Clostridium difficile NA REALIDADE BRASILEIRA

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TRATAMENTO

TRATAMENTO DIARRÉIA POR *C. DIFFICILE*

- vancomicina,
- metronidazole,
- fidaxomicina,
- acido fusidico,
- nitazoxanida,
- teicoplanina,
- rifampicina,
- rifaximina,
- bacitracina

Farmácia de manipulação

Vanco 125 mg/cp
Labs Tabajara – FUNCIONA!

Cochrane Database of Systematic Reviews, Issue 4, 2011

ANTIBIOTIC TREATMENT FOR *C. DIFFICILE*-ASSOCIATED DIARRHEA IN ADULTS
Nelson RL et al

Conclusões

• As evidências atuais não esclarecem se casos leves necessitam tratamento.

• Em portadores assintomáticos o placebo foi melhor do que vanco ou metronidazole para cura bacteriológica no follow-up.

• Se a opção for pelo tratamento, 2 propósitos devem ser contemplados: a melhora do paciente e a prevenção da disseminação da infecção do *C. difficile* para outros pacientes.

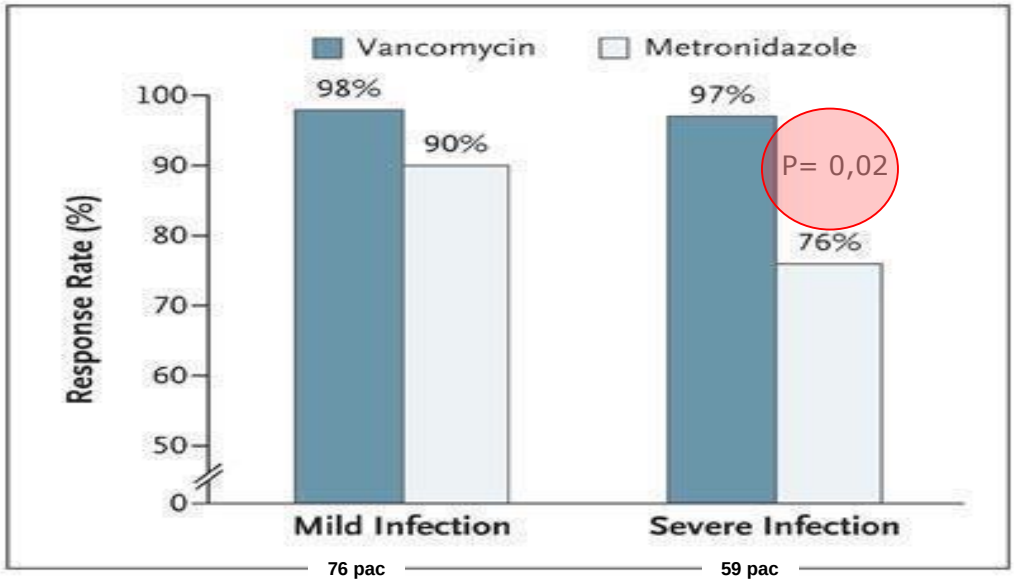
• A Teicoplanin parece ser a melhor opção porque é melhor do que a Vanco para a cura bacteriológica e marginalmente superior para a cura clínica.

? Porque não usamos?

A Comparison of Vancomycin and Metronidazole for the Treatment of *Clostridium difficile*–Associated Diarrhea, Stratified by Disease Severity

Clinical Infectious Diseases 2007; 45:302–7

Fred A. Zar,[1] Srinivasa R. Bakkanagari,[2] K. M. L. S. T. Moorthi,[2] and Melinda B. Davis[1]
[1]University of Illinois at Chicago, Chicago, and [2]Saint Francis Hospital, Evanston, Illinois



Leve a moderada:
leuco < 15 K,
cret < 1,5 x basal

Table 3. Rates of relapse of *Clostridium difficile*–associated diarrhea by disease severity and treatment.

Disease severity	No. of patients who experienced relapse/no. of patients who were cured (%)			P^a
	Mtz group	Vm group	Total	
Mild	3/37 (8)	2/39 (5)	5/76 (7)	.67
Severe	6/29 (21)	3/30 (10)	9/59 (15)	.30
All	9/66 (14)	5/69 (7)	14/135 (10)	.27

NOTE. Mtz, metronidazole; Vm, vancomycin.
[a] *P* values were calculated using Fisher's exact test.

Fatores de risco independentes para desenvolvimento de *C diff* grave

- Idade > 80 a
- F res > 20/min
- F card> 90 / min
- Leucócitos < 4 K ou > 20K
- PCR elevado (> 150mg/L)
- hipoalbuminemia (albumina <2,5 mg/L)
- Uréia elevada

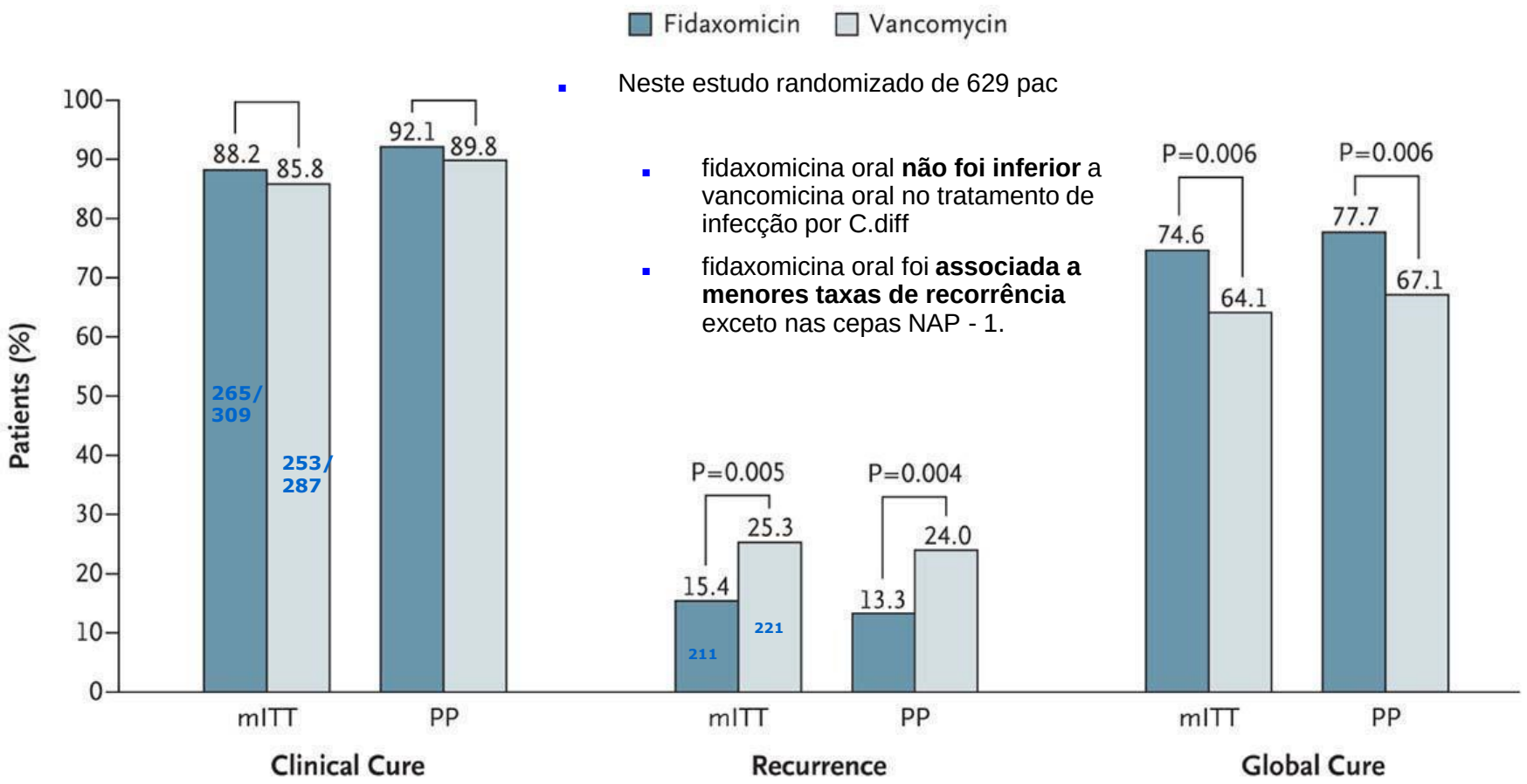
PODEM JUSTIFICAR TRATAMENTO E MONITORIZAÇÃO MAIS AGRESSIVOS

Factors Associated With Complications of Clostridium difficile Infection in a Multicenter Prospective Cohort
Chakra et al, 2015

Original Article

Fidaxomicin versus Vancomycin for *Clostridium difficile* Infection

Rates of Primary and Secondary End Points.

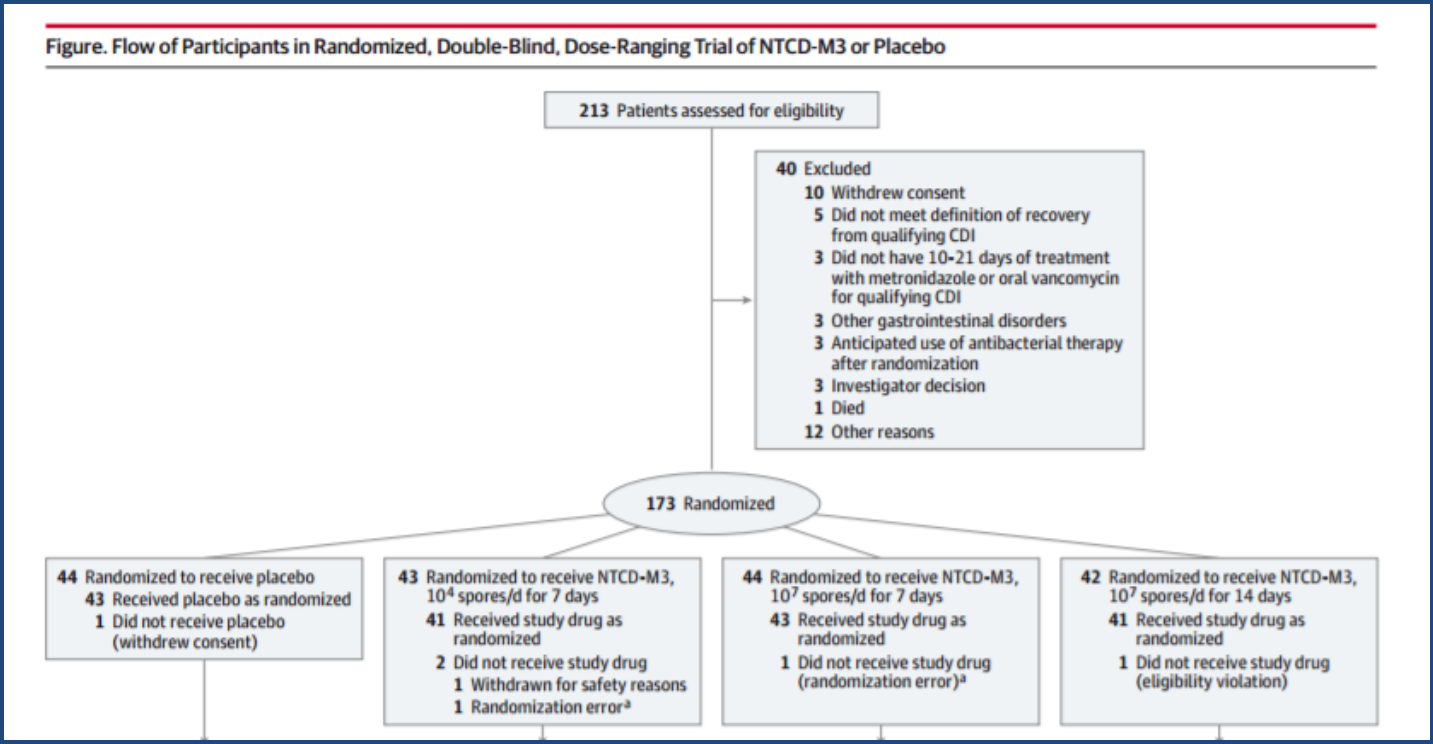


- Neste estudo randomizado de 629 pac
  - fidaxomicina oral **não foi inferior** a vancomicina oral no tratamento de infecção por C.diff
  - fidaxomicina oral foi **associada a menores taxas de recorrência** exceto nas cepas NAP - 1.

Louie TJ et al. N Engl J Med 2011;364:422-431

The NEW ENGLAND JOURNAL of MEDICINE

Administration of Spores of Nontoxigenic **Clostridium difficile** Strain M3 for Prevention of Recurrent *C difficile* Infection A Randomized Clinical Trial



Conclusão

Entre pacientes que se recuperaram clinicamente de um episódio de C diff após tratamento com vanco e/ou metronidazol, o uso de esporos de uma cepa não toxigêncica de C diff (NTCD-M3) foi bem tolerado e seguro. Quando a cepa NTCD – M3 colonizou o trato GI, reduziu significantemente a recorrência de C difficile (2%) versus 31% nos que não foram colonizados apesar de receberem a cepa, versus 30% dos que receberam placebo.

TRATAMENTO – Transplante fecal

TABLE 1

E van Nood (e.vannood@amc.nl)[1], P Speelman[1], E J Kuijper[2], J J Keller[3]

Faecal therapy for recurrent *C. difficile* infections: overview of the literature

Year	Patients (male/female)	Mean age	No. of relapses	Entry diagnosis	Cured (%)	Follow-up	Donor related to recipient?	Prepared with whole bowel lavage	No of faecal infusions	Amount of faeces	Route of installation		Reference
											Upper GI	Lower GI	
1958	4 (3/1)	56	*	PMC	4 (100)	10 days	Nd	No	1-3	Nd	0	4 (e)	[15]
1981	16 (7/9)	56	*	PMC	13 (81)	5 days-3 years	If possible	No	1-24	Nd	1	15	[34]
1984	1 (0/1)	65	6	CDI	1 (100)	9 months	Spouse	No	2x2	Nd	0	1	[35]
1989	2 (1/1) 1	60	3	CDI	1 (50)	6 months	Spouse/daughter	No	1	50 g	0	2	[36]
1991	1 (0/1)	64	7	CDI	1 (100)	3 days	Spouse	No	1	10 g	1	0	[37]
1994	7**	56	1-4	CDI	7 (100)	2 years	Spouse/relative	No	3	200 ml	0	7	[38]
1998	18**	Md	Md	CDI	15 (83)	Md	No	Md	1	Md	1	17	[39]
1999	32 (14/18)	27-89	Md	AAD	32 (100)	4-6 weeks	No	Md	1-2	5-10 g	0	32	[40]
2000	1 (0/1)	60	>5	CDI	1 (100)	1-6 months	Spouse	Yes	1	500 ml	0	1	[41]
2002	6 (1/5)	53	2-6	CDI/PMC	6 (100)	9-50 months	Yes	no	1	30 ml	0	6	[42]
2003	18 (5/13)	73	2-7	CDI	15 (83)	90 days	15 yes/3 no	No	1	30 g	18	0	[43]
2003	24 (11/13)	19-59	Md	CDI	20 (83)	Nd	Related and non-related donors	Yes	1-10	200-300 g	8	16	[44]
2006	5 (0/5)	82	>2	CDI	5 (100)	2,5-21 months	No	No	1	30 ml	0	5	[45]
2007	16 (5/11)	11-87	Md	CDI	15 (94)	4-6 weeks	Related and non-related donors	Yes	1-24	200-300 g	0	16	[46]
2008	7 (4/3)	67	3	CDI	7 (100)	30 days-1 year	6 yes/1 no	Yes	1-3	50-100 g	3	4	[47]
2008	1 (1/0)	69	1	CDI	1 (100)	2 days	Yes	No	1	45 g	0	1	[48]
	159				144/159 (91)						32	127	Total

AAD: antibiotic-associated diarrhoea; CDI: C. difficile-associated disease; GI: gastrointestinal tract; Md: missing data; Nd: not determined; PMC: pseudomembranous colitis

*unclear, since C. difficile at that time was not identified as the causative organism, so adequate antibiotics where not given.

** Sex unknown.

1- two patients treated with a faecal enema of which one failed. The failing patient and four others were treated with a new enema, consisting of a bacterial culture.

TRATAMENTO – Transplante fecal

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

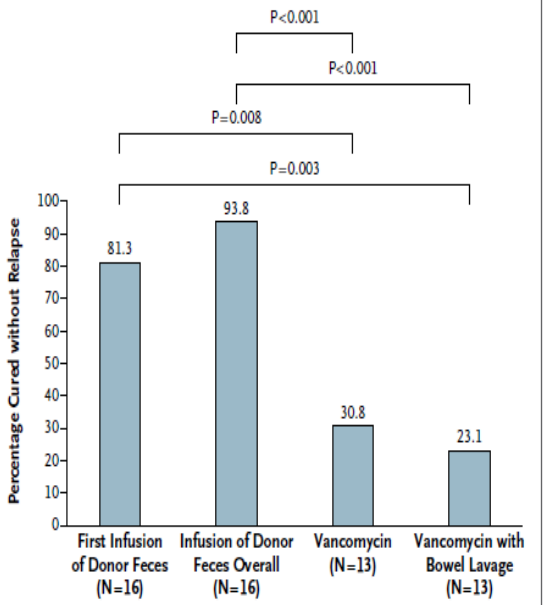


Figure 2. Rates of Cure without Relapse for Recurrent *Clostridium difficile* Infection.

Shown are the proportions of patients who were cured by the infusion of donor feces (first infusion and overall results), by standard vancomycin therapy, and by standard vancomycin therapy plus bowel lavage.

Conclusão:

Pacientes com infecção por C. difficile recorrente podem se beneficiar do transplante de fezes em comparação com o uso de vancomicina porém três grupos importantes foram excluídos (imunodeprimidos, UTI, em uso de outros antibióticos)

Sugestão: iniciar o transplante após a segunda recorrência

O estudo foi interrompido pois o benefício do transplante fecal foi muito maior do que vancomicina/lavagem intestinal.

N ENGL J MED 368;5 NEJM.ORG JANUARY 31, 2013

90. Fecal Microbial Transplantation: Highly Effective Treatment for Severe Clostridium difficile Infection

Part of Session: 28. New Considerations in C. difficile Prevention and Treatment

9:30 a.m.

LINDA BOBO, MD, PHD; Southern Illinois Healthcare/Medical Service, Carbondale, IL, ERICA KAUFMAN, MD; Southern Illinois Healthcare/Medical Services, Carbondale, IL and DIANA BIGGS, MT, ASCP, SM; Southern Illinois Healthcare, Herrin, IL

Background: Severe *Clostridium difficile* infection (CDI) has markedly increased. Age>60 years and multiple co-morbidities are positive predictors for poor CDI outcome. The purpose of this pilot study was to evaluate fecal microbial transplantation (FMT) in patients failing *C. difficile* antibiotic treatment.

Methods: Hospitalized FMT recipients (n=21) had: >3 watery stools or >200 ml/day output from ostomy, tested positive by *C. difficile* toxin B PCR or toxin A/B EIA, and were deteriorating clinically while on oral vancomycin +/- intravenous metronidazole. Suitable recipients weren't neutropenic, or on chemo/radiation therapy. Low risk donor blood and stool were tested for pathogens. A dedicated, screened donor (17/21) was used if no other available suitable donor. Fresh, filtered stool was used for transplantation, and was introduced via nasogastric tube followed by two rectal retention enemas. Signed, informed consent was obtained from all recipients or proxies. Enteritis and colitis were verified by computerized abdominal tomography, and pseudomembranous colitis by colonoscopy if needed.

Results: Recipient characteristics are in Table 1. There were no adverse events related to transplant, and cure at 30 days was 20/21 (95.2%). Relationship of FMT attempts vs: Horn Index ($p=0.1272^1$, $X^2=5.700,3$), disease severity (more attempts $p=0.0419$, $X^2=6.343,2$), and GI surgery ($p=0.1473$ $X^2=2.100,1$). Increased age was related to increased diarrhea duration ($p=0.0418$ $X^2=32.15,20$).

Conclusion: FMT of hospitalized patients with severe CDI, multiple co-morbidities, advanced age, and surgically altered gastrointestinal tracts, is safe and efficacious for those failing conventional CDI treatment. The data suggest that FMT should be evaluated as a primary treatment in these patients.

Idade média 70 a

Conclusão

Transplante de Microbiota Fecal de pacientes internados com C diff grave, múltiplas comorbidades, idade avançada e trato gastrointestinal alterado cirurgicamente é seguro e eficaz para aqueles que falharam com o tratamento convencional (vanco e/ou metronidazol) – 20/21 pacientes. Os dados sugerem que o Transplante de Microbiota Fecal deveria ser avaliado como tratamento primário nestes pacientes

ECCMID, 2013

CDAD
Quando indicar colectomia?

- **Megacolon tóxico**
- **Perfuração colon**
- **Abdome agudo**
- **Choque séptico com drogas vasopressoras**
- **Lactato > 20mg/100 ml**
- **Leucócito > 20.000/mm3**

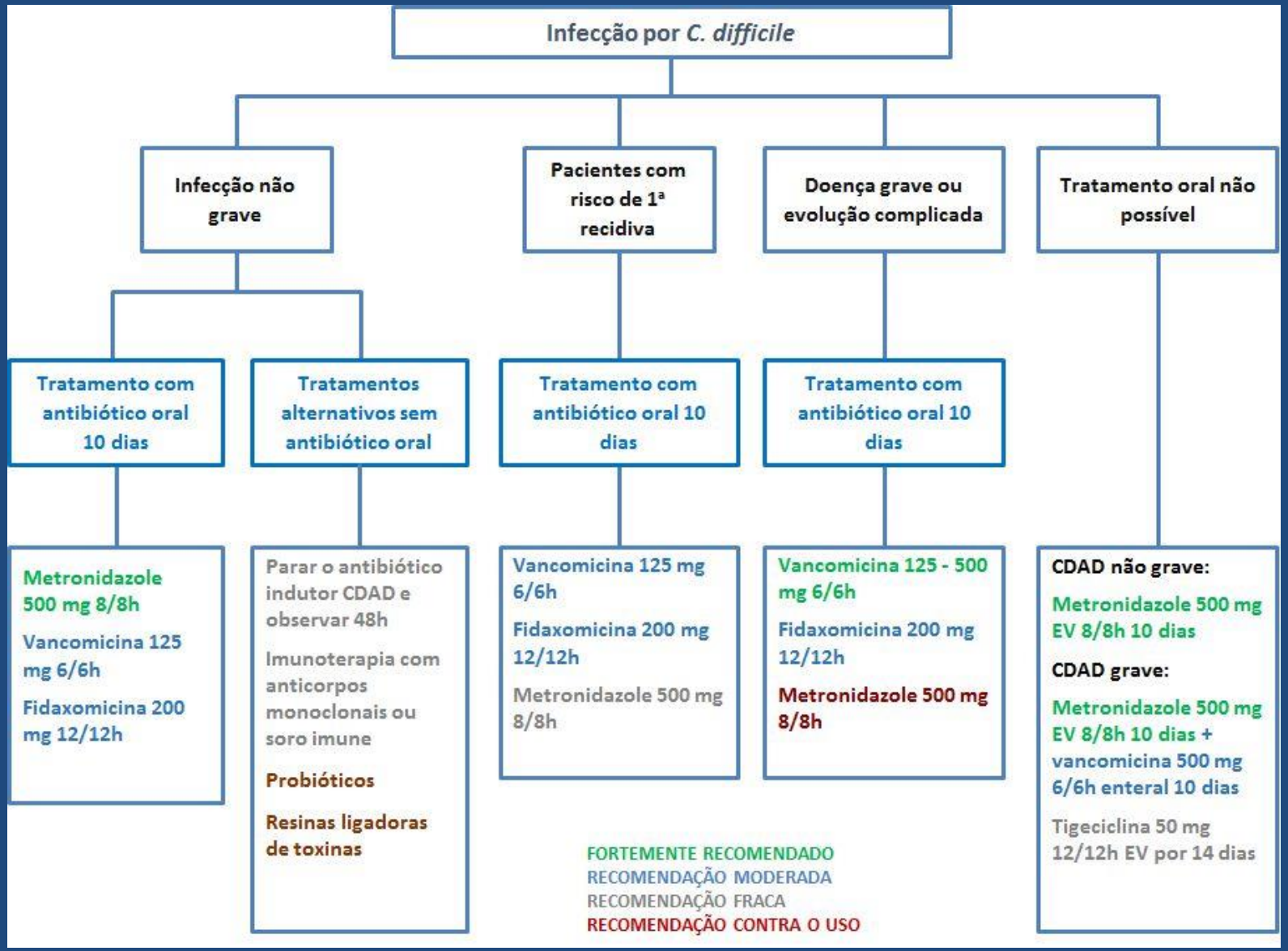
Lamontagne, F et al
Impact of Emergency Colectomy on Survival of Patients With Fulminant Clostridium difficile Colitis During an Epidemic Caused by a Hypervirulent Strain
Annals of Surgery, 2007

European Society of Clinical Microbiology and Infectious Diseases:

Update of the treatment guidance document for Clostridium difficile infection

S. B. Debast1,M. P. Bauer2, E. J. Kuijper3, on behalf of the Committee*

1) Department of Medical Microbiology, Radboud University Medical Center, Nijmegen, Departments of 2) Infectious Diseases and 3) Medical Microbiology, Centre for Infectious Diseases, Leiden University Medical Centre, Leiden, the Netherlands



Clinical Microbiology and Infection, Volume 20 Supplement 2, March 2014

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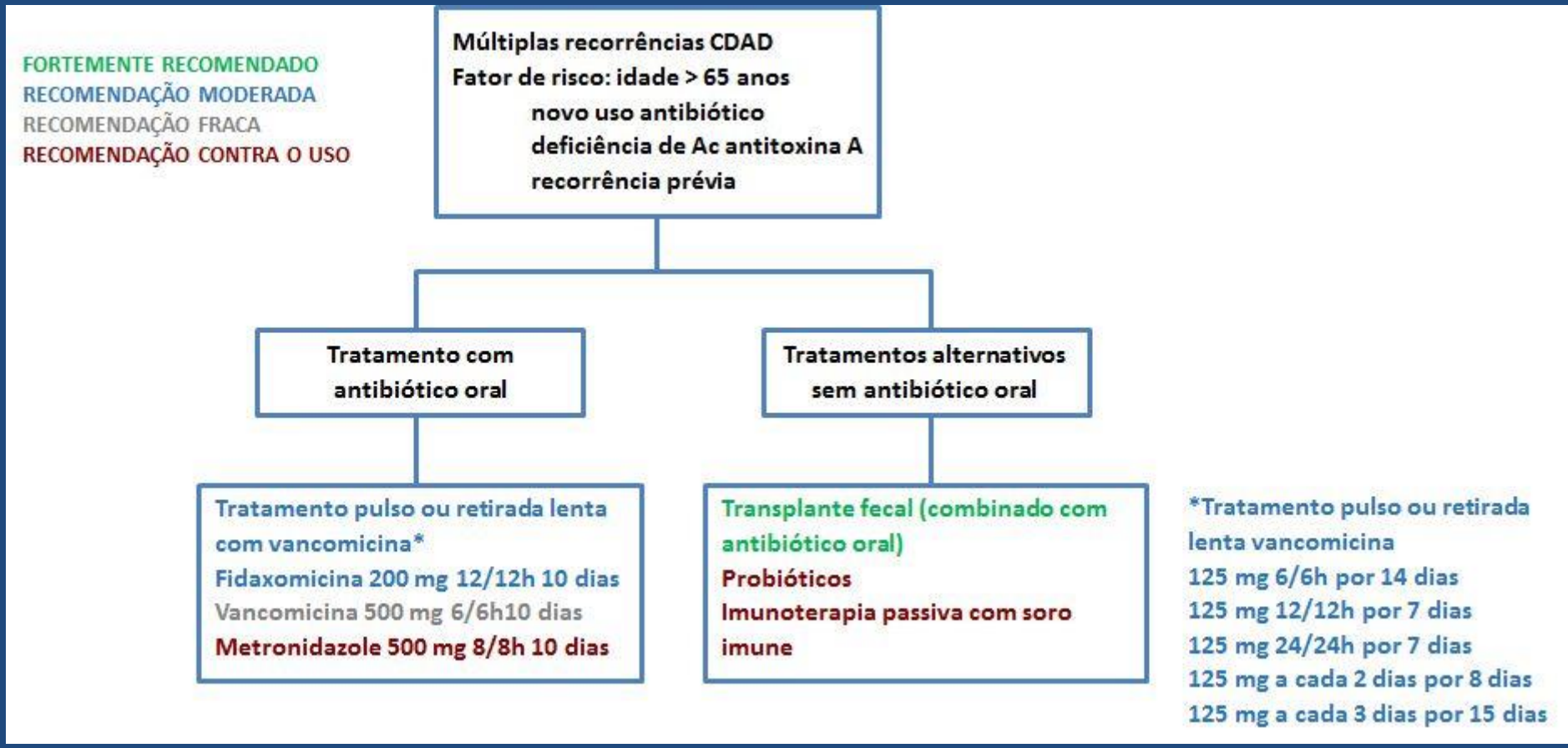

Clinical Microbiology and Infection, Volume 20 Supplement 2, March 2014

Clostridium difficile — More Difficult Than Ever

Ciáran et al N Engl J Med, 359(18):1932-1940,October 30, 2008

Obrigada

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H Sírio Libanes