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Review of the guidelines for complicated skin and soft tissue infections and intra-abdominal infections—are they applicable today?

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ABSTRACT

Difficult-to-treat infections in surgical patients, such as serious skin and soft tissue infections (SSTIs) and complicated intra-abdominal infections (cIAIs), are the cause of significant morbidity and mortality, and carry an economic burden. These surgical site infections are typically polymicrobial infections caused by a plethora of pathogens, which include difficult-to-treat organisms and multiresistant Gram-positive and Gram-negative strains. Optimal management of SSTIs and cIAIs must take into account the presence of resistant pathogens, and depends on the administration of appropriate antimicrobial therapy (i.e. the correct spectrum, route and dose in a timely fashion for a sufficient duration as well as the timely implementation of source control measures). Treatment recommendations from the Infectious Diseases Society of America and the Surgical Infection Society are available for guidance in the management of both of these infections, yet the increased global prevalence of multidrug-resistant pathogens has complicated the antibiotic selection process. Several pathogens of concern include methicillin-resistant *Staphylococcus aureus*, responsible for problematic postoperative infections, especially in patients with SSTIs, extended-spectrum β-lactamase-producing Gram-negative bacteria, including CTX-M-type-producing *Escherichia coli* strains, and multidrug-resistant strains of *Bacteroides fragilis*. New empirical regimens, taking advantage of potent broad-spectrum antibiotic options, may be needed for the treatment of certain high-risk patients with surgical site infections.

Keywords Complicated intra-abdominal infections, complicated skin and soft tissue infection, novel antimicrobials, resistant pathogens, treatment guidelines

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INTRODUCTION

Complicated intra-abdominal infections (cIAIs) and serious skin and soft tissue infections (SSTIs) are associated with considerable patient morbidity, mortality and escalating healthcare expenditures, due to the need for additional surgery and antimicrobial therapy, prolonged hospital stay and months of convalescence [1–3]. As such, the significant impact of these infections on patient outcome and survival is an important reason to reassess the management of these infections and the appropriate role of antimicrobial therapy. Furthermore, a better means of identifying and treating higher-risk patients with infections caused by potentially multiply antibiotic-resistant bacteria is needed.

By definition, cIAI is an infectious process that proceeds beyond the organ that is the source of the infection, and causes either localized peritonitis, also referred to as abdominal abscess, or diffuse peritonitis, depending on whether the patient's host responses can contain the process within the abdominal cavity [4]. Patients are considered to have complicated (c)SSTIs when there is a need for surgical intervention, if deep soft tissue involvement is suspected or confirmed, and/or when the patient has a complicating condition such as diabetes mellitus, peripheral vascular disease, or peripheral neuropathy [5].

Both cIAIs and cSSTIs are typically polymicrobial infections caused by a wide range of

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possible pathogens, which include difficult-to-treat organisms and multiresistant Gram-positive and Gram-negative strains [6,7]. IAIs are most commonly caused by multiple microorganisms that compose the intestinal flora, such as aerobes and facultative and obligate anaerobes, with *Enterobacteriaceae* (e.g. *Escherichia coli* and *Klebsiella pneumoniae*), enterococci and *Bacteroides fragilis* being isolated most often [4,7]. It is noteworthy that an increasing number of members of the gastrointestinal flora possess multiple resistance factors that express antimicrobial resistance (e.g. via extended-spectrum β-lactamase (ESBL) production) [8]. Outbreaks due to ESBL-producing *E. coli* and *K. pneumoniae* can negatively affect patient outcome, emphasizing the need for the judicious use of antimicrobials in order to minimize the spread of the infectious agents [8].

Likewise, the aetiological agents of cSSTIs also commonly comprise an array of organisms, often with multidrug-resistance phenotypes. A large surveillance study from North America, Europe and Latin America, analysing over 2500 isolates, found that the following organisms were most commonly implicated as causes of cSSTIs: *Staphylococcus aureus* (39.9%), *Pseudomonas aeruginosa* (12.1%), *E. coli* (9.7%), *Enterococcus* spp. (7.7%), *Klebsiella* spp. (5.8%), *Enterobacter* spp. (5.6%), coagulase-negative staphylococci (4.2%), *Proteus* spp. (3.7%), *Streptococcus* spp.(2.6%), *Acinetobacter* spp. (2.2%) and *Serratia* spp. (2%) [9]. In North America, the prevalence of these pathogens varied slightly: *S. aureus*, 45.9%; *P. aeruginosa*, 10.8%; *E. coli*, 7%; *Enterococcus* spp., 8.2%; *Klebsiella* spp., 5.1%; *Enterobacter* spp., 5.8%; coagulase-negative staphylococci, 3.4%; *Proteus* spp., 3.2%; *Streptococcus* spp., 2.7%; *Acinetobacter* spp., 1.6%; and *Serratia* spp., 2%. This surveillance study also revealed that the rate of methicillin-resistant *S. aureus* (MRSA) was 27.2% overall (29% in North America) [9]. The emergence of community-associated MRSA is also alarming, especially in patients with cSSTIs [10]. A retrospective meta-analysis of surveillance studies conducted in Europe confirmed that *S. aureus*, coagulase-negative staphylococci, *E. coli* and *P. aeruginosa* were the most common pathogens associated with cSSTIs/surgical site infections [11]. Certain patient risk factors, such as a history of intravenous drug use, must also be considered when attempting to predict the possible aetiologies of cSSTIs [12].

Successful management of cIAIs and cSSTIs is dictated, in part, by the likely presence of resistant pathogens, and depends on the administration of adequate antimicrobial therapy, and the timely implementation of source control measures [4,7]. Treatment recommendations are available to guide the clinician in the management of both of these infections [4,13,14]. However, because cSSTIs and cIAIs caused by multidrug-resistant pathogens have become more common over the last decade, alternative empirical treatments not currently outlined in the published guidelines may need to be considered for at-risk patients.

The primary purpose of this article is to discuss the impact of surgical site infections, including cSSTIs and cIAIs, on patient outcomes, to review the current treatment guidelines for surgical site infections, and to discuss the current treatment guidelines for cSSTIs and cIAIs in the context of the patterns of emerging resistance in Europe and the potential for monotherapy in empirical regimens.

COMPLICATED SKIN AND SOFT TISSUE INFECTIONS/SURGICAL SITE INFECTIONS

Surgically induced soft tissue surgical site infections (SSIs) are typically divided into the following categories: superficial incisional SSIs, deep incisional SSIs, and organ/space SSIs [15]. Superficial incisional SSIs involve only the subcutaneous space, between the skin and the underlying muscular fascia, and occur within 30 days of the index operation. A deep incisional SSI involves the deep layers of soft tissue (e.g. fascia and muscle) in the incision, and typically occurs within 30 days following the surgical procedure. An organ/space SSI is similar to a deep incisional SSI, except that it may involve any part of the anatomy (organs or spaces) other than the incision opened during the operation.

Assessing the total impact of cSSTIs/SSIs on patient morbidity and overall outcome is difficult because of incomplete data collection and reporting. A retrospective analysis of reported surgical site infections conducted in Europe attempted to calculate the incidence of these infections [11]. The estimated incidence varied widely, from 1.5% to 20%, suggesting that the true rate of SSTIs is currently unknown and is probably under-reported due to inconsistencies in data