

XI CURSO GIMUR

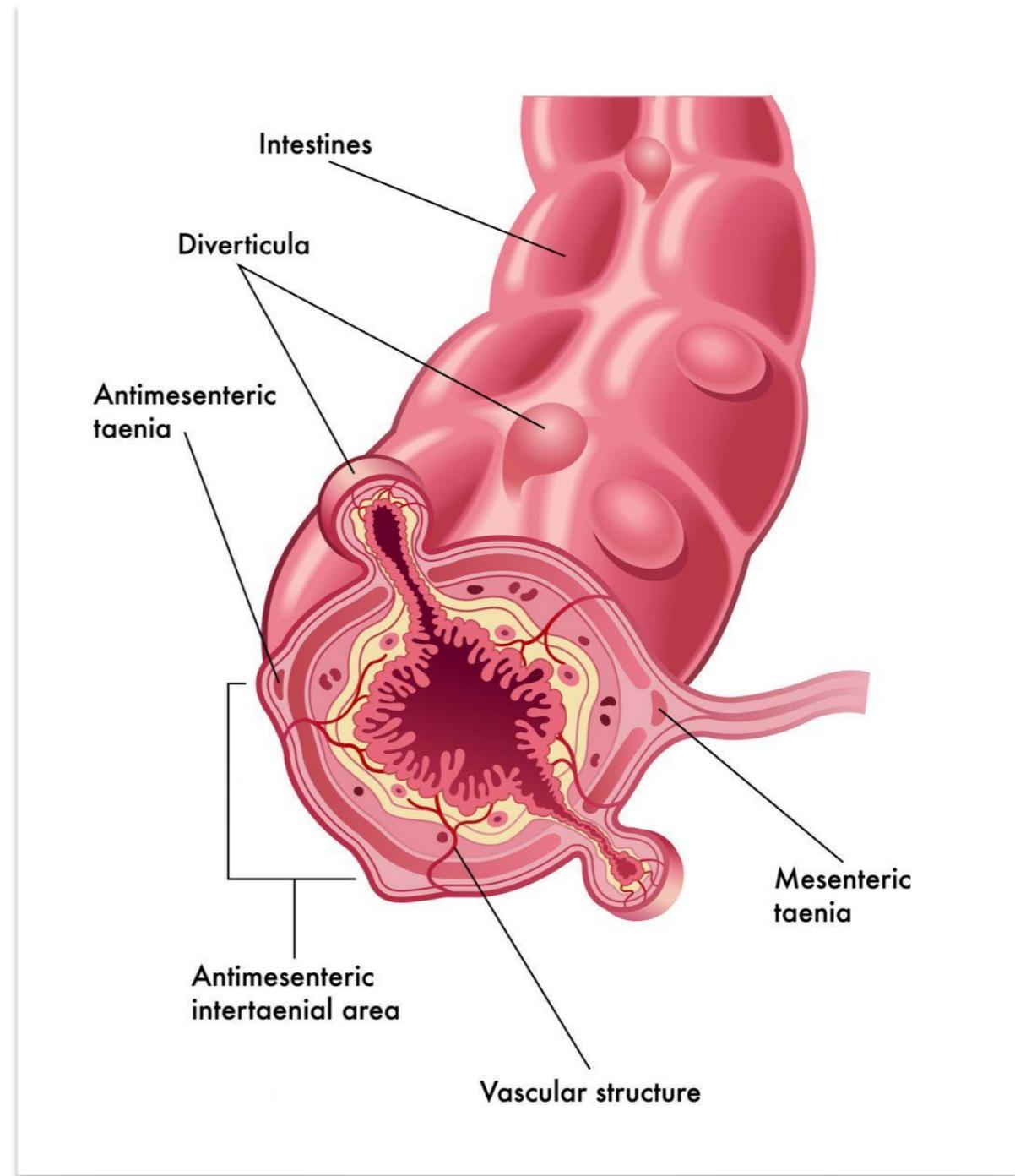
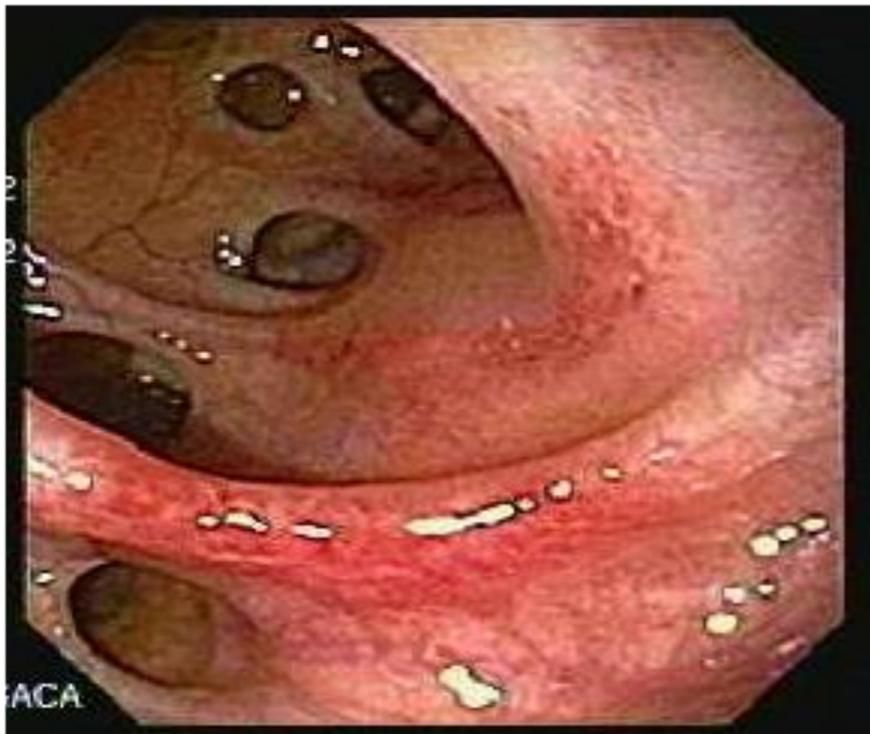
DIVERTICULITIS AGUDA

Jordi Roura Onaindia

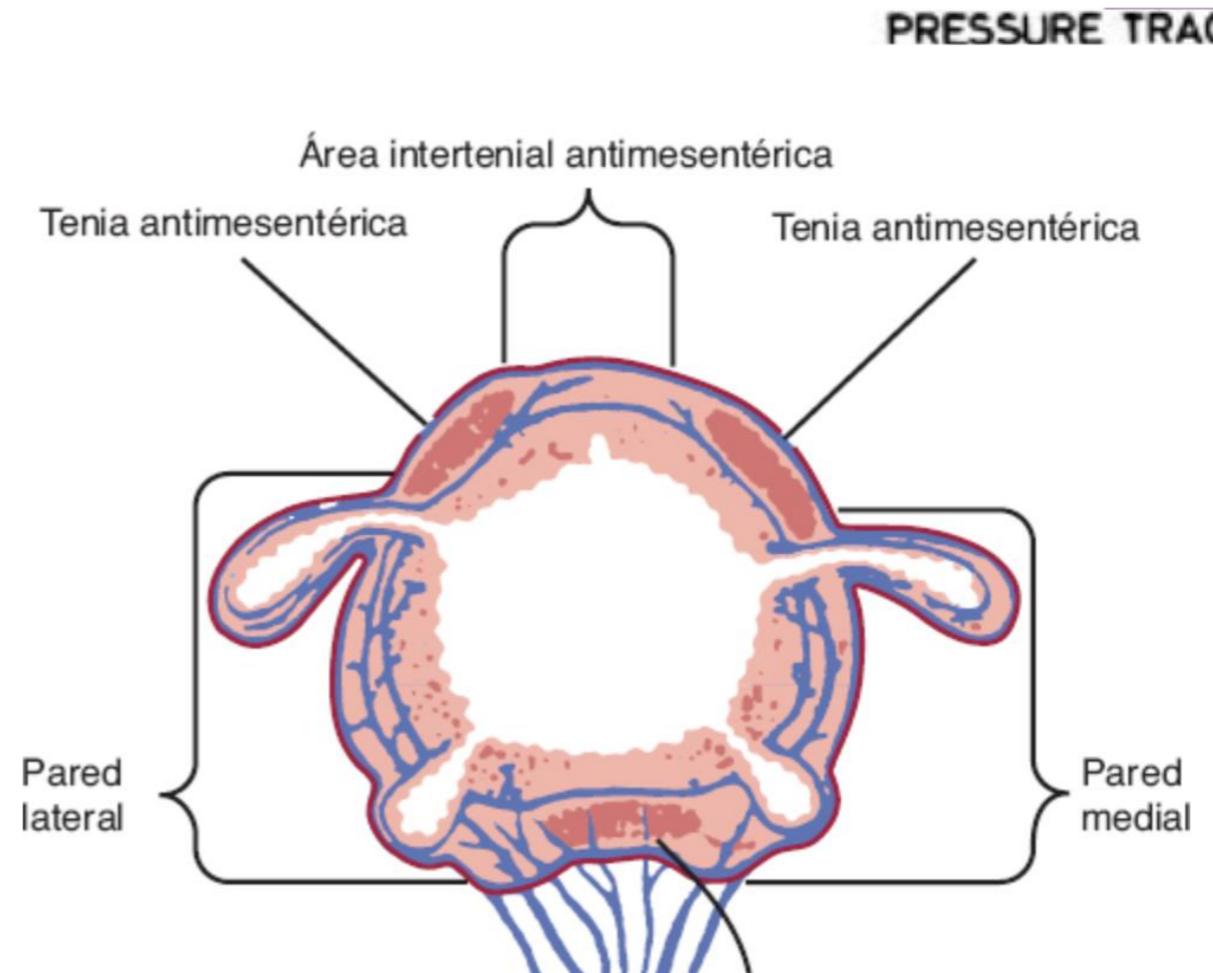
Médico Adjunto Servicio de Cirugía General y Digestiva HUGC

DEFINICIÓN

Abertura anormal o bolsa que se abre desde una víscera hueca



Clásico



Colorectal Dis. 2017 Jun;19(6):O168-O176. doi: 10.1111/codi.13692.

Limited evidence of abnormal intra-colonic pressure profiles in diverticular disease - a systematic review.

Jaung R¹, Robertson J¹, O'Grady G¹, Milne T¹, Rowbotham D², Bissett IP^{1,3}.

Herniación de la mucosa

PATOGENÉNESIS

Actual

MOTILIDAD

INFLAMACIÓN

Fibra



5 ASA

MICROBIOTA

Bifidobacterium longum y *animalis*

Rifaximin
Probióticos

HIPERSENSIBILIDAD

Mayo Clin Proc. 2016 Aug;91(8):1094-104. doi: 10.1016/j.mayocp.2016.03.012. Epub 2016 May 5.

Diverticulosis and Diverticulitis.

Feuerstein JD¹, Falchuk KR².

Diverticular Disease as a Chronic Illness:
Evolving Epidemiologic and Clinical Insights

Lisa L. Strate, MD, MPH¹, Rusha Modi, MD², Erica Cohen, MD³ and Brennan M.R. Spiegel, MD, MSHS²⁻⁵

Am J Gastroenterol 2012; 107:1486-1493; doi:10.1038/ajg.2012.194; published online 10 July 2012

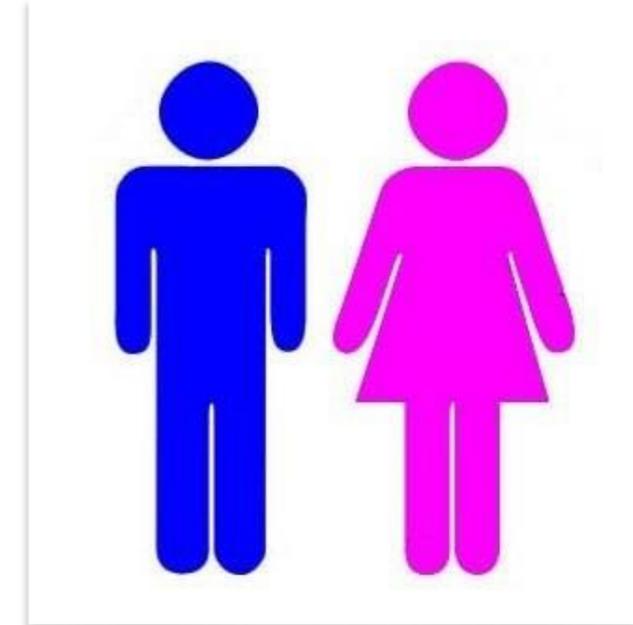
EPIDEMIOLOGÍA

M 98,6/100.000 vs H 76,3/100.000 <50 se invierte

Wheat CL, Strate LL. Trends in hospitalization for diverticulitis and diverticular bleeding in the United States from 2000 to 2010. *Clin Gastroenterol Hepatol.* 2016;14(1): 96-103.

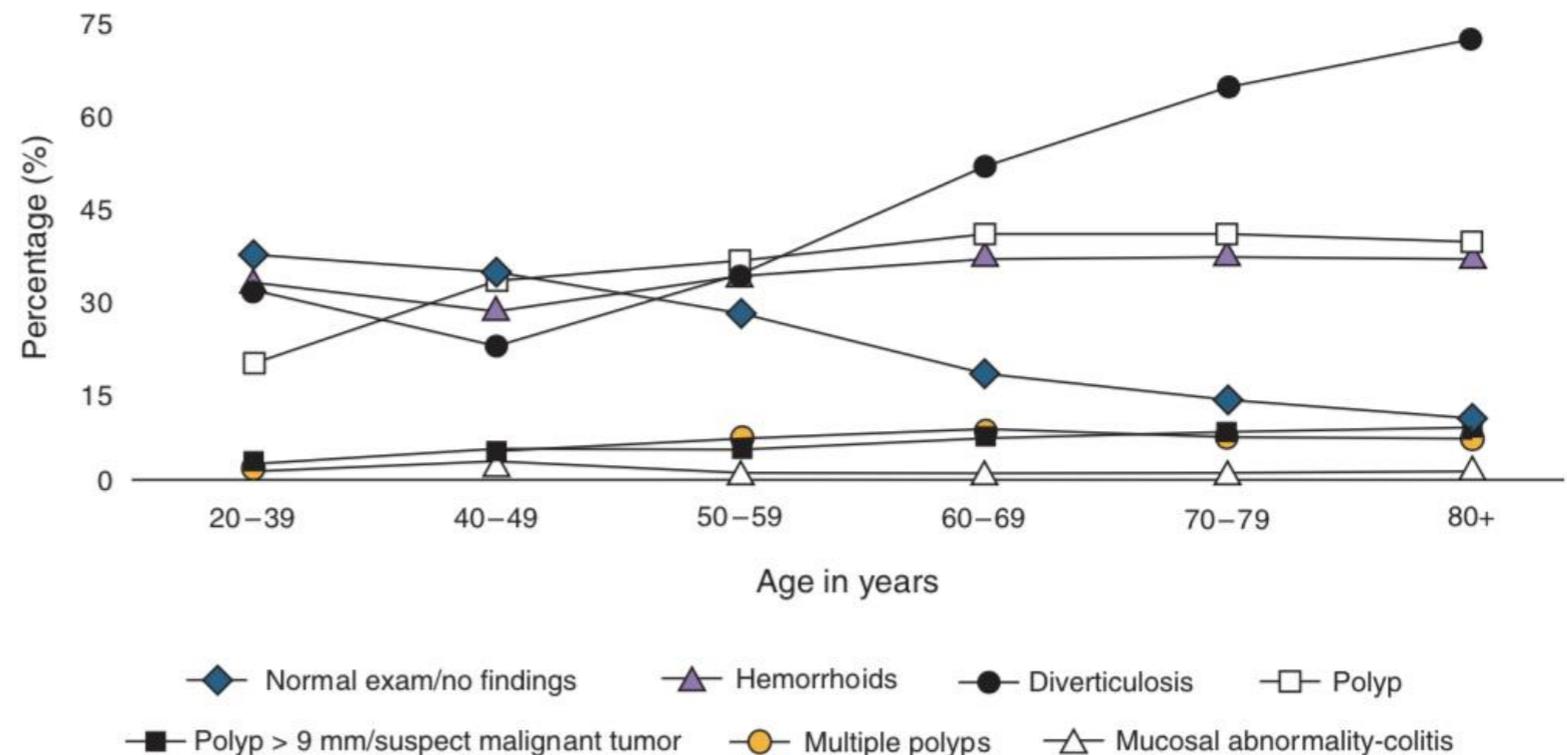
1998-2005 aumento 26% (18-44 años 82%)

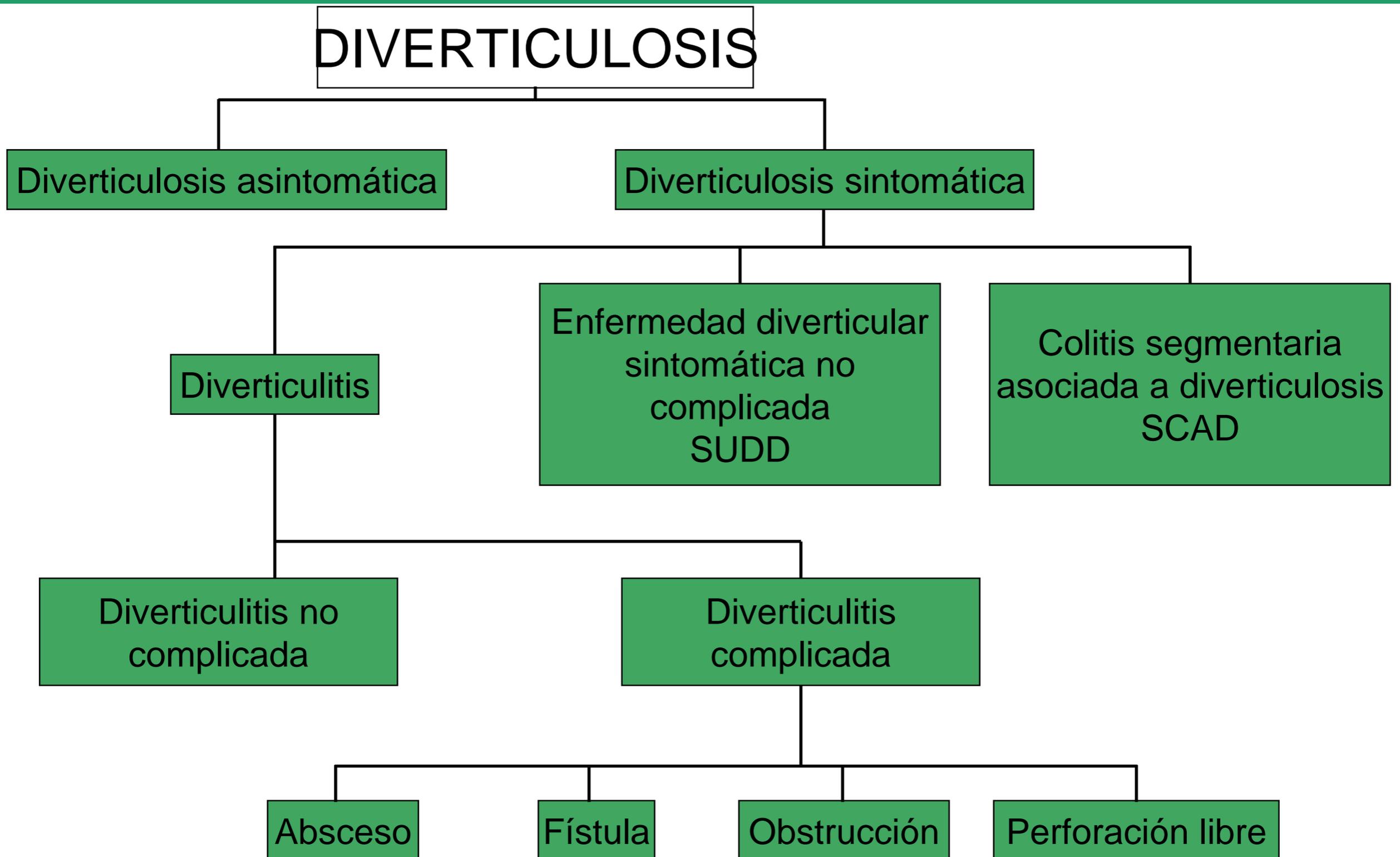
Masoomi H, Buchberg BS, Magno C, et al. Trends in diverticulitis management in the United States from 2002 to 2007. *Arch Surg.* 2011;146:400-406.



DIVERTICULOSIS

>50% de los mayores de 50 años
70% de los mayores de 80 años





Diverticular Disease: An Update on Pathogenesis and Management

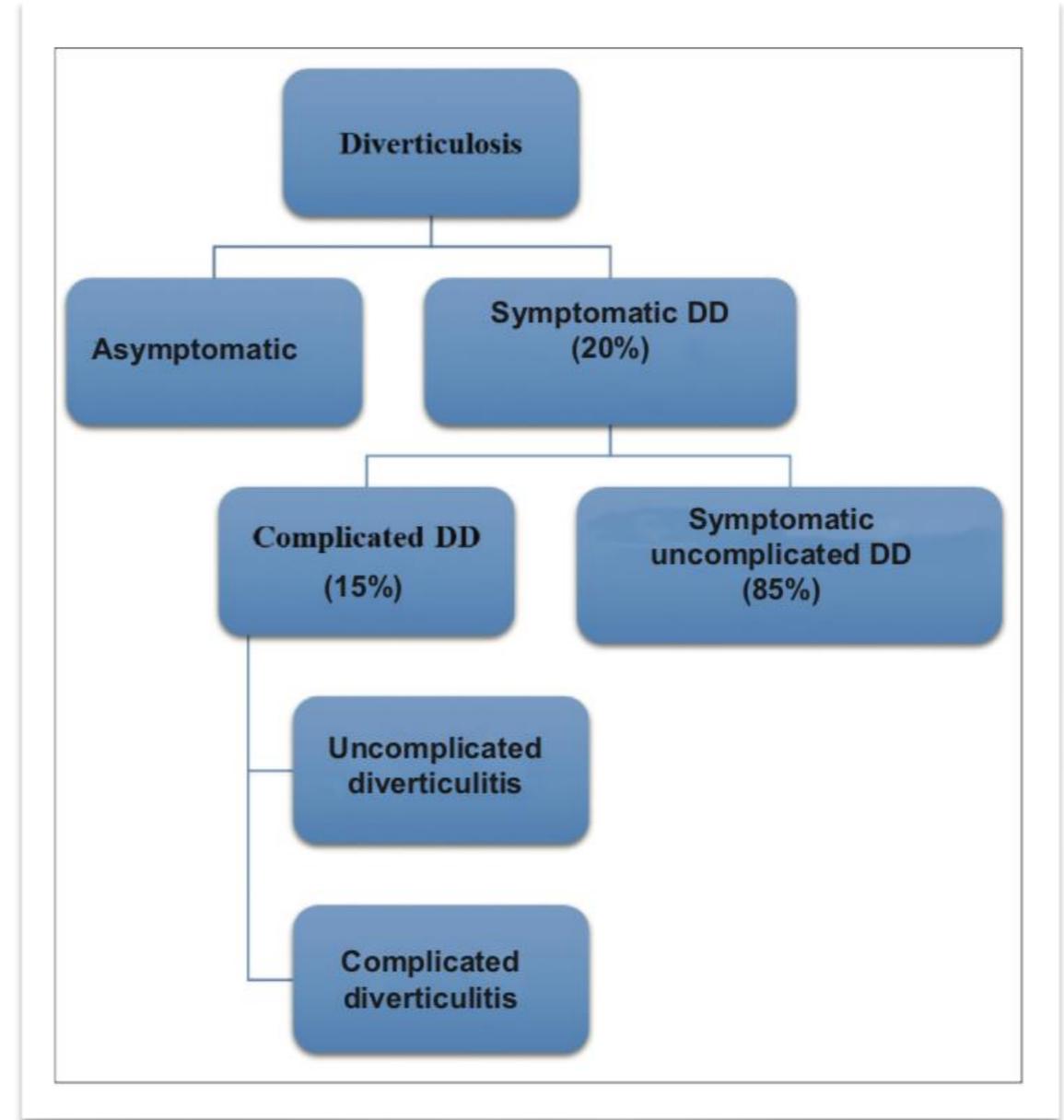
Mona Rezapour¹, Saima Ali², and Neil Stollman³ *Gut and Liver, Published online May 12, 2017*

DIVERTICULITIS AGUDA

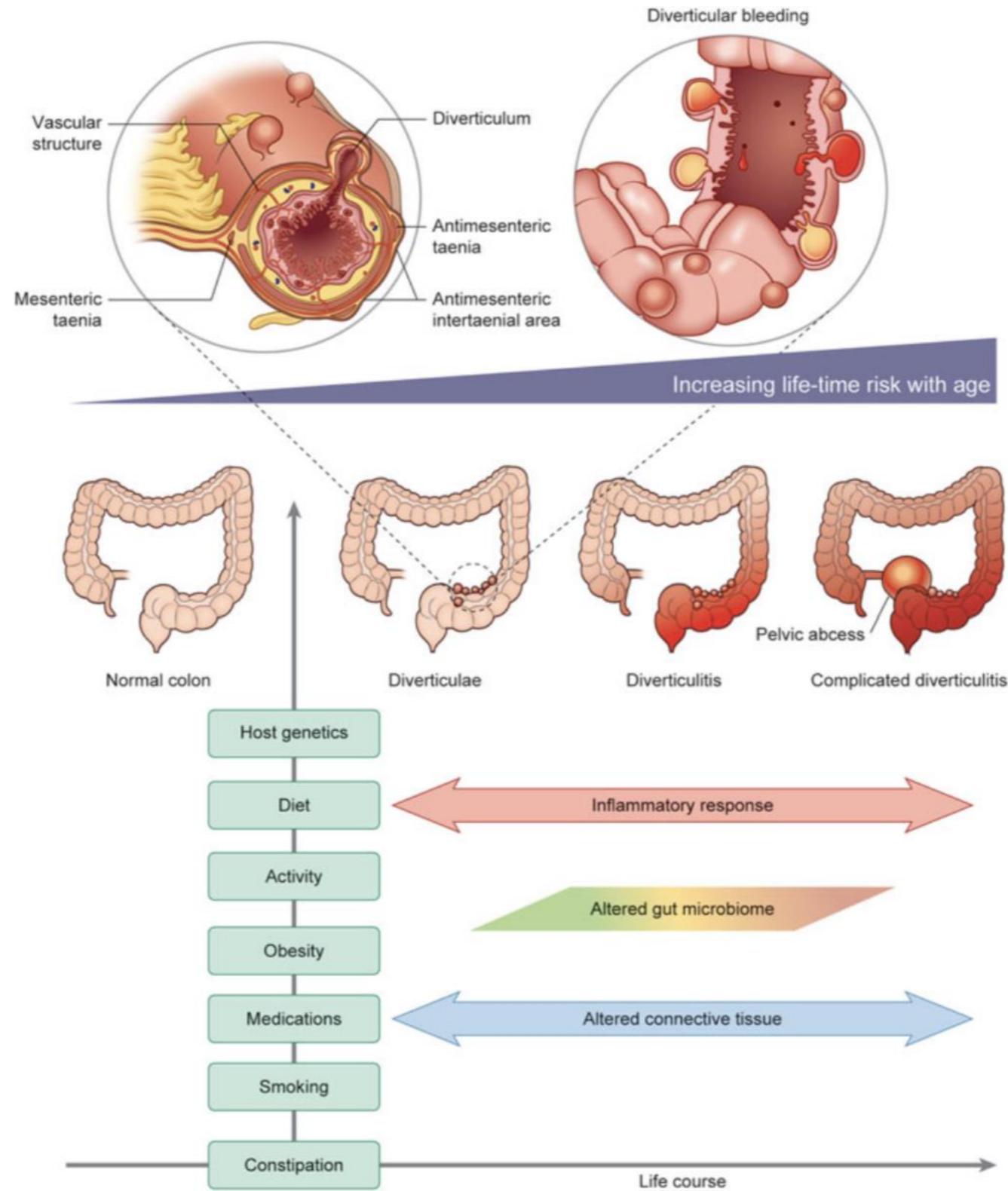
15-20% de los pacientes con diverticulosis

Estudios recientes señalan incidencia sobre no sería tan alta el 5%*

*Strate LL, Modi R, Cohen E, Spiegel BM. Diverticular disease as a chronic illness: evolving epidemiologic and clinical insights. Am J Gastroenterol. 2012;107(10):1486-1493.



FISIOPATOLOGÍA DIVERTICULITIS



2 ESCENARIOS

PACIENTE ESTABLE

Dolor cuadrante inferior izquierdo



Fiebre o febrícula



Síntomas urinarios
Truco



ABDOMEN AGUDO

Dolor cuadrante inferior izquierdo o generalizado

Temperatura $< 36^{\circ}\text{C}$ o $> 38^{\circ}\text{C}$

Frecuencia cardíaca > 90 latidos/min

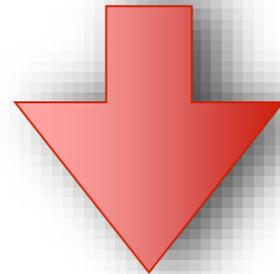
Frecuencia respiratoria > 20 rpm o $\text{PaCO}_2 < 32$ mm Hg

Leucocitos en sangre $> 12 \times 10^9/\text{L}$, o $< 4 \times 10^9/\text{L}$

75%-85% de los episodios de diverticulitis

Reacción inflamatoria limitada localmente

DIVERTICULITIS NO COMPLICADA

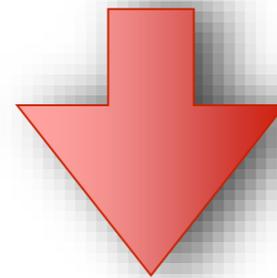


DIAGNOSTICO DIFERENCIAL

ESTUDIOS COMPLEMENTARIOS

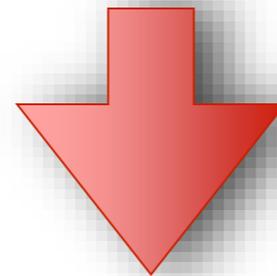
20% de los episodios de diverticulitis

Reacción inflamatoria GENERALIZADA



DIVERTICULITIS COMPLICADA

Resucitación



DIAGNOSTICO DIFERENCIAL

ESTUDIOS COMPLEMENTARIOS

DIAGNÓSTICO DIFERENCIAL

APENDICITIS

PATOLOGÍA
GINECOLÓGICA

TORSIÓN APÉNDICE
EPIPLOICO

NEFROLITIASIS CON O SIN
INFECCIÓN URINARIA

CANCER DE COLON

OCCLUSIÓN INTESTINAL

ENFERMEDAD INFLAMATORIA

COLITIS (isquémica, infecciosa)

COLON IRRITABLE

PATOLOGÍA
VASCULAR

ISQUEMIA
MESENTÉRICA

DIAGNÓSTICO

- HISTORIA CLÍNICA
- EXAMEN FÍSICO
- LABORATORIO
 - Hemograma
 - Sedimento
 - PCR (150mg/l)
- RADIOLOGÍA SIMPLE

Recomendación 1C



IMAGEN

- TC ABDOMINAL SENSIBILIDAD 98% ESPECIFICIDAD 99%
- RESONANCIA SENSIBILIDAD 94% ESPECIFICIDAD 92%
- ECO ABDOMINAL PRECISIÓN DIAGNOSTICA 97%

Recomendación 1B

Recomendación 1C

Van Randen A, Lameris W, van Es HW et al (2011) A comparison of the accuracy of ultrasound and

computed tomography in common diagnoses causing acute abdominal pain. Eur Radiol 21(7):1535–1545

Contemporary Review of Risk-Stratified Management in Acute Uncomplicated and Complicated Diverticulitis

Marja A. Boermeester¹ • David J. Humes^{2,6} • George C. Velmahos³ • Kjetil Søreide^{4,5} World J Surg 2016 DOI 10.1007/s00268-016-3560-8

ESCORES CLÍNICOS

- Ausencia de vómitos
- Defensa en cuadrante inferior izquierdo
- PCR>50mg/L

DISCRIMINAR 34 Y 68%

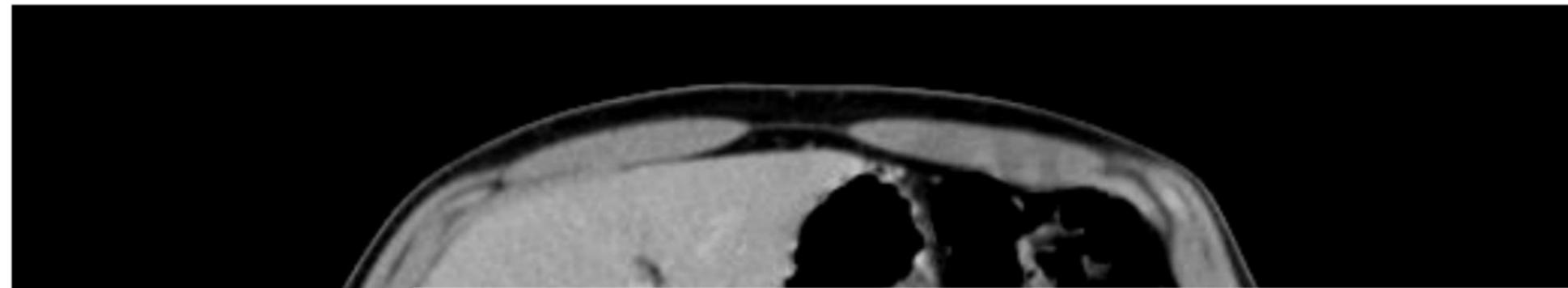
- Ausencia de vómitos
- Defensa en cuadrante inferior izquierdo
- PCR>50mg/L
- Edad >50 años
- Episodio previo de DA
- Aumento del dolor con del movimiento

DISCRIMINAR 86%

TOMOGRAFÍA AXIAL COMPUTERIZADA



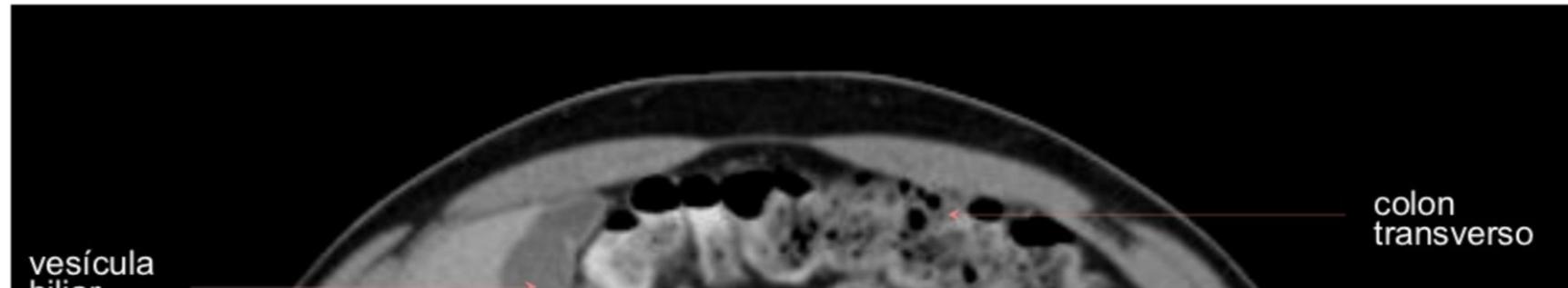
DIAGNÓSTICO



lóbulo caudado

crura diafragmática

arco costal



colon transverso

vesícula biliar

proceso uncinado pancreático

m.psoas



ciego

a. ilíaca ext.

a. ilíaca int.

m. ilíaco

m. glúteo medio

articulación sacroilíaca

sigmoides

v. ilíaca

m.psoas

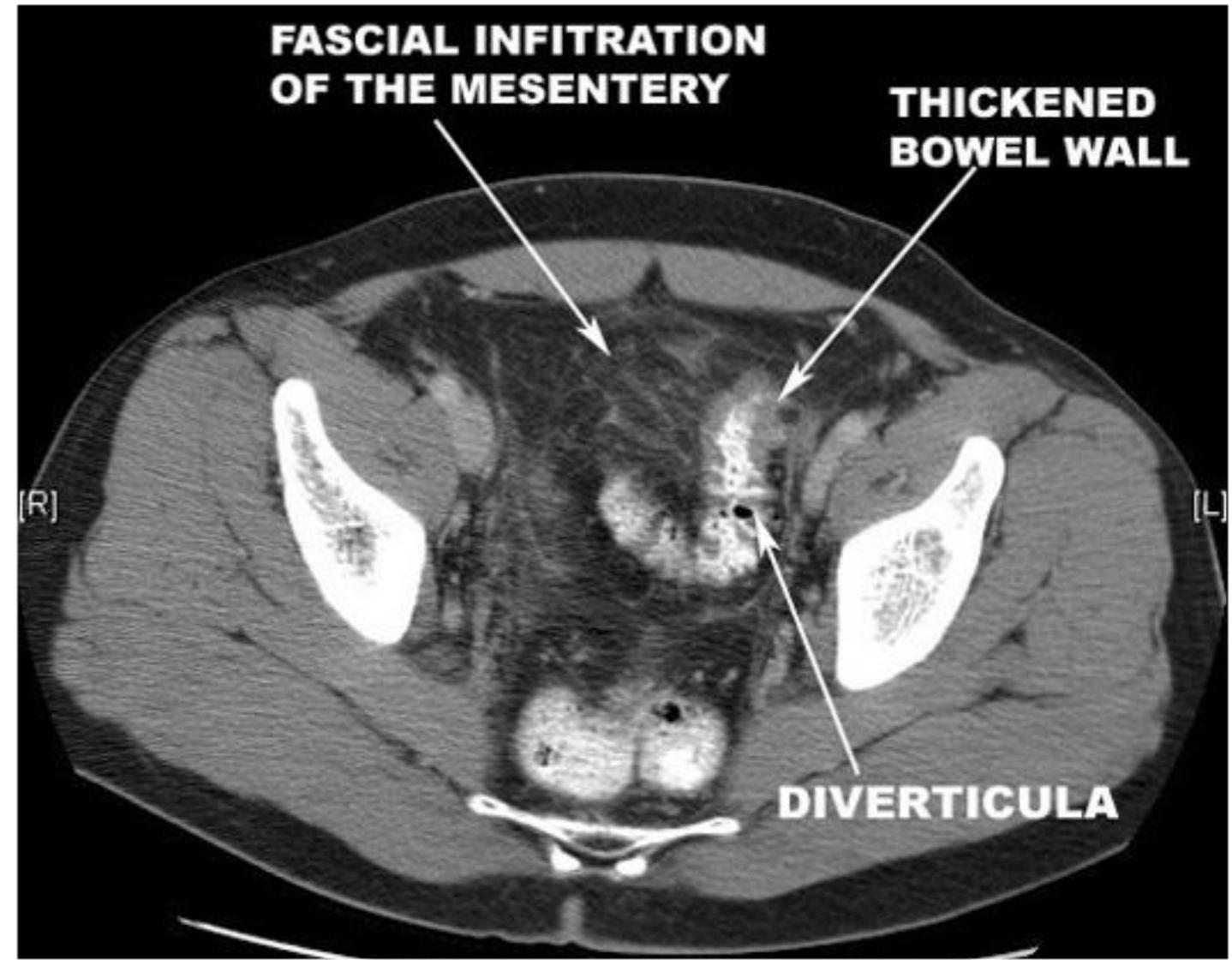
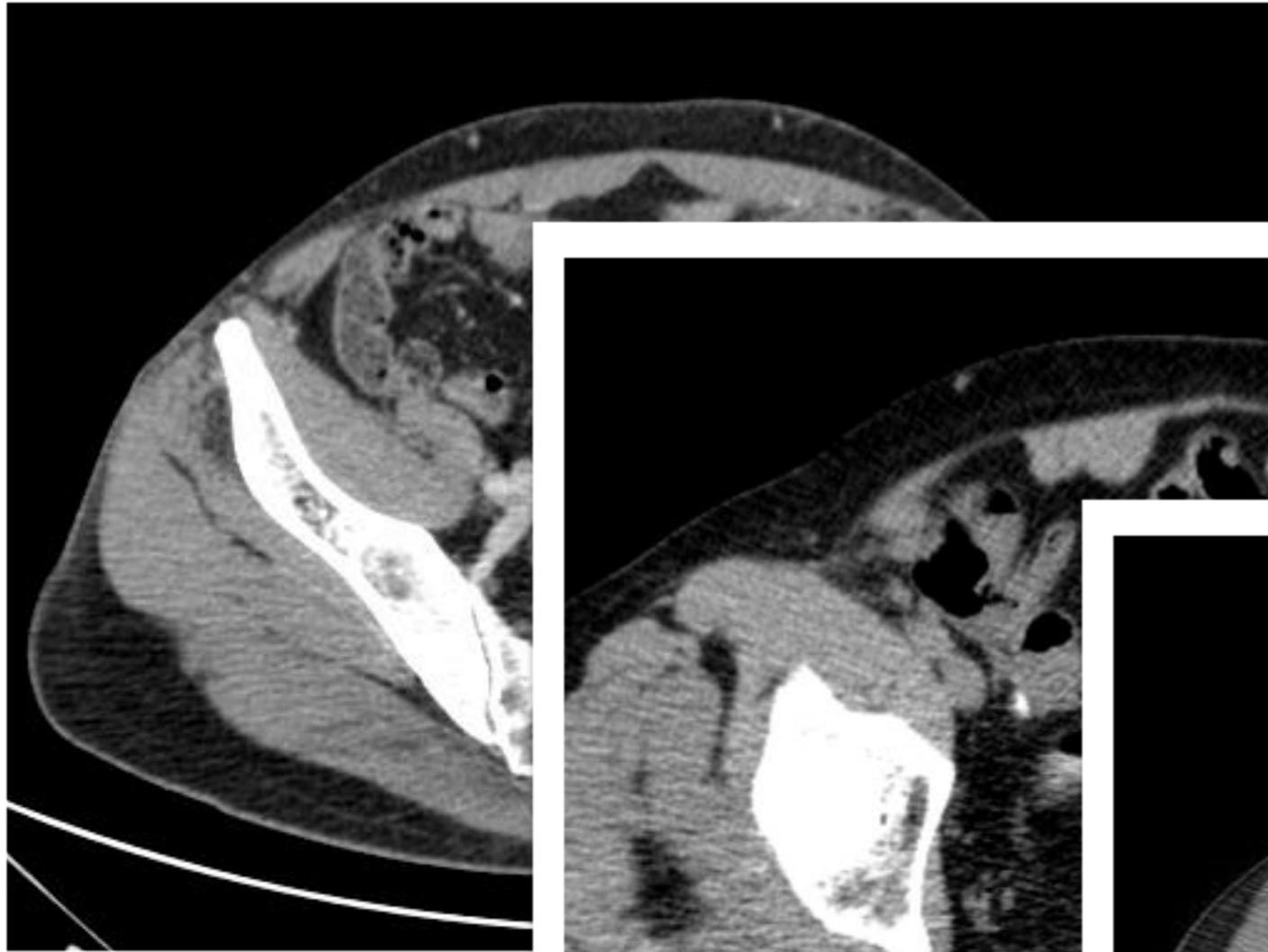
sacro

iliaco

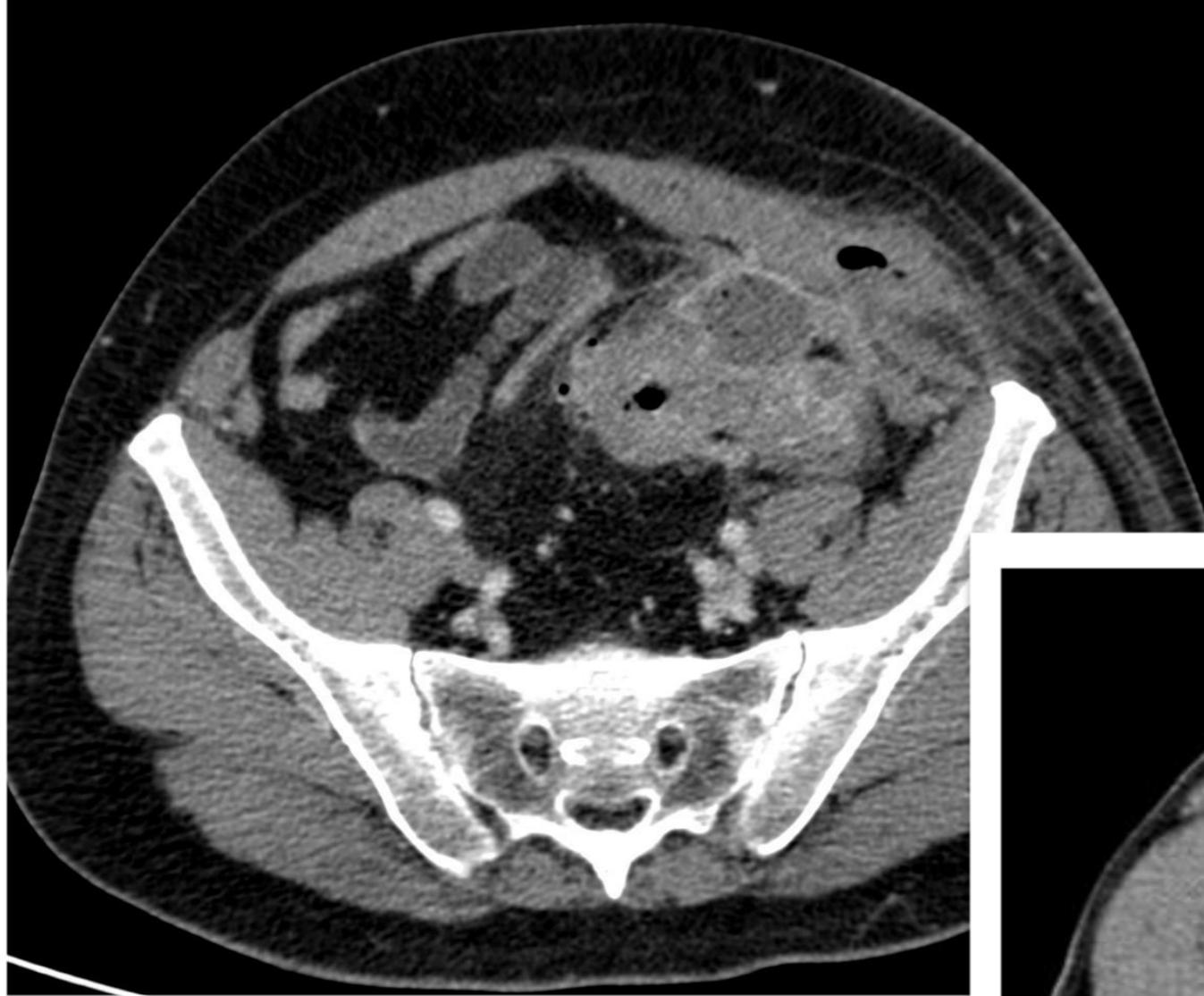
m. glúteo mayor

TC ABDOMINAL NORMAL





TC ABDOMINAL
PATOLÓGICO



TC ABDOMINAL
PATOLÓGICO

DIAGNÓSTICO

Table 1 Classification

Original Hinchey classification [16]

I Pericolic abscess or phlegmon

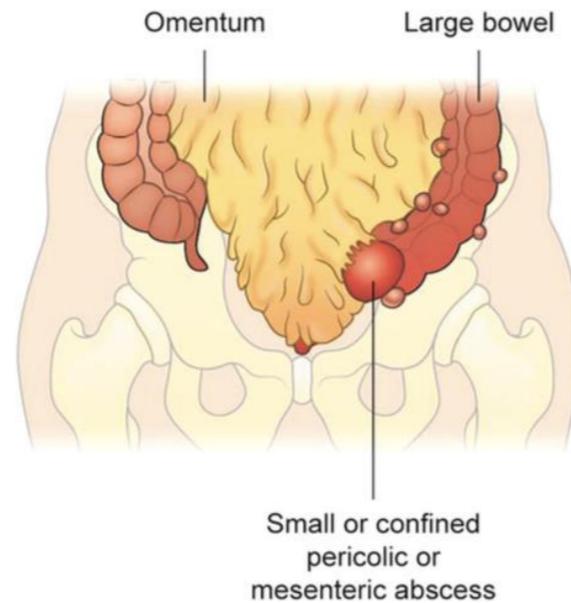
II Pelvic, intraabdominal, or retroperitoneal abscess

III Generalized purulent peritonitis

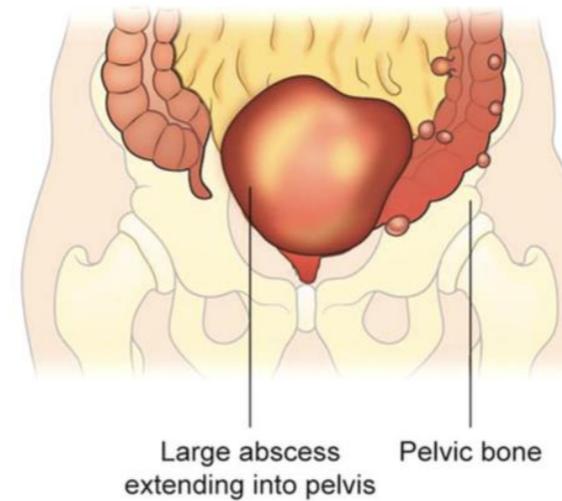
IV Generalized fecal peritonitis

Hinchey classification

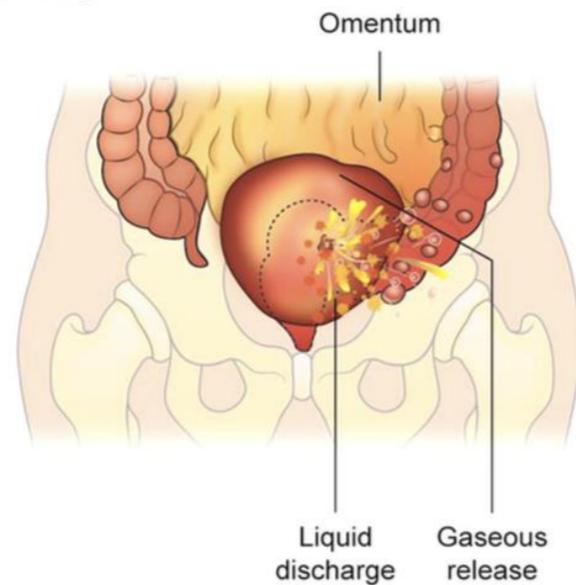
A Stage 1



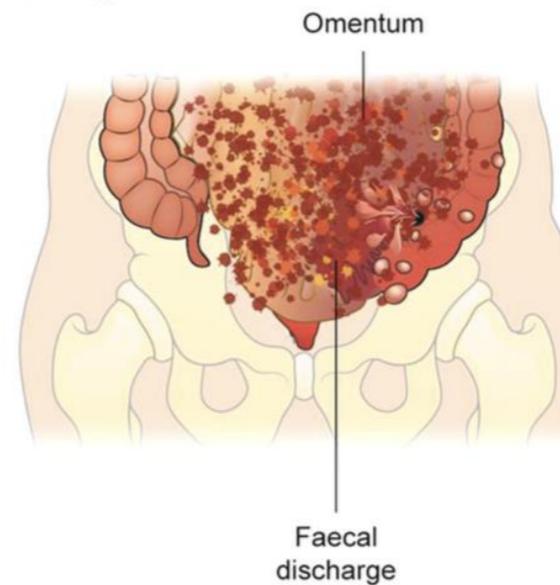
B Stage 2



C Stage 3



D Stage 4



marajan
licated diverticulitis
)]

ocalized free air
(mesocolic) without
cess

ollection of free air
(2 cm) or Abscess
(4 cm)

ollection of free air
(2 cm) or Abscess
(4 cm)

ee air with non-
calized free fluid in the
ritoneal cavity

World Journal
of Surgery

CLASIFICACIÓN WSES

No Complicada

- Estadio 0

Divertículos, pared del colon engrosada o trabeculación de la grasa periódica.

Complicada

- Estadio 1a

Burbujas de gas pericolónicas o un poco de líquido pericolónico sin absceso (a menos de 5cm del colon afecto)

- Estadio 1b

Absceso \leq 4cm

- Estadio 2a

Absceso $>$ 4 cm

- Estadio 2b

Aire a distancia más allá de 5cm del segmento de colon inflamado.

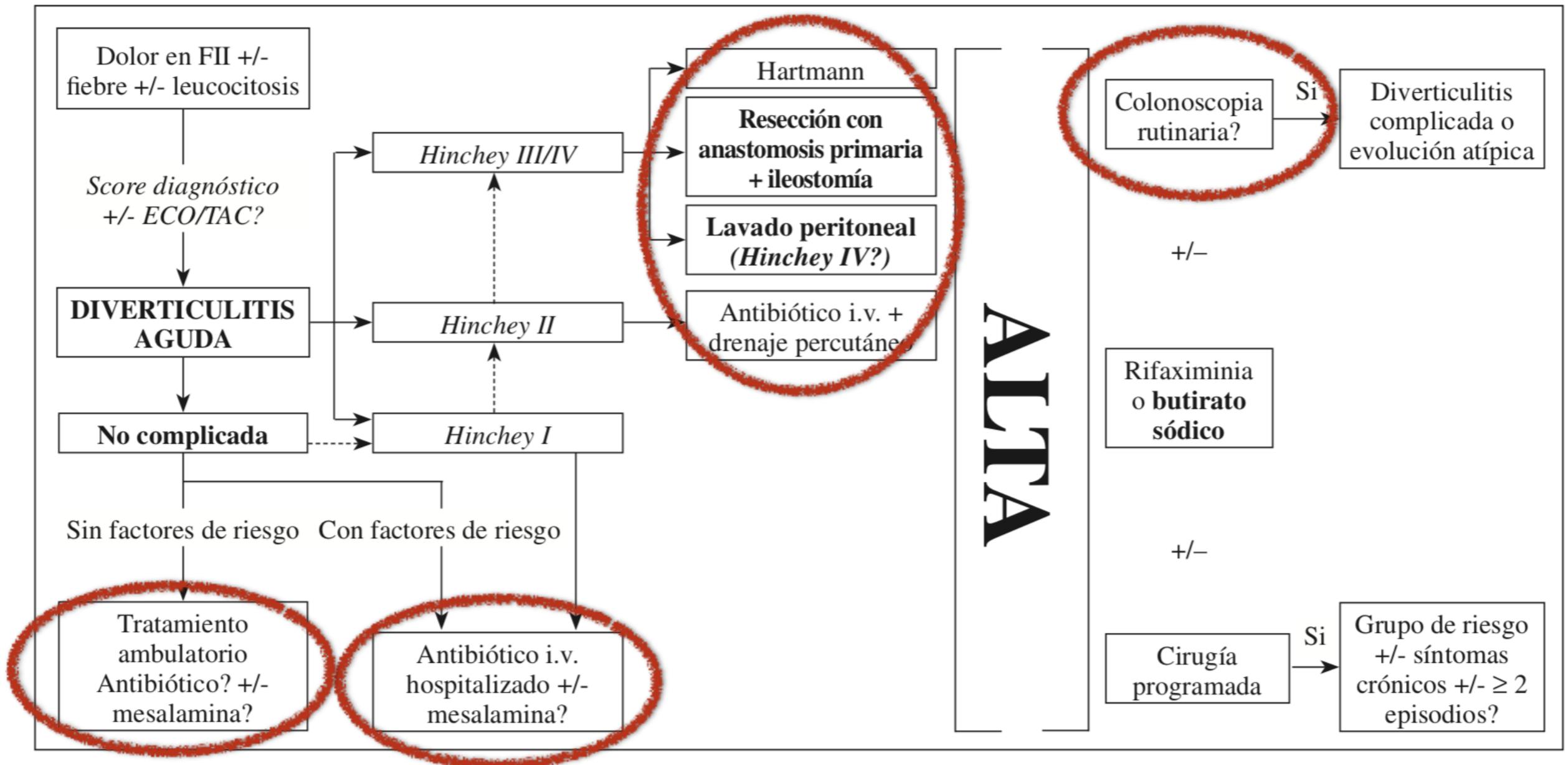
- Estadio 3

Líquido difuso SIN aire libre a distancia (no hay agujero en el colon)

- Estadio 4

Líquido libre difuso y aire libre a distancia (agujero persistente en el colon)

TRATAMIENTO



Diverticulitis aguda no complicada

Tratamiento antibiótico

Tratamiento antibiótico que debería cubrir germen aeróbicos y anaerobios.

Si no hay factores de riesgo se puede considerar tratamiento ambulatorio oral (recomendación

1B)

Table 2 Published guidelines and practise parameters

Organization	Year	Antibiotics	Original	Which	Original	Route of administering	Original
and Rectal Surgeons[24]				negative and anaerobes		depending on clinical status	
Society of Surgery of the Alimentary Tract[26]	2007	Yes	None	Broad spectrum antibiotics	None	Oral or intravenous, depending on clinical status	None
World Gastroenterology Organization[27]	2007	Yes	None	Covering both Gram negative and anaerobes	None	Oral or intravenous, depending on clinical status	None
SWAB[28]	2009	No, not primarily	None	Broad spectrum antibiotics	None	Oral or intravenous, depending on clinical status	None

El tratamiento antibiótico se podría obviar en pacientes inmunocompetentes sin manifestaciones sistemicas de infección (Recomendación 1A)

Randomized clinical trial

Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis

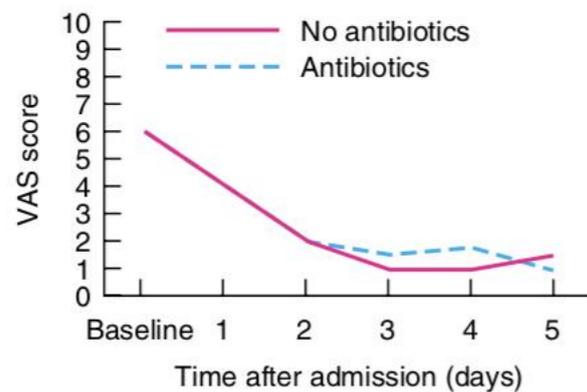
A. Chabok¹, L. Pählman², F. Hjern³, S. Haapaniemi⁴ and K. Smedh¹, for the AVOD Study Group

British Journal of Surgery 2012; 99: 532–539

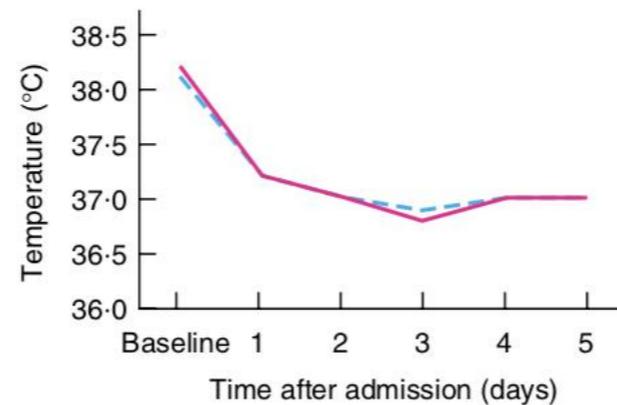
	No antibiotics (n = 309)	Antibiotics (n = 314)	P†
Complications	6 (1.9)	3 (1.0)	0.302
Sigmoid perforation	3 (1.0)	3 (1.0)	0.985
Abscess	3 (1.0)	0 (0)	0.080
Sigmoid resections	7 (2.3)	5 (1.6)	0.541
During hospital stay	1 (0.3)	3 (1.0)	0.324
During follow-up	6 (1.9)	2 (0.6)	0.148
Hospital stay (days)*	2.9(1.6)	2.9(1.9)	0.717‡
Recurrent diverticulitis	47 of 290 (16.2)	46 of 292 (15.8)	0.881

COMPLICACIONES
1,9 VS 1

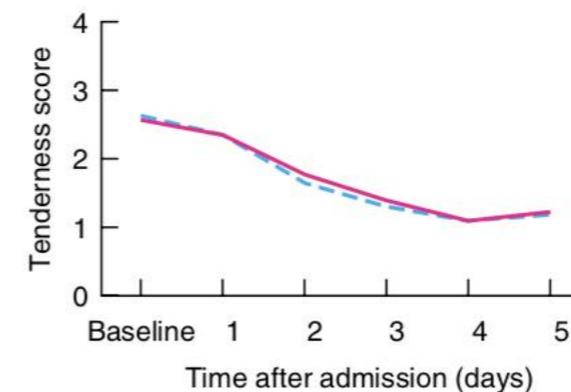
PARA DEMOSTRAR DIFERENCIAS SE
NECESITARIAN 5000 PACIENTES



a Abdominal pain



b Temperature



c Abdominal tenderness

TRATAMIENTO

Randomized clinical trial

Randomized clinical trial of observational *versus* antibiotic treatment for a first episode of CT-proven uncomplicated acute diverticulitis

BJS

L. Daniels¹, Ç. Ünlü^{1,4}, N. de Korte⁵, S. van Dieren², H. B. Stockmann⁶, B. C. Vrouenraets³,

	Observation (n = 262)	Antibiotics (n = 266)	Unadjusted P¶	Adjusted P**
Outpatient treatment	34 (13.0)	1 (0.4)	< 0.001	0.006
Duration of initial admission (days)*	2 (1-3)	3 (2-3)	< 0.001#	0.006
Recovery within 6 months	234 (89.3)	248 (93.2)	0.055	0.183
Readmission within 6 months	46 (17.6)	32 (12.0)	0.037	0.148
Total number of readmissions	66	35		
Proportion of time outside hospital within 6 months	0.989 (0.978-0.994)	0.983 (0.978-0.989)	< 0.001#	0.006
Complicated diverticulitis within 6 months‡	10 (3.8)	7 (2.6)	0.220	0.377
Abscess (> 5 cm)	2 (0.8)	2 (0.8)	0.682	0.682
Perforation	3 (1.1)	3 (1.1)	0.650	0.678
Obstruction	4 (1.5)	2 (0.8)	0.336	0.448
Fistula	1 (0.4)	0 (0)	0.496	0.553
Bleeding	2 (0.8)	0 (0)	0.246	0.390
At index admission	3 (1.1)	6 (2.3)	0.260	0.390
Intervention‡				
Percutaneous	2 (0.8)	1 (0.4)	0.494	0.553
Surgery	8 (3.1)	5 (1.9)	0.192	0.354
Ongoing diverticulitis within 6 months	19 (7.3)	11 (4.1)	0.061	0.183
Imaging-proven	10	5		
Needing admission	15	4		
Recurrent diverticulitis within 6 months	9 (3.4)	8 (3.0)	0.391	0.494
Imaging-proven	7	4		
Needing admission	4	5		
Sigmoid resection within 6 months	10 (3.8)	6 (2.3)	0.148	0.323
Emergency	2 (0.8)	3 (1.1)	0.507	0.553
Elective	8 (3.1)	3 (1.1)	0.106	0.254
Morbidity‡§	127 (48.5)	145 (54.5)	0.083	0.221
Mild	89 (34.0)	114 (42.9)	0.018	0.086
Serious	69 (26.3)	61 (22.9)	0.182	0.354
Antibiotic-related	1 (0.4)	22 (8.3)	< 0.001	0.006
Mortality§	3 (1.1)	1 (0.4)	0.306	0.432

Diverticulitis aguda no complicada

Ingreso

- Se puede tratar ambulatoriamente en paciente sin comorbilidades, poca sintomatología y buen soporte familiar. (Recomendación 1A)

Biondo S, Golda T, Kreisler E, Espin E, Vallribera F, Oteiza F, et al. Outpatient versus hospitalization management for uncomplicated diverticulitis: a prospective, multicenter randomized clinical trial (DIVER Trial). *Ann Surg.* 2014;259:38–44.

- Los pacientes tratados de forma ambulatoria se debería monitorizar de forma ambulatoria y reevaluar a los 7 días para constatar la resolución del proceso inflamatorio. Una reevaluación más temprana es imprescindible si el paciente empeora (Recomendación 1B)

Sartelli et al. *World Journal of Emergency Surgery* (2016) 11:37
DOI 10.1186/s13017-016-0095-0

World Journal of
Emergency Surgery

REVIEW

Open Access



WSES Guidelines for the management of acute left sided colonic diverticulitis in the emergency setting

Diverticulitis aguda no complicada

Mesalazina y rifaximina



AGA desaconseja el uso de mesalazina

Papel de mesalazina en SUDD

Datos no concluyentes para recomendar su uso



American
Gastroenterological
Association

Parece que el uso de Rifaximina combinado con fibra reduce los síntomas (64%vs36%)

Bianchi M, Festa V, Moretti A, et al. Meta-analysis: long-term therapy with rifaximin in the management of uncomplicated diverticular disease. Aliment Pharmacol Ther 2011;33:902-910.

Diverticulitis aguda complicada Hinchey I y II

- Pacientes con aire y líquido pericolónico detectado por TC se deben tratar con antibioterapia (Recomendación 1C)
- Paciente con absceso diverticular pequeño (<4-5cm) se deben tratar sólo con antibioterapia (Recomendación 1C)
- Pacientes con abscesos grandes (>5cm) es mejor tratarlos con drenaje percutáneo y antibioterapia (Recomendación 1C)
- Si el drenaje del absceso no es posible, basándonos en el estado clínico del paciente, este se puede tratar sólo con antibióticos, pero es imprescindible una buena monitorización clínica (Recomendación 1C)

Diverticulitis aguda complicada Hinchey III y IV

- Los pacientes con hallazgos de el **TC de aire distante, sin fluido difuso pueden tratarse con tratamiento conservador** en casos seleccionados. Sin embargo, existe un riesgo de fracaso del tratamiento y es posible que se requiera una cirugía de emergencia. La supervisión cuidadosa es obligatoria. Una tomografía computarizada debe repetirse sobre la base de la evaluación clínica y de laboratorio. (Recomendación 1C)
- **Si el tratamiento conservador falla** en pacientes con aire distante sin fluido difuso, se sugiere resección quirúrgica y anastomosis con o sin estoma o resección de Hartmann de acuerdo con las condiciones clínicas del paciente y las comorbilidades (Recomerndación 1B)
- El lavado y drenaje peritoneal laparoscópico no debe considerarse el tratamiento de elección en pacientes con peritonitis generalizada (Recomendación 1A) SCANDIV, DILALA, LOLA

Diverticulitis aguda complicada

Hinchey III y IV

- La resección de **Hartmann** todavía se recomienda para el manejo de la peritonitis difusa en pacientes críticos y en pacientes con comorbilidades múltiples. Sin embargo, en pacientes clínicamente estables sin comorbilidades, se puede realizar una resección primaria con anastomosis con o sin un estoma desviado. (Recomendación 1B) HASTA UN 25% NECESITARÁN CIRUGÍA

- La **sigmoidec**

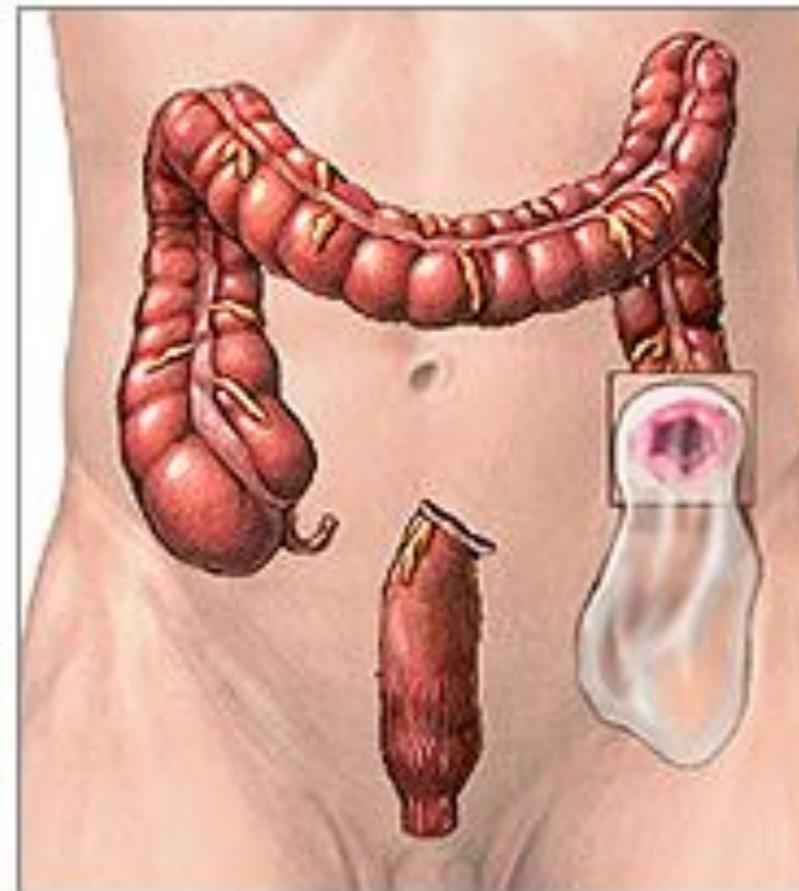
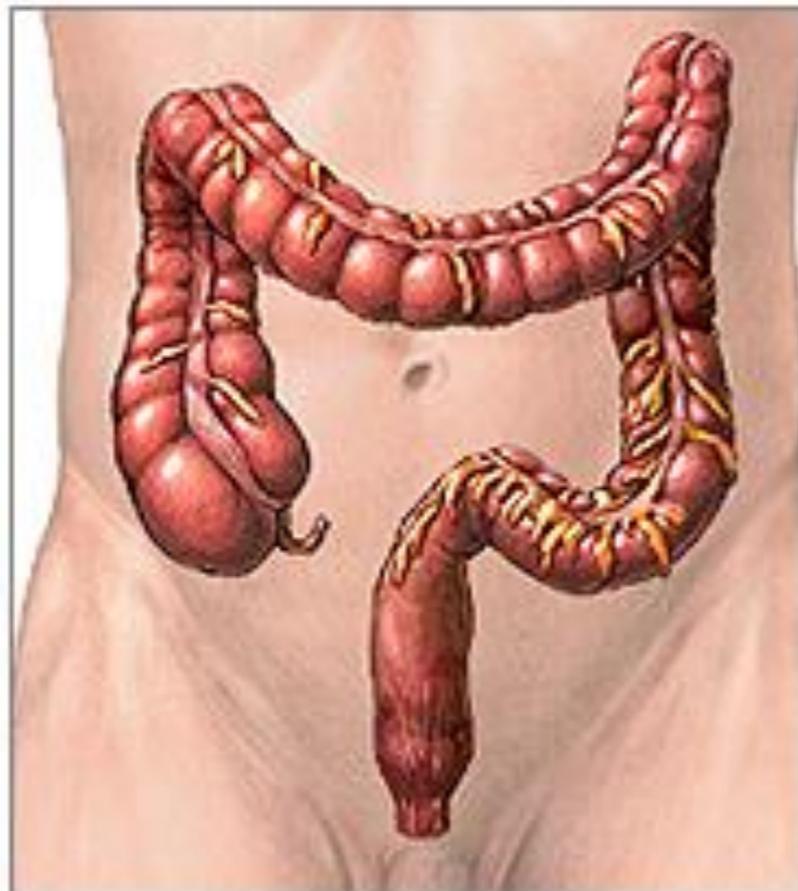
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por manos ex

- La estrategia
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diverticulitis a

WSES Guidelines for t
World Journal of Emer



ulitis perforada
ean manejados

mente

ión 1B)

s clínicos y de

atoria en la

endación 1A)

Riesgo de recurrencia 7-62%

Serie más larga 2366 pacientes
seguimiento 9 años...recurrencia del 13.3%

Riesgo de DC tras DNC 5% a los 8 años

Estudio DIVER Biondo 2014 la probabilidad de
perforación baja a la 1/2 tras cada recurrencia
25%..12%..6%..1%...

SEGUIMIENTO

- En pacientes con diverticulitis no complicada comprobada por CT tratada conservadoramente (sin otros factores de riesgo), **no se requiere una colonoscopia de seguimiento precoz**. Los pacientes de 50 años o más deberían participar en programas de detección de cáncer colorrectal (Recomendación 1C) (no aumento del riesgo de CCR, ni mayor asociación con pólipos)
- **Los factores relacionados con el paciente** y no el número de episodios previos de diverticulitis, deben considerarse en la planificación de la **resección sigmoidea** electiva en pacientes con diverticulitis aguda complicada tratados conservadoramente (Recomendación 1 C)
- Después de un episodio de diverticulitis aguda complicada, tratado de forma conservadora se debe planificar una resección **sigmoidea electiva en pacientes de alto riesgo**, como pacientes inmunocomprometidos (Recomendación 1 C).

FIBRA

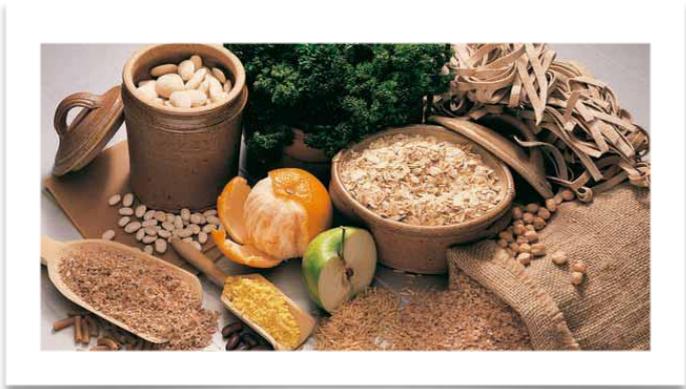


Table 1 Fiber in diverticulosis and symptomatic diverticular disease

Study	Trial design	No of patients	Randomization	Outcomes assessed	Length of follow up	Results
Brodibb	Double-blind	18	Wheat crispbread 0.6 g/day vs. bran crisp bread 6.7 g/day	Reduction in global symptom score in SUDD	3 months	High-fiber vs. low-fiber group has significant reeuction in symptoms score (34.3-8.1 vs. 42.0-35.1, P<0.002)
Ornstein <i>et al</i>	Randomized, cross-over, double-blind, placebo	58	Bran (6.99 g/day) vs. ispaghula (9.04 g/day) vs. placebo (2.34 g/day)	Reduction in global symptom score in SUDD	16 weeks	No difference was found between the three arms (from 16.3, 18.4 and 15.6-5.9, 6.7 and 6.3, P=n.s.) No difference between bran and ispaghula consumption (5.9 vs. 6.7)
Hodgson	Double-blind, randomized, Placebo controlled	30	Methylcellulose 2 tablets/day vs. placebo 2 tablets/day	Reduction in global symptom score in SUDD	3 months	Symptom score decreased significantly in the methylcellulose group (from 19+6 to 13+4, P<0.01) but not in the placebo group (from 21+7 to 17+9, P=n.s.)
Crowe <i>et al</i>	Prospective, cohort study	47.033	Vegetarian vs. non vegetarian diet (>25.5 g/day for women and >26.1 g/day for men) vs. lower fiber consumption	Occurrence of DD; Hospital admission for DD complications	11.6 years	Vegeterians had a 31% lower risk of DD occurrence (P=0.001) high-fiber intake had a 25% lower risk of developing DD (P=0.018). Hospital admission of death for DD was 4.4% for meat eaters and 3.0% in vegetarian of vegans
Peery <i>et al</i>	Cross-sectional study	2104	Fiber or high-fiber consumption (>50 g/day) vs. normal diet	Diverticulosis occurrence	12 years	High-fiber consumption had higher risk to develop diverticulosis (P=0.004) Soluble fiber had higher risk to develop diverticulosis (P=0.038)
Strate <i>et al</i>	Prospective cohort study	47.228	Lower (less than once per month) vs. higher (at least twice per week) nut, corn, or popcorn consumption	Diverticulitis occurrence Diverticulitis bleeding occurrence	18 years	Higher nut, corn or popcorn consumption had lower risk of diverticulitis occurrence (P=0.034). No difference in diverticular bleeding occurrence between higher or lower consumption of nut, corn or popcorn (P=0.56, 0.64 and 0.52 respectively)
Leahy <i>et al</i>	Prospective case-control	56	Lower (<25 g/day) vs. high (>25/day) fiber diet	Symptoms recurrence occurrence of complications surgery due to DD	66 months	High-fiber diet has significantly lower symptom recurrence (19.35% vs. 44%, P<0.05), occurrence of complications (6.45% vs. 20.25%, P<0.05) and surgery due to DD (6.45% vs. 32%) than low-fiber diet

SUDD, symptomatic uncomplicated diverticular disease; DD, diverticular disease

RIFAXIMINA

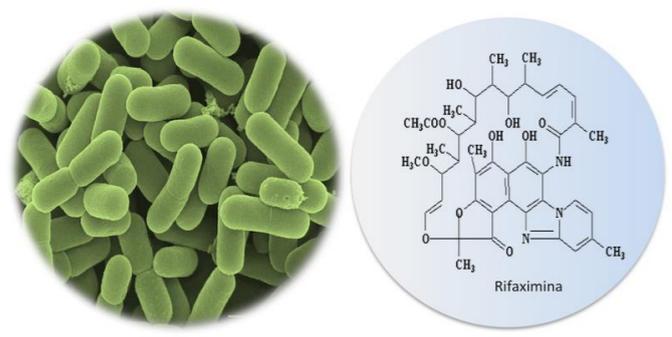


Table 2 Controlled trials in using rifaximin in treating diverticular disease

Study	Trial design	No of patients	Randomization	Outcomes assessed	Length of follow up	Results
Papi <i>et al</i>	Open-label, prospective, randomized	217	RFX 800 mg/plus GM 2 g/day for 7 days vs. GM 2 g/day for 7 days each month	Reduction in global symptomatic score in SUDD	12 months	RFX+GM 63.9% reduction score vs. GM alone 47.6% (P<0.001)
Papi <i>et al</i>	Double-blind, randomized, placebo-controlled	168	RFX 800 mg/plus GM 2 g/day for 7 days vs. placebo plus GM 2 g/day for 7 days each month	Reduction in global symptomatic score in SUDD prevention of diverticulitis occurrence	12 months	RFX+GM 68.9% reduction score vs. placebo+GM 39.5% (P=0.001). No difference in preventing diverticulitis occurrence (1.3% vs. 1.5%, P=n.s.)
Latella <i>et al</i>	Prospective, randomized, open-label	968	RFX 800 mg/plus GM 4 g/day for 7 days vs. GM 4 g/day for 7 days each month	Reduction in global symptomatic score in SUDD prevention of DD complications (acute diverticulitis and diverticular bleeding)	12 months	RFX+GM 56.5% reduction score vs. GM alone 29.2% (P<0.001). RFX+GM 1.34% occurrence of DD complications vs. GM alone 3.22% (P<0.05)
Lanas <i>et al</i>	Open-label, prospective, randomized	165	RFX 800 mg/plus fiber 7 g/day for 7 days vs. fiber 7 g/day for 7 days each month	Prevention of diverticulitis recurrence	12 months	RFX/fiber 10.4% diverticulitis recurrence vs. fiber alone 19.3% (P=0.025)

RFX, rifaximin; GM, glucomannan; SUDD, symptomatic uncomplicated diverticular disease; DD, diverticular disease

PROBIÓTICOS

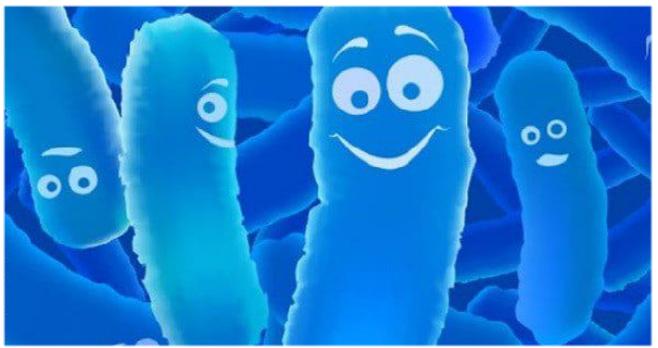


Table 4 Controlled trials in using probiotics for symptomatic diverticular disease

Study	Trial design	No of patients	Randomization	Outcomes assessed	Length of follow up	Results
Annibal <i>et al</i>	Prospective, randomized, open-label	50	Group A, high-fiber diet alone; Group B, twice daily 1 sachet of probiotic lactobacillus paracasei sub paracasei F19 for 14c days/month+high-fiber diet). Group C twice daily 2 sachets of probiotic <i>Lactobacillus paracasei</i> sub, <i>paracasei</i> F19 for 4 days/month+high-fiber diet	Decrease in VAS score after treatment in SUDD	6 months	Bloating decreased significantly in Groups B and C (group B: 4.6+2.6 vs. 2.3+2.0, P<0.05, group C: 3.9+2.9 vs. 1.8+2.1, P<0.05)
Dughera <i>et al</i>	Prospective, randomized, open-label	83	Polybacterial lysate suspension of <i>Escherichia coli</i> + <i>Proteus vulgaris</i> for 2 weeks every month plus fiber 15 g/day vs. fiber 15 g/day alone	Prevention of diverticulitis recurrence	3 months	Polybacterial lysate plus fiber had significant superiority to fiber alone at 1 and 3 months in controlling symptoms and preventing diverticulitis recurrence (P<0.05 and P<0.01 respectively)
Lahner <i>et al</i>	Prospective, randomized, open-label	30	Methylcellulose 2 tablets/day vs. placebo 2 tablets/day		3 months	Symptom score decreased significantly in the methylcellulose group (from 19+6 to 13+4, P<0.01) but not in the placebo group (from 21+7 to 17+9, P=n.s.)
Tursi <i>et al</i>	Double-blind, randomized, placebo-controlled	210	Mesalazine 800 mg twice a day and mesalazine 800 mg twice a day+ <i>Lactobacillus casei</i> 750 mg a day vs. <i>Lactobacillus casei</i> 750 mg a day vs. placebo		12 months	Remission was maintained in 93.33% in combined treatment group. 85.45% in probiotic group and 54% of placebo group (P=0.0001) acute diverticulitis occurred in 0% in combined treatment group. 1.82% in probiotic group and 12% in the placebo group (P=0.003)
Tursi <i>et al</i>	Prospective, randomized, open-label	30	Balsalazide 2.25 g daily for 10 days every month plus probiotic mixture VSL #3 450 billion/day for 15 days every month (Group A) vs. VSL#3 alone 450 billion /day for 15 days every month (Group B)		12 months	6.66% of group A and 13.33% of group GB pts had recurrence of the disease (P=n.s.)

VAS, visual analogic scale; DD, diverticular disease; SUDD, symptomatic uncomplicated diverticular disease

MESALAZINA

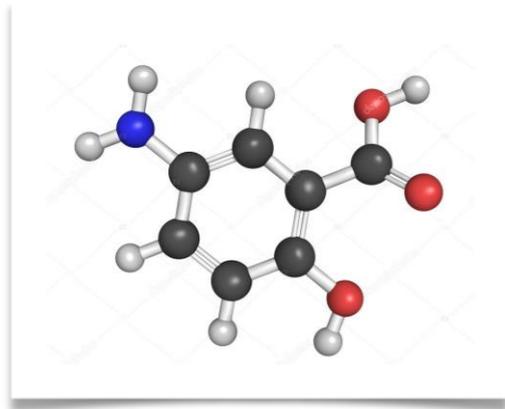


Table 3 Fully published placebo-controlled trials in using mesalazine in diverticular disease

Study	Trial design	No of patients	Randomization	Outcomes assessed	Length of follow up	Results
Kruis <i>et al</i>	Double-blind, randomized, placebo controlled	117	Mesalazine granules 3 g/day vs. placebo in SUDD	Pain control in SUDD	3	Mesalazine had higher percentage of pain control (62.5% vs. 50.81%, P=0.374 on ITT and P=0.05 on PP)
Tursi <i>et al</i>	Double-blind, randomized, placebo controlled	210	Mesalazine Eudragit L 2.4 g/day vs. mesalazine 2.4 g/day+ <i>Lactobacillus casei</i> 750 mg/day vs. <i>Lactobacillus casei</i> 750 mg/day vs. placebo in SUDD	Reducing gastrointestinal symptoms in SUDD preventing diverticulitis occurrence	12	Mesalazine, alone or in combination, had high remission rate (93.33% and 85.45% vs. 54%, P=0.0001)* Mesalazine, alone or in combination, had lower diverticulitis occurrence (0% and 1.81% vs. 12%, P=0.003)*
Stollman <i>et al</i>	Double-blind, randomized, placebo controlled	117	Mesalazine eudragit L 2.4 g/day vs. Mesalazine 2.4 g/day+ <i>Bifidobacterium infantis</i> 35624 vs. placebo following acute diverticulitis	Reducing gastrointestinal symptoms preventing diverticulitis recurrence	12	Mesalazine, alone or in combination, had higher symptoms' improvement rate (59.3% and 54.8% vs. 27.3%, P=0.0346).* Mesalazine, alone or in combination, had no higher remission rate in preventing diverticulitis recurrence (28.1%, 37% vs. 31% placebo, P=n.s.)*
Parente <i>et al</i>	Double-blind, randomized, placebo controlled	92	Mesalazine eudragit L 2.4 g/day for 10 days/month vs. placebo following acute diverticulitis	Preventing diverticulitis recurrence improvement quality of life	24	Mesalazine had higher but no significant remission rate in preventing diverticulitis recurrence (13% vs. 28%, P=0.1011).* Mesalazine had higher quality of life score (P=0.022)*
Raskin <i>et al</i>	Double-blind, randomized, placebo controlled	1182 (590 in PREVEN T1 and 592 in PREVEN T2)	Mesalazine MMX 1.6 g/day vs. 2.4 g/day vs. 4.8 g/day vs. placebo following acute diverticulitis	Preventing diverticulitis recurrence	24	Mesalazine did not reduce the rate of diverticulitis recurrence both in PREVENT 1 (53-63% vs. 65%, P=n.s.)* and in PREVENT 2 (59-69% vs. 68%, P=n.s.)*

*All results reported are on ITT analysis

ITT, intention-to-treat analysis; PP, per-protocol analysis; SUDD, symptomatic uncomplicated diverticular disease



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