SOCIEDADE PAULISTA DE INFECTOLOGIA

I FÓRUM PAULISTA DE INFECÇÕES INTRA-ABDOMINAIS

18 de fevereiro de 2017

Infecção do Sítio Cirúrgico
Quando Iniciar a Terapia Antifúngica ?

Claudio Penido Campos Jr.
HCRP/FMRP-USP

USP - RIBEIRÃO
assistência • ensino • pesquisa

Potenciais Conflitos de Interesse

- **Não há conflitos de interesse para esta apresentação**

Resolução CFM nº 1.595/2000
Resolução Anvisa 102/2000

Descrição histológica e clínica de infecções invasivas do trato gastrointestinal por Candida há cerca de 150 anos

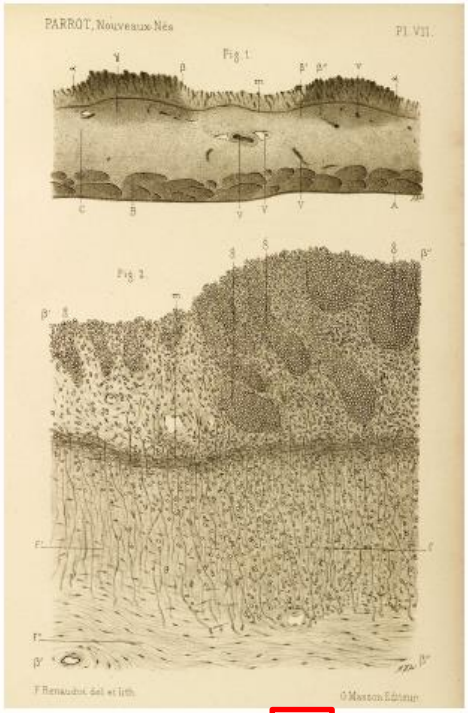


Figure 5. Systemic candidiasis: drawings by Parrot, published in 1877 ([203] Plate VII). (Fig. 1 — upper part), section through wall of stomach attacked by thrush fungus. (Fig. 2 — lower part) cells of *Candida albicans* can be seen in the epithelial digestive mucosa, the yeast's filaments penetrating deeply into submucosal and muscular strata. A, peritoneum; B, muscular layer; C, cellular layer (*couche celluleuse*); V, vessel occluded by clot; m, submucosa; g, gastric glands filled with *Candida* cells

Table 1. Some of the earlier reports of different places of infection by *Candida albicans* (after Odds [194])

Date	Area of lesion	Reference
1825	Oesophageal	Veron [274]
1849	Vaginal	Wilkinson [290]
1862	Cerebral	Zenker [298]
1869	Intestinal	Parrot [200–202]
1890	Renal	Schmorl [235]
1904	Nail bed (onychomycosis)	Dübendorfer [71]
1907	Cutaneous	Jacobi [119]
1912	Broncho-pulmonary	Castellani [45]
1925	Nail-fold (paronychia)	Kingery and Thienes [135]
1928	Bone (osteomyelitis)	Connor [59]
1940	Heart (endocarditis)	Joachim and Polayes [123]
1943	Eye (endophthalmitis)	Miale [177]
1953	Corneal	Mendelblatt [174]

Barret JA. Yeast 2008;25:385-417.

Intensive Care Med (2013) 39:2226–2230
DOI 10.1007/s00134-013-3134-2

EDITORIAL

Philippe Montravers
Herve Dupont
Philippe Eggimann

Intra-abdominal candidiasis: the guidelines—forgotten non-candidemic invasive candidiasis

Table 2 Unsolved questions in the field of intra-abdominal candidiasis

Field of investigation	Specific points to address	Type of investigation
Pathophysiological role of *Candida* spp isolated from the peritoneum	–Synergisms and antagonisms with bacteria (*Pseudomonas* spp, *Enterococci*, *Staphylococci*…)	In vitro experimental studies
	–Mechanisms of adhesion/invasion of the epithelial intestinal cell	In vivo animal models
	–Role of biofilms	In vivo epidemiological studies
	–Role of host defense mechanisms (innate immunity)	
Distinction between colonization and infection	–Enhanced predictivity of described tools in high risk groups:	Multicenter clinical studies
	–Exclusion of low risk patients by negative predictive value of colonization index, of clinical scores and of predictive rules	
	–Positive predictive value of biomarkers in these patients	
	–Role of fungi isolated from mixed cultures	
	–Time course of colonization and infection	
Prophylaxis and preemptive antifungal treatment	–When, how, to whom, what drug	Clinical studies
	–What dose, for how long time	
Therapeutic challenges	–Comparison of antifungal agents (fungicidal versus fungistatic)	In vivo animal models
	–Effects of combinations of antifungals	
	In different but homogenous clinical settings:	Clinical studies
	–Severe or mild to moderate fungal infection	
	–Community-acquired versus nosocomial/health-care associated infections	
	–Prolonged or persistent fungal peritonitis	
	–Clinical and biological makers of clinical and microbiological response	
	–Optimal duration of treatment	
	–Feasibility and advantages of de-escalation	

Intensive Care Med (2013) 39:2226–2230
DOI 10.1007/s00134-013-3134-2

EDITORIAL

Philippe Montravers
Herve Dupont
Philippe Eggimann

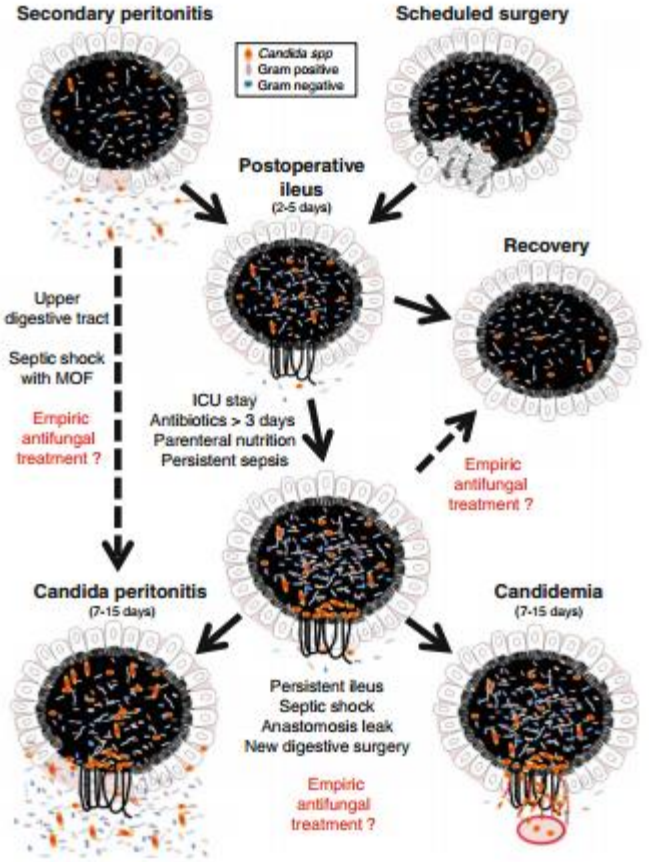
Intra-abdominal candidiasis: the guidelines—forgotten non-candidemic invasive candidiasis

1. Isolados de Candida na primeira reabordagem cirúrgica e na ausência choque séptico: **não indicar terapia antifúngica**

2. Peritonite secundária após a primeira reabordagem cirúrgica: **indicar terapia empírica ?**

3. Peritonites Terciárias: **indicar terapia antifúngica empírica**

Fig. 1 Specific characteristics of *Candida* peritonitis. Secondary perforation of the hollow viscus releases *Candida* cells within the peritoneum. Except for patients with septic shock and multiple organ failure, antifungals are not recommended in this setting. In recurrent peritonitis, such as anastomotic leakage, invasive candidiasis might be more significant, and early empirical antifungal treatment might be beneficial. Intermediate between these situations, such as patients who underwent a first re-operation for postoperative peritonitis, the prediction of *Candida* peritonitis is challenging, and an emergency antifungal treatment is not a validated approach. *ICU* Intensive Care Unit



OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Intra-Abdominal Candidiasis: The Importance of Early Source Control and Antifungal Treatment

Pascalis Vergidis, Cornelius J. Clancy, Ryan K. Shields, Seo Young Park, Brett N. Wildfeuer, Richard L. Simmons, M. Hong Nguyen

Published: April 28, 2016 • http://dx.doi.org/10.1371/journal.pone.0153247

- **163 pacientes com infecções intra-abdominais por Candida**
  - **Abscessos intra-abdominais: 55% dos casos**
  - **Peritonites: 33% dos casos**
    - **Peritonite primária: 5%**
    - **Abscesso pancreático: 5%**
    - **Colecistites/Colangites: 3%**
  - ***Candida albicans*: 56%; *Candida glabrata: 24%***
  - **Candidemia concomitante: 6%**

Classificação e Critérios de Definição

Table 1. Classification of types of intra-abdominal candidiasis (IAC).

IAC classification*	Definition
Primary peritonitis	Peritoneal inflammation** associated with recovery of *Candida* spp., occurring in the absence of an apparent breach of the GI tract or a pathologic process in a visceral organ.
Secondary peritonitis stemming from a GI tract source	Peritoneal *Candida* infection resulting from a pathologic process or breach of the GI tract (stomach, small bowel or colon), such as perforation, surgical leak or trauma.
Intra-abdominal abscess stemming from a GI tract source	Localized collection of *Candida* and pus that is walled-off from healthy tissue, resulting from a pathologic process or breach of the GI tract. Collections may be identified by imaging studies*** or intra-operatively.
Secondary peritonitis stemming from a hepatobiliary or pancreatic source	Peritoneal *Candida* infection resulting from a pathologic process of the liver, gallbladder, biliary or hepatic ducts, or pancreas.
Intra-abdominal abscess stemming from a hepatobiliary or pancreatic source	Abscess (as defined above) resulting from a pathologic process of the liver, gallbladder, biliary or hepatic ducts, or pancreas. Infected bilomas, pancreatic pseudocysts or other (peri)pancreatic collections are categorized as abscesses.
Infected pancreatic necrosis	*Candida* infection of non-vitalized pancreatic tissue resulting from chronic pancreatitis.
Cholecystitis, cholangitis	*Candida* infection of the gallbladder or biliary tract.

* In the classification scheme, sources of peritonitis and abscesses are divided into: a) gastrointestinal (GI) tract (stomach and intestines), and b) hepatobiliary system (liver, gallbladder, and associated ducts) or pancreas.

** Peritoneal inflammation was defined by neutrophil counts >250/mm^3.

*** A majority of patients in this study received computed tomography scans.

doi:10.1371/journal.pone.0153247.t001

Vergidis P et al. PLOS ONE | DOI:10.1371/journal.pone.0153247 April 28, 2016

Preditores de Mortalidade

Table 4. Predictors of 100-day mortality for all subjects with IAC.

Parameter	Non-survivors* (n = 46)	Survivors (n = 117)	Univariate OR (95% CI)	Univariate *P* value	Multivariate OR (95% CI)	Multivariate *P* value
Age, median (interquartile range)	64 (57–77)	58 (46–67)	1.04 (1.01–1.06)	0.002	1.06 (1.03–1.09)	<0.001
Male sex	29 (63)	60 (51)	1.62 (0.80–3.26)	0.18		
Solid organ transplant	9 (20)	11 (9)	2.34 (0.90–6.10)	0.08	3.04 (0.98–9.43)	0.054
Obesity (BMI >30)	15 (33)	36 (31)	1.09 (0.52–2.26)	0.82		
Healthcare-associated disease	39 (85)	94 (80)	1.36 (0.54–3.44)	0.51		
APACHE II score, mean (range)	17 (7–29)	15 (3–29)	1.04 (0.96–1.12)	0.32		
Septic shock	15 (33)	15 (13)	3.29 (1.45–7.48)	0.004	…	…
Presence of abscess	15 (33)	74 (63)	0.28 (0.14–0.58)	0.001	0.25 (0.11–0.57)	0.001
Bacterial co-infection	26 (57)	84 (72)	0.51 (0.25–1.04)	0.06	…	…
C. glabrata infection	11 (24)	32 (27)	0.83 (0.38–1.84)	0.65		
Candidemia	3/36 (8)	5/89 (6)	1.53 (0.35–6.76)	0.57		
Surgical intervention	26 (57)	70 (60)	0.87 (0.44–1.74)	0.70		
Surgical intervention (within 5d)	19 (41)	58 (50)	0.51 (0.23–1.14)	0.34		
Source control intervention (within 5d)	25 (54)	93 (79)	0.38 (0.18–0.76)	0.002	0.23 (0.11–0.57)	0.001
Antifungal treatment (within 5d)	31 (67)	86 (74)	0.74 (0.36–1.56)	0.44		
Infectious disease consultation	21 (46)	58 (50)	0.85 (0.43–1.69)	0.65		

Data are presented in absolute numbers (percentages), unless otherwise indicated. Variables in ellipsis were removed from the multivariable analysis using backward elimination.

*Cause of death: sepsis (20), multi-organ failure (4), heart failure/cardiac event (4), respiratory failure (4), liver failure (2), hemorrhage/ischemia (2), hospice (7), unknown (3)

Abbreviation: OR, odds ratio.

Vergidis P et al. PLOS ONE | DOI:10.1371/journal.pone.0153247 April 28, 2016

Preditores-Sobrevida

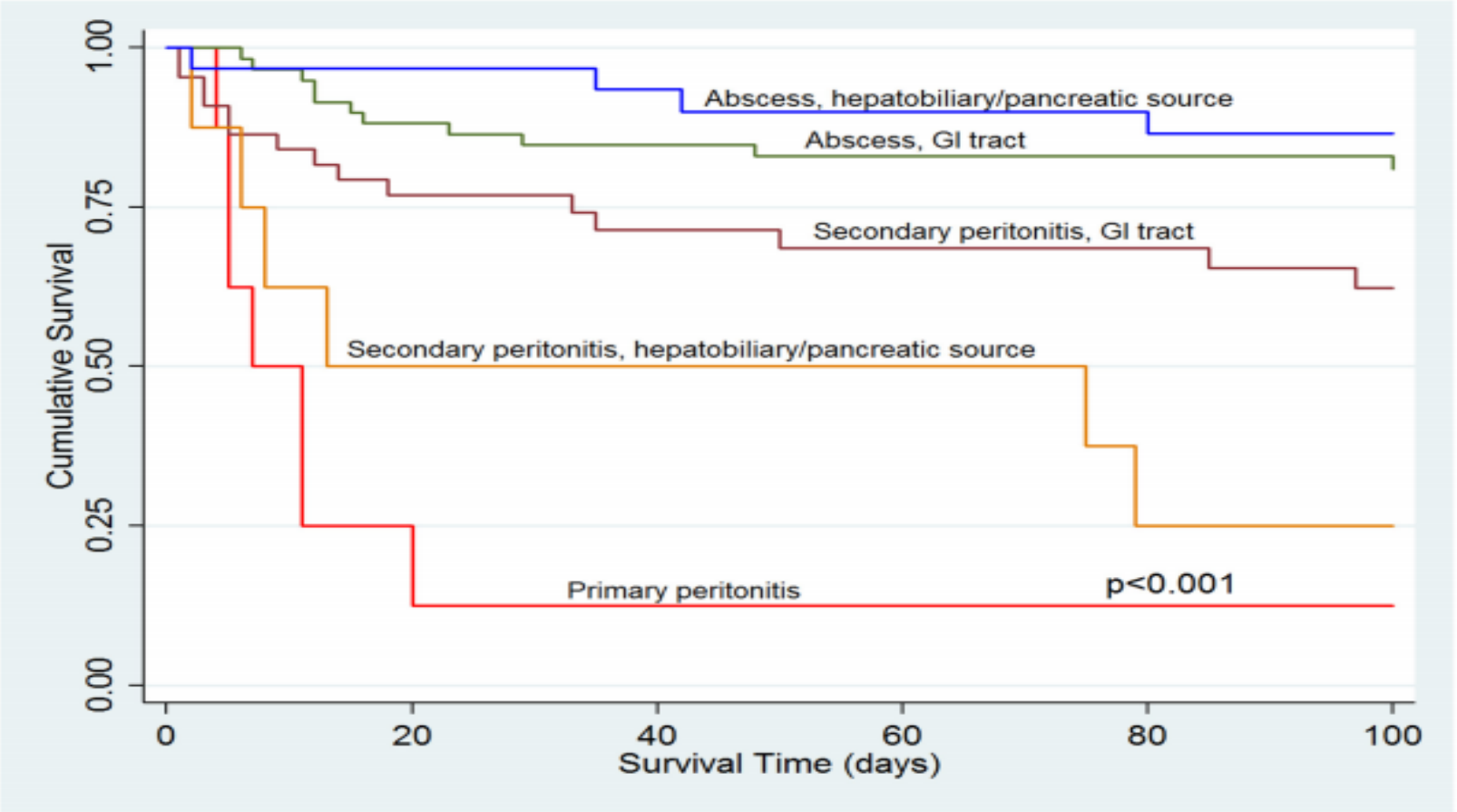


Fig 1. Survival analysis by type of intra-abdominal candidiasis.

Vergidis P et al. PLOS ONE | DOI:10.1371/journal.pone.0153247 April 28, 2016

Intensive Care Med (2015) 41:1601–1610
DOI 10.1007/s00134-015-3866-2

ORIGINAL

Matteo Bassetti
Elda Righi
Filippo Ansaldi
Maria Merelli
Claudio Scarparo
Massimo Antonelli
Jose Garnacho-Montero
Ana Diaz-Martin
Inmaculada Palacios-Garcia
Roberto Luzzati
Chiara Rosin
Leonel Lagunes
Jordi Rello
Benito Almirante
Pier Giorgio Scotton
Gianmaria Baldin
George Dimopoulos
Marcio Nucci
Patricia Munoz
Antonio Vena
Emilio Bouza
Viviana de Egea
Arnaldo Lopes Colombo
Carlo Tascini
Francesco Menichetti
Enrico Tagliaferri
Pierluigi Brugnaro
Maurizio Sanguinetti
Alessio Mesini
Gabriele Sganga
Claudio Viscoli
Mario Tumbarello

A multicenter multinational study of abdominal candidiasis: epidemiology, outcomes and predictors of mortality

- 481 pacientes, 52,4% em UTI
- Candidíase Intra-abdominal
- Duas Síndromes: Peritonites e Abscessos por Candida
- Candida no TGI: 5% `a 41%
- Até 40% de peritonites terciárias com envolvimento de Candida
- Mortalidade de até 60%

Intensive Care Med (2015) 41:1601–1610
DOI 10.1007/s00134-015-3866-2

ORIGINAL

Matteo Bassetti
Elda Righi
Filippo Ansaldi
Maria Merelli
Claudio Scarparo
Massimo Antonelli
Jose Garnacho-Montero
Ana Diaz-Martin
Inmaculada Palacios-Garcia
Roberto Luzzati
Chiara Rosin
Leonel Lagunes
Jordi Rello
Benito Almirante
Pier Giorgio Scotton
Gianmaria Baldin
George Dimopoulos
Marcio Nucci
Patricia Munoz
Antonio Vena
Emilio Bouza
Viviana de Egea
Arnaldo Lopes Colombo
Carlo Tascini
Francesco Menichetti
Enrico Tagliaferri
Pierluigi Brugnaro
Maurizio Sanguinetti
Alessio Mesini
Gabriele Sganga
Claudio Viscoli
Mario Tumbarello

A multicenter multinational study of abdominal candidiasis: epidemiology, outcomes and predictors of mortality

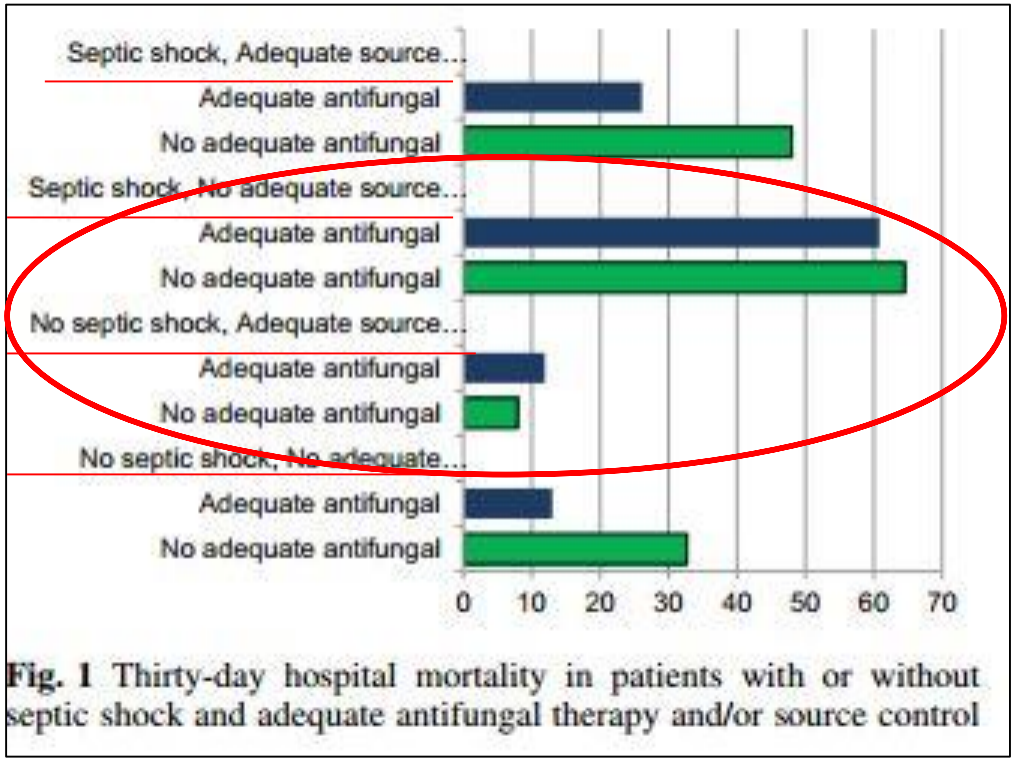


Fig. 1 Thirty-day hospital mortality in patients with or without septic shock and adequate antifungal therapy and/or source control

ESCMID PUBLICATIONS 10.1111/1469-0691.12039

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

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

- Candidemia
- Infecção Urinária
- Endocardite
- Osteomielite
- Ocular
- Meningite

Infecção Intra-abdominal ?

Cornely AO et al. Clin Microbiol Infect 2012;18(7):19-37.

Clinical Infectious Diseases
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]

- **Terapia empírica para pacientes com infecção intra-abdominal e com fatores de risco para Candidemia**
- **Controle do foco: drenagem e/ou desbridamento**
- Equinocandinas como terapia de escolha
- Duração da terapia de acordo com controle do foco e evolução clínica

VIII. What Is the Treatment for Intra-abdominal Candidiasis?

Recommendations

54. Empiric antifungal therapy should be considered for patients with clinical evidence of intra-abdominal infection and significant risk factors for candidiasis, including recent abdominal surgery, anastomotic leaks, or necrotizing pancreatitis *(strong recommendation; moderate-quality evidence).*
55. Treatment of intra-abdominal candidiasis should include source control, with appropriate drainage and/or debridement *(strong recommendation; moderate-quality evidence).*
56. The choice of antifungal therapy is the same as for the treatment of candidemia or empiric therapy for nonneutropenic patients in the ICU (See sections I and V) *(strong recommendation; moderate-quality evidence).*
57. The duration of therapy should be determined by adequacy of source control and clinical response *(strong recommendation; low-quality evidence).*

Pappas PG et al. Clin Infect Dis 2016:62:e1-50

The Brazilian Journal of
INFECTIOUS DISEASES
www.elsevier.com/locate/bjid

Original article

Brazilian guidelines for the management of candidiasis – a joint meeting report of three medical societies: Sociedade Brasileira de Infectologia, Sociedade Paulista de Infectologia and Sociedade Brasileira de Medicina Tropical☆

Arnaldo Lopes Colombo[a,*,1], *Thaís Guimarães*[b,1], *Luis Fernando Aranha Camargo*[a,1], *Rosana Richtmann*[c,1], *Flavio de Queiroz-Telles*[d,1], *Mauro José Costa Salles*[e,1], *Clóvis Arns da Cunha*[f,1], *Maria Aparecida Shikanai Yasuda*[g,1], *Maria Luiza Moretti*[h,1], *Marcio Nucci*[i,1]
Marcio Nucci[i,1]

- Abordagem direta do tema
- Controvérsias na interpretação de isolados de Candida em secreções do TGI
- **Avaliar ``caso a caso``**
- Terapia: Anfotericina B, Fluconazol e Equinocandinas

``Take Home Messages``

- Assunto ``quase resolvido``
- **Síndrome Infecciosa bem definida**
- Alta morbimortalidade
- Tratamento multimodal
- **Controle do foco**
- **Terapia antifúngica dirigida em peritonites secundárias e isolamento de Candida**
- Terapia antifúngica empírica nas peritonites terciárias
- **Equinocandinas**
- Papel dos biomarcadores (?)
- Profilaxia (?)