugs	All patients had received parenteral nutrition.
Measures	
Not mentioned	

Scand J Infect Dis. 1998;30(2):137-42.

Outbreak of Candida albicans fungaemia in a neonatal intensive care unit.

Huang YC[1], Lin TY, Peng HL, Wu JH, Chang HY, Leu HS.

Author information

Abstract

During a 4-month period, 9 premature infants hospitalized in a neonatal intensive care unit (NICU) developed Candida albicans fungaemia. All 9 infants received antifungal agents. Fluconazole was administered in 7 patients and successfully eradicated this organism in 6 with no adverse effects. For epidemiological investigation, 64 environmental specimens and hand-washings of all 54 staff members involved in the NICU were examined for the presence of this organism. No C. albicans could be identified from environmental sources, while the hand-washing of 1 nurse was C. albicans-positive. Two genotyping methods, including electrophoretic karyotyping using contour-clamped homogeneous electric field gel electrophoresis and polymerase chain reaction-based direct sequencing of rRNA gene, were used in the analysis of the isolates recovered from blood cultures of the infants, the hand-washing of the nurse and 7 control isolates. Both methods yielded comparable results and revealed that all 13 isolates from infected infants as well as the isolate from hand washing of the nurse were of the same genotype while the control isolates were distinct. These results suggest that the outbreak of C. albicans fungaemia was caused by a particular strain and possibly via cross-infection. In addition, we showed that fluconazole seemed to be safe and effective in treating C. albicans fungaemia in neonates, although the data were limited.

PMID: 9730299 [PubMed - indexed for MEDLINE]

Development

Type	Description	Phase
Sources		
Personnel	No C.albicans could be identified from environmental sources, while the hand-washing of one nurse was C.albicans positive.	
Medical equipment/device		
Transmissions		
Contact		
Invasive technique		
Risk Factors		
Personnel		
Device(s)		
Patient	Very low birth weight infants.	
Drugs		
Measures		
Isolation/cohorting	All 9 infants received antifungal agents.	
Personnel training	Strict hand-washing with appropriate disinfectants before and after contact with patients cannot be overemphasized enough.	
Personnel screening/surveillance		
Hand washing/hand disinfection		
Patient screening/surveillance		
Protective clothing		

Development

Type	Description	Phase
Sources		
Personnel	No C.albicans could be identified from environmental sources, while the hand-washing of one nurse was C.albicans positive.	
Medical equipment/device		
Transmissions		
Contact		
Invasive technique		
Risk Factors		
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Personnel screening/surveillance		
Hand washing/hand disinfection		
Patient screening/surveillance		
Protective clothing		

EL HİJYENİ

The Turkish Journal of Pediatrics 2010; 52: 42-49 *Original*

Nosocomial transmission of *Candida pelliculosa* fungemia in a pediatric intensive care unit and review of the literature

Ayşe Kalkancı[1], Murat Dizbay[2], Özden Turan[3], Işıl Fidan[1], Burçe Yalçın[1], İbrahim Hirfanoğlu[3], Semra Kuştimur[1], Firdevs Aktaş[2], Takashi Sugita[4]

Departments of [1]Microbiology, [2]Infectious Diseases and Infection Control Committee, and [3]Pediatrics, Gazi University Faculty of Medicine, Ankara, Turkey, and [4]Department of Microbiology, Meiji Pharmaceutical University, Kiyose, Tokyo, Japan

Development

Type	Description	Phase
Sources		
Unknown		
Transmissions		
Contact	At the time of investigation, no C. pelliculosa could identified in any of the other clinical, surveillance, or environmental samples that were tested. Horizontal transmission of C. pelliculosa between the babies was emphasized. At the time the candidemia cases were detected, the four affected patients were in the same room. Their periods of hospitalization overlapped, and they were all cared for by NICU staff members.	
Risk Factors		
Not mentioned		
Measures		
Personnel screening/surveillance	Physicians and nursing staff of the ICU were screened for oral and hand carriage of Candida spp.	
Environmental screening	Extensive sampling was undertaken from fomites and other environmental sources of the ward (floors, disinfectant solutions, multidose vials, infusion pumps, commercially prepared parenteral nutrition bags, and other medical equipment), and cultures were performed.	
Hand washing/hand disinfection	Compliance with standard infection control measures, including rigorous handwashing, was emphasized.	
Modification of care/equipment	Infusion sets were changed to a new one at the 48th hour (h) of insertion, instead of at 24 h.	

Development

Type	Description	Phase
Sources		
Unknown		
Transmissions		
Contact	At the time of investigation, no C. pelliculosa could identified in any of the other clinical, surveillance, or environmental samples that were tested. Horizontal transmission of C. pelliculosa between the babies was emphasized. At the time the candidemia cases were detected, the four affected patients were in the same room. Their periods of hospitalization overlapped, and they were all cared for by NICU staff members.	
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EL HİJYENİ

Table I. Clinical Characteristics of Four Patients with *Candida pelliculosa* Fungemia

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4
Age (gestational week)	24	29	38	37
Birth weight (g)7	50	790	3460	3240
Underlying disease	Prematurity, RDS, Intracranial hematoma	PDA,ASD, VSD,NEC	Pulmonary hypertension Intraparanchymal hematoma, ASD	Pyloric stenosis
Potential risk factors for candidemia				
CVC	Yes	Yes	Yes	Yes
Mechanic ventilation	Yes	Yes	Yes	No
TPN	Yes	Yes	Yes	No
Prior antibiotic usage	Ampicillin+ amikacin / Meropenem+ teicoplanin	Ampicillin+ amikacin / Meropenem+ teicoplanin	Meropenem+ teicoplanin	Ampicillin + amikacin
Prior antifungal prophylaxis	No	No	No	No
Thoracal tube	Yes	No	No	No
Ventriculo-peritoneal shunt	No	No	Yes	No
Blood culture	*C. pelliculosa* (peripheral vein) + *Enterococcus faecalis* (CVC)	*C. pelliculosa* (peripheral vein)	*C. pelliculosa* + CNS (peripheral vein)	*C. pelliculosa* (CVC)
Therapy				
Antifungal therapy	FL, AB + VO	FL, AB	AB	No
Catheter removal	Yes	Yes	Yes	Yes
Outcome				
Candidemia	Cleared	Cleared	Cleared	Cleared
Clinical	Recovery	Recovery	Recovery	Recovery

An Outbreak of *Candida* spp. Bloodstream Infection in a Tertiary Care Center in Bogotá, Colombia

Carlos A. DiazGranados[1,2,3], Adriana Martinez[2], Ceneth Deaza[2] and Sandra Valderrama[2]

[1]Emory University School of Medicine, Atlanta, GA, USA; [2]Jorge Piñeros Corpas Clinic; [3]Fundación Universitaria de Ciencias de la Salud; Bogotá, Colombia

The Brazilian Journal of Infectious Diseases 2008;12(5):390-394.

Development

Type	Description
Sources	
Unknown	
Transmissions	
Unknown	Our documentation of hand colonization in some HCW and our observation of poor hand-hygiene practices suggest that nosocomial transmission could have been facilitated from HCW hands as transient reservoirs.
Risk Factors	
Procedure	
Device(s)	Parenteral nutition, presence of a central line, and severity of illness were associated with candidemia in bivariate analysis.
Measures	
Environmental screening	The micribiological investigation was comprised of culturing HCW hands, ventilator tubing in the intensive care unit and coronary care unit, latex gloves, surgical tape, bandages, cotton, IV catheters, IV solutions, IV medication containers, and IV medication transportation bags.
Modification of care/equipment	
Disinfection/Sterilization	
Personnel training	The outbreak was controlled after elimination of plastic bags used for transportation, instauration of daily disinfection of IV medication containers, aquisition of sterile alcohol swabs for port disinfection and staff education.

CANDIDA PARAPSILOSIS BLOODSTREAM INFECTION IN PEDIATRIC ONCOLOGY PATIENTS: RESULTS OF AN EPIDEMIOLOGIC INVESTIGATION

Brunella Posteraro, PhD; Stefania Bruno, MD; Stefania Boccia, BS; Antonio Ruggiero, MD; Maurizio Sanguinetti, MD; Vincenzo Romano Spica, MD; Gualtiero Ricciardi, MD; Giovanni Fadda, MD, PhD

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Vol. 25 No. 8 INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY 641

CANDIDA PARAPSILOSIS BLOODSTREAM INFECTION IN PEDIATRIC ONCOLOGY PATIENTS: RESULTS OF AN EPIDEMIOLOGIC INVESTIGATION

Brunella Posteraro, PhD; Stefania Bruno, MD; Stefania Boccia, BS; Antonio Ruggiero, MD; Maurizio Sanguinetti, MD; Vincenzo Romano Spica, MD; Gualtiero Ricciardi, MD; Giovanni Fadda, MD, PhD

Development

Type	Description	F
Sources		
Unknown		
Transmissions		
Contact	Transmission occurred (probably during CVC dressing changes) by nurses whose hands were colonized with C. parapsilosis.	
Risk Factors		
Device(s)	All children had an indwelling CVC.	
Measures		
Modification of care/equipment	[ME] other: The CVCs were removed and cultures of the three catheter tips revealed C. parapsilosis. Of the 30 environmental cultures that were performed, none was positive.	
Hand washing/hand disinfection	More frequent handwashing and antisepsis was enforced.	
Patient screening/surveillance	Surveillance cultures (oropharyngeal and nasal swabs and urine and stool samples) performed on admission were negative in all three cases.	
Personnel screening/surveillance	Samples for skin cultures were taken from the hands of the medical and paramedical staff. Six of the 20 nurses tested were positive for C. parapsilosis.	
(Change) antibiotic therapy	In all cases, the candidemia cleared with amphotericin B therapy.	

CANDIDA PARAPSILOSIS BLOODSTREAM INFECTION IN PEDIATRIC ONCOLOGY PATIENTS: RESULTS OF AN EPIDEMIOLOGIC INVESTIGATION

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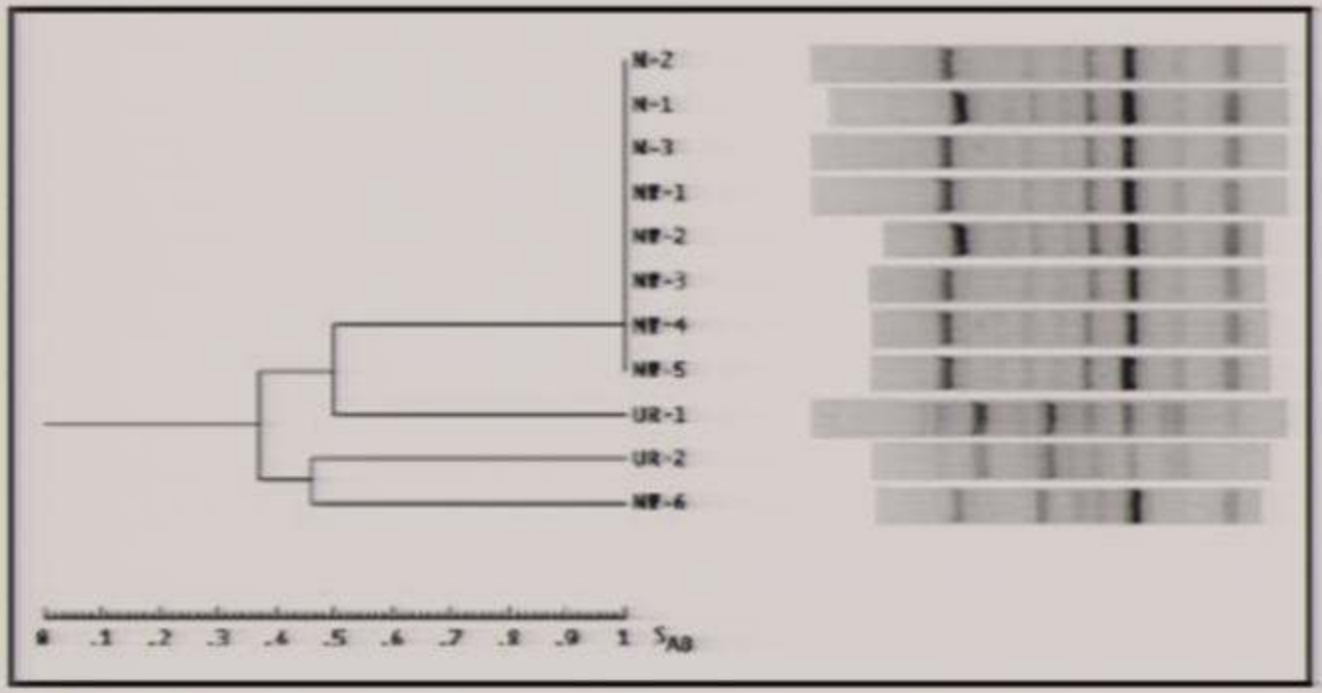

FIGURE. Dendrogram illustrating the similarity of DNA fingerprinting patterns (shown on the right) obtained with arbitrarily primed polymerase chain reaction using 8F primer for 11 *Candida parapsilosis* isolates: 3 (N-1, N-2, and N-3) representative of the isolates recovered from each patient in the pediatric oncology unit, 6 (NW-1 through NW-6) recovered from the hands of 6 nurses caring for these patients, and 2 (UR-1 and UR-2) epidemiologically unrelated controls recovered from patients in other areas of the same medical center. Similarity coefficients (S_{AB}) indicated that isolates N-1 to N-3 and NW-1 to NW-5 were identical ($S_{AB} = 1$). Isolate NW-6 was clearly unrelated to the 8 isolates ($S_{AB} = 0.37$), as were isolates UR-1 ($S_{AB} = 0.50$) and UR-2 ($S_{AB} = 0.37$).

About the Outbreak Article

Title	Candida parapsilosis bloodstream infection in pediatric oncology patients: results of an epidemiologic investigation
Authors	Posteraro B, Bruno S, Boccia S, et al.
Reference	Infect Control Hosp Epidemiol. (25 / 2004) [p. 641 to 645]
Language	English
Publication Type	original
Study Type	case report
Further Outbreaks	0
Comments	All of the staff reported much greater attention to the practice of strict handwashing, particularly before engaging in CVC dressing changes, and there have been no additional cases of C. parapsilosis BSI in the pediatric oncology unit since that time.
URL	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15357154
Articles Related	

JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 2004, p. 4468–4472 Vol. 42, No. 10
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.10.4468–4472.2004

Epidemiologic and Molecular Characterization of an Outbreak of *Candida parapsilosis* Bloodstream Infections in a Community Hospital

Thomas A. Clark,[1,2]* Sally A. Slavinski,[3] Juliette Morgan,[2] Timothy Lott,[2] Beth A. Arthington-Skaggs,[2] Mary E. Brandt,[2] Risa M. Webb,[3,4] Mary Currier,[3] Richard H. Flowers,[4] Scott K. Fridkin,[2]* and Rana A. Hajjeh[2]

Epidemic Intelligence Service, Epidemiology Program Office, Division of Applied Public Health Training,[1] and Mycotic Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases,[2] Centers for Disease Control and Prevention, Atlanta, Georgia, and Mississippi State Department of Health[3] and University of Mississippi Medical Center,[4] Jackson, Mississippi

Measures

Modification of care/equipment	[ME] other: Infection control and isolation policies and practices were reviewed. Three surreptitious observational studies of health care worker hand hygiene practices were conducted. The rate of compliance with hand hygiene was similar to that reported in prior studies, which typically observe rates of compliance of less than 50%. A multi-disciplinary program was created, designed to improve HCW adherence to recommended hand hygiene practices. Samples for surveillance cultures were obtained from central venous catheter insertion sites and medical devices. C. parapsilosis was recovered from 1 patient care device (blood pressure cuff tubing), but

1. Candida parapsilosis
Genotyping by randomly amplified polymorphic DNA (RAPD) analysis, electrophoretic karyotyping, and Southern blotting with the complex Cp3-13 probe.

Type	Description
	no yeasts were recovered from cultures of CVC hubs or insertion sites sampled.
Personnel screening/surveillance	Twenty-six percent of the health care workers surveyed demonstrated hand colonization with C. parapsilosis, and one hand isolate was higly related to all case-patient isolates by tests with the DNA probe Cp3-13.
(Change) antibiotic therapy	Fluconazole use practices were reviewed.

TABLE 2. Description of environmental and hand carriage samples obtained and culture results by type of sample, hospital A, Mississippi, 2001

Specimen cultured	No. (%) of samples: Positive for *C. parapsilosis*	Obtained
Total HCW hand pairs	19 (28)	68
Nurses	14 (26)	53
Physicians	3 (43)	7
Other	2 (25)	8
CVC insertion s	0	8
Medical device	1 (6)	16
Blood pressure cuff tubing	1 (13)	8
Electrocardiograph lead	0	8

EL HİJYENİ

JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 2007, p. 942–947 Vol. 45, No. 3
0095-1137/07/$08.00+0 doi:10.1128/JCM.01878-06

Evidence for a Pseudo-Outbreak of *Candida guilliermondii* Fungemia in a University Hospital in Brazil▽

Eduardo Alexandrino Servolo Medeiros,[1]* Timothy J. Lott,[2] Arnaldo Lopes Colombo,[3] Patrício Godoy,[3] Ana Paula Coutinho,[1] Monica Santos Braga,[1] Marcio Nucci,[4] and Mary E. Brandt[2]

Hospital Infection Program, Division of Infectious Diseases, Federal University of São Paulo, São Paulo, Brazil[1]; Mycotic Diseases Branch, Division of Foodborne, Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333[2]; Division of Infectious Diseases, Federal University of São Paulo, São Paulo, Brazil[3]; and Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil[4]

Received 9 September 2006/Returned for modification 7 November 2006/Accepted 1 January 2007

Fungal infections due to *Candida* species represent an important cause of nosocomial bloodstream infections. We report a large pseudo-outbreak of *Candida guilliermondii* fungemia that occurred in a university hospital in Brazil. *C. guilliermondii* was identified in 64 (43%) of the 149 blood samples drawn between June 2003 and July 2004. The samples were from patients in different wards of the hospital but concentrated in pediatric units. None of the patients had clinical signs of fungemia, and observational analysis revealed errors in the collection of blood samples. During the investigation of the pseudo-outbreak, *C. guilliermondii* was isolated from environmental surfaces and from the skin and nails of members of the nursing team. Through a subtyping analysis it was found that some of the nonpatient isolates were highly related to the patient isolates, and all the patient isolates were highly related. This is consistent with the hypothesis that the pseudo-outbreak was from a limited number of common sources. The adoption of intervention measures was effective in resolving the outbreak, supporting the hypothesis that the outbreak was due to poor techniques of drawing blood samples for culture.

TABLE 3. Parameters considered during the observational analysis of the collection of blood samples and resulting observations (n = 15)

Parameter	No. of observations (%)
Product for hand hygiene	
Common soap	11 (73.3)
Chlorhexidine (2%)	3 (20.0)
None	1 (6.7)
Product for aseptic prepn of the puncture site	
Common soap	9 (60.0)
Iodopolvidine solution	1 (6.7)
70% alcohol	5 (33.3)
Type of gloves	
Nonsterile (procedure) gloves	7 (46.6)
Sterile gloves	8 (53.4)

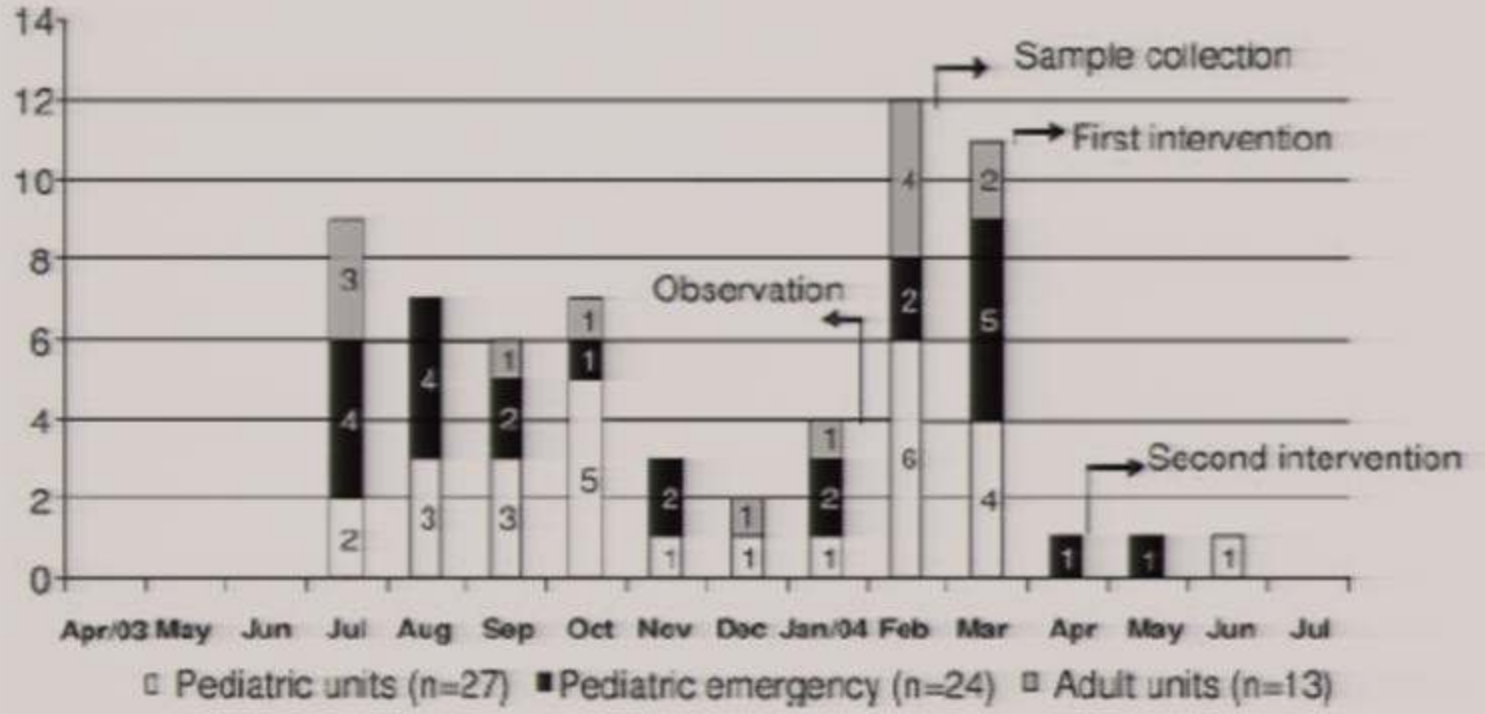

FIG. 1. Distribution of *C. guilliermondii* cases isolated at the Hospital São Paulo, São Paulo, Brazil, from April 2003 to July 2004 and intervention measures. The numbers on the *y* axis and in the bars are the numbers of cases.

TEDAVİ

IDSA GUIDELINES

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]

[1]University of Alabama at Birmingham, Birmingham; [2]University of Michigan and Ann Arbor Veterans Administration Health Care System, Ann Arbor, and [3]Wayne State University, Detroit, Michigan; [4]University of Wisconsin, Madison; [5]Duke University Medical Center, Durham, North Carolina; [6]Harbor–University of California at Los Angeles Medical Center, Torrance; [7]Medical College of Georgia, Augusta; [8]University of Texas at Houston, Houston; [9]Cooper Hospital, Camden, New Jersey; [10]National Cancer Institute, Bethesda, Maryland; [11]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [12]Nijmegen University Centre for Infectious Diseases, Nijmegen, The Netherlands; and [13]Astra Zeneca Pharmaceuticals, Manchester, United Kingdom

CMI
CLINICAL MICROBIOLOGY
AND INFECTION

Review

Management and diagnostic guidelines for fungal diseases in infectious diseases and clinical microbiology: critical appraisal

S. Leroux and A. J. Ullmann*

Article first published online: 21 NOV 2013

DOI: 10.1111/1469-0691.12426

Issue

Clinical Microbiology and Infection

Volume 19, Issue 12, pages 1115–1121, December 2013

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CLINICAL MICROBIOLOGY
AND INFECTION

ESCMID PUBLICATIONS

FREE

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], A. J. Ullmann[24] and for the ESCMID Fungal Infection Study Group (EFISG)

Article first published online: 9 NOV 2012

DOI: 10.1111/1469-0691.12038

Issue

Clinical Microbiology and Infection

Special Issue: ESCMID Guideline for the Diagnosis and Management of Candida Diseases

Volume 18, Issue Supplement s7, pages 9–18, December 2012

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CLINICAL MICROBIOLOGY
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ESCMID PUBLICATIONS

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

FREE

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Table 3. Recommendations on antifungal prophylaxis in ICU patients

Population	Intention	Intervention	SoR	QoE	Ref	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal *Candida* infection	Fluconazole 400 mg/day	B	I	[8]	Placebo *N* = 43
		Caspofungin 70/50 mg/day	C	II_u	[9]	Single arm *N* = 19
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

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]
ICU patients persistently febrile, but without microbiological evidence	To reduce overall mortality	Fluconazole or echinocandin	C	II_u	[28] [163] [164] [7] [27]
ICU patients with candida isolated from respiratory secretions	To cure invasive candidiasis or candidaemia early	Any antifungal	D	II_u	[42]
ICU patients with positive (1,3)-β-D-glucan test[a]	To cure invasive candidiasis or candidaemia early	Any antifungal	C	II_u	[39] [31] [37] [35] [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]

APACHE, acute physiology and chronic health evaluation.

[a]The (1,3)-β-D-glucan tests have low specificity and sensitivity with false-positive results in the presence of haemodialysis, other fungal or bacterial infection, wound gauze, albumin or immunoglobulin infusion.

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Clinical practice guidelines for the management of invasive *Candida* infections in adults in the Middle East region: Expert panel recommendations

Adel F. Alothman[a,*], Tariq Al-Musawi[b], Hail M. Al-Abdely[c], Jameela Al Salman[d], Muna Almaslamani[e], Nadine Yared[f], Adeel A. Butt[g], Nirvana Raghubir[h], Waleed El Morsi[h], Abdulhakeem O. Al Thaqafi[i]

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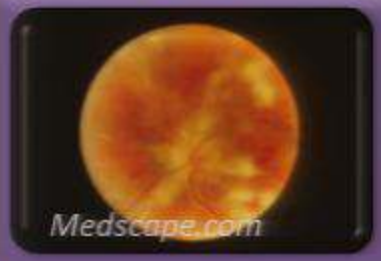


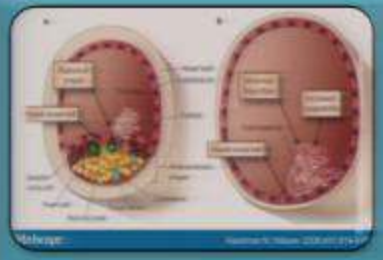
Haftalık fundoskopi yapılmalı...

Okuler tutulum % 16

Çoğunluğu koryoretinit

TEE yapılması....

Endokardit % 8.3



Trombüs araştırılmalı

Özellikle santral kateteri olanlarda

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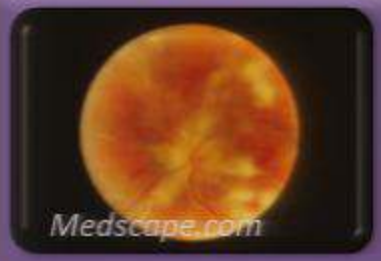

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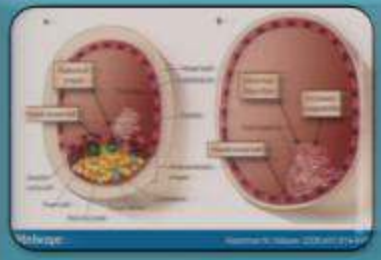

Trombüs araştırılmalı

Özellikle santral kateteri olanlarda

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INVAZİF CANDİDA SALGINI VAR İSE...

Gerçek bir salgın mı?

...

Olgu Tanımı

Kaynak?

Çevre kültürleri?

El kültürleri?

Moleküler çalışmalar..

Epidemiyolojik veriler...

Tedavi

Takip


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1903


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