Le infezioni intra-addominali

17 Settembre

LA COMPLESSITA' IN MALATTIE INFETTIVE.
NUOVI PARADIGMI GESTIONALI. Parte Seconda.

Dott. Filippo Trapani

Outline

- Introduction
- Classifications
- Epidemiology
- Source control among certain Intra-abdominal infections
- Antimicrobial debate among certain Intra-abdominal infections
- Antifungal coverage in Intra-abdominal infections
- Proposal of empirical antimicrobial regimes to treat cIAI

Introduction

- Intra-abdominal infections (IAIs) encompass a variety of pathological conditions, ranging from uncomplicated appendicitis to fecal peritonitis.
- The most common are acute appendicitis, diverticulitis, ascending cholangitis, acute cholecystitis, post-operative intra-abdominal infections, pancreatic infection during acute pancreatitis.
- Other potential IAIs include:
- Colonic carcinoma perforation
- Colonic perforation following colonoscopy
- Post-traumatic bowel injuries
- Gastroduodenal perforation
- Small bowel perforations

Introduction

- Infection may be in the retroperitoneal space or within the peritoneal cavity.
- In addition, infection may be contained within the intra-abdominal viscera.
- Abscesses also frequently form around diseased viscera and between adjacent loops of bowel (i.e., interloop abscesses)
- **Intra-abdominal infection is the second most common cause of infectious mortality in the intensive care unit.**
- **Mortality is approximately 25% to 35%, but may exceed 70%.**
- **Most common cause of readmission.**
- **Common features--> Source control.**

Classifications

- **Community acquired and Health care-related acquired**

Presence of invasive device at time of admission, History of MDR infection or colonization, History of surgery, hospitalization, dialysis or residence in a long-term care facility in the last 12 month, Hospital onset of IAI (> 48 h)

- **Complicated and uncomplicated**

Complicated intra-abdominal infection extends beyond the hollow viscus of origin into the peritoneal space and is associated with either abscess formation or peritonitis.

Patients with such infections **can be treated with either surgical intervention or antibiotics.** **When the infection is effectively resolved by means of surgery, a 24-hour regimen of perioperative antibiotics is typically sufficient.**

Classifications

Peritonitis

- **Primary.** The peritoneal infection is not related directly to other intra-abdominal abnormalities. Sometimes referred to as *spontaneous bacterial peritonitis*. Primary peritonitis occurs at all ages. Among adults, primary peritonitis has usually been reported in patients with cirrhosis and ascites. A polymorphonuclear leukocyte count in peritoneal fluid greater than 250 cells/mm3 is considered diagnostic of primary peritonitis, even when culture of ascitic fluid yields negative results. Primary peritonitis is managed medically.

- **Secondary.** An intra-abdominal process is evident. Example include: perforation of a peptic ulcer, traumatic perforation of the uterus, urinary bladder, stomach, or small or large bowel; spontaneous perforation associated with typhoid, tuberculous, amebic, Strongyloides, or cytomegalovirus ulcers in immunocompromised persons; appendicitis, diverticulitis, or intestinal neoplasms; gangrene of the bowel from strangulation, bowel obstruction, or mesenteric vascular obstruction; suppurative cholecystitis; bile peritonitis; pancreatitis; operative contamination of the peritoneum or disruption of a surgical anastomosis site; septic abortion, puerperal sepsis, postoperative uterine infection, or endometritis complicating an intrauterine device; gonococcal salpingitis or gonococcal vulvovaginitis in children; suppurative prostatitis; and rupture of an intraperitoneal or visceral abscess, such as renal or perinephric, tubo-ovarian, liver, splenic, or pancreatic abscess

Classifications

Peritonitis

- **Tertiary.** When clinical peritonitis and signs of sepsis and multiorgan failure persist or recur after treatment for primary or secondary peritonitis. More common among critically ill or immunocompromised patients and is characteristically without a surgically treatable focus, following an earlier surgical intervention and source control. Usually associated to MDR infections. These organisms may gain access to the peritoneal cavity through contamination during operative interventions, through selection from the initial polymicrobial peritoneal inoculum by antibiotic therapy, or through translocation of bowel flora.

Epidemiology

Table 8. Organisms Identified in 3 Randomized Prospective Trials of Investigational Antibiotics for Complicated Intra-abdominal Infection, including 1237 Microbiologically Confirmed Infections

Organism	Patients, % (*n* = 1237)
Facultative and aerobic gram-negative	
Escherichia coli	71
Klebsiella species	14
Pseudomonas aeruginosa	14
Proteus mirabilis	5
Enterobacter species	5
Anaerobic	
Bacteroides fragilis	35
Other *Bacteroides* species	71
Clostridium species	29
Prevotella species	12
Peptostreptococcus species	17
Fusobacterium species	9
Eubacterium species	17
Gram-positive aerobic cocci	
Streptococcus species	38
Enterococcus faecalis	12
Enterococcus faecium	3
Enterococcus species	8
Staphylococcus aureus	4

Complicated intra-abdominal infections in Europe: a comprehensive review of the CIAO study

Sartelli M. et al. *World Journal of Emergency Surgery* 2012, 7:36

2,152 patients with either community-acquired or healthcare-associated complicated intra-abdominal infections (IAIs) were included in the study over a six months period (Jan-Jun 2012.
Intraperitoneal specimens were collected from 1338 patients (62.2%).
The overall mortality rate was 7.5% (163/2.152).

Table 7 Candida isolates identified in peritoneal fluid

Candida	138
Candida albicans	110 (79.7%)
(Candida albicans resistant to Fluconazole)	4 (2.9%)
Non-albicans Candida	28 (20.3%)
(non-albicans Candida resistant to Fluconazole)	5 (3.6%)

Community-acquired IAIs	Isolates n°	Healthcare-associated (nosocomial) IAIs	Isolates n°
Aerobic bacteria	988 (100%)	Aerobic bacteria	567 (100%)
Escherichia coli	480 (48.6%)	Escherichia coli	152 (26.8%
(Escherichia coli resistant to third generation cephalosporins)	30 (3%)	(Escherichia coli resistant to third generation cephalosporins)	34 (6%)
Klebsiella pneumoniae	52 (5.2%)	Klebsiella pneumoniae	57 (10%)
(Klebsiella pneumoniae resistant to third generation cephalosporins)	11 (1,7%)	(Klebsiella pneumoniae resistant to third generation cephalosporins)	22 (6.7%)
Pseudomonas	42 (4.2%)	Pseudomonas	38 (6.7%)
Enterococcus faecalis	78 (7.9%)	Enterococcus faecalis	91 (16%)
Enterococcus faecium	39 (3.9%)	Enterococcus faecium	43 (7.6%)

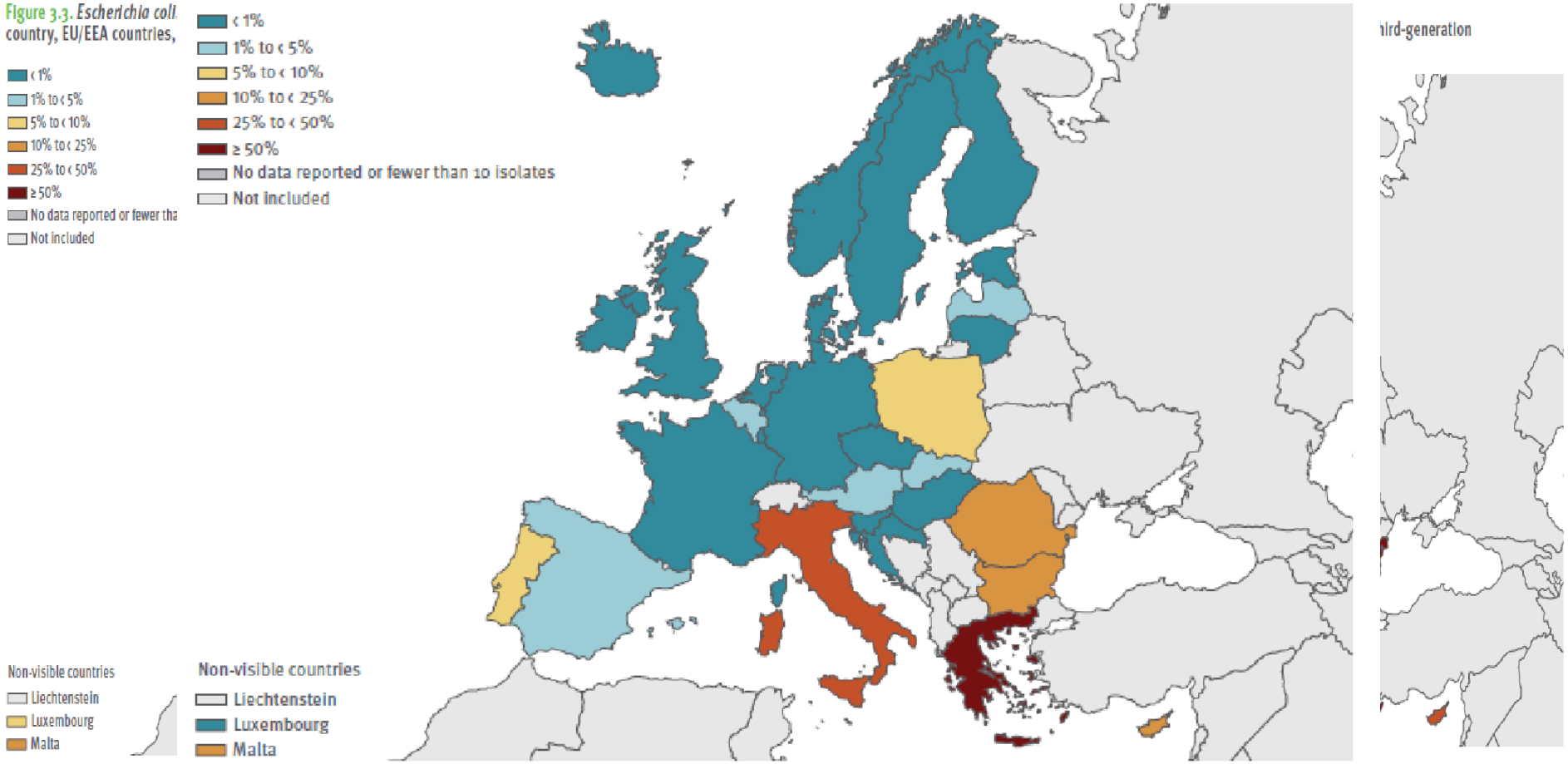
ESBL

Table 1. Recent incidences of extended-spectrum β-lactamase producers among *Eschericia coli* and *Klebsiella pneumoniae* from intra-abdominal infections [Study for Monitoring Antimicrobial Resistance Trends (SMART) program]

		E. coli		*K. pneumoniae*		
Area/country	Year of isolates	Number producing isolates	% of ESBL isolates	Number producing isolates	% of ESBL	Reference
Global	2008–2009	N/A	N/A	2841	22.4	[6]
USA	2007–2008	447	2	183	3.1	[7]
USA	2009	2885	6.8	N/A	N/A	[8]
Latin America	2008	504	26.8	151	37.7	[9]
Europe	2008	1495	11.6	319	17.9	[10]
Europe	2008–2009	3160	11	N/A	N/A	[11]
Asia-Pacific region	2009	1817	36.1	689	25.3	[12]
China	2009	285	64.9	94	31.9	[13]

Chen YH et al. Curr Opin 2012

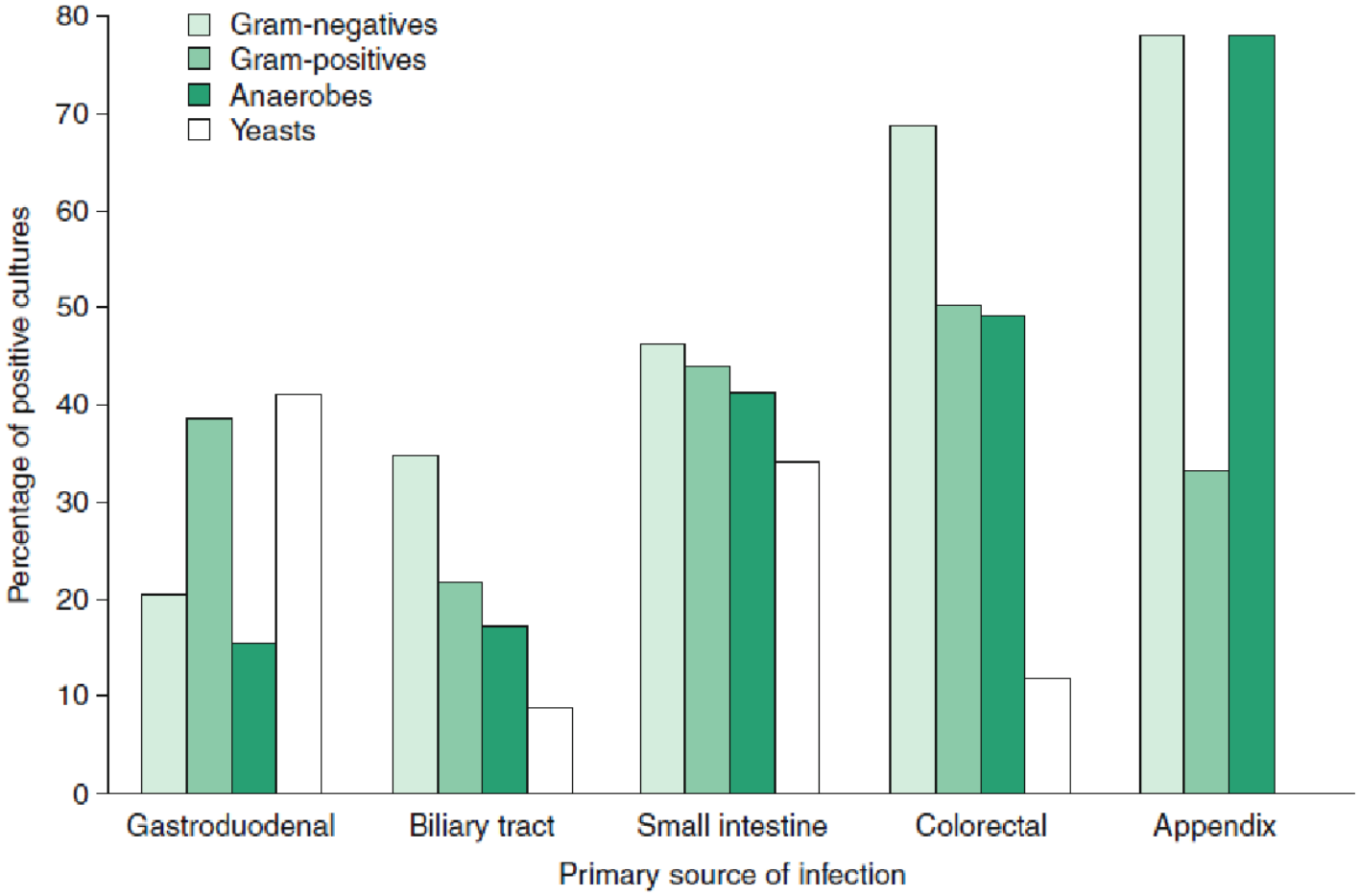
Figure 3.11. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2017



Essentials for Selecting Antimicrobial Therapy for Intra-Abdominal Infections

Stijn Blot, et al. Drugs 2012; 72 (6): e17-e32

- Infection source and etiology



Courtesy of Prof. Giannella

Complicated intra-abdominal infections in Europe: a comprehensive review of the CIAO study

Sartelli M. et al. *World Journal of Emergency Surgery* 2012, 7:36

Table 3 Source of Infection

Source of infection	Patients N 2152° (100%)
Appendicitis	798 (37%)
Cholecystitis	289 (13.4%)
Post-operative	342 (15,9%)
Colonic non diverticular perforation	158 (7.3%)
Gastroduodenal perforations	156 (7.3%)
Diverticulitis	166 (7.7%)
Small bowel perforation	103 (4.8%)
Others	110 (5.1%)
PID	18 (0.8%)
Post traumatic perforation	12 (0.6%)

Table 9 Multivariate analysis: risk factors for occurrence of death during hospitalization

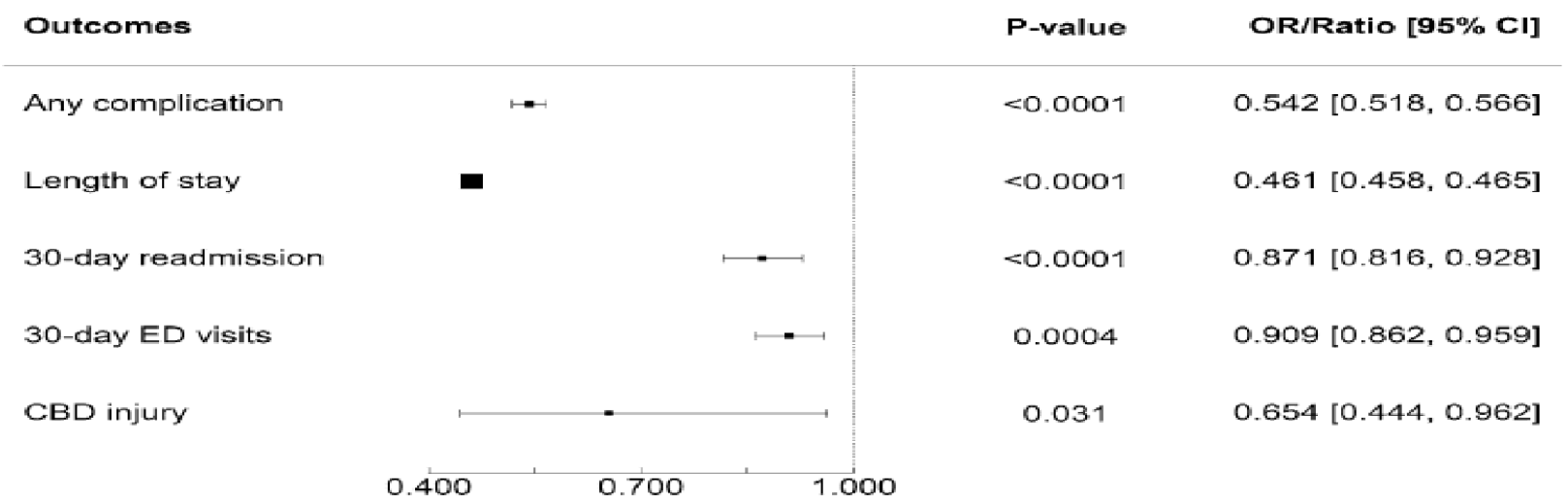
Risk factors	Odds ratio	95%CI	p
Age	3.3	2.2-5	<0.0001
Severe sepsis in the immediate post-operative course	27.6	15.9-47.8	<0.0001
Septic shock in the immediate post-operative course	14.6	8.7-24.4	<0.0001
Colonic non diverticular perforation	4.7	2.5-8	<0.0001
Diverticulitis	2.3	1.5-3.7	<0.0001
Small bowel perforation	21.4	8-57.4	<0.0001
Delayed initial intervention	2.4	1.5-3.7	0.0001

Early cholecystectomy (< 72 h) is associated with lower rate of complications and bile duct injury: a study of 109,862 cholecystectomies in the state of New York

Maria S. Altieri, et al. Surg Endosc. 2019 Aug 2. doi: 10.1007/s00464-019-07049-6. [Epub ahead of print]

- There were 109,862 patients who presented to an ED from 2005 to 2016 with the diagnosis of acute cholecystitis. The majority of patients underwent early (within 72 hours) cholecystectomy (*n* = 93,761, 85.3%), whereas only 16,101 patients underwent late cholecystectomy (14.7%).
- Early vs late groups were compared in terms of overall complications, bile duct injury (BDI), hospital length of stay (LOS), 30-days ED visits and readmissions.

- The rationale for performing early cholecystectomy within 72 h of symptoms is due to pathological observation that past that time period, inflammatory changes become more vascular and fibrotic which may lead to a more difficult dissection and greater potential for conversion to open operation or injuring the bile duct.



Essentials for Selecting Antimicrobial Therapy for Intra-Abdominal Infections

Stijn Blot, et al. Drugs 2012; 72 (6): e17-e32

Infection site	Clinical context	Duration of therapy
Abscess	Exclusive liver or spleen abscesses	3–7 days after surgery or drainage
Acalculous cholecystitis	Percutanous drainage	1–7 days according to clinical response
Appendicitis	No perforation Gangrenous Perforation	Only peri-operative prophylaxis 1–3 days 3–7 days
Ascending cholangitis	No device Device	Up to 24 hours after drainage 7 days in moderate to severe cases Prolonged therapy if case of liver abscess 5 days after drainage and device removal
Cholecystitis	Non-operative approach Surgical approach	5–10 days
	• no perforation • perforation	• up to 24 hours • 5 days
Diverticulitis	No perforation Perforation	5–7 days 3–7 days
Gastro-duodenal perforation	Time to intervention	
	• <24 hours • >24 hours	• Peri-operative prophylaxis only • 3–7 days
Pancreatitis	Proven infection or after 10 days of multiple organ dysfunction	3–7 days
Peritonitis/anastomotic leakage	Localized or generalized	3–7 days

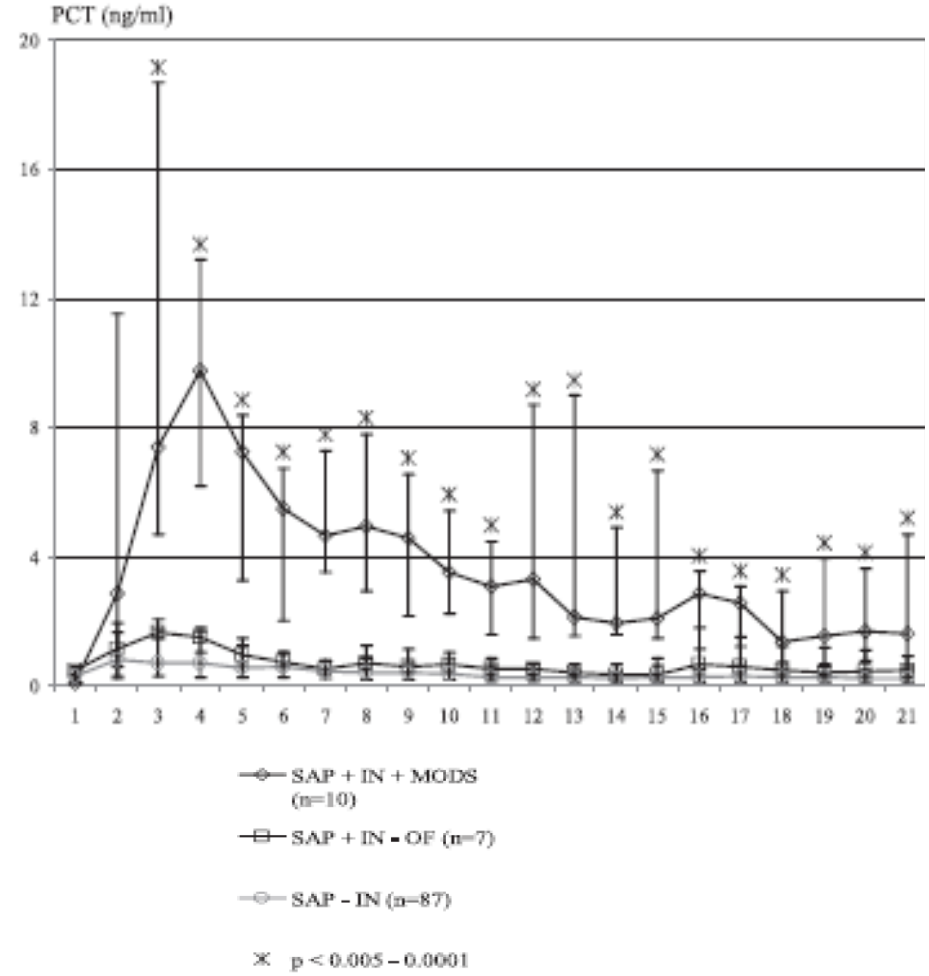
Early Assessment of Pancreatic Infections and Overall Prognosis in Severe Acute Pancreatitis by Procalcitonin (PCT).

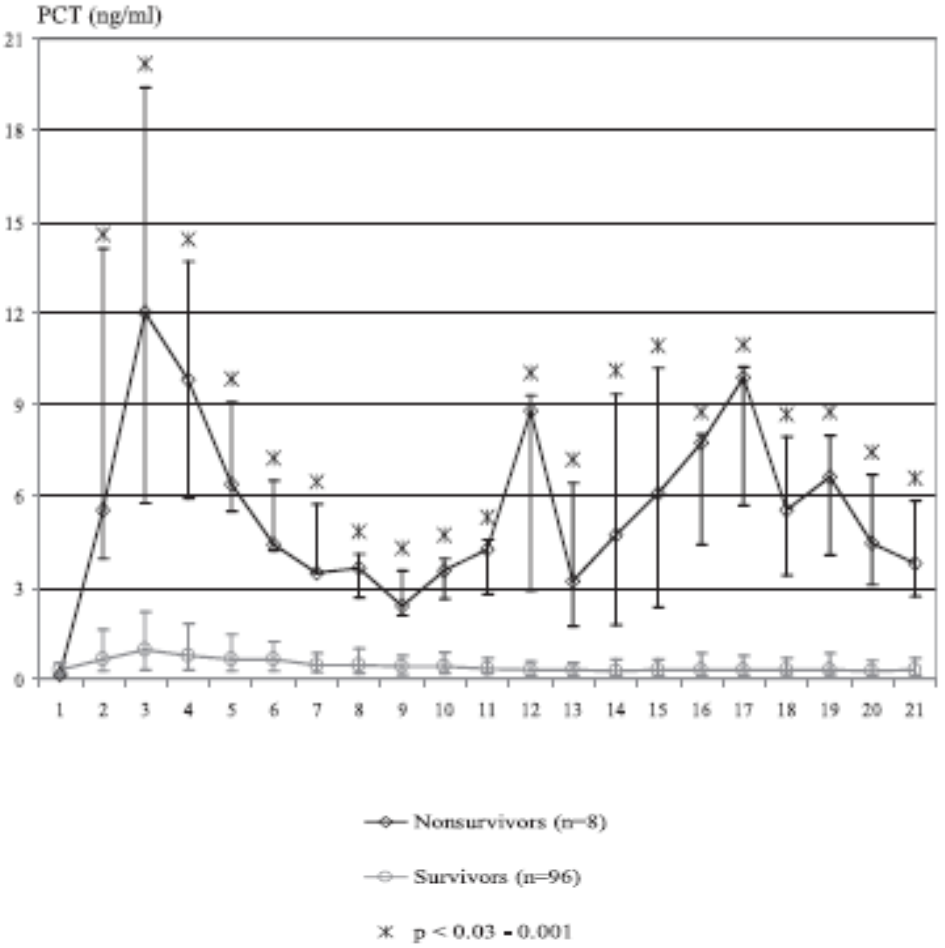
A Prospective International Multicenter Study

Bettina M. Rau, et al. *Ann Surg* 2007;245: 745–754

A total of 104 patients with predicted severe AP were enrolled in five European academic surgical centers within 96 hours of symptom onset. PCT was measured prospectively by a semiautomated immunoassay in each center, C-reactive protein (CRP) was routinely assessed.

Both parameters were monitored over a maximum of 21 consecutive days and in weekly intervals thereafter.





Early Assessment of Pancreatic Infections and Overall Prognosis in Severe Acute Pancreatitis by Procalcitonin (PCT).

A Prospective International Multicenter Study

Bettina M. Rau, et al. *Ann Surg* 2007;245: 745–754

TABLE 4. Sensitivity, Specificity, PPV, NPV, and Optimum Cutoff Levels for the Overall Assessment of Major Complications in Severe Acute Pancreatitis

	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Infected necrosis					
PCT (ng/mL)	≥4.0	65	89	52	93
CRP (mg/L)	≥390	41	92	50	89
Infected necrosis + MODS					
PCT (ng/mL)	≥5.6	90	89	47	99
CRP (mg/L)	≥430	50	99	83	95
Death					
PCT (ng/mL)	≥3.5	100	82	32	100
CRP (mg/L)	≥310	63	67	14	96
Infected necrosis + MODS or death					
PCT (ng/mL)	≥3.5	93	88	56	99
CRP (mg/L)	≥430	40	100	100	91

TABLE 5. Sensitivity, Specificity, PPV, NPV, and Optimum Cutoff Levels for the Early Assessment (day 3 and 4)* of Major Complications in Severe Acute Pancreatitis

	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Infected necrosis					
PCT (ng/mL)	≥1.5	82	69	34	95
CRP (mg/L)	≥420	35	93	50	88
Infected necrosis + MODS					
PCT (ng/mL)	≥3.8	80	90	47	98
CRP (mg/L)	≥440	40	96	50	94
Death					
PCT (ng/mL)	≥3.8	86	89	35	99
CRP (mg/L)	≥310	71	59	11	97
Infected necrosis + MODS or death					
PCT (ng/mL)	≥3.8	79	93	65	97
CRP (mg/L)	≥430	36	97	63	91

Trial of Short-Course Antimicrobial Therapy for Intra-abdominal Infection

Sawyer RG et al N Engl J Med 2015; 372:1996-2005

We randomly assigned 518 patients with complicated intraabdominal infection and adequate source control to receive antibiotics until 2 days after the resolution of fever, leukocytosis, and ileus, with a **maximum of 10 days of therapy (control group)**, or **to receive a fixed course of antibiotics (experimental group) for 4± 1 calendar days**.
The **primary outcome** was a composite of surgical-site infection, recurrent intraabdominal infection, or death within 30 days after the index source-control procedure, according to treatment group.
Secondary outcomes included the duration of therapy and rates of subsequent infections.

Characteristics of index infection	Control Group (N = 260)	Experimental Group (N = 258)
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)

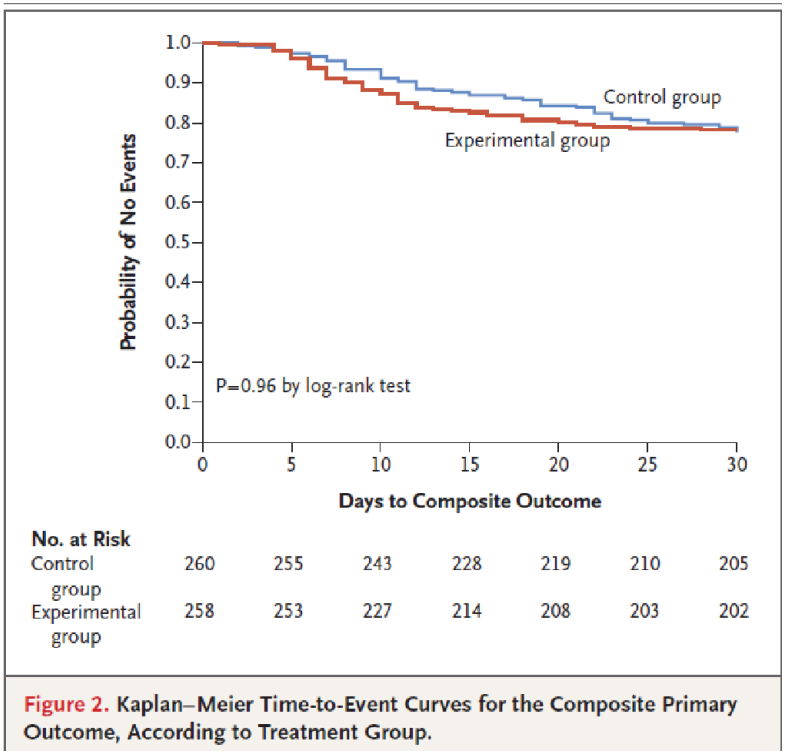


Figure 2. Kaplan–Meier Time-to-Event Curves for the Composite Primary Outcome, According to Treatment Group.

Trial of Short-Course Antimicrobial Therapy for Intra-abdominal Infection

Sawyer RG et al N Engl J Med 2015; 372:1996-2005

Variable	Control Group (N = 260)	Experimental Group (N = 257)	P Valu
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
Site of extraabdominal infection — no. (%)			
Any site†	13 (5.0)	23 (8.9)	0.11
Urine	10 (3.8)	13 (5.1)	0.65
Blood	3 (1.2)	5 (1.9)	0.71
Lung	3 (1.2)	3 (1.2)	0.99
Area of skin other than surgical site	1 (0.4)	4 (1.6)	0.36
Vascular catheter	0 (0)	2 (0.8)	0.47
Clostridium difficile infection — no. (%)	3 (1.2)	5 (1.9)	0.71
Extraabdominal infection with resistant pathogen — no. (%)	6 (2.3)	2 (0.8)	0.29
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	

- Antifungal coverage:

✓ patients with severe sepsis or septic shock

- i) post-operative peritonitis
- ii) recurrent gastrointestinal perforation
- iii) post-operative hepatobiliary and/or pancreatic disorders
- iv) post-operative intra-abdominal abscess
- v) anastomotic leak

❖ broad-spectrum antibiotics,

❖ intravenous access devices,

❖ total parenteral nutrition,

❖ mechanical ventilation,

❖ hemodialysis, diabetes mellitus, corticosteroids, neutropenia or neutrophil dysfunction, and Candida colonization, cancer chemotherapy, prolonged ICU stay

Early diagnosis of candidemia in intensive care unit patients with sepsis: a prospective comparison of (1-3)-b-D-glucan assay, Candida score, and colonization index.

Posteraro et al. *Critical Care* 2011, 15:R249

A prospective single-center observational study was conducted to compare the diagnostic value of BG assay, Candida score (CS), and colonization index in intensive care unit (ICU) patients at risk for Candida sepsis.
Methods: Of 377 patients, consecutively admitted to ICU for sepsis, 95 patients having an ICU stay of more than five days were studied. **Blood specimens** for fungal culture and BG measurement **were obtained at the onset of clinical sepsis.**

Table 3 Performances of (1→3)-β-D-glucan assay (BG), *Candida* score (CS), and colonization index for detection of invasive candidiasis in 95 patients

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	PLR (%) (95% CI)	NLR (%) (95% CI)
BG cut-off value, 80 pg/mL	92.9 (66.1 to 99.8)	93.7 (85.8 to 97.9)	72.2 (46.5 to 90.3)	98.7 (92.8 to 99.9)	14.74 (4.65 to 47.52)	0.07 (0.02 to 0.39)
CS ≥3	85.7 (57.2 to 98.2)	88.6 (79.5 to 94.7)	57.1 (34.0 to 78.2)	97.2 (90.3 to 99.7)	7.51 (2.79 to 18.29)	0.16 (0.02 to 0.54)
Colonization index ≥0.5	64.3 (35.1 to 87.2)	69.6 (58.2 to 79.5)	27.3 (13.3 to 45.5)	91.7 (81.6 to 97.2)	2.12 (0.84 to 4.25)	0.51 (0.16 to 1.11)

The combination of a positive BG result and a CS value ≥3 increased the sensitivity (100% (95% CI, 76.8% to 100%)) and NPV (100% (95% CI, 94.6% to 100%)) for diagnosis of IC, compared to 92.9% and 97.2% for the BG test alone, respectively.
Conversely, the specificity (83.5% (95% CI 73.5% to 90.9%)) and PPV (51.8% (95% CI, 31.9% to 71.3%)) based on combined tests was lower than those of the BG test (93.7% and 72.2%, respectively).

b-Glucan Antigenemia Anticipates Diagnosis of Blood Culture–Negative Intraabdominal Candidiasis

Frederic Tissot, et al. Am J Respir Crit Care Med Vol 188, Iss. 9, pp 1100–1109, Nov 1, 2013

Objectives: The aim of this prospective Fungal Infection Network of Switzerland (FUNGINOS) cohort study was to assess accuracy of 1,3-b-D-glucan (BG) antigenemia for diagnosis of IAC.

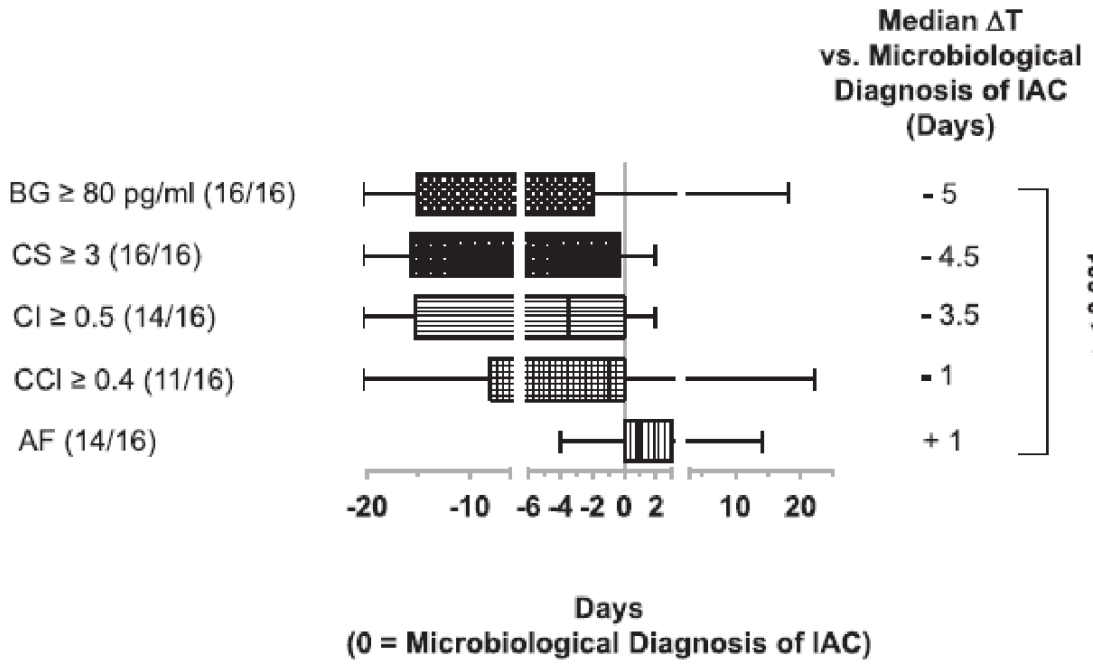
Four hundred thirty-four patients with abdominal surgery or acute pancreatitis admitted to the ICU for 72 hours or longer were screened during the 30-month study period. Eighty-nine (20.5%) were included.

TABLE 3. ACCURACY OF 1,3-β-D-GLUCAN, *Candida* SCORE, *Candida* COLONIZATION INDEX, AND CORRECTED *Candida* COLONIZATION INDEX FOR THE DIAGNOSIS OF INTRAABDOMINAL CANDIDIASIS (N = 29)

	Sensitivity	Specificity	PPV	NPV	Efficiency, %
BG ⩾ 80 pg/ml 1×					
At inclusion	0.76 (0.56–0.90)	0.59 (0.43–0.74)	0.56 (0.40–0.72)	0.78 (0.60–0.90)	66
At infection*	0.83 (0.64–0.94)	0.40 (0.26–0.57)	0.49 (0.34–0.64)	0.77 (0.55–0.92)	58
BG ⩾ 80 pg/ml 2×†					
At inclusion	0.66 (0.45–0.82)	0.83 (0.69–0.93)	0.73 (0.52–0.88)	0.78 (0.63–0.89)	76
At infection*	0.65 (0.46–0.82)	0.78 (0.63–0.90)	0.68 (0.48–0.84)	0.77 (0.61–0.88)	73
CS ⩾ 3					
At inclusion	0.86 (0.68–0.96)	0.50 (0.34–0.66)	0.54 (0.39–0.69)	0.84 (0.64–0.95)	65
At infection*	0.86 (0.68–0.96)	0.38 (0.23–0.54)	0.49 (0.35–0.63)	0.80 (0.56–0.94)	58
CI ⩾ 0.5					
At inclusion	0.26 (0.10–0.48)	0.76 (0.61–0.87)	0.35 (0.14–0.62)	0.67 (0.53–0.80)	59
At infection*	0.88 (0.69–0.97)	0.34 (0.19–0.52)	0.49 (0.34–0.64)	0.80 (0.52–0.96)	57
CCI ⩾ 0.4					
At inclusion	0.14 (0.03–0.36)	0.77 (0.61–0.88)	0.23 (0.05–0.54)	0.65 (0.50–0.77)	56
At infection*	0.50 (0.29–0.71)	0.43 (0.28–0.60)	0.35 (0.20–0.53)	0.59 (0.39–0.76)	46

b-Glucan Antigenemia Anticipates Diagnosis of Blood Culture–Negative Intraabdominal Candidiasis

Frederic Tissot, et al. Am J Respir Crit Care Med Vol 188, Iss. 9, pp 1100–1109, Nov 1, 2013



Main results:

- In patients with recurrent GI tract perforation, BG greater than or equal to 80 pg/ml discriminated IAC from colonization with 72% PPV and 80% NPV and was superior to CI, CCI, and CS.

  BG greater than or equal to 80 pg/ml performed better in patients with recurrent GI tract perforation than in those with acute necrotizing pancreatitis

  BG preceded microbiological documentation of IAC with intraabdominal cultures and start of antifungal therapy by a median of 5 and 6 days, respectively, which suggests its potential role for guiding prompt and targeted initiation of antifungal therapy on a preemptive basis.

- **BG kinetics reflected severity of infection, response to antifungal therapy, and clinical outcome.**

Microbiological Laboratory Testing in the Diagnosis of Fungal Infections in Pulmonary and Critical Care Practice
An Official American Thoracic Society Clinical Practice Guideline

Chadi A. Hage, et al.; Am J Respir Crit Care Med Vol 200, Iss 5, pp 535–550, Sep 1, 2019

Question 3

In critically ill patients with suspected IC, is the BDG assay alone sufficient for diagnostic decision-making?

- A total of 10 ICU-based studies encompassing 1,510 subjects were pooled to determine the performance characteristics of BDG in the critically ill population.

Results of all 10 studies reporting, on a per-patient basis, the performance characteristics of BDG in potential cases of IC in the ICU

	Pooled ICU population at risk of IC	ICU patient at High risk of IC (10%)
SENSITIVITY	**0.81** (95% CI, 0.74–0.86)	
SPECIFICITY	**0.60** (95% CI, 0.49–0.71).	
PPV		**0.19**
NPV		**0.50**

Recommendation.
In critically ill patients in whom there is clinical concern for IC,
we suggest against reliance solely on results of serum BDG testing alone for diagnostic decision-making (*conditional recommendation, low-quality evidence*).

Empirical therapy of cIAI

	No risk factors for DTTPs	**Alternative regimen (β-lactam allergy)**	**Risk factors for DTTPs**	**Alternative regimen (β-lactam allergy)**
Mild disease (Sepsis without MOF or qSOFA<2)	Amoxicillin/clavulanate	Moxifloxacin or Ciprofloxacin + metronidazole	Piperacillin/tazobactam/Ceftolozane/tazobactam + tigecycline	Ciprofloxacin + tigecycline
Severe disease (Severe sepsis or qSOFA ≥2, and septic shock)	Piperacillin/tazobactam/ ertapenem ± tigecycline	Ciprofloxacin + tigecycline	Meropenem/imipenem/doripenem/ceftolozane/tazobactam/ceftazidime/avibactam + tigecycline + antifungals	Aztreonam or ciprofloxacin + tigecycline + antifungals

DTTPs: MDR Gram negative bacteria (ESBL, CRE, NF-GNB), enterococci, Candida spp.

Courtesy of Prof. Giannella