Non surgical treatment of Intraabdominal infection

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Management of Intraabdominal infections

- Source control remains the cornerstone
- Timing of adequate antimicrobial therapy and source control have an impact on outcome
- Too many studies orienting the guidelines have included patients with low to moderate severity

RESEARCH Open Access

Adverse effects of delayed antimicrobial treatment and surgical source control in adults with sepsis: results of a planned secondary analysis of a cluster-randomized controlled trial

Hendrik Rüddel[1,2], Daniel O. Thomas-Rüddel[1,2], Konrad Reinhart[3,4], Friedhelm Bach[5], Herwig Gerlach[6], Matthias Lindner[7], John C. Marshall[8], Philipp Simon[9], Manfred Weiss[10], Frank Bloos[1,2], Daniel Schwarzkopf[1,2,11]* and the MEDUSA study group

Rüddel *et al. Critical Care* (2022) 26:51
https://doi.org/10.1186/s13054-022-03901-9

Table 1 Baseline characteristics of patients stratified by timing of start of antimicrobial treatment

Variable	No. of patients with complete data	All patients ($N=4792$)	Timing of antimicrobial therapy		
			Within 1 h ($N=1311$)	More than 1 h ($N=3481$)	*p* value
Time to beginning of antimicrobial therapy (minutes)	4792	150 [60, 378.5]	30 [15, 50]	240 [120, 518]	–
Age	4791	70 [59, 77]	71 [60, 77]	70 [59, 77]	0.435
Sex: male	4792	2986 (62.3%)	800 (61%)	2186 (62.8%)	0.27
Origin of infection: Community acquired	4791	2273 (47.4%)	779 (59.4%)	1494 (42.9%)	≤0.001
Nosocomial (ICU/IMC)		1112 (23.2%)	208 (15.9%)	904 (26%)	
Nosocomial (general ward)		1406 (29.3%)	324 (24.7%)	1082 (31.1%)	
Location at onset of sepsis: ICU	4792	2233 (46.6%)	559 (42.6%)	1674 (48.1%)	≤0.001
Emergency department		948 (19.8%)	333 (25.4%)	615 (17.7%)	
Operating room		428 (8.9%)	167 (12.7%)	261 (7.5%)	
General ward		692 (14.4%)	127 (9.7%)	565 (16.2%)	
Ambulance service		211 (4.4%)	48 (3.7%)	163 (4.7%)	
IMC		280 (5.8%)	77 (5.9%)	203 (5.8%)	
Focus of infection: respiratory	4789	2057 (43%)	510 (38.9%)	1547 (44.5%)	≤0.001
Focus of infection: abdominal	4789	1657 (34.6%)	464 (35.4%)	1193 (34.3%)	0.474
Focus of infection: urogenital	4789	695 (14.5%)	209 (16%)	486 (14%)	0.089
Focus of infection: bones/soft tissue/wound	4789	531 (11.1%)	154 (11.8%)	377 (10.8%)	0.38
Focus of infection: other/unknown	4789	644 (13.4%)	161 (12.3%)	483 (13.9%)	0.154
Infection microbiologically confirmed	4781	3514 (73.5%)	965 (73.7%)	2549 (73.4%)	0.854
Bacteremia: Gram positive	4754	806 (17%)	223 (17.2%)	583 (16.9%)	0.005
Gram negative		712 (15%)	226 (17.4%)	486 (14.1%)	
Other/several		166 (3.5%)	41 (3.2%)	125 (3.6%)	
No pathogen detected		2281 (48%)	627 (48.3%)	1654 (47.9%)	
No blood culture taken		789 (16.6%)	182 (14%)	607 (17.6%)	
Vasopressor use within 12 h after first organ dysfunction	4781	3595 (75.2%)	982 (75.2%)	2613 (75.2%)	1

Descriptive statistics given as N (%) or median [interquartile range]. *p* values obtained by Mann-Whitney-U test, Fisher's exact test or Pearson's Chi-squared test, as appropriate

ICU: intensive care unit; IMC: intermediate care unit

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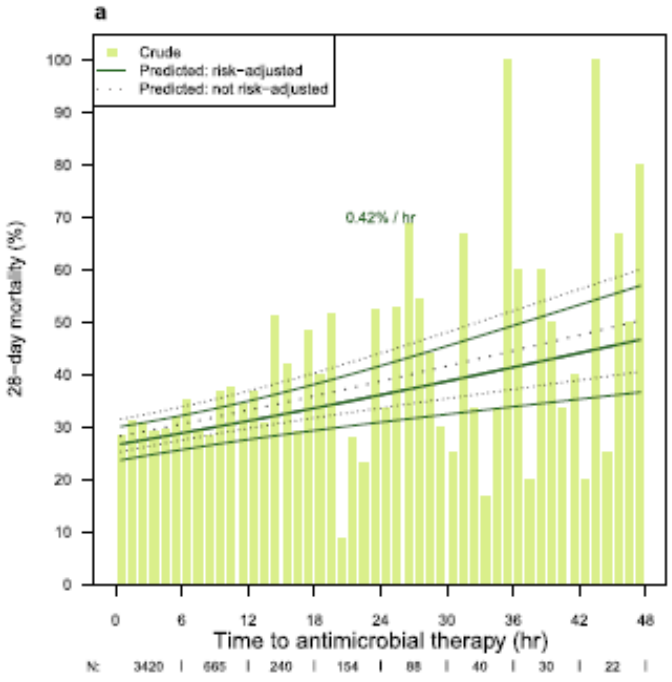

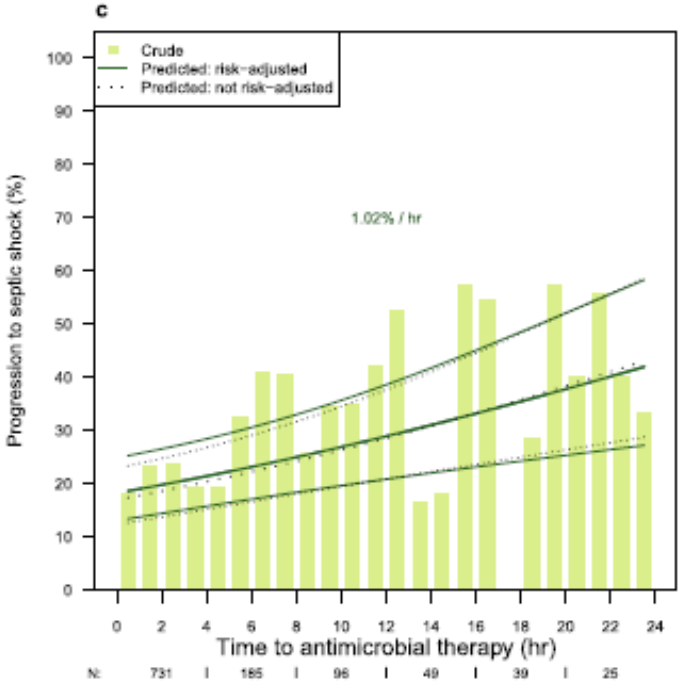

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Predictor	No. of patients	Observed mortality	Risk-adjusted mortality	OR (95% CI)	P-value
Timing of antimicrobial therapy	4659/4792				0,008*
0–1 hr		364/1270 (28.7)	25.3 (22, 28.9)	1	
1–3 hrs		418/1352 (30.9)	27.8 (24.4, 31.6)	1.14 (0.95, 1.36)	0.149
3–6 hrs		255/836 (30.5)	26 (22.3, 30.2)	1.04 (0.85, 1.27)	0.715
>6 hrs		437/1201 (36.4)	31.5 (27.5, 35.7)	1.36 (1.12, 1.63)	0,001
Timing of surgical source control	1563/1595				0.22*
0–1 hr		92/327 (28.1)	25.1 (19.1, 32.3)	1	
1–3 hrs		85/287 (29.6)	26.4 (20.8, 32.9)	1.07 (0.71, 1.61)	0.743
3–6 hrs		93/293 (31.7)	27.1 (21.3, 33.8)	1.11 (0.71, 1.72)	0,646
>6 hrs		240/656 (36.6)	31.9 (26.7, 37.5)	1.4 (0.94, 2.08)	0.102
Success of source control	1563/1595				
Not successful		179/262 (68.3)	68.7 (60.7, 75.7)	1	
Successful		331/1301 (25.4)	20.2 (16.5, 24.5)	0.12 (0.08, 0.16)	<=0,001

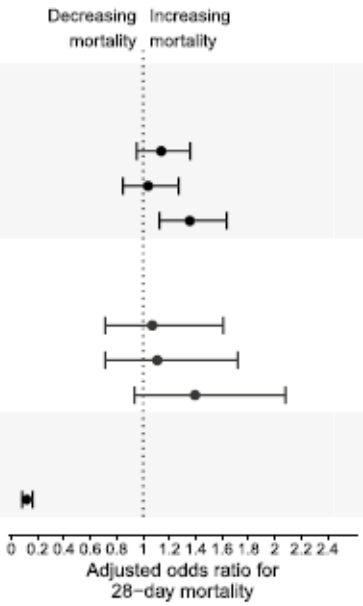
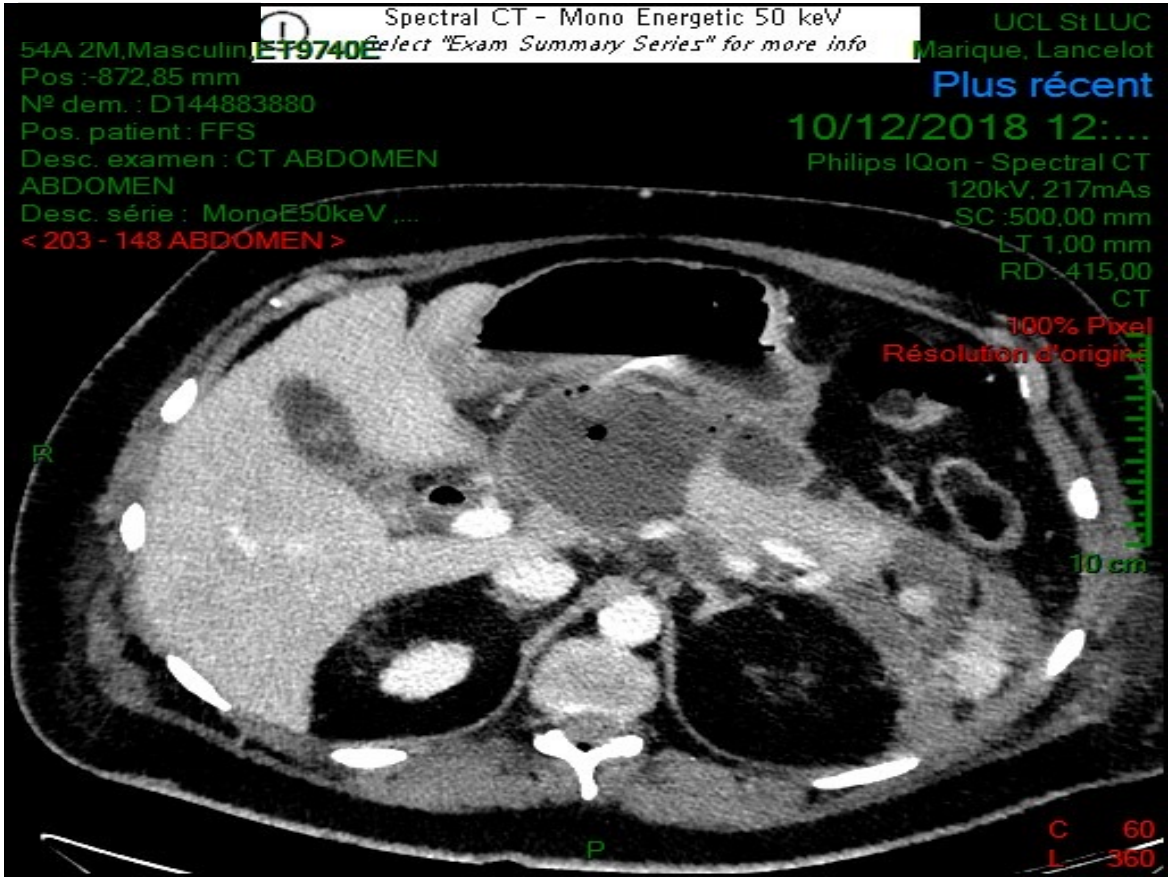


Fig. 2 Effects of antimicrobial therapy and of surgical source control on 28-day mortality. Effects were tested in a logistic hierarchical linear model with a random intercept adjusting for covariates. Risk-adjusted mortality estimates were obtained as predictive margins that were calculated for the average of continuous variables and for the most common category of categorical variables. No. of patients gives the number of cases with complete data compared to the total number of patients suitable for the respective analysis. * marks the p-value of the overall test of significance for the categorical variables on timing conducted by a likelihood-ratio test, while the other p-values give the results of tests of single categories against the reference category. Models adjusted for the following covariates: age and gender, origin of infection, location of the patient at the onset of sepsis, focus of infection, microbiological confirmation of infection, study phase (trial vs. surveillance phase), and group the hospital was randomized to (intervention vs. control)

Source control in IAI?

- Diverticulitis ?
- Appendicitis ? (conservative ?)
- WON in Pancreatitis ? (delayed ?)
- Liver Abscess ? (delayed?)

- Decompartment, decompression..


Spectral CT - Mono Energetic 50 keV
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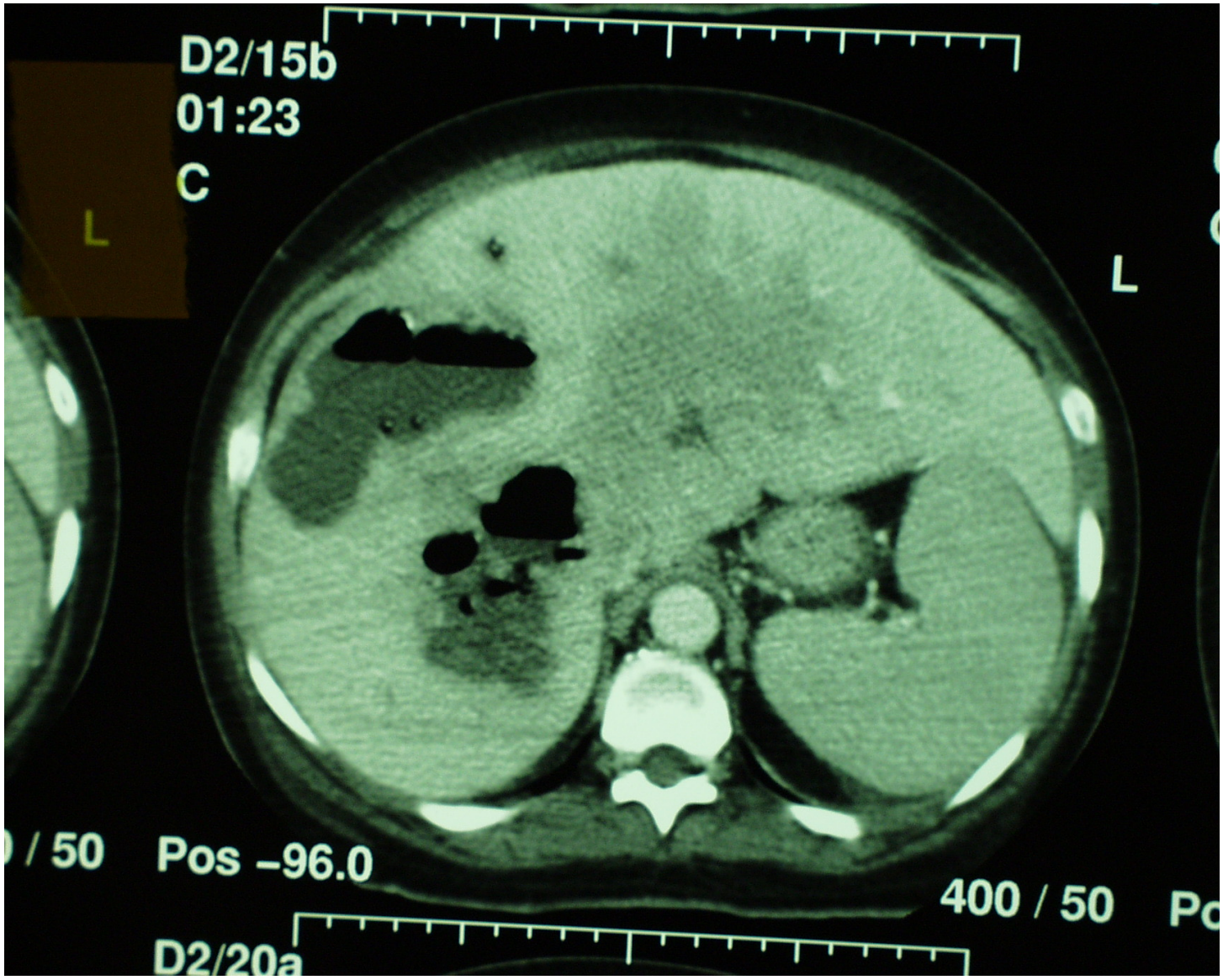
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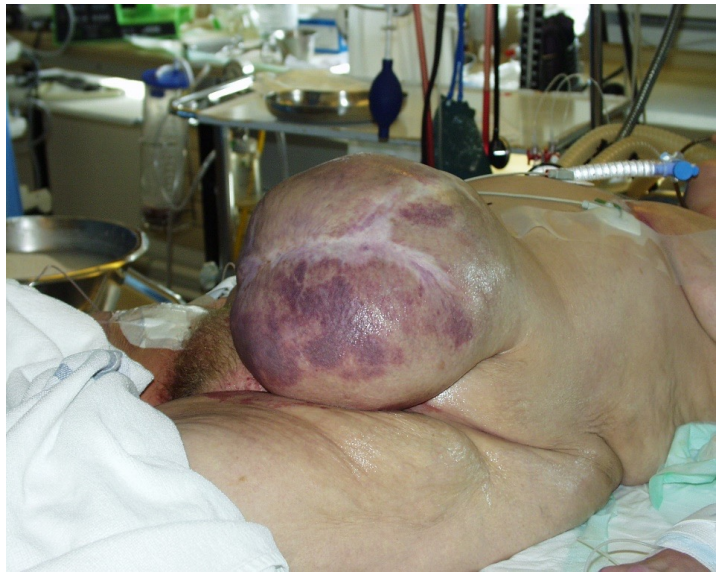
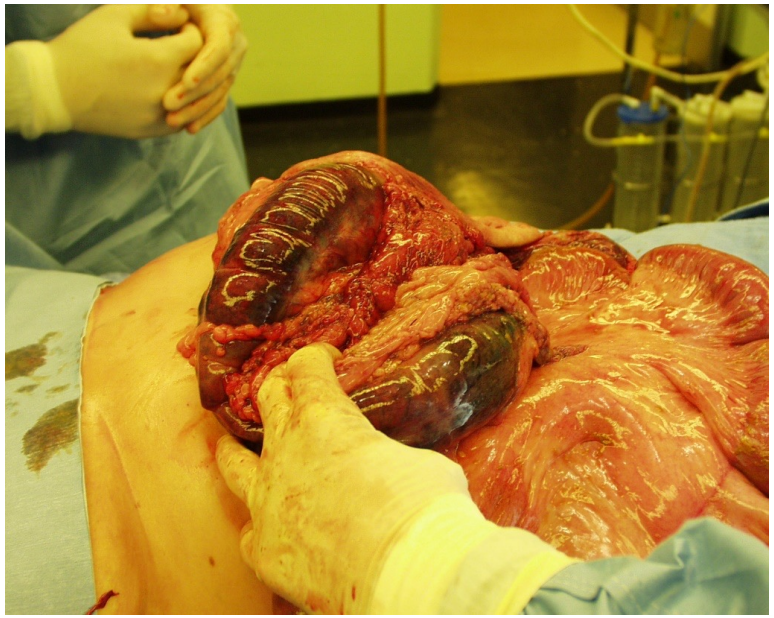
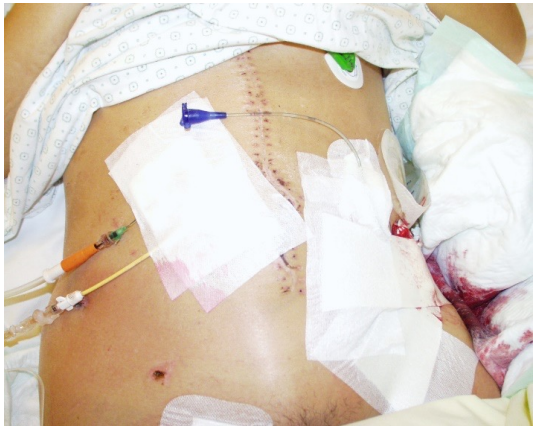
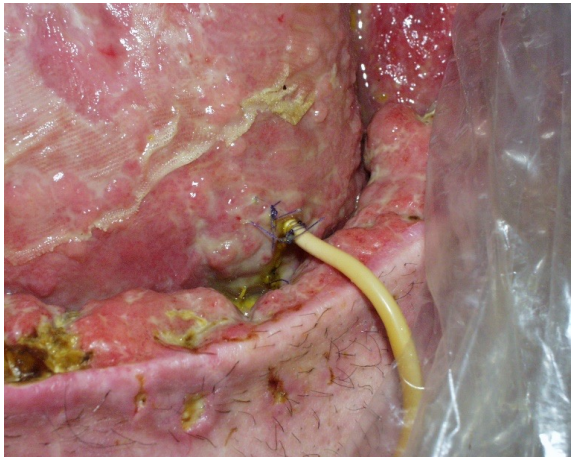


Bowel necrosis and
« ischemia-translocation »
issues ?
Role of antimicrobials alone



SAP, surgery and secondary GI-tract fistula ?





Antimicrobial therapy for IAI ?

Insufficient β-lactam concentrations in the early phase of severe sepsis and septic shock

Fabio Silvio Taccone[1], Pierre-François Laterre[2], Thierry Dugernier[3], Herbert Spapen[4], Isabelle Delattre[5], Xavier Wittebole[2], Daniel De Backer[1], Brice Layeux[6], Pierre Wallemacq[5], Jean-Louis Vincent[1] and Frédérique Jacobs*[6]

Taccone *et al. Critical Care* 2010, **14**:R126
http://ccforum.com/content/14/4/R126

Revisiting the loading dose of amikacin for patients with severe sepsis and septic shock

Fabio Silvio Taccone[1], Pierre-François Laterre[2], Herbert Spapen[3], Thierry Dugernier[4], Isabelle Delattre[5], Brice Layeux[6], Daniel De Backer[1], Xavier Wittebole[2], Pierre Wallemacq[5], Jean-Louis Vincent[1] and Frédérique Jacobs*[6]

Taccone *et al. Critical Care* 2010, **14**:R53
http://ccforum.com/content/14/2/R53

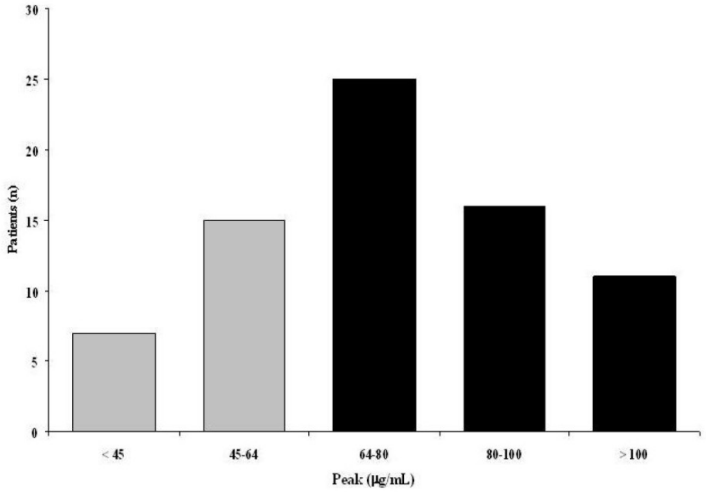


Figure 2 Distribution of peak concentrations. Black bars, peak >64 µg/ml; gray bars, peak <64 µg/ml.

Short-course antibiotic therapy for critically ill patients treated for postoperative intra-abdominal infection: the DURAPOP randomised clinical trial

Philippe Montravers[1,18*], Florence Tubach[2], Thomas Lescot[3], Benoit Veber[4], Marina Esposito-Farèse[5], Philippe Seguin[6], Catherine Paugam[7], Alain Lepape[8], Claude Meistelman[9], Joel Cousson[10], Antoine Tesniere[11], Gaetan Plantefeve[12], Gilles Blasco[13], Karim Asehnoune[14], Samir Jaber[15], Sigismond Lasocki[16], Herve Dupont[17] and For the DURAPOP Trial Group

Intensive Care Med (2018) 44:300–310

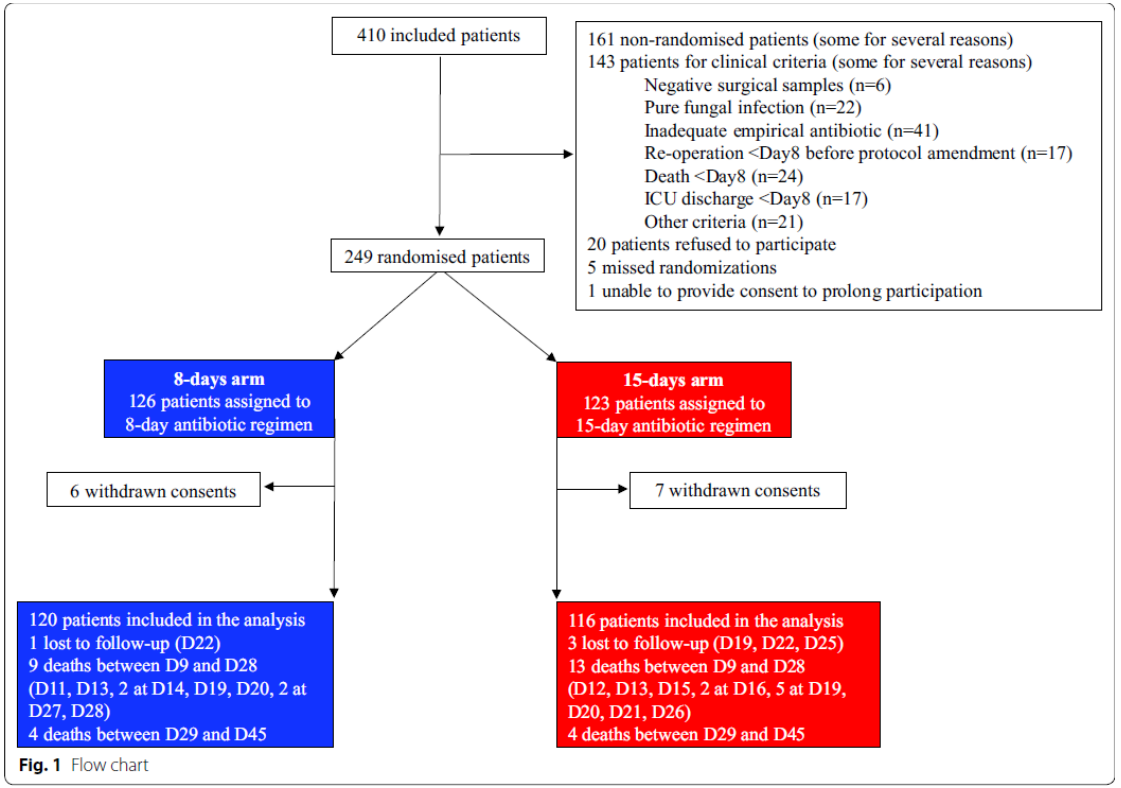


Fig. 1 Flow chart

Short-course antibiotic therapy for critically ill patients treated for postoperative intra-abdominal infection: the DURAPOP randomised clinical trial

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Table 1 Demographic and clinical characteristics and antibiotic regimens of the study patients according to treatment arm

Variable	Missing data Control/experimental arms	15-day arm (n = 116)	8-day arm (n = 120)
Characteristics on the day of enrolment (Day 0)			
Age, years, median [IQR]	0/0	66·5 [59–77]	66 [57–76]
Patients aged > 80 years, n (%)	0/0	18 (16)	12 (10)
Male sex, n (%)	0/0	70 (60)	82 (68)
No underlying disease, n (%)	0/1	60 (52)	72 (61)
Charlson score, median [IQR]	0/0	5 [3–7]	4 [2–7]
Body mass index, kg/m^2, median [IQR]	9/10	27.3 [23–31.6]	28.1 [24–33]
Body mass index > 35 kg/m^2, n (%)	9/10	16 (15)	20 (18)
SAPS II score, median [IQR]	10/6	45 [34–51.8]	44.5 [35–56.8]
SAPS II score > 40, n (%)	10/6	63 (59)	73 (64)
SOFA score, median [IQR]	16/11	6 [3–8]	7 [4–9]
Mechanical ventilation, n (%)	16/11	83 (74)	96 (84)
Vasoactive agents, n (%)	16/11	79 (71)	78 (68)
Sedation, n (%)	16/11	77 (71)	91 (81)
Renal replacement therapy, n (%)	16/11	11 (10)	13 (11)
Source of contamination, n (%)			
Colon or rectum, n (%)	0/0	49 (42)	57 (48)
Small bowel, n (%)	0/0	37 (32)	39 (32)
Gastroduodenal, n (%)	0/0	15 (13)	13 (11)
Perforation, n (%)	0/1	61 (53)	53 (45)
Ischaemia/bowel necrosis, n (%)	0/1	17 (15)	19 (16)
Abscess, n (%)	0/1	23 (20)	17 (14)

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Primary and secondary outcomes	15-day arm (n=116)	8-day arm (n=120)	Odd-ratios (95%CI)	P value
Primary outcome				
Antibiotic-free days on Day28, median [IQR][a]	12 [6—13]	15 [6—20]	1.08 (1.04—1.125)	1.9×10^{-4}
Secondary outcome				
Length of ICU stay between Day0 and Day45, median [IQR][b]	12 [7—20]	13 [7.75—25]	1.02 (0.99—1.04)	0.14
Length of hospital stay between Day0 and Day45, median [IQR][c]	30 [20—45]	30.5 [18.75—45]	0.80 (0.46—1.38)	0.42
Secondary outcomes				
Organ failure on Day15, n (%)[d]	17/96 (18)	15/90 (17)	1.08 (0.47—2.50)	1.00
Organ failure on Day28, n (%)[e]	4/60 (5)	3/63 (6)	0.78 (0.11—4.82)	1.00
45-day mortality, n (%)	17/116 (15)	13/120 (11)	0.71 (0.30—1.64)	0.43
Additional source control between Day8 and Day45, n (%)	34/116 (28)	48/120 (40)	1.61 (0.90—2.87)	0.101
Reoperations between Day8 and Day45, n (%)	27/166 (23)	31/120 (26)	1.15 (0.61—2.17)	0.65
Percutaneous drainages between Day8 and Day45, n (%)	11/116 (9)	23/120 (19)	2.26 (0.99—5.41)	0.041
Recurrent infection, n (%)[f]	13/14 (93)	14/19 (74)	0.22 (0.004—2.40)	0.21
Superinfection, n (%)[e]	11/32 (34)	14/44 (32)	0.65 (0.05—5.52)	1
New antibiotic therapy, n (%)	45/116 (39)	51/120 (42)	1.17 (0.67—2.03)	0.59
New antibiotic therapy between Day16 and Day28, n (%)	25/102 (25)	29/106 (27)	1.16 (0.56—2.27)	0.75
Bacteraemia between Day8 and Day45, n (%)	5/116 (4)	13/120 (11)	2.69 (0.86—9.96)	0.059
Clinical failure between Day8 and Day45, n (%)	16 (14)	28 (24)	1.18 (0.68—2.05)	0.54
Microbiological failure between Day8 and Day45, n (%)	18 (16)	28 (23)	1.65 (0.82—3.40)	0.13
Emergence of MDR bacteria in surveillance samples, n (%)[g]	23/104 (22)	20/107 (19)	0.81 (0.39—1.67)	0.54
Emergence of MDR bacteria in clinical isolates, n (%)[d]	40/104 (38)	38/108 (35)	0.87 (0.47—1.58)	0.72
Emergence of MDR bacteria in both surveillance samples and clinical isolates confounded, n (%)[g]	52/104 (50)	46/108 (43)	0.74 (0.41—1.32)	0.28
Emergence of fungi, n (%)[g]	27/106 (25)	22/107 (21)	0.75 (0.37—1.51)	0.39

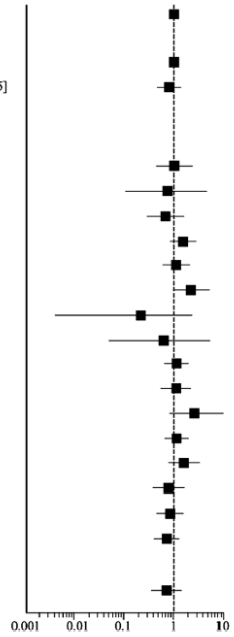

Fig. 2 Primary and secondary outcomes (two-sided analyses on ITT population). [a]Deceased patients have 0 days free of antibiotics; [b]deceased patients leave the ICU on the day of death; [c]deceased patients leave the hospital on the day of death; [d]among patients still hospitalised at day 15; [e]among patients still hospitalised at day 28; [f]among those who underwent reoperation or additional drainage; [g]among those who underwent surveillance samples or additional clinical isolates. Clinical and microbiological failures: see definitions in "Materials and methods". *IQR* interquartile range, *ICU* intensive care unit, *MDR bacteria* multidrug-resistant bacteria

ORIGINAL ARTICLE

Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection

R.G. Sawyer, J.A. Claridge, A.B. Nathens, O.D. Rotstein, T.M. Duane, H.L. Evans, C.H. Cook, P.J. O'Neill, J.E. Mazuski, R. Askari, M.A. Wilson, L.M. Napolitano, N. Namias, P.R. Miller, E.P. Dellinger, C.M. Watson, R. Coimbra, D.L. Dent, S.F. Lowry,* C.S. Cocanour, M.A. West, K.L. Banton, W.G. Cheadle, P.A. Lipsett, C.A. Guidry, and K. Popovsky, for the STOP-IT Trial Investigators†

N Engl J Med 2015;372:1996-2005.
DOI: 10.1056/NEJMoa1411162

Table 1. Baseline Demographic and Clinical Characteristics, According to Study Group.*

Variable	Control Group (N=260)	Experimental Group (N=258)
Age — yr	52.2±1.0	52.2±1.0
Male sex — no. (%)	145 (55.8)	144 (55.8)
Race or ethnic group — no. (%)†		
White	208 (80.0)	196 (76.0)
Black	43 (16.5)	51 (19.8)
Asian	5 (1.9)	6 (2.3)
American Indian or Alaskan Native	2 (0.8)	1 (0.4)
Hispanic — no. (%)	20 (7.7)	15 (5.8)
Other	2 (0.8)	4 (1.6)
Characteristics of index infection		
APACHE II score‡	9.9±0.4	10.3±0.4
Maximum white-cell count — per mm^3	15,600±0.4	17,100±0.7
Maximum body temperature — °C	37.8±0.1	37.7±0.1
Organ of origin — no. (%)		
Colon or rectum	80 (30.8)	97 (37.6)
Appendix	34 (13.1)	39 (15.1)
Small bowel	31 (11.9)	42 (16.3)
Source-control procedure — no. (%)		
Percutaneous drainage	86 (33.1)	86 (33.3)
Resection and anastomosis or closure	69 (26.5)	64 (24.8)
Surgical drainage only	55 (21.2)	54 (20.9)
Resection and proximal diversion	27 (10.4)	37 (14.3)
Simple closure	20 (7.7)	12 (4.7)
Surgical drainage and diversion	3 (1.2)	4 (1.6)

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Table 2. Primary and Major Secondary Outcomes.*

Variable	Control Group (N=260)	Experimental Group (N=257)	P Value
Primary outcome: surgical-site infection, recurrent intraabdominal infection, or death — no. (%)	58 (22.3)	56 (21.8)	0.92
Surgical-site infection	23 (8.8)	17 (6.6)	0.43
Recurrent intraabdominal infection	36 (13.8)	40 (15.6)	0.67
Death	2 (0.8)	3 (1.2)	0.99
Time to event — no. of days after index source-control procedure			
Diagnosis of surgical-site infection	15.1±0.6	8.8±0.4	<0.001
Diagnosis of recurrent intraabdominal infection	15.1±0.5	10.8±0.4	<0.001
Death	19.0±1.0	18.5±0.5	0.66
Secondary outcome			
Surgical-site infection or recurrent intraabdominal infection with resistant pathogen — no. (%)	9 (3.5)	6 (2.3)	0.62
Duration of outcome — days			
Antimicrobial therapy for index infection			<0.001
Median	8	4	
Interquartile range	5–10	4–5	
Antimicrobial-free days at 30 days			<0.001
Median	21	25	
Interquartile range	18–25	21–26	
Hospitalization after index procedure			0.48
Median	7	7	
Interquartile range	4–11	4–11	
Hospital-free days at 30 days			0.22
Median	23	22	
Interquartile range	18–26	16–26	

ORIGINAL ARTICLE

Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection

R.G. Sawyer, J.A. Claridge, A.B. Nathens, O.D. Rotstein, T.M. Duane, H.L. Evans, C.H. Cook, P.J. O'Neill, J.E. Mazuski, R. Askari, M.A. Wilson, L.M. Napolitano, N. Namias, P.R. Miller, E.P. Dellinger, C.M. Watson, R. Coimbra, D.L. Dent, S.F. Lowry,* C.S. Cocanour, M.A. West, K.L. Banton, W.G. Cheadle, P.A. Lipsett, C.A. Guidry, and K. Popovsky, for the STOP-IT Trial Investigators†

N Engl J Med 2015;372:1996-2005.
DOI: 10.1056/NEJMoa1411162

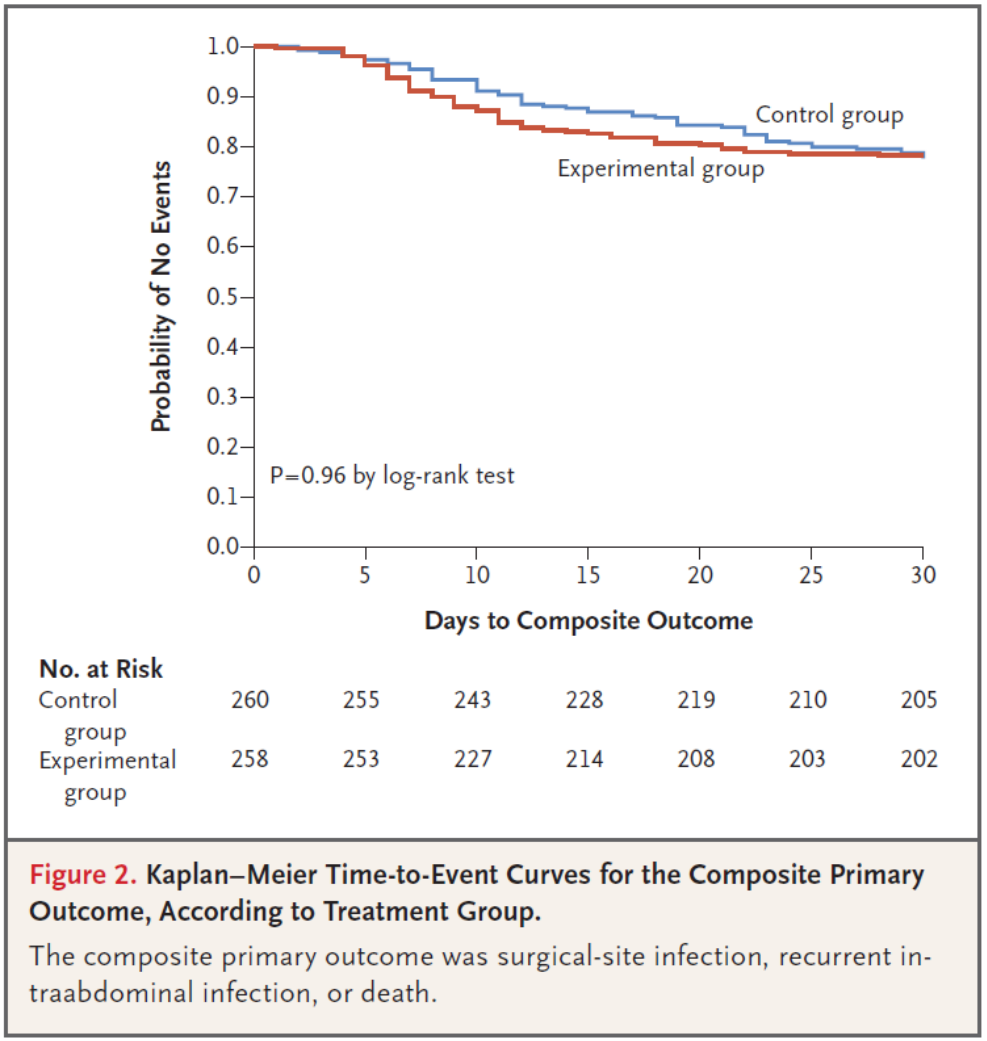

Figure 2. Kaplan–Meier Time-to-Event Curves for the Composite Primary Outcome, According to Treatment Group.

The composite primary outcome was surgical-site infection, recurrent intraabdominal infection, or death.

Composite Criteria for Non-Operative Management of Acute Non-Complicated Appendicitis Result in Low Failure Rates

Shahaf Shay[1] · Amram Kupietzky[1] · Daniel Joshua Weiss[1] · Roi Dover[1] · Nachum Emil Eliezer Lourie[1] · Tzlil Mordechay-Heyn[1] · Haggi Mazeh[1] · Ido Mizrahi[1]

World J Surg (2022) 46:69–75
https://doi.org/10.1007/s00268-021-06330-x

Methods Patients admitted to our institution between March 2016 and October 2019 with non-complicated AA were grouped according to their initial management: non-operative versus surgical. Our unique protocol for non-operative management includes: pain < 3 days; afebrile upon admission; non-gravid; WBC <15,000 ($\times 10^9$/L); CRP < 5 mg/dl; appendix diameter < 1 cm; no appendicolith on imaging; no prior episode of AA; no history of Inflammatory Bowel Disease; no evidence of peritonitis on physical examination. The primary outcome measured was failure of non-surgical management during the index admission. Secondary outcomes included recurrence rate, readmissions, complications, length of antibiotic treatment and length of stay (LOS).

Composite Criteria for Non-Operative Management of Acute Non-Complicated Appendicitis Result in Low Failure Rates

Shal
Nacl

Table 1 Comparison of patient demographics and clinical presentation

Characteristics	Conservative treatment ($N = 259$)	Surgical treatment ($N = 436$)	p value
Age (years)	21.3 ± 13.4	24.4 ± 16.8	0.006
Gender			
Female	128 (47.5%)	161 (37.2%)	0.007
Male	141 (52.5%)	277 (62.8%)	
Fever at home	31 (12.0%)	80 (18.2%)	0.026
Length of pain prior to admission (hours)	33.1 ± 45.2	27.3 ± 28.8	0.04
Fever at admission (celsius)	36.7 ± 0.6	36.8 ± 0.7	0.20
White blood count ($\times 10^9$/L)	11.2 ± 3.9	14.6 ± 4.7	< 0.001
CRP (mg/dl)	2.1 ± 3.6	3.9 ± 6.0	< 0.001
Diagnostic imaging modality			
Ultrasound (US)	161 (59.9%)	237 (54.4%)	0.23
Computed tomography (CT)	97 (36.1%)	185 (42.2%)	
Both	11 (4.1%)	14 (3.2%)	
Radiological findings			
Largest appendix diameter (mm)	8.2 ± 1.9	10.8 ± 3.2	< 0.001
Appendicolith	11 (4.2%)	130 (29.8%)	< 0.001

Composite Criteria for Non-Operative Management of Acute Non-Complicated Appendicitis Result in Low Failure Rates

Shahaf Shay[1] · Amram Kupietzky[1] · Daniel Joshua Weiss[1] · Roi Dover[1] · Nachum Emil Eliezer Lourie[1] · Tzlil Mordechay-Heyn[1] · Haggi Mazeh[1] · Ido Mizrahi[1]

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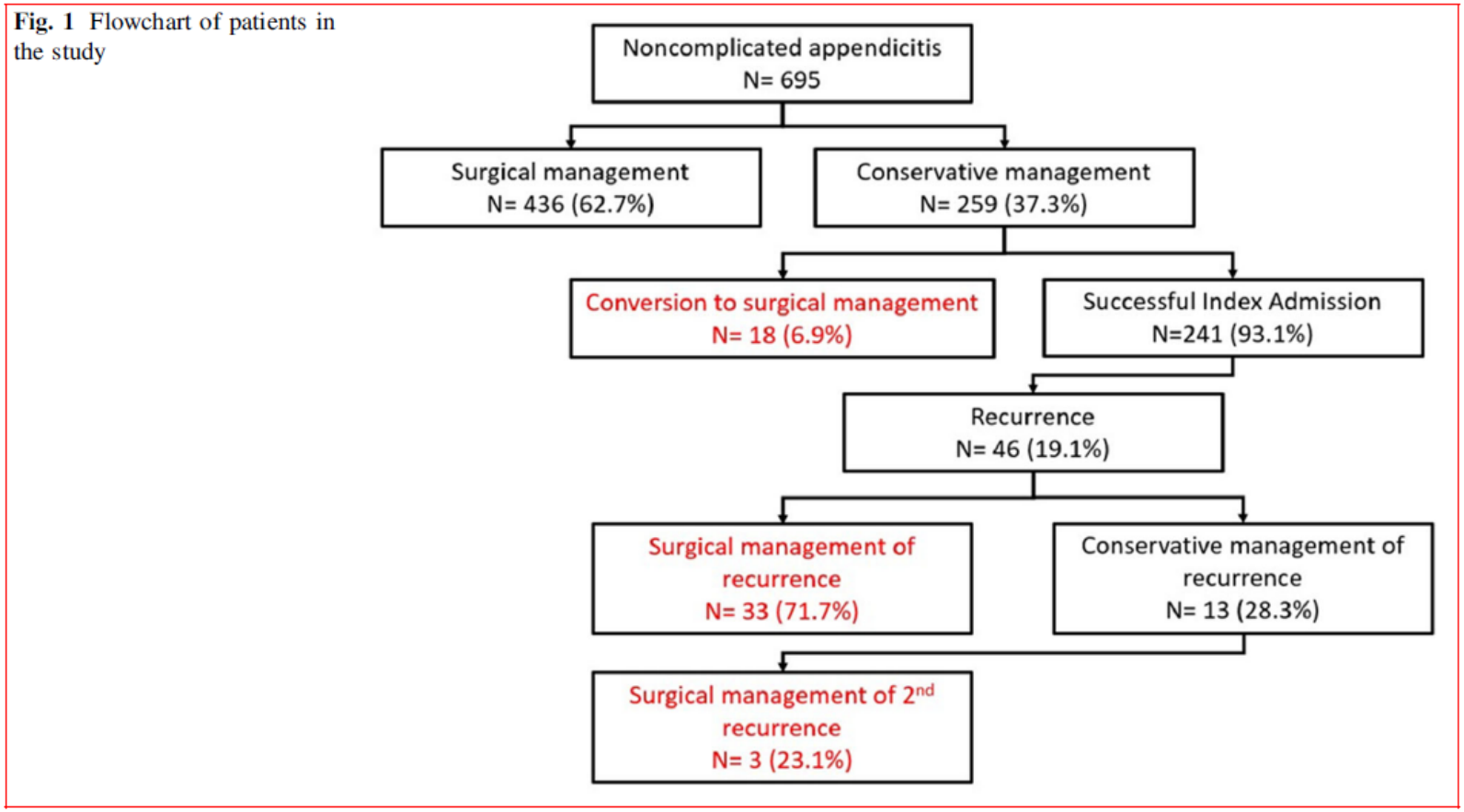

Fig. 1 Flowchart of patients in the study

Composite Criteria for Non-Operative Management of Acute Non-Complicated Appendicitis Result in Low Failure Rates

Shahaf Shay[1] · Amram Kupietzky[1] · Daniel Joshua Weiss[1] · Roi Dover[1] · Nachum Emil Eliezer Lourie[1] · Tzlil Mordechay-Heyn[1] · Haggi Mazeh[1] · Ido Mizrahi[1]

World J Surg (2022) 46:69–75
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Table 2 Index admission data

Characteristics	Conservative treatment ($N = 259$)	Surgical treatment ($N = 436$)	p value
IV antibiotic treatment (days)	2.9 ± 1.2	2.4 ± 1.8	< 0.001
PO antibiotic treatment at home (days)	5.3 ± 1.8	0.4 ± 1.4	< 0.001
Total antibiotic treatment (days)	7.9 ± 2.5	2.8 ± 2.7	< 0.001
LOS (days)	3.5 ± 1.1	3.7 ± 1.8	0.11

Composite Criteria for Non-Operative Management of Acute Non-Complicated Appendicitis Result in Low Failure Rates

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World J Surg (2022) 46:69–75
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Table 4 Comparison of successful versus unsuccessful conservative treatment characteristics

Characteristics	Successful treatment (n = 195)	Unsuccessful treatment (n = 64)	p value
Age (years)	21.6 ± 13.8	18.8 ± 10.8	0.10
Gender			
Female	103 (52.8%)	22 (34.4%)	0.10
Male	92 (47.2%)	42 (65.6%)	
Fever at home	22 (11.3%)	9 (14.1%)	0.55
Length of pain at home (hours)	35.8 ± 43.9	28.7 ± 43.0	0.32
Fever at admission (celsius)	36.7 ± 0.6	36.8 ± 0.6	0.37
White blood count ($\times 10^9$/L)	11.0 ± 4.1	11.8 ± 3.5	0.16
CRP (mg/dl)	1.7 ± 2.9	3.0 ± 4.9	0.05
Radiological findings			
Largest appendix diameter (mm)	8.1 ± 1.9	8.5 ± 1.9	0.24
Appendicolith	7 (3.6%)	4 (6.3%)	0.36

Short-course antibiotic therapy for critically ill patients treated for postoperative intra-abdominal infection: the DURAPOP randomised clinical trial

Intensive Care Med (2018) 44:300–310

Philippe Montravers[1,18*], Florence Tubach[2], Thomas Lescot[3], Benoit Veber[4], Marina Esposito-Farèse[5], Philippe Seguin[6], Catherine Paugam[7], Alain Lepape[8], Claude Meistelman[9], Joel Cousson[10], Antoine Tesniere[11], Gaetan Plantefeve[12], Gilles Blasco[13], Karim Asehnoune[14], Samir Jaber[15], Sigismond Lasocki[16], Herve Dupont[17] and For the DURAPOP Trial Group

Table 1 Demographic and clinical characteristics and antibiotic regimens of the study patients according to treatment arm

Variable	Missing data Control/experimental arms	15-day arm (n = 116)	8-day arm (n = 120)
Characteristics on the day of enrolment (Day 0)			
Age, years, median [IQR]	0/0	66·5 [59–77]	66 [57–76]
Patients aged > 80 years, n (%)	0/0	18 (16)	12 (10)
Male sex, n (%)	0/0	70 (60)	82 (68)
No underlying disease, n (%)	0/1	60 (52)	72 (61)
Charlson score, median [IQR]	0/0	5 [3–7]	4 [2–7]
Body mass index, kg/m^2, median [IQR]	9/10	27.3 [23–31.6]	28.1 [24–33]
Body mass index > 35 kg/m^2, n (%)	9/10	16 (15)	20 (18)
SAPS II score, median [IQR]	10/6	45 [34–51.8]	44.5 [35–56.8]
SAPS II score > 40, n (%)	10/6	63 (59)	73 (64)
SOFA score, median [IQR]	16/11	6 [3–8]	7 [4–9]
Mechanical ventilation, n (%)	16/11	83 (74)	96 (84)
Vasoactive agents, n (%)	16/11	79 (71)	78 (68)
Sedation, n (%)	16/11	77 (71)	91 (81)
Renal replacement therapy, n (%)	16/11	11 (10)	13 (11)
Source of contamination, n (%)			
Colon or rectum, n (%)	0/0	49 (42)	57 (48)
Small bowel, n (%)	0/0	37 (32)	39 (32)
Gastroduodenal, n (%)	0/0	15 (13)	13 (11)
Perforation, n (%)	0/1	61 (53)	53 (45)
Ischaemia/bowel necrosis, n (%)	0/1	17 (15)	19 (16)
Abscess, n (%)	0/1	23 (20)	17 (14)

Short-course antibiotic therapy for critically ill patients treated for postoperative intra-abdominal infection: the DURAPOP randomised clinical trial

Philippe Montravers[1,18*], Florence Tubach[2], Thomas Lescot[3], Benoit Veber[4], Marina Esposito-Farèse[5], Philippe Seguin[6], Catherine Paugam[7], Alain Lepape[8], Claude Meistelman[9], Joel Cousson[10], Antoine Tesniere[11], Gaetan Plantefeve[12], Gilles Blasco[13], Karim Asehnoune[14], Samir Jaber[15], Sigismond Lasocki[16], Herve Dupont[17] and For the DURAPOP Trial Group

Intensive Care Med (2018) 44:300–310

Primary and secondary outcomes	15-day arm (n=116)	8-day arm (n=120)	Odd-ratios (95%CI)	P value
Primary outcome				
Antibiotic-free days on Day28, median [IQR][a]	12 [6—13]	15 [6—20]	1.08 (1.04—1.125)	1.9×10^{-4}
Secondary outcome				
Length of ICU stay between Day0 and Day45, median [IQR][b]	12 [7—20]	13 [7.75—25]	1.02 (0.99—1.04)	0.14
Length of hospital stay between Day0 and Day45, median [IQR][c]	30 [20—45]	30.5 [18.75—45]	0.80 (0.46—1.38)	0.42
Secondary outcomes				
Organ failure on Day15, n (%)[d]	17/96 (18)	15/90 (17)	1.08 (0.47—2.50)	1.00
Organ failure on Day28, n (%)[e]	4/60 (5)	3/63 (6)	0.78 (0.11—4.82)	1.00
45-day mortality, n (%)	17/116 (15)	13/120 (11)	0.71 (0.30—1.64)	0.43

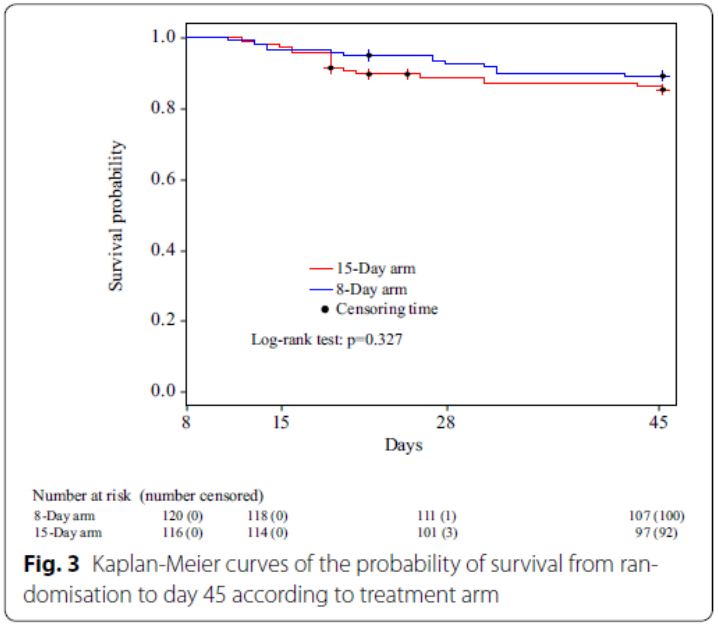


Fig. 3 Kaplan-Meier curves of the probability of survival from randomisation to day 45 according to treatment arm

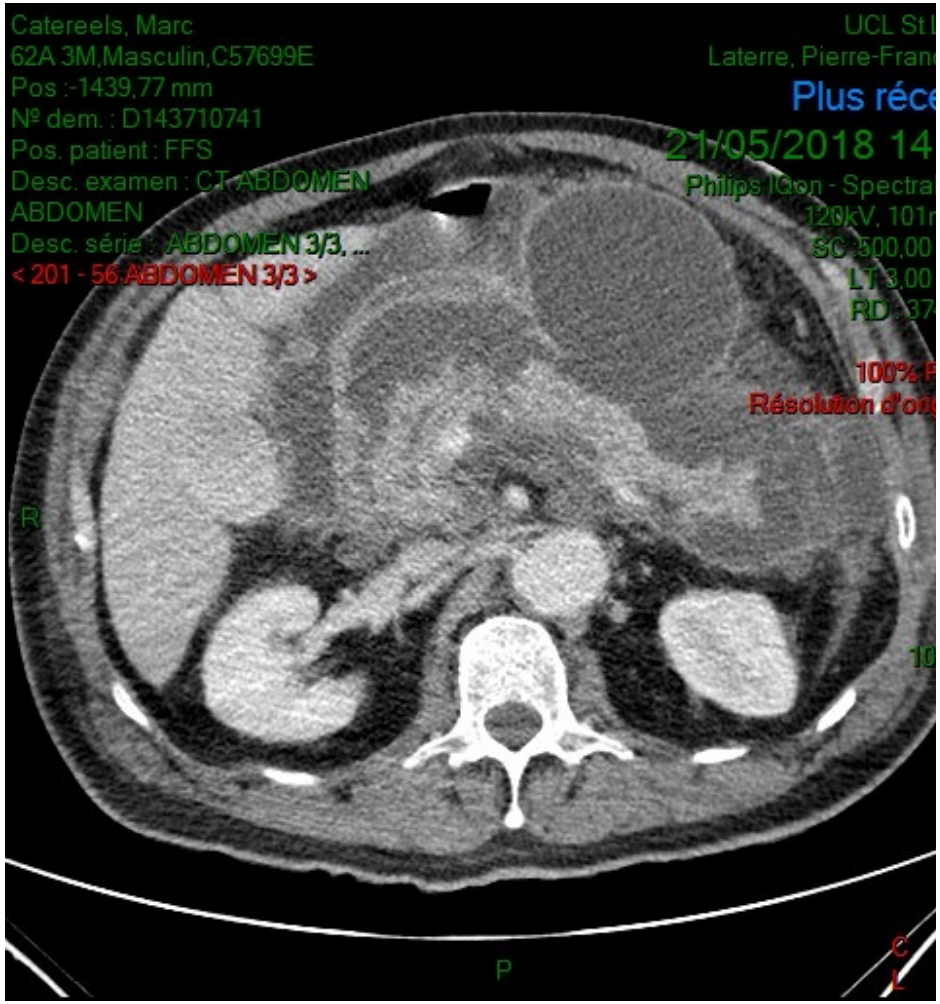
Patients with Complicated Intra-Abdominal Infection Presenting with Sepsis Do Not Require Longer Duration of Antimicrobial Therapy

Rishi Rattan, MD, Casey J Allen, MD, Robert G Sawyer, MD, Reza Askari, MD, Kaysie L Banton, MD, Jeffrey A Claridge, MD, MS, FACS, Christine S Cocanour, MD, FACS, FCCM, Raul Coimbra, MD, PhD, FACS, Charles H Cook, MD, FACS, FCCM, Joseph Cuschieri, MD, FACS, E Patchen Dellinger, MD, Therese M Duane, MD, FACS, FCCM, Heather L Evans, MD, MS, FACS, Pamela A Lipsett, MD, MHPE, FACS, FCCM, John E Mazuski, MD, PhD, Preston R Miller, MD, Patrick J O'Neill, MD, PhD, FACS, Ori D Rotstein, MD, MSc, FRCSC, FACS, Nicholas Namias, MD, MBA,

J Am Coll Surg 2016;222:440–446.

Table 1. Baseline Demographic and Clinical Characteristics, According to Study Group

Characteristic	Control group (n = 45)*	Experimental group (n = 67)
Age, y, mean ± SD	53 ± 16	51 ± 16
Male sex, n (%)	24 (53.3)	37 (55.2)
Race or ethnic group, n (%)†		
White	37 (82.2)	54 (80.6)
Black	8 (17.8)	11 (16.4)
Other	0 (0)	2 (3.0)
Characteristic of index infection		
APACHE II score, mean ± SD‡	11.2 ± 6.6	11.2 ± 5.9
Maximum WBC, 1000 per mm^3, median (range)	17.1 (15.2–20.4)	18.5 (15.1–21.6)
Maximum body temperature, °C, mean ± SD	38.5 ± 0.4	38.5 ± 0.4
Organ of origin, n (%)		
Colon or rectum	18 (40.0)	21 (31.3)
Appendix	6 (13.0)	11 (16.4)
Small bowel	4 (8.9)	10 (14.9)
Source-control procedure, n (%)		
Percutaneous drainage	10 (22.2)	23 (34.3)
Resection and anastomosis or closure	13 (28.9)	11 (16.4)
Surgical drainage only	16 (35.6)	19 (28.4)
Resection and proximal diversion	5 (11.1)	10 (14.9)
Simple closure	1 (2.2)	4 (6.0)
Surgical drainage and diversion	0 (0)	0 (0)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62A 3M,Masculin,C57699E
Pos :-1439,77 mm
Nº dem. : D143710741
Pos. patient : FFS
Desc. examen : CT ABDOMEN
ABDOMEN
Desc. série : ABDOMEN 3/3, ...
< 201 - 56 ABDOMEN 3/3 >
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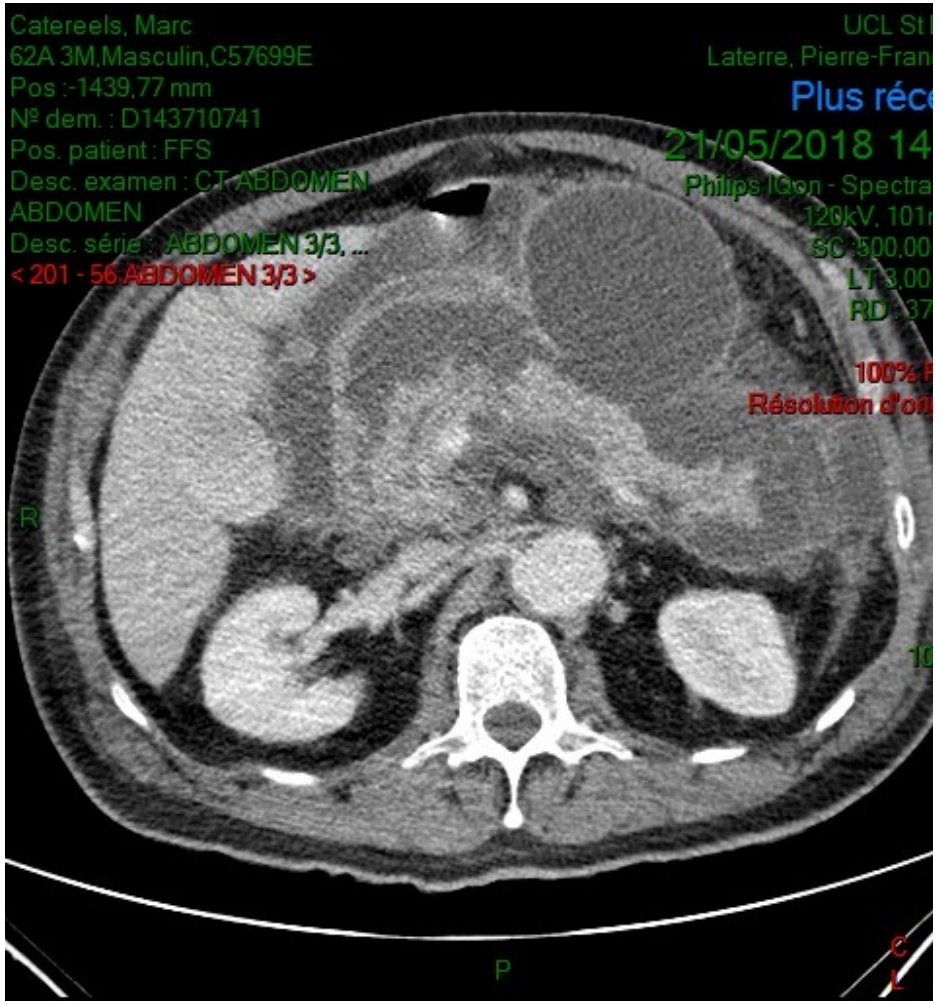
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Guidelines for management of intra-abdominal infections

Philippe Montravers [a,*], Hervé Dupont [b], Marc Leone [c], Jean-Michel Constantin [d], Paul-Michel Mertes [e], and the Société française d'anesthésie et de réanimation (Sfar), Société de réanimation de langue française (SRLF), Pierre-Francois Laterre [f], Benoit Misset [g], Société de pathologie infectieuse de langue française (SPILF), Jean-Pierre Bru [h], Rémy Gauzit [i], Albert Sotto [j], Association française de chirurgie (AFC), Cecile Brigand [k], Antoine Hamy [l], Société française de chirurgie digestive (SFCD), Jean-Jacques Tuech [m]

Anaesth Crit Care Pain Med 34 (2015) 117–130

R11 – Empirical antibiotic therapy protocols for community-acquired IAI must be established on the basis of regular analysis of national and regional microbiological data in order to quantify and monitor the course of microbial resistance in the community.

(Grade 1+) STRONG agreement

Rationale: In view of the potential difficulty of selecting appropriate anti-infective therapy, local and regional antibiotic therapy protocols must be established on the basis of the community origin, patient characteristics (comorbidities), clinical severity, presence of documented beta-lactam allergy and by taking local bacterial resistance data into account [7,26–28]. These protocols must be elaborated by multidisciplinary teams (anaesthetists-intensive care physicians, microbiologists, surgeons, infectious disease specialists and pharmacists).

Patients with Complicated Intra-Abdominal Infection Presenting with Sepsis Do Not Require Longer Duration of Antimicrobial Therapy

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J Am Coll Surg 2016;222:440–446.

Table 2. Primary and Major Secondary Outcomes: As-Treated Analysis

Outcome	Control group (n = 45)	Experimental group (n = 67)	p Value
Primary outcome			
Surgical site infection, n (%)	4 (8.9)	8 (11.9)	0.759
Recurrent intra-abdominal infection, n (%)	6 (13.3)	8 (11.9)	1.000
Death, n (%)	0 (0)	1 (1.5)	1.000
Time to event, days after index source-control procedure			
Diagnosis of surgical site infection, mean ± SD	21.3 ± 6.1	6.9 ± 3.5	<0.001
Diagnosis of recurrent intra-abdominal infection, mean ± SD	18.0 ± 8.1	12.5 ± 6.6	0.185
Death, median (range)	—	7.0 (7.0–7.0)	—
Secondary outcome			
Surgical site infection with resistant pathogen, n (%)	0 (0)	2 (3.0)	0.515
Recurrent intra-abdominal infection with resistant pathogen, n (%)	1 (2.2)	0 (0)	0.402
Any extra-abdominal infection, n (%)	3 (6.7)	7 (10.4)	0.523
Clostridium difficile infection, n (%)	0 (0)	0 (0)	1.000
Duration of outcome, d, mean ± SD			
Antimicrobial therapy for index infection	7.2 ± 2.5	4.4 ± 0.6	<0.001
Antimicrobial-free days at 30 d	21.3 ± 3.9	23.6 ± 4.9	0.009
Hospitalization after index procedure	9.0 ± 7.5	7.4 ± 5.5	0.227
Hospital-free days at 30 d	20.6 ± 7.0	21.6 ± 6.4	0.436

The Surgical Infection Society Revised Guidelines on the Management of Intra-Abdominal Infection

SURGICAL INFECTIONS
Volume 18, Number 1, 2017
Mary Ann Liebert, Inc.

TABLE 6. FACTORS POTENTIALLY IDENTIFYING PATIENTS WITH INTRA-ABDOMINAL INFECTION AT HIGHER RISK

Phenotypic/physiologic risk factors
Advanced age (≥70 y)
Malignancy
Significant cardiovascular compromise
Significant liver disease or cirrhosis
Significant renal disease
Hypoalbuminemia
Extent of infection/adequacy of initial source control
Diffuse, generalized peritonitis
Elevated MPI score
Delayed initial source control
Inability to achieve adequate source control
Microbiologic characteristics
Suspected infection with resistant pathogens

MPI = Mannheim Peritonitis Index.

TABLE 7. CRITERIA FOR HEALTHCARE- OR HOSPITAL-ACQUIRED INTRA-ABDOMINAL INFECTION

Infection developing greater than 48 h after initial source control.
Hospitalized for greater than 48 h during current admission or within the previous 90 d.
Residence in a skilled nursing or other long-term care facility within the previous 30 d.
Home infusion therapy, home wound care, or dialysis within the preceding 30 d.
Use of broad-spectrum antimicrobial therapy for 5 d or more during the preceding 90 d.

Inadequate Source Control and Inappropriate Antibiotics are Key Determinants of Mortality in Patients with Intra-Abdominal Sepsis and Associated Bacteremia

SURGICAL INFECTIONS
Volume 16, Number 6, 2015

TABLE 9. MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

Variable	*AOR, 95% CI*	p
Inadequate source control	7.46, 2.08–26.32	0.002
Inappropriate antibiotics	3.86, 1.28–11.64	0.016
APACHE II score (1 point increments)	0.93, 0.87– 1.01	0.084

Hosmer-Lemeshow p=0.943, AUROC=0.776.
AOR=adjusted odds ratio; CI=confidence interval; APACHE=Acute Physiology and Chronic Health Evaluation.

BMJ Open A randomised placebo-controlled

BMJ Open 2018;**8**:e023623.

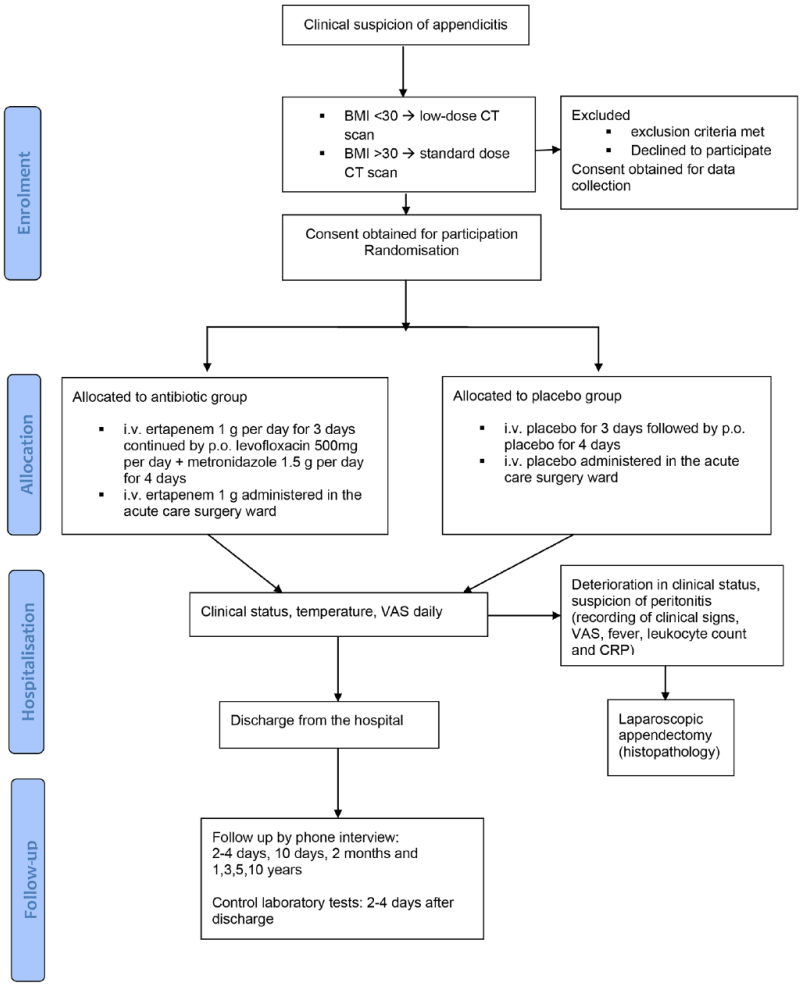

Figure 1 Flow chart of the APPAC III (APPendicitis ACuta III) study protocol. BMI, body mass index; CRP, C reactive protein; i.v., intravenous; p.o., orally; VAS, Visual Analogue Scale.

Short-course antimicrobial treatment for acute cholangitis with Gram-negative bacillary bacteremia☆

Shunsuke Uno[a,*], Ryota Hase[b], Masayoshi Kobayashi[c], Toshiyasu Shiratori[c], So Nakaji[c], Nobuto Hirata[c], Naoto Hosokawa[b]

International Journal of Infectious Diseases 55 (2017) 81–85

Table 2
Summary of patient demographic and clinical characteristics and treatments provided.

	Before May 2013 ($n=40$)	After May 2013 ($n=52$)	p-Value
Age, years			
Mean ± SD	81.7 ± 7.95	76.0 ± 11.1	0.007[a]
Median (range)	83.5 (56–92)	76 (46–98)	
Sex, male, n (%)	23 (57.5)	35 (67.3)	0.227[b]
Community-acquired, n (%)	37 (92.5)	51 (98.1)	0.217[b]
History of acute cholangitis, n (%)	7 (17.5)	13 (25.0)	0.273[b]
Diagnosis according to TG13 criteria			
Definite	34 (85.0)	49 (94.2)	
Suspected	6 (15.0)	3 (5.8)	
Severity grading defined in TG13, n (%)			0.138[c]
Grade I (mild)	15 (37.5)	27 (51.9)	
Grade II (moderate)	13 (32.5)	15 (28.8)	
Grade III (severe)	12 (30.0)	10 (19.2)	
Pitt bacteremia score, median (IQR)	1 (0–2)	0.5 (0–2)	0.953[c]
Charlson comorbidity index, median (IQR)	2 (0–3)	1 (0–3)	0.533[c]

Table 3
Study outcomes.

	Before May 2013 ($n=40$)	After May 2013 ($n=52$)	p-Value
Treatment duration, median days (IQR)	14.5 (14–15)	10.0 (7.25–12.75)	<0.001[a]
Hospital length of stay, median days (IQR)	17.5 (16–22.5)	14.0 (10.0–17.0)	<0.001[a]
30-day mortality rate, n/n (%)	2/35 (5.7)	0/47 (0.0)	0.179[b]
Recurrence rate within 3 months, n/n (%)	4/30 (13.3)	0/37 (0.0)	0.036[b]

Short-course antimicrobial treatment for acute cholangitis with Gram-negative bacillary bacteremia☆

Shunsuke Uno[a,*], Ryota Hase[b], Masayoshi Kobayashi[c], Toshiyasu Shiratori[c], So Nakaji[c], Nobuto Hirata[c], Naoto Hosokawa[b]

International Journal of Infectious Diseases 55 (2017) 81–85

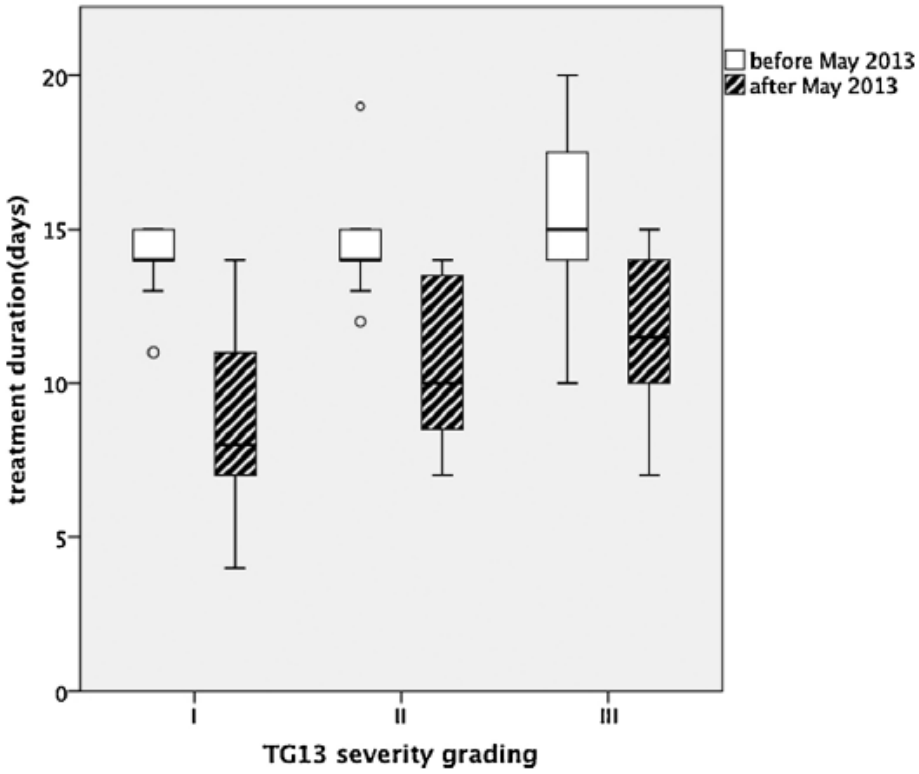

Figure 2. Comparison of treatment duration.

Therapeutic management of peritonitis: a comprehensive guide for intensivists

P. Montravers[1*], S. Blot[2,10], G. Dimopoulos[3], C. Eckmann[4], P. Eggimann[5], X. Guirao[6], J. A. Paiva[7,11], G. Sganga[8] and J. De Waele[9]

Intensive Care Med (2016) 42:1234–1247
DOI 10.1007/s00134-016-4307-6

Table 3 Surgical and non-surgical infectious complications in patients with diffuse secondary peritonitis

Complications	Clinical setting	Frequency	Treatment
Severe bleeding	Haemodynamic instability Significant blood loss	++	Reoperation, bleeding control
SSI (superficial/deep)	Putrid wound secretion	+++	Incision and drainage
SSI (organ space)	Faecal wound secretion	++	Relaparotomy, source control, open wound therapy
Dehiscence of abdominal fascia	Fascia necrosis/abdominal compartment syndrome	+	Relaparotomy, mesh implant/open abdomen/ negative pressure therapy
Intra-abdominal abscess	Evidence on imaging (CT, US)	+/++	CT-guided drainage
Anastomotic leakage	Evidence on imaging, drain fluid	+/++	Relaparotomy, source control/drainage
Rectal stump insufficiency	Putrid anal secretion following Hartmann procedure	(+)	Transrectal drainage, negative pressure therapy
Rupture of stoma	Stool in soft tissue around stoma	(+)	Reoperation, reinsertion of stoma
Tertiary peritonitis	Persistent abdominal infection despite adequate source control	+	Antibiotic and/or antifungal treatment Source control sufficient?
Septic shock	Haemodynamic instability	++	Haemodynamic stabilization, anti-infective treatment Diagnostic investigations for source of infection
Pneumonia	Respiratory insufficiency, unplanned (re)intubation	+++	Antibiotic therapy
Urinary tract infection (UTI)	Lower UTI or pyelonephritis	+	Antibiotic therapy, source control

(+) very rare (<1 %), + rare (1–5 %), ++ common (5–10 %), +++ very common (>10 %)

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Intensive Care Med (2016) 42:1234–1247
DOI 10.1007/s00134-016-4307-6

Table 4 Potential pathogens in peritonitis

Microorganism	Predisposing clinical condition requiring coverage beyond standard first-line antimicrobial therapy	Resistance considerations
Gram-positive bacteria		
Streptococci	None. Covered by first-line antibiotic regimen	No clinically relevant resistance problem
Enterococci	Septic shock, failure of early surgical source control, recent antibiotic exposure (particularly prolonged cephalosporin treatment), immunosuppression and prosthetic heart valves	Resistance likely in healthcare-associated infections, especially when caused by *E. faecium*. Ampicillin resistance and associated production of beta-lactamases are a concern in some geographical areas, as well as glycopeptide resistance
Coagulase-negative staphylococci	Clinical relevance uncertain	Methicillin-resistance likely in healthcare-associated infection
Staphylococcus aureus	None. Methicillin-susceptible *S. aureus* is covered by first-line antibiotic regimen	Methicillin-resistance possible in healthcare-associated infection
Gram-negative bacteria		
Enterobacteriaceae (*Escherichia coli*, *Enterobacter* spp., *Klebsiella* spp., *Serratia* spp., *Proteus* spp., etc.)	None. Non-extended-spectrum beta-lactamase (ESBL)-producing strains are covered by first-line antibiotic regimen	ESBL-producing strains likely in healthcare-associated infection and should be considered in patients with a history of recent travel in regions with high prevalence (Egypt, Thailand, India). Fluoroquinolone-resistance of *E. coli* may be as high as 20 % in some geographical areas
Non-fermenting Gram-negative bacteria (*Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, etc.)	Healthcare-associated infection, especially with length of hospital stay >5 days. Recent antibiotic exposure. Chronic underlying diseases leading to immunocompromised status (e.g. due to corticosteroid use)	Multidrug resistance most likely in healthcare-associated infection
Anaerobe bacteria (*Bacteroides fragilis*, *Clostridium* spp., etc.)	None. Covered by first-line antibiotic regimen	High rates of resistance to clindamycin and cefoxitin in certain geographical areas. Resistance to metronidazole is rare
Candida spp.	Immunodeficiency and prolonged antibiotic exposure. Tertiary peritonitis following failure of source control, especially in peritonitis originating from upper GI tract perforation	Selection towards *Candida* non-albicans spp. with dose-dependent susceptibility to fluconazole in patients with prior fluconazole exposure

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DOI 10.1007/s00134-016-4307-6

Table 5 Empirical antibiotic regimens proposed in recent guidelines for community-acquired and healthcare-associated infections

Expert groups	Community-acquired peritonitis		Healthcare-associated peritonitis	
	Mild to moderate cases	Severe or at-risk cases	Mild to moderate cases	Severe or at-risk cases
2006—Belgium [42]	Amoxicillin/clavulanate, cefuroxime + metronidazole Fluoroquinolones + metronidazole		Piperacillin/tazobactam or carbapenems Allergy to β-lactams: fluoroquinolones or aztreonam + metronidazole ± vancomycin	
2009—Spain [41]	Amoxicillin/clavulanate, ceftriaxone or cefotaxime + metronidazole, ertapenem In case of β-lactams allergy: gentamicin or aztreonam + metronidazole, tigecycline For suspected MDR *Enterobacteriaceae* ertapenem or tigecycline	Piperacillin/tazobactam or imipenem, meropenem or tigecycline (+ antipseudomonal drug in case of septic shock) In case of β-lactam allergy: tigecycline	Piperacillin/tazobactam or imipenem, meropenem or tigecycline In case of β-lactam allergy: tigecycline	Imipenem or meropenem + linezolid or daptomycin or glycopeptide Tigecycline + ceftazidime or amikacin
2009—USA [8]	Monotherapy: cefoxitin, ertapenem, moxifloxacin, tigecycline or ticarcillin/clavulanate Combination therapy: cefazolin, cefuroxime, ceftriaxone, cefotaxime, ciprofloxacin or levofloxacin + metronidazole	Monotherapy: imipenem, meropenem, doripenem or piperacillin/tazobactam Combination therapy: cefepime, ceftazidime, ciprofloxacin, or levofloxacin + metronidazole	Piperacillin/tazobactam or imipenem, meropenem ± aminoglycoside Ceftazidime or cefepime + metronidazole ± aminoglycoside MRSA infection: vancomycin	
2010—Canada [7]	Mild to moderate cases: monotherapy: cefoxitin, amoxicillin/clavulanate, ticarcillin/clavulanate, ertapenem, moxifloxacin, tigecycline Combination therapy: cefuroxime, ceftriaxone, cefotaxime or ciprofloxacin + metronidazole	Piperacillin/tazobactam or Imipenem or meropenem ± aminoglycoside ceftazidime or cefepime or ciprofloxacin + metronidazole tigecycline + ciprofloxacin	Piperacillin/tazobactam or imipenem or meropenem ± aminoglycoside Ceftazidime or cefepime or ciprofloxacin + metronidazole Tigecycline + ciprofloxacin MRSA or enterococcal infections: vancomycin or linezolid or daptomycin or tigecycline	
2013—International [5]	Amoxicillin/clavulanate, ciprofloxacin + metronidazole At risk of ESBL infection: ertapenem or tigecycline Biliary tract infections and at risk of ESBL infection: tigecycline	Piperacillin/tazobactam At risk of ESBL infection: imipenem or meropenem Biliary tract infections: piperacillin/tazobactam Biliary tract infections and at risk of ESBL infection: piperacillin + tigecycline	Piperacillin + tigecycline Imipenem or meropenem + teicoplanin	
2015—France [10]	Amoxicillin/clavulanate + gentamicin or cefotaxime/ceftriaxone + metronidazole In case of β-lactams allergy: levofloxacin + gentamicin + metronidazole, or tigecycline	Piperacillin/tazobactam + gentamicin	Piperacillin/tazobactam + amikacin ± vancomycin Allergy to β-lactams: ciprofloxacin or aztreonam + amikacin + metronidazole + vancomycin Or tigecycline + ciprofloxacin	Severe cases or patients at risk of MDR bacteria Imipenem or meropenem ± amikacin ± vancomycin

Regional differences ?

Tissue penetration ?

Table 9 Biliary penetration ability of the most common antibiotics

Good penetration efficiency	Low penetration efficiency
Piperacillin/tazobactam	Ceftriaxone
Tigecycline	Cefotaxime
Amoxicillin/clavulanate	Meropenem
Ciprofloxacin	Ceftazidime
Ampicillin/sulbactam	Vancomycin
Cefepime	Amikacin
Levofloxacin	Gentamicin

Severe acute pancreatitis

Quinolones ?
Carbapenems ?

Statement (type of antibiotics)

1. In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis should be used (1B).
2. In patients with infected necrosis, the spectrum of empirical antibiotic regimen should include both aerobic and anaerobic Gram-negative and Gram-positive microorganisms. Routine prophylactic administration of antifungal is not recommended in patients with infected acute pancreatitis, although *Candida* spp. are common in patients with infected pancreatic necrosis and indicate patients with a higher risk of mortality (1B).

Discussion Aminoglycoside antibiotics (e.g., gentamicin and tobramycin) in standard intravenous dosages fail to penetrate into the pancreas in sufficient tissue concentrations to cover the minimal inhibitory concentration (MIC) of the bacteria that are commonly found in secondary pancreatic infections [71].

Acylureidopenicillins and third-generation cephalosporins have an intermediate penetration into pancreas tissue and are effective against gram-negative microorganisms and can cover the MIC for most gram-negative organisms found in pancreatic infections [72]. Among these antibiotics, only piperacillin/tazobactam is effective against gram-positive bacteria and anaerobes.

Quinolones (ciprofloxacin and moxifloxacin) and carbapenems both show good tissue penetration into the pancreas the additional benefit of excellent anaerobic coverage [73–76]. However, because of quinolones high rate of resistance worldwide, quinolones should be discouraged and used only in patients with allergy to beta-lactam agents. Carbapenems due to the spread of carbapenem resistant *Klebsiella pneumoniae* should be always optimized and should be used only in very critically ill patients.

Antifungal therapy ?

- Not for CA IAI
- Upper GI-tract perforation ?
- Previous antimicrobial therapy ?
- Tertiary IAI ?
- Septic shock in tertiary IAI ?

- Azoles or Echinocadins ?

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

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

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

Recommendation

1. In patients with recent abdominal surgery and recurrent gastrointestinal perforation or anastomotic leakage, prophylaxis with fluconazole should be considered (BI); an echinocandin should be considered if there is a high likelihood of azole resistance (CII).

Recommendations

1. Fungicidal agents such as echinocandins or lipid formulations of amphotericin B should be used for targeted therapy of all critically ill patients or for patients with previous exposure to azoles (BII).
2. In this setting, the presence of organ failures should lead to the choice of the drug (BIII).
3. For the subgroup of patients infected with *C. parapsilosis*, lipid formulations of amphotericin B or fluconazole should be preferred (BII).
4. Azoles can be used for targeted therapy of non-critically ill patients with IAC due to susceptible strain(s) (BII).
5. Amphotericin B deoxycholate should not be used due to its well-documented significant toxicity (DII).

Conclusions