OLGULAR EŞLİĞİNDE İAE'DA ANTİFUNGAL TEDAVİ

Dr. Behice Kurtaran
Ç.Ü.T.F. Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

IDSA GUIDELINE

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Peter G. Pappas,[1] Carol A. Kauffman,[2] David R. Andes,[3] Cornelius J. Clancy,[4] Kieren A. Marr,[5] Luis Ostrosky-Zeichner,[6] Annette C. Reboli,[7] Mindy G. Schuster,[8] Jose A. Vazquez,[9] Thomas J. Walsh,[10] Theoklis E. Zaoutis,[11] and Jack D. Sobel[12]

IDSA-Non-nötropenik hastalarda invaziv kandidiyazis

- Kandidemi
- YBÜ hastalarında ampirik tedavi
- Solunum yolu örneklerinde kandida
- Üriner sistem enfeksiyonları
- Endokardit
- İntaabdominal enfeksiyonlar
- Kemik eklem enfeksiyonları
- SSS enfeksiyonları
- Özefajit
- Endoftalmit
- Yenidoğan kandida enfeksiyonu

Olgu

- 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 S nedeniyle tx

İlaçlar: Certican (everolimus) 0.25 mg 2x1

Soy geçmiş: özellik yok

Fizik muayene

Bilinç konfüze

Ateş 40°C,

TA: 180/100mmHg,

Kalp hızı: 120/dk

Bilateral solunum sesleri kaba

Batın muayenesinde yaygın hassasiyet

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
- Arteriyel kan gazında laktat 1.8 HCO_3:14 pH:7.30
- İzleminde konfüzyonunda artma
- Hemodiyalize alındı
- Gram (-) sepsis düşünülerek meropenem başlandı
- Ateş yanıtı alınamadı

Kan kültürü

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 *Candida* türleri	İnvaziv cerrahi işlemler (öz. 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 *Candida* türleri	Yoğun bakımda uzun yatış süresi Geniş spektrumlu antibiyotik kullanımı Kanser kemoterapisi, Transplantasyon H2 reseptör blokörü kullanımı Prematüre yenidoğan Renal yetmezlik/hemodiyaliz Mukozal kandida kolonizasyonu Bakteriyel enfeksiyon

3

4

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 2016)

Başlangıç tedavisi

- Mikafungin 100 mg
- Anidulafungin 200/100 mg
- Caspofungin 70/50 mg

} EKİNOKANDİNLER

(Güçlü öneri, yüksek düzey kanıt)

- Amfoterisin B 3-5 mg/kg

YBÜ'de invaziv kandida enfeksiyonlarının tedavisi

İki ana ilke

Erken tanı

Doğru tedavi

Mortalite ↓

Tedavi / Mortalite

7 randomize kontrollü çalışmanın değerlendirmesi, 1915 hasta

APACHE II
İleri yaş
C. tropicalis

KÖTÜ PROGNOZ

Andes DR et al. Clin Infect Dis 2012;54:1110–22.

Nötropenik olmayan kandidemili hastalarda tedavi (IDSA 2016)

Başlangıç tedavisi

- Flukonazol (12 mg/kg; 6 mg/kg gün)

400–800 mg/gün

Kritik olmayan hasta, hemodinamik olarak stabil

Öncesinde azol kullanımı olmayan

Azol dirençli kandida beklenmeyen hasta grubunda alternatif tedavi

C. glabrata: İleri yaş, malignite, diyabet

(Güçlü öneri, yüksek düzey kanıt)

De-eskalasyon

Ekinokandin → Flukonazol

- Nötropenik olmayan hastalarda (5-7 günlük tedavi)
  - Klinik durum stabil
  - *C. albicans* veya flukonazole duyarlı *Candida* türü
  - Tekrarlanan kan kültürlerinde üreme olmaması

(Güçlü öneri, orta düzey kanıt)

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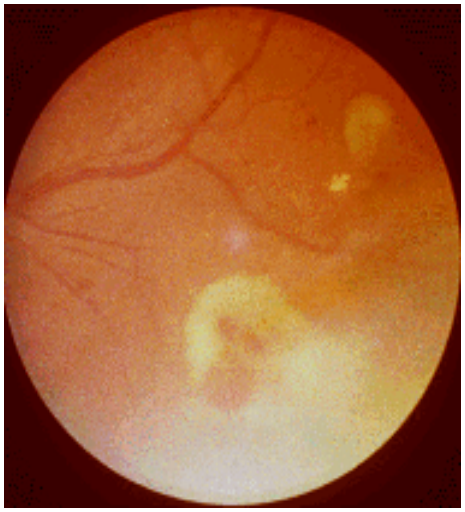
Göz dibi muayenesi

Kandidemi: Antifungal tedavi başlangıcından sonra bir hafta içinde dilate fundoskopi

(Güçlü öneri, düşük düzey kanıt)

%16 göz tutulumu



Korioretinit varsa tedavi göz dibi muayenesi normalleşinceye kadar devam ettirilmelidir

Oude Lashof AM, et al. Antimicrob Agents Chemother 2012; 56:3133–7.

Kontrol kan kültürleri ne zaman alınmalı?

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

(Güçlü öneri, düşük düzey kanıt)

Tedavi süresi

Semptomların düzelmesi ve metastatik enfeksiyon olmaması durumunda;

İlk negatif kan kültüründen 2 hafta sonrasına kadar

(Güçlü öneri, orta düzey kanıt)

YBÜ ampirik antifungal tedavi olgu

- 44 yaşında, kadın
- Brid ileus, jejunum perforasyonu (Genel Cerrahi operasyon)
- Post-op solunum yetmezliği, hipotermi, septik şok → YB (MV)
- Noradrenalin
- Meropenem

3. gün

- Noradrenalin, TPN
- Meropenem tedavisi altında yüksek ateş (39,3^{0}C)
- Lökosit:16.600/mm^3, CRP:26,3 mg/dl
- Prokalsitonin:9,5 ng/dl
- ARDS -Prone pozisyonu
- Kan kültürlerinde üreme yok
- Ampirik vankomisin eklendi

4. gün

- İdrarda *Candida* spp.

Kolonizasyon taraması

- 7 bölgeden örnek alındı
  - İdrar
  - DTA
  - Ağız sürüntü
  - Dren sıvısı
  - Dren çevresi sürüntü
  - Rektal sürüntü
  - Koltuk altı sürüntü

5(+)

- Ekinokandin

6. gün

- DTA: *Acinetobacter* spp.
- CRP 29.4, Prokalsitonin 11.9
- Tedaviye Kolistin ekleme
- Anastomoz kaçağı →
- Genel Cerrahi kaynak kontrolü

12. gün

- MV, hemodinamik olarak stabil
- Ekinokandin -----Flukonazol
- 20. günde genel durumu iyi, GC servisine devir

1. Acinetobacter baumannii complex
(**Üreme Düzeyi :** 100.000 Koloni/ml)

Antibiyogram Adı	I
Colistin	S
Ampisilin/sulbaktam	R
Sefepim	R
Doksisiklin	I
İmipenem	R
Meropenem	R
Amikasin	S
Siprofloksasin	R
Trimetoprim/sulfametoksazol	R
Seftazidim	R
Levofloksasin	R
Sefoperazon/sulbaktam	R
Tetrasiklin	R
Tigesiklin	S

Ampirik tedavi - Nötropenik olmayan hasta (YBÜ invaziv kandidozdan şüphelenildiğinde)

- İnvaziv kandida enfeksiyonu için risk faktörlerinin varlığında,
- Ateşi açıklayacak başka bir neden yoksa,
- Kandida serolojisi pozitifse ve/veya steril olmayan bölgelerden alınan kültür (+)
  - Mannan, anti-mannan, beta D-glukan, PCR
- Ampirik AF tedavi septik şok ve risk faktörleri olan hastada en erken sürede başlanmalı

(Güçlü öneri, orta düzey kanıt)

Risk grubu

- Kandida kolonizasyonu
- Ağır hastalık
- Geniş spektrumlu antibiyotik
- Majör cerrahi (özellikle abdominal cerrahi)
- Nekrotizan pankreatit
- Diyaliz
- Parenteral nutrisyon
- Kortikosteroid
- Santral kateter

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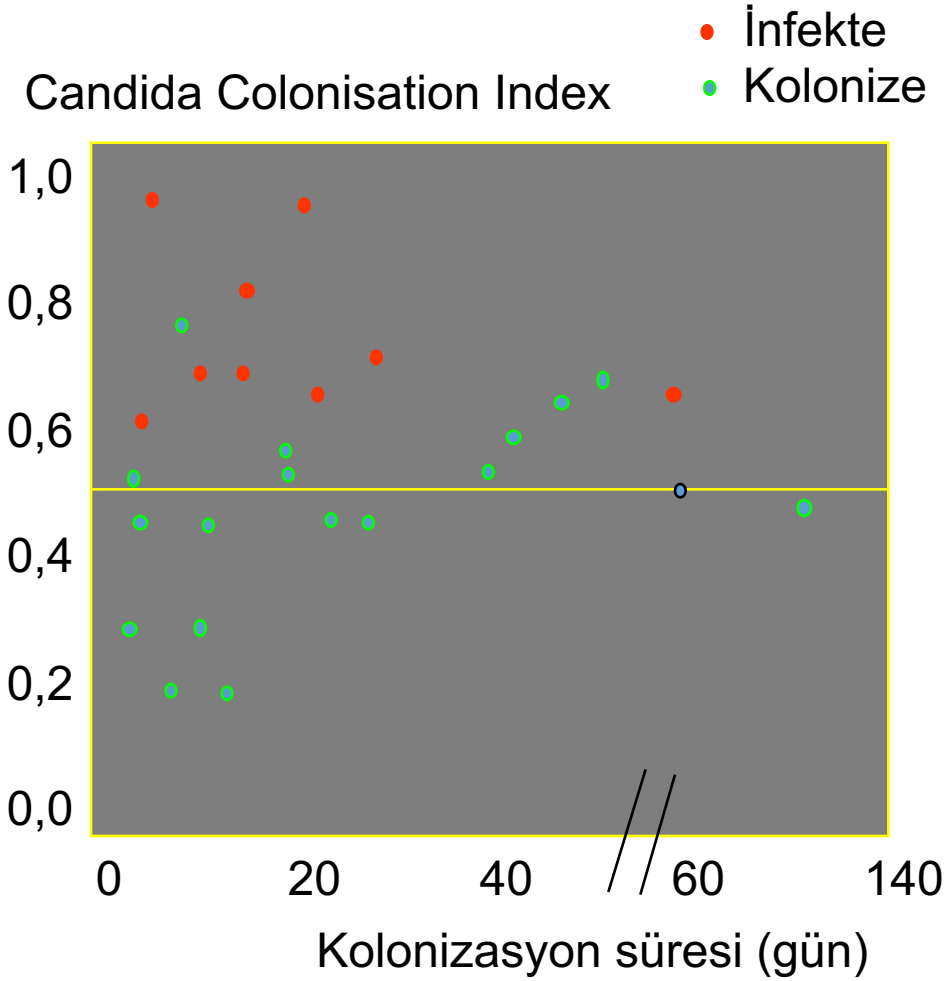
Yüksek risk grubu

- Tekrarlayan gastrointestinal perforasyon
- Anastomoz kaçağı
- Akut nekrotizan pankreatit

IDSA 2016 Kandidiyaz Tedavi Kılavuzu

Kolonizasyon/Enfeksiyon



- Prospektif kohort çalışması
- 5 farklı bölge/hasta

- Kolonizasyon İndeksi :

$$\frac{\text{Kolonize bölge sayısı}}{\text{Örnek alınan bölge sayısı}}$$

KKi >0.5
Klinik önemi

Candida skoru

- Lojistik regresyon analizinde bağımsız risk faktörleri olarak belirlenen

• Sepsis	: 2 puan
• Multifokal kandida kolonizasyonu	: 1 puan
• Cerrahi	: 1 puan
• TPN	: 1 puan

- Sınır değeri: 2.5 (%81 duyarlı, %74 özgül)
- Eğer bir hastanın *Candida* skoru >2.5 ise invaziv kandidoz riski 7.75 kat fazla

- Erken tedavi başlamada ve antifungallerin aşırı kullanımını önlemede değerli

Leon C. Crit Care Med 2006

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

Ampirik tedavi süresi

- Tedaviye klinik ve laboratuvar olarak yanıt veren hastalarda
  - Kandidemideki gibi

- Tedaviye yanıt vermeyen olgularda (4-5 günlük tedavi sonrası)
  - ampirik tedavi sonlandırılmalıdır

IDSA 2016 Kandidiyaz Tedavi Kılavuzu

Profilaksi

- İnvaziv kandida enfeksiyonu gelişme riski >%5 olan riskli hasta grubunda Flukonazol 800/400 mg/gün

  (Zayıf öneri, orta düzey kanıt)

- Ekinokandinler (alternatif)

  (Zayıf öneri, düşük düzey kanıt)

- Günlük klorheksidin banyosu kandidemi dahil kan dolaşımı enfeksiyonlarında azalma

  (Zayıf öneri, orta düzey kanıt)

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

İntraabdominal kandidoz

- Ampirik tedavi
  - İntaabdominal enfeksiyon kanıtları
  - Risk faktörleri: yeni geçirilmiş abdominal cerrahi
  - Anastomoz kaçağı (Güçlü öneri, orta düzey kanıt)
  - Nekrotizan pankreatit (Güçlü öneri, orta düzey kanıt)
- AF seçimi kandidemideki gibi (Güçlü öneri, orta düzey kanıt)
- Kaynak kontrolü, drenaj, debritman
- Tedavi süresi: Yeterli kaynak kontrolü ve klinik yanıta göre (Güçlü öneri, düşük düzey kanıt)

Intensive Care Med (2013) 39:2092–2106
DOI 10.1007/s00134-013-3109-3

ORIGINAL

A research agenda on the management of intra-abdominal candidiasis: results from a consensus of multinational experts

Matteo Bassetti
Monia Marchetti
Arunaloke Chakrabarti
Sergio Colizza
Jose Garnacho-Montero
Daniel H. Kett
Patricia Munoz
Francesco Cristini
Anastasia Andoniadou
Pierluigi Viale
Giorgio Della Rocca
Emmanuel Roilides
Gabriele Sganga
Thomas J. Walsh
Carlo Tascini
Mario Tumbarello
Francesco Menichetti
Elda Righi
Christian Eckmann
Claudio Viscoli
Andrew F. Shorr
Olivier Leroy
George Petrikos
Francesco Giuseppe De Rosa

Table 1 Strength of ESCMID recommendations by quality of evidence [16]

Strength of recommendation	
Grade A	ESCMID *strongly* supports a recommendation for use
Grade B	ESCMID *moderately* supports a recommendation for use
Grade C	ESCMID *marginally* supports a recommendation for use
Grade D	ESCMID *supports* a recommendation against use
Quality of evidence	
Level I	Evidence from at least one properly designed randomized, controlled trial
Level II	Evidence from at least one well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time series; or from dramatic results of uncontrolled experiments
Level III	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies

GİRİŞ

- Sekonder ve tersiyer peritonitlerin %30-40'ında intraabdominal kandidoz
- Sıklıkla abdominal cerrahi sonrası gelişen peritonit veya intraabdominal apse
- *Candida* peritoniti mortalitesi %25-60
- *C.albicans* %65-82; takiben *C.glabrata*

Table 2 Risk factors for intra-abdominal *Candida* infection

Risk factor	Notes	References
1. Specific		
Recurrent abdominal surgery	Laparoscopies included	[33]
GI tract perforations	Recurrent perforations and/or perforations untreated within 24 h[a]	[17]
Gastrointestinal anastomosis leakage	More severe if the leakage is in the upper GI tract[b]	[2, 3, 17, 31]
Multifocal colonization by *Candida* spp.		
2. Additional nonspecific		
Acute renal failure, central venous catheter placement, total parenteral nutrition, ICU stay, severity of sepsis, diabetes and immunosuppression, prolonged broad-spectrum antibacterial therapy		[20, 31]

[a] Surgical control of upper gastrointestinal perforations is more problematic [65]

[b] Gastroduodenal surgery, in particular that involving the esophagus

Table 4 Principal recommendations on the management of intra-abdominal candidiasis

Topic	Recommendation	Quality of evidence and strength of recommendation
Diagnosis	Direct microscopy examination for yeast detection from purulent and necrotic intra-abdominal specimens obtained during surgery or by percutaneous aspiration is recommended in all patients with nonappendicular abdominal infections including secondary and tertiary peritonitis	AII
	Samples obtained from drainage tubes are not valuable except for study of colonization	DIII
	Blood cultures should be taken through peripheral vein punctures upon diagnosis or suspicion of intra-abdominal infections and tertiary peritonitis, and specific media for fungi are recommended, if available	AII
	Antifungal susceptibility test should be performed on yeast isolates from blood, sterile sites, and other appropriate specimens. MICs should be reported to the clinicians, specifying the reference method used (CLSI versus EUCAST)	BIII
Culture interpretation	Systemic antifungal treatment should be considered when adequate intra-abdominal specimens (obtained surgically or within 24 h from external drainage) are positive for *Candida*, irrespective of the fungal concentration and the associated bacterial growth	AII
	Positive cultures from drains should not be treated, especially if the drains are in place for more than 24 h	DIII
Nonculture test	When available, mannan and antimannan tests and BDG should be performed in patients with secondary or tertiary peritonitis and at least one specific risk factor for IAC	BII
Prophylaxis	Patients with recent abdominal surgery and recurrent gastrointestinal perforation or anastomotic leakage should receive treatment with fluconazole	BII
	An echinocandin should be considered if there is a high likelihood of azole resistance	CII
Empirical therapy	Empirical antifungal treatment may be considered in patients with a diagnosis of intra-abdominal infection and at least one specific risk factor for *Candida* infection (Table 2)	CIII
	In patients with intra-abdominal infection with or without specific risk factor for *Candida* infection, empirical antifungal treatment should be administered if a positive mannan/antimannan or BDG or PCR test result is present	BII
	Fungicidal antifungal agents (i.e., echinocandins or lipid formulation of amphotericin B) should be prescribed for the empirical therapy of all critically ill patients or patients with previous exposure to azoles	AII
	Azoles can be adopted for the empirical therapy of non-critically ill patients without previous exposure to azoles unless they are known to be colonized with a *Candida* strain with reduced susceptibility to azoles	BII
Targeted therapy	Fungicidal agents such as echinocandins or lipid formulations of amphotericin B should be used for targeted therapy of all critically ill patients or patients with previous exposure to azoles	BII
	For the subgroup of patients infected with *C. parapsilosis*, lipid formulations of amphotericin B or fluconazole should be preferred	BII
	Azoles (fluconazole) can be used for targeted therapy of non-critically ill patients without previous exposure to azoles unless there is evidence of multisite colonization with a *Candida* strain characterized by reduced susceptibility to azoles	BII
Treatment duration	In patients with IAC and clinically ameliorating, antifungal treatment should be continued for at least 10–14 days after the beginning of treatment for IAC	CIII
	In patients without proven *Candida* infection but clinically improved, empirical antifungal therapy should be discontinued after 3–5 days	BIII
	In patients without proven *Candida* infection and not clinically improved, empirical antifungal therapy should be stopped	BIII
Step-down therapy	Treatment can be simplified to an azole (fluconazole or voriconazole) after 5–7 days of echinocandins or lipid formulations of amphotericin B, if the species is susceptible and the patient is clinically stable	BIII

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Sekonder ve tersiyer peritonit dahil non-appendiküler abdominal cerrahide per-op kültür veya perkütan aspirasyon kültürü ve mikroskopisi önerilmektedir

Table 4 Principal recommendations on the management of intra-abdominal candidiasis

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24 saatten uzun süre kalmış drenlerden tanısal amaçlı kültür almak önerilmemektedir!

Table 5 Treatment recommendations

Strategy	Drug	Quality of evidence and strength of recommendation
Prophylaxis	Fluconazole	BII
	Caspofungin	CII
Empirical therapy	Caspofungin	AII
	Micafungin	
	Anidulafungin	
	Liposomal amphotericin B	AII
	Amphotericin B lipid complex	
	Fluconazole	BII
	Voriconazole	
	Amphotericin B deoxycholate	DII
Targeted therapy	Caspofungin	AII
	Micafungin	
	Anidulafungin	
	Liposomal amphotericin B	AII
	Amphotericin B lipid complex	
	Fluconazole	BII
	Voriconazole	
	Amphotericin B deoxycholate	DII

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Special article

EPICO 3.0. Recommendations on invasive candidiasis in patients with complicated intra-abdominal infection and surgical patients with ICU extended stay

Emilio Maseda[a,*], Alejandro H. Rodríguez[b], Gerardo Aguilar[c], Javier Pemán[d], Rafael Zaragoza[e], Ricard Ferrer[f], Pedro Llinares[g], Santiago Grau[h], EPICO Project Group[1]

[a] Servicio de Anestesiología, Hospital Universitario La Paz, Madrid, Spain
[b] Servicio de Medicina Intensiva, Hospital Universitario de Tarragona Joan XXIII/URV/IISPV/CIBERES, Spain
[c] Servicio de Anestesia y Reanimación, Hospital Clínico Universitario de Valencia, Spain
[d] Servicio de Microbiología, Hospital Universitario La Fe de Valencia, Spain
[e] Servicio de Medicina Intensiva, Hospital Universitario Vall D'Hebron, Spain
[f] Servicio de Medicina Intensiva, Hospital Universitario Mútua de Terrassa, Spain
[g] Unidad de Enfermedades Infecciosas, Complejo Hospitalario Universitario A Coruña, Spain
[h] Servicio de Farmacia, Hospital del Mar, Barcelona, Spain

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ABSTRACT

Background: Although in the last decade the management of invasive fungal infections has improved, a number of controversies persist regarding the management of complicated intra-abdominal infection and surgical extended length-of-stay (LOS) patients in intensive care unit (ICU).

Aims: To identify the essential clinical knowledge and elaborate a set of recommendations, with a high level of consensus, necessary for the management of postsurgical patients with complicated intra-

1. *Agreement regarding the variables considered risk factors to initiate early empirical antifungal treatment in patients with community-acquired peritonitis, located in the upper GI tract (above the angle of Treitz).*

Answers provided by the coordinators: Recent or current immunosuppressive therapy, pancreatic neoplasm, severe sepsis or septic shock, previous antibiotic treatment (5 days), upper GI neoplasm, and chronic PPT-antiH2 treatment.

2. *Agreement on the microbiological diagnostic techniques based on their positive predictive value and their possible usefulness to initiate empirical therapy in patients with intra-abdominal candidiasis.*

Answers provided by the coordinators: blood culture, direct examination of abdominal fluid, (1 → 3)-β-D-glucan, and PCR.

3. *Agreement on the microbiological diagnostic techniques based on their negative predictive value (NPV) and their possible usefulness to discontinue empirical/early antifungal therapy in patients with intra-abdominal candidiasis.*

Answers provided by the coordinators: blood culture, direct examination of the abdominal fluid, (1 → 3)-β-D-glucan, and PCR.

4. *Agreement on the systematic initiation of empirical/early antifungal treatment in patients with anastomotic leakage (independent of the CS).*

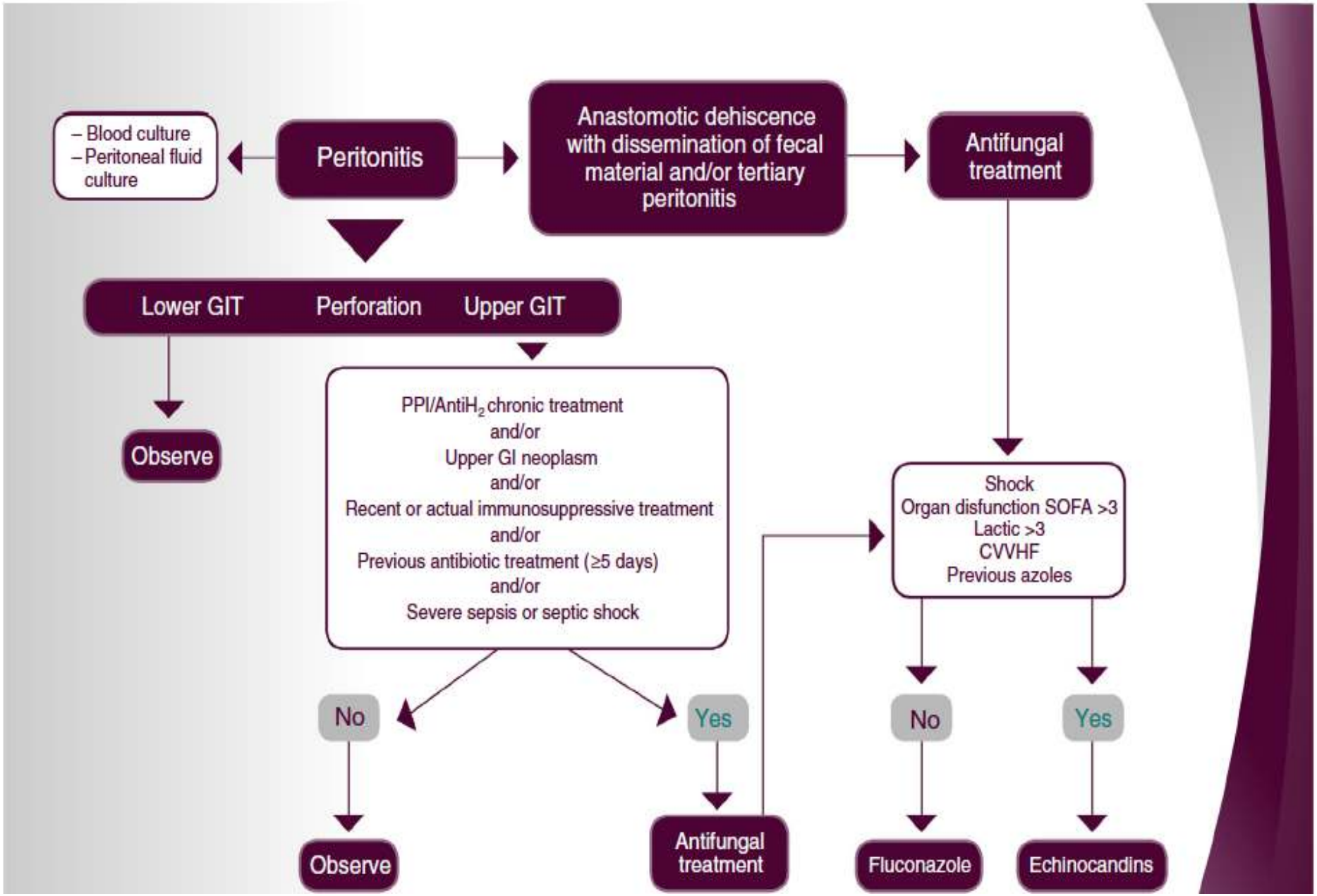
Most of the experienced consultants (75%) agreed on the need to initiate empirical/early antifungal treatment in every patient with anastomotic leakage, regardless of the presence of IC. Specif-

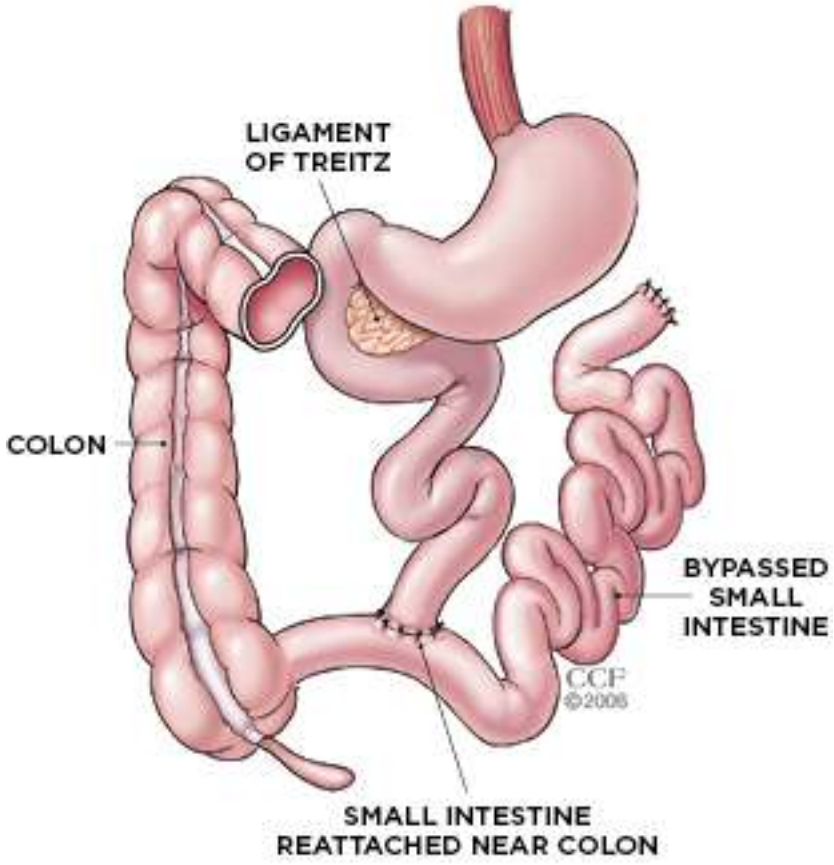
5. *Agreement on the usefulness of the CS to decide on an empirical/early antifungal treatment in patients with anastomotic leaks, and/or tertiary peritonitis.*

The vast majority of the board members (82%) agreed to consider the use of the CS to determine empirical/early antifungal therapy useful in this population. Specifically, and using a 0–10

7. *Agreement on the prescription of the following antifungal drugs as first-line empirical/early treatment in unstable patients with intra-abdominal infection and/or with serum lactate >3 mmol/l, previous azoles intake and/or continuous renal replacement therapy.*

Answers provided by the coordinators: fluconazole, amphotericin lipid B complex, liposomal amphotericin B, anidulafungin, caspofungin, and micafungin.


– Blood culture
– Peritoneal fluid culture
Peritonitis
Anastomotic dehiscence with dissemination of fecal material and/or tertiary peritonitis
Antifungal treatment
Lower GIT
Perforation
Upper GIT
Observe
PPI/AntiH2 chronic treatment
and/or
Upper GI neoplasm
and/or
Recent or actual immunosuppressive treatment
and/or
Previous antibiotic treatment (≥5 days)
and/or
Severe sepsis or septic shock
Shock
Organ disfunction SOFA >3
Lactic >3
CVVHF
Previous azoles
No
Yes
No
Yes
Observe
Antifungal treatment
Fluconazole
Echinocandins


LIGAMENT
OF TREITZ
COLON
BYPASSED
SMALL
INTESTINE
CCF
©2006
SMALL INTESTINE
REATTACHED NEAR COLON

Surgical patients with ICU extended stay

1. *Agreement on the variables considered as risk factors for IC in abdominal surgical patients.*

Answers provided by the coordinators: parenteral nutrition, patients with extended burns, high severity (APACHE II $\geq$ 25 points), upper abdominal surgery (above the angle of Treitz), broad-spectrum antibiotic intake for more than 72 h, extended hospitalization (>10 days in ICU or hospital), presence of solid neoplasm, and lower abdominal surgery.

2. *Agreement on the need to consider the presence of multi-colonization as a mandatory variable of the CS to prescribe an early antifungal treatment.*

Most of the panel members (75%) agreed on considering the presence of multi-colonization necessary to prescribe an antifungal treatment in this situation. Specifically, on a scale of 0–10,

3. *Agreement on initiating fungal treatment based on the following results of the CS in stable (no shock) post-operative abdominal surgery patients, IC risk factors and sepsis with no evident focus.*

Answers provided by the coordinators: CS = 3, CS = 4, and CS = 5.

4. *Agreement on the performance of the following actions in stable (no shock) post-operative abdominal surgery patients, IC risk factors and sepsis with no evident focus, CS= 3 and high clinical suspicion.*

Answers provided by the coordinators: determining non-culture-based microbiological techniques to diagnose IC, and initiating antifungal treatment in the event of a positive non-culture-based microbiological method.

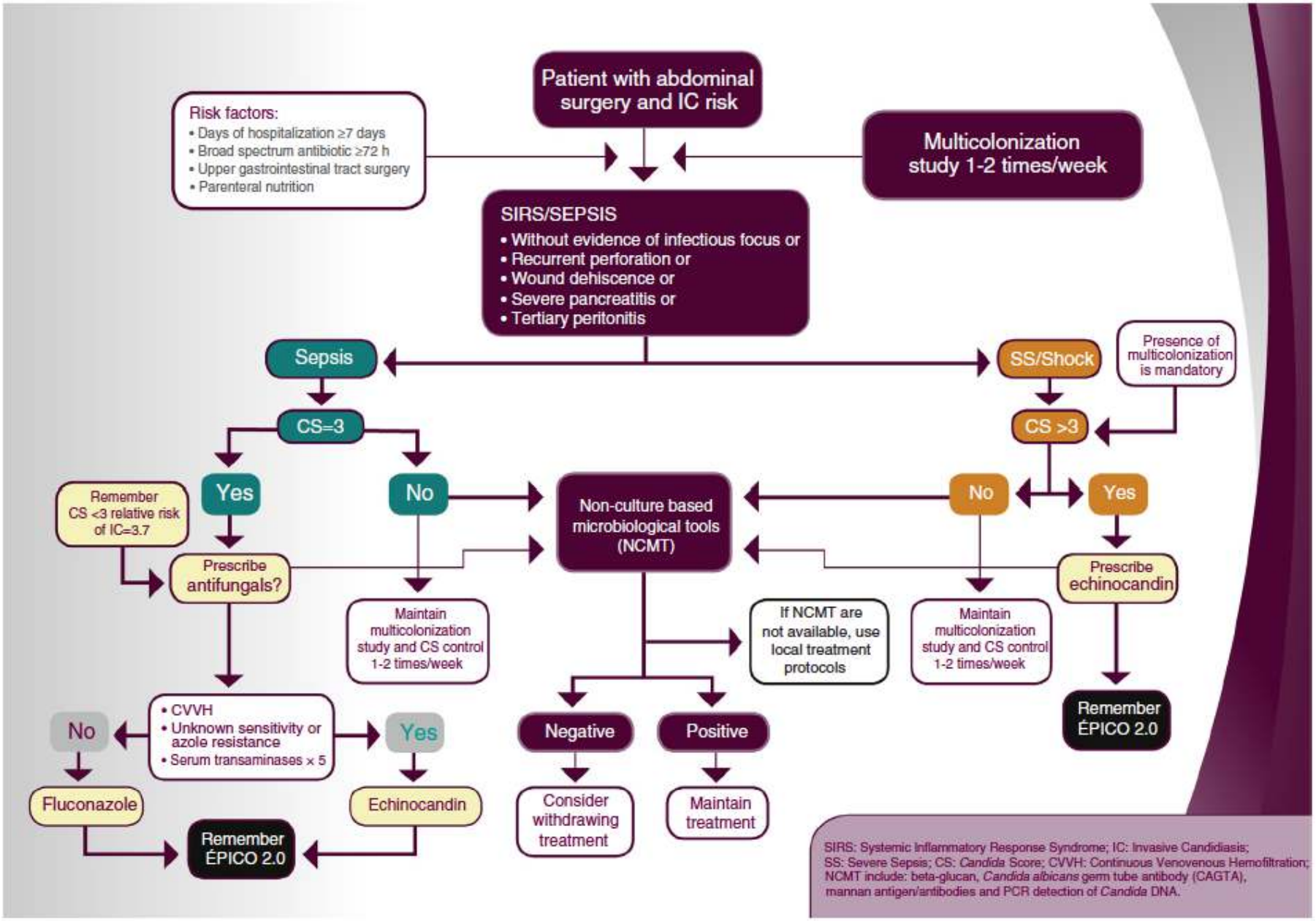


Fig. 2. Algorithm for extended length-of-stay surgical patients.

Hekimlik Zor
İnsanlık Zorda
Barış Dolu Yıllar.....