Intensive Care Med
https://doi.org/10.1007/s00134-019-05841-5

NARRATIVE REVIEW

Post-operative abdominal infections: epidemiology, operational definitions, and outcomes

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Abstract

Postoperative abdominal infections are an important and heterogeneous health challenge in intensive care units (ICU) and encompass postoperative infectious processes developing within the abdominal cavity that may be caused by either bacterial or fungal pathogens. In this narrative review, we discuss postoperative bacterial and fungal abdominal infections, covering also multidrug-resistant (MDR) pathogens. We also cover clinically preeminent aspects such as the definition of postoperative abdominal infections, which still remains difficult owing to their heterogeneity in patient characteristics, clinical presentation, ecology and antimicrobial treatment. With regard to treatment, modifiable factors such as source control and antimicrobial therapy play a key role in influencing the prognosis of postoperative abdominal infections, but several conditions may hamper their correct application; thus efforts should necessarily be devoted towards improving their appropriateness and timing. Hot topics regarding the characteristics and management of postoperative abdominal infections are discussed in this narrative review.

Keywords: IAI, Source control, Antimicrobial resistance, Peritonitis, Candidiasis, Abdominal infections

Introduction

Postoperative abdominal infections are an important and heterogeneous health challenge in intensive care units (ICU). They encompass infectious processes developing within the abdominal cavity and that may be caused by either bacterial or fungal pathogens. Complicated intra-abdominal infections (cIAI) belong to the three most frequent organ-specific reasons for septic shock in ICU, with reported mortality rates up to 30-40% [1–3].

Some major factors contribute to influencing the prognosis of postoperative IAI. First, postoperative IAI add to non-infectious surgical complications and may precipitate pre-existing organ dysfunction [4]. Second, they are healthcare-associated infections, implying that resistant organisms may be involved in endemic areas and hospitals. This may reduce the chance of prompting an active primary antimicrobial regimen, thereby increasing both mortality and costs. Third, a delayed or incomplete source control may also participate in significantly and unfavourably affecting survival.

Although an adequate primary antibiotic treatment and an early source control may both seem intuitive and easy measures to be adopted, the combination of subtle clinical presentation, inaccurate diagnosis, operational difficulties, failure to recognize the risk of resistant organisms, and the possible lack of therapeutic options for pan-resistant bacteria may sometimes hamper their correct application in the everyday clinical practice. Furthermore, peculiar challenges should be taken into account regarding fungal infections. Indeed, there is a

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need for more solid evidence to firmly guide the use of rapid fungal diagnostics, and also to optimize the administration of antifungals according to updated PK/PD data in patients with either proven or suspected postoperative intra-abdominal candidiasis (IAC) [5].

In the present narrative review, we discuss the current literature and future perspectives about the epidemiology, operational definitions, and factors influencing the outcome of postoperative IAI in critically ill patients in ICU wards.

Methods

A panel of experts was selected by MB for writing the present narrative review. Separated PubMed/MEDLINE searches using various combination of keywords pertinent to the different paragraphs (e.g., IAI, abdominal surgery, postoperative infection, definition* for the paragraph "operational definitions") were conducted by the different authors. Further inductive searches were also conducted, prompted by the first research results. Subsequently, each author was asked to write a 300–500-word draft for a single assigned major paragraph, selecting up to a maximum of 10 references on the basis of the perceived importance of the topic. Eventually, the different drafts were assembled, and the final manuscript was reviewed and approved by all authors.

Aetiology and risk factors for postoperative abdominal bacterial infections

In complicated abdominal infections, the infectious process extends to the peritoneum. In this regard, postoperative peritonitis is the most frequent form of intra-abdominal infection [6] accounting for up to 65% of all abdominal infections observed in ICU patients [1].

Peri-operative cultures are indicated for further monitoring emergence of multi-drug resistant (MDR) microorganisms and adjusting empirical antibiotic therapy [7, 8]. However, the value of perioperative samples remains debated as the variety of cultured pathogens represents only a limited part of gastrointestinal flora. In addition, culture results cannot discriminate contaminating/saprophytic bacteria from true infectious pathogens. This issue is of particular relevance for enterococci. The cultured micro-organisms include a spectrum of aerobic and anaerobic Gram-positive/negative bacteria with a highly variable mix depending on several factors including the site of perforation (above/below transverse mesocolon) [9, 10]. Gram-negative and anaerobic bacteria are increasingly involved, ranging from about 15–20% in gastroduodenal perforation to about 80% in intestinal/colonic-related peritonitis while the proportions of Gram-positive bacteria vary only minimally remaining about 30–40% of the isolates [9, 10].

Take-home message

Early source control and appropriate antimicrobial therapy influenced by the local microbiological epidemiology remains essential to effectively deal with postoperative abdominal infections in an era of multidrug-resistant pathogens.

Postoperative infections are associated with an increased frequency of multi-drug resistant (MDR) microorganisms including methicillin-resistant staphylococci, vancomycin-resistant enterococci, extended-spectrum beta-lactamase and/or carbapenemase-producing *Enterobacterales*, and *Pseudomonas aeruginosa* and *Acinetobacter baumannii* [1, 11, 12]. Many factors predisposing to MDR bacteria have been identified including immunosuppression or corticosteroid use, recent exposure to broad-spectrum antibiotics, underlying conditions such as liver or pulmonary disease, and a length of hospitalization > 5 days [11, 13]. Geographical and hospital microbial ecology should also be considered. Patients with a recent history of stay/hospitalization in regions known to have particular resistance issues deserve special care. In addition, emergence of MDR bacteria increases progressively with the number of reoperation and the prolonged antibiotic therapy (Fig. 1) [14]. While inadequate empirical therapy is an important element in the poor prognosis of postoperative peritonitis [12], the part played by MDR bacteria as such rather than complicated courses or underlying conditions remains debated [10, 12, 13].

However, all the data demonstrating resistance issues in postoperative peritonitis were obtained in wealthy western countries. This approach might be too restrictive and should be considered in a broader perspective. Indeed, the results of AbSeS prospective observational cohort, gathering 2621 IAI patients admitted in 309 ICUs worldwide suggest that multidrug resistance is equally reported in community-acquired (26.2%) as in early-onset (< 7 days) (30.1%) and late-onset (24.5%) hospital-acquired infections [15].

Epidemiology and search for a standard definition of postoperative abdominal fungal infections

Fungi play a non-negligible role as causative agents of postoperative IAI in ICU patients. In the Extended Prevalence of Infection in the ICU (EPIC) II study, among 1392 patients with IAI from 1265 ICUs in 75 countries, 1083 were surgical patients (78%). Fungi (mostly *Candida* spp.) were responsible for 10% of IAI episodes [1]. Among 23 European ICU (3 surgical, 5 medical, and 15 mixed medical plus surgical) a cumulative incidence of 1.84 episodes of IAC per 1000 ICU admission during the

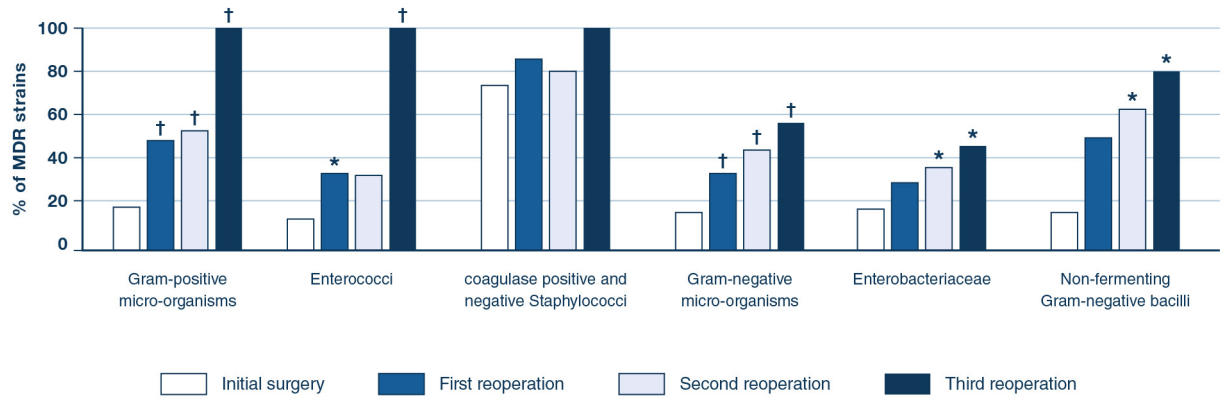

Fig. 1 The emergence of multi-drug resistant (MDR) bacteria is expressed as proportions of the respective species obtained from surgical samples at the time of initial surgery and first, second and third reoperation (adapted from [14]). *$P < 0.05$, †$P < 0.01$ versus initial surgery

years 2015 and 2016 was recently registered within the EUCANDICU project [16].

Prolonged length of hospital stay and previous antibiotic treatment are the most widely recognized risk factors for ICU-acquired IAC, but also other potential predictors such as upper gastrointestinal tract origin of peritonitis and intraoperative cardiovascular failure have been suggested [17].

Candida albicans was responsible for 76% of IAC in the EPIC II study, and its predominance was also reported (although reduced, 58%) in another study conducted using data form the prospective, multicenter AmarCand cohort [18]. In a retrospective, multicenter study conducted from 2011 to 2013 in 13 hospitals across Italy, Brazil, Greece, and Spain, *C. albicans* was responsible for 63% of 129 episodes of ICU-acquired IAC. This latter study also highlighted a high prevalence of septic shock among patients with IAC (41%) and that concomitant candidemia was observed only in 10–15% of all IAC episodes [3].

Of note, a clear comparison of IAC prevalence or incidence data between different studies is frequently hampered by two factors: (1) the inclusion among counted IAC episodes of only *Candida* peritonitis vs. the inclusion also of other infections such as abdominal abscesses and/or biliary tract infections [3]; (2) the use of different definitions of IAC, with the risk either of overestimation by including contaminations or of underestimation by including only patients with a positive culture, although this risk seems reduced after the publication of a recent expert consensus [19]. In addition, the currently ongoing FUNDICU initiative, aimed at developing standard definitions for invasive fungal diseases in ICU patients, will further help to delineate a clear definition of IAC for both clinical and research purposes [20].

Operational definitions

Postoperative intra-abdominal infections are not well defined. This is due to their heterogeneity in patient characteristics, clinical presentation, ecology and antimicrobial treatment. Various classification approaches have been published in the international literature [4, 21–23]. The Infectious Diseases Society of America (IDSA) defines complicated and uncomplicated IAI. In complicated IAI the infection extends beyond the hollow viscus of origin into the peritoneal space and is associated with either abscess formation or peritonitis [23]. Postoperative IAI are not specifically addressed; they are summarized under the term "healthcare-associated complicated IAI". A frequently used clinical approach defines different types of peritonitis, i.e., primary, secondary (community-acquired and postoperative), and tertiary peritonitis [4, 21, 22]. In contrast to community-acquired IAI, nosocomial (postoperative) IAI are: intra-abdominal postoperative abscess, postoperative secondary peritonitis and tertiary peritonitis. The following differentiation appears to be useful for clinical practice (Table 1):

- Postoperative intra-abdominal abscess is a postoperative collection of infected fluid within the intrabdominal cavity. It is usually treated by a combination of interventional measures (i.e. percutaneous drainage) and anti-infective therapy [4, 24]. Exact criteria for drainage of an abscess (i.e. diameter, method, necessity for surgery) are not standardized. Surgical intervention in intra-abdominal abscesses is rare (< 10% of all cases) and usually follows ineffective interventional treatment [24].
- Postoperative (post-interventional, post-traumatic) secondary peritonitis is a nosocomial peritonitis form and defined as an infectious abdominal com-

Table 1 Clinical classification of postoperative intra-abdominal infection

Diagnosis	Current definition	Example	Treatment	Comments/issues	Possible future definition approach
Postoperative Intra-abdominal abscess	Intra- abdominal collection of infected fluid	Liver abscess following biliary surgery	Interventional drainage + antimicrobial therapy	Exact diameter for drainage indication not well defined Subgroup of pts needs surgical drainage	Interventionally treated postoperative IAI
Postoperative (post-traumatic, post interventional) secondary peritonitis	Perforation of the GI tract following a procedure (e.g. colonoscopy, operation)	Anastomotic leakage following low anterior resection	Surgery + antimicrobial therapy	Low accuracy of diagnostics Transition to non-surgical treatment occurs (e.g. VAC device for leakage)	Surgically treated postoperative IAI
Tertiary peritonitis	Ongoing peritonitis despite adequate source control	Laparostomy complicated by *Candida* peritonitis	Antimicrobial therapy	Vague definition as transition to secondary peritonitis occurs frequently	Conservatively treated postoperative IAI

VAC negative pressure (vacuum-assisted) treatment

plication with peritonitis following a previous intervention (e.g. anastomotic leakage following colorectal resection) [11, 25] requiring by definition a surgical intervention.

- Tertiary peritonitis is a persistent IAI following an earlier surgical intervention and successful source control [19, 21]. Intraabdominal compartment syndrome and open abdomen treatment are clinically evident risk factors for the development of a tertiary peritonitis. In most cases the infection is maintained because of a state of immunodeficiency and due to resistant bacteria selection following previous antibiotic treatment. Compared to postoperative peritonitis, the tertiary form does not require source control [19]. Tertiary peritonitis is a vague term and difficult to assess. Abdominal CT scan is mandatory in order to avoid unnecessary and potentially harmful surgery. In uncertain cases of critically ill patients an uncontributive reoperation has to prove that the patient does not need source control [21].

A possible future approach for more accurate clinical definitions, allowing better comparability of collectives, could follow the primary treatment approach (conservative, interventional, surgical), but needs to be validated (Table 1).

Source control

Timing and adequacy of source control are the most important issues in the management of post-operative peritonitis, because inadequate and late operation may have a negative effect on the outcome. Source control should be performed early, although when exactly is still controversial [26]. Classically, in unstable patients it is recommended to obtain source control within 6–12 h [27]. However, some recent studies pointed out to the possible benefits of the earliest the better [28, 29], which would inevitably imply the need for a 24/7 access to surgery/radiology services. Overall, this topic remains preeminent, and further high-level, confirmatory evidence is warranted.

Early control of the septic source can be achieved either by nonoperative or operative means (Table 3). Nonoperative interventional procedures include percutaneous drainages of abscesses. Ultrasound and CT guided percutaneous drainage of abdominal and extraperitoneal localized abscesses in selected patients are safe and effective. Numerous studies in the surgery and radiology literature have documented the effectiveness of percutaneous drainage in selected patients with IAI, with cure rates of 62%–91% and with morbidity and mortality rates equivalent to those of surgical drainage [30–33]. Therefore, the minimal invasive, non-surgical therapy should always be the first approach for treatment of intraabdominal collections, whenever feasible. The principal cause for failure of percutaneous drainage is misdiagnosis of the magnitude, extent, complexity, location of the abscess [34]. In these rare cases of ineffective/non-feasible minimal invasive interventional treatment of abscesses surgical drainage should be performed.

Surgery is the most important therapeutic measure to control post-operative peritonitis. Generally, the choice of the procedure depends on the anatomical source of infection, on the degree of peritoneal inflammation, on the generalized septic response and on the patient's general conditions. The primary objectives of surgical intervention include: (1) determining the cause of peritonitis; (2) draining fluid collections; (3) controlling the origin of the abdominal sepsis.

Patients with ongoing infections may benefit from aggressive surgical treatment following an initial emergency laparotomy to control multiple organ dysfunction syndrome caused by ongoing intra-abdominal infection [35]. Surgical strategies of re-laparotomy include both "re-laparotomy on demand" (when required by the patient's clinical condition) and planned re-laparotomy in the 36- to 48-h post-operative period (when relaparotomy is planned after first operation) [35]. The open abdomen procedure is the easiest means to perform a planned re-laparotomy and is now a viable option for treating critically ill patients with intra-abdominal sepsis. Open abdomen approach may be useful, required for various reasons including to extend the concept of damage control surgery to critical patients preventing the appearance of the abdominal compartment syndrome [36]. However, the use of the open abdomen, although a lifesaving technique, presents a clinical challenge because it may be associated with significant morbidity [36].

Treatment with antimicrobials

Early and adequate source control is mandatory for a successful treatment of postoperative IAI. A delay in reoperation has been shown to be a significant risk factor for emergence of MDR bacteria [14]. Nevertheless, appropriate antimicrobial treatment of postoperative IAI is necessary, too. Postoperative IAI are characterized by a higher likelihood of isolation of MDR Gram-positive [e.g. methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE)] and Gram-negative bacteria (e.g. extended-spectrum beta-lactamases [ESBL] producers, carbapenem-resistant *Enterobacterales*, *Pseudomonas* spp., *Acinetobacter* spp.). This shift towards resistant pathogens calls for a differentiated use of antimicrobial agents compared with community-acquired IAI.

There is only limited data about efficacy of antibiotics used in postoperative IAI. Therefore, the level of evidence for any recommendation in postoperative IAI is low and rarely exceeds expert opinion. Significant differences in the bacterial ecology of regions, hospitals and wards require a thorough analysis of surveillance data followed by local guidelines fitted to the expected bacterial spectrum [23]. Initial antimicrobial regimens with broad spectrum of activity are recommended, because adequate empirical therapy appears to be important to reduce mortality. In postoperative IAI, the globally most frequent problem with antimicrobial resistance is posed by ESBL-producing *Enterobacterales*. Empiric therapy directed against ESBL producers is almost always recommended in postoperative peritonitis [4, 37]. Enterococci, *Pseudomonas* spp., and *Acinetobacter* spp. are microorganisms that may play an important role in postoperative peritonitis. They have been a subject of debate in recent years, but empiric therapy directed against those pathogens is recommended under specific circumstances [4, 37].

Table 2 shows a clinically driven approach for the antimicrobial treatment of postoperative IAI. Patients suffering from postoperative intra-abdominal abscess are mainly hemodynamically stable. Tigecycline (active against MRSA, VRE, ESBL producers, carbapenemase-producing *Enterobacterales*, and *Acinetobacter* spp., but not against *Pseudomonas* spp.) has been used successfully in this indication [38], but is not recommended as a single agent in septic shock. Alternatively, in specific regions, in which susceptibility for ESBL-producing *Enterobacterales* exceeds 90%, piperacillin/tazobactam combined with daptomycin, linezolid or vancomycin (Gram-positive coverage) can be used in non-bacteremic patients. Meropenem can be used as well, but a balanced use as a carbapenem-sparing strategy appears to be reasonable [37].

On the contrary, postoperative diffuse secondary and tertiary peritonitis is frequently associated with septic shock. A recent multicentre trial comparing piperacillin-tazobactam with meropenem in the treatment of bacteremia caused by ceftriaxone-resistant *E. coli* and *K. pneumoniae* (including a non-negligible number of IAI patients) revealed an increased mortality for patients treated with piperacillin/tazobactam, thus suggesting a possible advantage of carbapenems also for IAI patients, to be further explored through adequately powerful confirmatory studies [39]. Meropenem or imipenem covers the expected spectrum in many cases. Tigecycline (gram-positive and gram-negative coverage excluding *Pseudomonas* spp.), linezolid and daptomycin (Gram-positive coverage including VRE), vancomycin (Gram-positive coverage excluding VRE) can be used as combination partners according to the likelihood of a specific difficult to treat pathogen in the respective unit.

Ceftolozane/tazobactam, ceftazidime/avibactam, meropenem/vaborbactam, and eravacycline have also recently been approved for the treatment of IAI [16, 40–43]. These agents have strong activity against selected MDR Gram-negative pathogens [44, 45]. Ceftazidime/avibactam and meropenem/vaborbactam have demonstrated consistent activity against KPC-producing organisms, eravacycline against MDR *A. baumannii* and other MDR Gram negatives, and ceftazidime/avibactam and ceftolozane/tazobactam against ESBLs and MDR *P. aeruginosa*. Ceftazidime/avibactam and ceftolozane/tazobactam should be combined with metronidazole due to limited activity against some *Bacteroides* species.

A start of antimicrobial therapy within 1 h after admission to ICU has been shown to improve survival in

Table 2 Antiinfective treatment recommendations for postoperative intra-abdominal infections in ICU

Diagnosis	Hemodynamic situation/likelihood of septic shock	Empirical antibiotic regimen	Dose adjustment according to PK/PD parameters	Consider empirical antifungal treatment	Empirical antifungal regimen
Postoperative intra-abdominal abscess	Stable/low	Tigecycline Eravacycline Piperacillin/tazobactam ± linezolid or daptomycin	Recommended	Primarily no	Fluconazole or Echinocandin (anidulafungin or caspofungin or micafungin)
Postoperative (post-traumatic, post interventional) secondary peritonitis	Unstable/high	Meropenem ± linezolid or vancomycin or daptomycin Meropenem ± tigecycline or eravacycline Piperacillin/tazobactam + gentamycin or amikacin ± linezolid or vancomycin or daptomycin Ceftolozane/tazobactam or Ceftazidime/avibactam + metronidazole ± linezolid or vancomycin or daptomycin Ceftolozane/tazobactam or Ceftazidime/avibactam + tigecycline or eravacycline Meropenem/vaborbactam ± linezolid or vancomycin or daptomycin	Recommended	Yes	Echinocandin (anidulafungin or caspofungin or micafungin) Step down to fluconazole possible if *Candida* spp. is susceptible
Tertiary peritonitis	Varying/varying	Stable/no septic shock: Tigecycline Eravacycline Piperacillin/tazobactam ± linezolid or daptomycin	Recommended	Primarily no	Fluconazole or Echinocandin (anidulafungin or caspofungin or micafungin)
		Unstable/septic shock: see postoperative secondary peritonitis	Recommended	Yes	Echinocandin (anidulafungin or caspofungin or micafungin)

All mentioned antimicrobial agents/combination regimens should be tailored to local epidemiological situation and culture results (see text)

patients suffering from septic shock including those with abdominal sepsis [46]. Septic shock usually requires dose adjustment according to pharmacokinetic parameters. De-escalation from broad-spectrum agents to standard antibiotics is recommended after having received the culture results. Four to 5 days of antibiotics is adequate in the majority of hemodynamically stable patients with postoperative IAI and adequate source control [47]. In critically ill patients, treatment regimen of 8 days has been shown to be as effective as 15 days but reduces antibiotic exposure significantly, although the increased rates of post-day-8 drainages and bacteremia in the 8 days arm deserves further investigation [48]. Inefficacy of an antibiotic therapy should initiate intensive investigations for incomplete source control. Procalcitonin is a possible tool to discontinue antibiotic therapy, but the results in IAI are controversial. The value of its use to determine antibiotic therapy duration in postoperative IAI remains under debate [37, 48].

The isolation of *Candida* species in postoperative IAI is clinically significant and is usually associated with poor prognosis [19]. The inclusion of an anticandidal drug in empirical regimens for postoperative IAI seems to be appropriate in hemodynamically unstable patients. In critically ill patients, echinocandins (anidulafungin, caspofungin, micafungin) are preferred to fluconazole according to many international guidelines. Discontinuation of empirical antifungal therapy is recommended, if culture results show no growth of *Candida* species. In proven *Candida* peritonitis a step-down approach from an echinocandin to fluconazole appears to be feasible and safe, if the final culture results reveal fluconazole

Table 3 Potential research agenda on postoperative intrabdominal infections

Domain	Research aim
Definition/Diagnosis	Achieving improvements in the standardization of definitions and classification of IAI Developing standardized definition for intrabdominal candidiasis for both clinical and research purposes Elucidating the role of novel rapid phenotypic/molecular tests for the diagnosis of both bacterial and fungal postoperative IAI, preferably through assessment on their impact on actual therapeutic choices and patients' outcomes in randomized clinical trial Exploring the role of precision medicine and artificial intelligence/machine learning algorithms for improving our ability to define risks and interpret combined results of different diagnostic markers
Therapy	Defining exact criteria for primarily non-successful minimal invasive treatment of intraabdominal abscesses Evaluating the impact of determinant of resistance-level antimicrobial choices for treating IAI caused by MDR organisms Providing external validation of the DURAPOP study and better definition of treatment durations for critically ill patient populations different from those included in the trial Providing evidence about the most effective schedule and type of follow-up cultures/biomarkers results for monitoring response to treatment Improving our knowledge and implementation of PK/PD-based dosage adjustments

IAI intrabdominal infections, *MDR* multidrug resistant, *PK/PD* pharmacokinetics/pharmacodynamics

susceptibility. A treatment duration of 10–14 days although not evidence-based, has become common sense [4, 19].

Outcomes and future perspectives

Mortality of postoperative IAI remains high [1, 3, 49]. As detailed in previous sections, modifiable factors such as antimicrobial therapy and source control play a key role in influencing the prognosis of IAI, and efforts should, therefore, be devoted towards improving their appropriateness and timing. Major baseline factors that can impact the prognosis of postoperative IAI (besides their inherent healthcare-associated nature) are the presence of sepsis or septic shock, the site of origin, the presence of immunosuppression, and older age [49].

Peculiar of postoperative IAI, as already stressed in several occasions in previous paragraphs, is the risk of infection by resistant organism in endemic areas and hospitals [22]. Against this background, an always updated knowledge of the local microbiological epidemiology appears essential to guide correct empirical antibiotic choices, paired with the use of mortality risk assessments [49]. Another critical related aspect is the need to progress the diagnosis of postoperative IAI. Indeed, while there is firm indication for collecting blood cultures in unstable patients, for performing cultures on intraoperative specimens, and for the role of Gram stain for suggesting fungal infections [23, 37], high-level clinical evidence (about the actual impact on therapeutic choices and on patients' outcome and not only about diagnostic accuracy) should be provided in the future with regard to the role of rapid tests (e.g., PCR) and their interpretation in the context of postoperative IAI. For example, future studies will need to clearly characterize whether high sensitivity molecular methods may be of help for the etiological diagnosis of postoperative IAI in patients with negative blood cultures. The attempt to improve sensitivity for anaerobic organisms by means of molecular methods is another field of interest for future research. With regard to IAC, obtaining more high-level evidence about the tissue penetration of antifungals and the performance of single and combined diagnostic markers of fungal infection should also be among the key objectives of future research [5]. Potential research priorities for diagnosis and treatment of postoperative IAI are also summarized in Table 3.

The appropriate use of novel agents recently approved for the treatment of the most problematic resistant organisms (i.e., timely use for patients at high risk of resistance and avoidance of indiscriminate use for patients at low risk) could be paramount both for effectively treating patients in the present and for preserving efficacy in the future [44]. In our opinion, this also implies a possible shift in the perspective of how we classify patients at risk of resistant organisms, for the purpose of both empirical and targeted therapy. Indeed, the classical division, for example in MDR and extensively drug-resistant (XDR) organisms, relies on the phenotypic expression of resistance, whereas novel agents are now available that are active against strains expressing specific resistance determinants (e.g., KPC enzymes). Against this backdrop, the knowledge of the local molecular epidemiology (and not only of the resistance phenotypes) could change the ways we stratify the risk and we choose empirical agent/s, whereas the use of rapid molecular tests able to identify specific resistance genes/enzymes could influence the way we manage patients with proven MDR infections. Nonetheless, dedicated RCT remain necessary to validate these molecular-based approaches, and to evaluate their true impact on patients' outcome and local resistance epidemiology in different fields, including that of postoperative IAI.

With this increasing requirement for expertise in both novel infectious diseases (ID) diagnostic technologies and the molecular-level specificity of novel antimicrobials, we

think the role of ID consultants and microbiologists will continue to become increasingly essential. This is also true from an antimicrobial stewardship perspective. For example, ID consultants may help discriminate infected from non-infected postoperative pancreatitis, reducing useless administrations of broad-spectrum agents. Finally, antimicrobial stewardship efforts are also likely to participate in reducing mortality of postoperative IAI due to resistant organisms, and the importance both of a standardized multidisciplinary approach and of dedicated educational activities has been recently highlighted by an international panel composed by participants in the Antimicrobials: A Global Alliance for Optimizing their Rational Use in Intra-Abdominal Infections (AGORA) project and antimicrobial stewardship experts [50].

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Compliance with ethical standards

Conflicts of interest
Outside the submitted work, MB has received funding for scientific advisory boards, travel and speaker honoraria from Angelini, Astellas, AstraZeneca, Basilea, Bayer, BioMérieux, Cidara, Correvio, Cubist, Menarini, Molteni, MSD, Nabriva, Paratek, Pfizer, Roche, Shionogi, Tetraphase, Thermo Fisher, and The Medicine Company. DRG reports personal fees from Stepstone Pharma GmbH and an unconditioned grant from MSD Italia. PM has received funding for scientific advisory boards travel and speaker honoraria from Astra Zeneca, Basilea, Bayer, Menarini, MSD, Parexel, The Medicines Company, Pfizer and Tetraphase. CE has received speaker honoraria from Angelini, Astellas, AstraZeneca, Menarini, MSD, Nabriva and Pfizer. MS declares no conflict of interest.

Publisher's Note

Received: 3 September 2019 Accepted: 23 October 2019
Published online: 07 November 2019

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