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REVIEW

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Abdominal Sepsis: An Update

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Abstract

Despite the significant development and advancement in antibiotic therapy, life-threatening complication of infective diseases cause hundreds of thousands of deaths world. This paper updates some of the issues regarding the etiology and treatment of abdominal sepsis and summaries the latest guidelines as recommended by the Intra-abdominal Infection (IAI) Consensus (2017). Prognostic scores are currently used to assess the course of peritonitis. Irrespective of the initial cause, there are several measures universally accepted as contributing to an improved survival rate, with the early recognition of IAI being the critical matter in this respect. Immediate correction of fluid balance should be undertaken with the use of vasoactive agents being prescribed, if necessary, to augment and assist fluid resuscitation. The WISS study showed that mortality was significantly affected by sepsis irrespective of any medical and surgical measures. A significant issue is the prevalence of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae in the clinical setting, and the reported prevalence of ESBLs intra-abdominal infections has steadily increased in Asia. Europe, Latin America, Middle East, North America, and South Pacific. Abdominal cavity pathology is second only to sepsis occurring in a pulmonary site. Following IAI (2017) guidelines, antibiotic therapy should be initiated as soon as possible after a diagnosis has been verified.

Keywords: abdominal sepsis, septic shock, peritonitis

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Background

Despite significant developments and advancements in antibiotic therapy life-threatening complication of infective diseases cause hundreds of thousands of deaths in the USA and millions more worldwide [1, 2].

Sepsis is the body's overwhelming and life-threatening response to infection which can lead to multiple organ systems failure. It is the body's immune system overresponse to infection following the release of inflammatory mediators such as cytokines into the blood circulation [3, 4]. Pro-coagulation factors in endothelial cells are activated causing local damages which will lead to a systemic inflammatory response syndrome (SIRS), septic shock and multiple organ dysfunction syndrome (MOSF) [5]. During such severe inflammatory stages, patients are often sedated and intubated, and the collection of relevant data requires well-developed communication skills [6]. This paper updates matters of abdominal sepsis etiology and treatment in the light of the latest guidelines outlined by the Intraabdominal Infection (IAI) Consensus (2017) [7].

Prognostic scores

A diversity of prognostic scores are currently used to assess the course of peritonitis and intra-abdominal infections according to age, sex, the origin of sepsis, the degree of peritonitis, the time between any perforation to an operation and the type of exudates. Their objective is the early classification of patients presenting with peritonitis and intra-abdominal sepsis through an objective scoring system, to aid in patient select for specific treatment modalities as well as to compare the results of different treatment regimens (Table I). Unfortunately, none of the current scoring systems satisfies all prerequisites [8-14].

Peritonitis classification

Peritonitis can be classified by the anatomical integrity of the abdominal cavity. Primary peritonitis is associated with undamaged intra-abdominal cavity organs. It is also known as spontaneous bacterial peritonitis and is treated without surgical interven-

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tion. The source of infection is often hard to establish and is usually found occurring in infants and cirrhotic patients. Secondary peritonitis is an infection of the peritoneal cavity after hollow viscus perforation, anastomotic leak, ischemic necrosis, or other injuries of the gastrointestinal tract.

Secondary peritonitis, a common occurrence in critical surgical patients, is defined as an infection of the peritoneal cavity resulting from hollow viscus perforation, anastomotic leak, ischemic necrosis, or other injuries of the gastrointestinal tract. Tertiary peritonitis is defined as a serious recurrent or persistent intra-abdominal infection after the ostensibly successful control of secondary peritonitis [15-17].

Medical treatment of abdominal sepsis

Irrespective of the cause, several measures are available and accepted as improving the survival rate, the most important being the early recognition of IAI. Efforts to achieve fluid balance should be initiated immediately to replace any intravascular insufficiency. Vasoactive agents may be necessary to augment and assist fluid restoration [18].

The WISS study showed that sepsis significantly influences mortality rate, this being only 1.2% in the absence of sepsis, increasing to 4.4% when sepsis is present and 71.8% when septic shock occurs [19].

Associated Microorganisms

Associated microorganisms differ according to the type of peritonitis and with the levels of perforation in secondary and tertiary peritonitis. When perforation is higher up in the alimentary tract, i.e. the stomach or the duodenum, bacterial contamination usually has less serious consequences whereas perforation of the colon and rectum leads to severe bacterial contamination which can be life-threatening and is the leading cause of sepsis and septic shock [20].

Primary bacterial peritonitis is associated with gram-negative *Enterobacteriaceae and*, *Streptococcus spp*., whereas secondary bacterial peritonitis is mainly linked to a polymicrobial infection of gram-negative *Enterobacteriaceae*, gram-positive *Enterococci and Staphylococci*, or anaerobes and candida. Tertiary peritonitis has a similar poly-microbial infection to secondary peritonitis, with common organisms isolated from patients being *Enterococcus*, *Candida*, and *Staphylococcus epidermidis* and are more likely to involve antibiotic-resistant strains [20].

Antibiotic therapy

The Study for Monitoring Antimicrobial Resistance Trends (SMART) monitored the patterns of clinical gram-negative bacilli to antimicrobial agents. It reported the prevalence of extended-spectrum β-lactamase (ESBL)-producing *Enterobacteriaceae* in the clinical setting, to be of significant importance and acknowledged it to be increasing worldwide. In addition to the expected increased resistance to beta-lactams, fluoroquinolone resistance in ESBL-positive *Escherichia coli* causing intra-abdominal infections, ranges from 60 to 93 % [21,22]. A comprehensive list of currently acceptable antibiotic therapy treatment related to peritonitis severity is given in Table II [23].

Surgical treatment of abdominal sepsis

IAI guidelines have published graded guidelines, A, B, C, D, for the medical and surgical treatment of abdomi-

Table I. Prognostic scores used to evaluate the prognostic of abdominal infection

Prognostic scores	Etiology
Peritonitis Severity Score (PSS)	Left-sided colon perforation
Boey Score Jabalpur Index Hacettepe Score PULP Score	Gastroduodenal ulcers perforations
Postoperative peritonitis	Dutch leakage score
P-POSSUM Score Mannheim Peritonitis Index (MPI) Peritonitis Index Altona (PIA) WSES complicated IAI score (WISS study)	Peritonitis of all causes

nal sepsis, A, is a strong recommendation and D, one that is less robust in its recommendation[7].

Laparoscopic appendectomy is the primary treatment modalities recommended for perforated appendicitis. Antibiotic-therapy is used to supplement surgery or to delay a surgical procedure, though, on its own, it does not usually control an intraperitoneal infection [7]. According to Kong (2015), following retractable septic shock, the median overall length of hospital stay was five days, and the mortality rate was 1% [24].

In left colic perforated diverticular disease associated with a small abscess, treatment is commenced with antibiotics, with percutaneous drainage undertaken in cases of large abscess formation. The Hartmann procedure is used in cases of diffuse peritonitis and when progression to sepsis has occurred [25, 26], and in perforated colonic carcinoma, the Hartmann procedure is the first option of surgical treatment [27].

When local conditions allow, perforation subsequent to colonoscopy should be treated immediately by primary suture, if not the resection of the large bowel containing the perforation may be necessary [28, 29].

In gastroduodenal ulcer perforations, primary suturing, with or without an omentum patch, performed open or laparoscopically, is the treatment of choice [30,31].

In small bowel perforation, primary suturing is the first option, but if it is associated with a large perforation or with a local ischemic condition, segmental resection is mandatory [32,33].

Early cholecystectomy in acute cholecystitis is now recommended as being superior to the previously held opinion of delaying cholecystectomy, with a laparoscopic technique being the procedure of choice. The alternative, and considered to be the best option, especially when complications occurs, is a classical approach [34].

Endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard for biliary decompression in patients with moderate to severe acute cholangitis, failing which, percutaneous biliary drainage (PTBD) is the second option[35,36]. Ineffective control of the septic source is associated with significantly elevated mortality rates [37].

Pelvic inflammatory disease (PID) usually responds to antibiotic therapy, though surgical drainage is usually required in patients with a tubo-ovarian abscess [38,39].

In cases of trauma accompanied by perforation, repair or anastomosis of the intestinal injuries should be considered in all cases. A colostomy is to be considered in colorectal injuries involving all layers when multiple injuries or comorbid conditions are present [40,41].

Discussion

Sepsis originates from infections caused by microorganisms such as bacteria, fungi, viruses or parasites. A clinical diagnosis of the source of infection, be it lung, cutaneous or kidney, or an abdominal abscess, or infection with or without neoplasia [42], is the initial step of identification of the causative agent [1]. Pathogenic agents have changed in recent years, due to the use of newer antibiotics [1]. The gram-negative bacteria, the *Pseudomonas aeruginosa* and gram-positive *Staphylococcus aureus* continue to be the most frequent pathogenic agent isolated from blood [1]. A recent increase in *Candida albicans* can be attributed to the use of anti-

Table II. Currently acceptable antibiotic therapy treatment related to peritonitis severity

Diagnosis	Monotherapy	Combination therapy
Primary peritonitis	Ampicillin/Sulbactam	2nd generation Cephalosporin
Secondary peritonitis low risk (localized peritonitis)	Ampicillin/Sulbactam	2nd generation Cephalosporin + Metronidazole
	Carbapenem	3rd generation Cephalosporin + Metronidazole
Secondary peritonitis low risk (diffuse peritonitis)	Ampicillin/Sulbactam Piperacillin/Tazobactam Carbapenem (group 1/2) Fluoroquinolone 4th generation Tigecycline	2nd generation fluoroquinolone + Metronidazole 3rd or 4th generation Cephalosporin + Metronidazole
Secondary peritonitis high risk	Piperacillin/Tazobactam Carbapenem (group 1/2) Tigecycline	4th generation Cephalosporin + Metronidazole
Tertiary peritonitis	According to resistance from microbiology	Antifungal therapy in high-risk patients

biotic therapy and immunosuppressants [43]. Though extremely rare, sepsis caused by malaria-causing *Plasmodium falciparum* has been reported in the literature [44].

Stearns-Kurosawa (2011) outlined the pathogenesis of the severity of sepsis and septic shock and charted the criteria for the systemic inflammatory response syndrome (SIRS) [45].

SIRS may be induced by trauma, pulmonary emboli, or myocardial infarction [46].

Sepsis is considered to occur when SIRS is associated with an infection, and if sepsis progresses and there is resultant arterial hypotension, then septic shock ensues[47]. Sepsis by itself can lead to the development of secondary abdominal compartment syndrome, which severely compromises the patient's progress [48,49].

The key relationship in the pathogenesis of sepsis is the gram-negative bacterial endotoxin lipopolysaccharide (LPS) being recognized as a marker for the detection of bacterial pathogen invasion and responsible for the development of an inflammatory response. Release of LPS into the circulation triggers a strong systemic pro-inflammatory response [43].

Cytokines release also represents a response against aggression. Tumor necrosis factor-a (TNF-a) and IL-1b are very well known in sepsis and septic shock involvement [50]. A systemic inflammatory response syndrome is triggered by high blood levels of cytokines one of them being IL-6 , initially described as B-cell–stimulating factor. IL-6, encoded by a gene located in the chromosome 7p2 region, is a cytokine with an initial pro-inflammatory role in a systemic inflammatory response to infectious injuries [51]. The importance of IL6 as a prognostic factor has been studied with the development of IL6 inhibitors, such as monoclonal neutralizing antibodies against IL-6 and its gp80 receptor, as well as a soluble gp130 Fc fusion protein that inhibits IL-6/sIL-6R trans-signaling. As a result of multiple studies, tocilizumab, a monoclonal antibody that acts as an IL-6 receptor antagonist, has been approved for the treatment of rheumatoid arthritis [52].

Conclusions

Abdominal cavity pathology is the second most common site of sepsis, with perforated appendicitis being the most frequent source of an abdominal infection. If it is not recognized, it can progress to septic shock with a 1% mortality rate. The intra-abdominal compartment syndrome is a complication of the progression of peritonitis. According to IAI guidelines, depending on the degree of the condition, antibiotic- therapy should be initiated as soon as possible.

Conflict of interest

None to declare.

References

1. Alexandraki I, Palacio C. Gram-negative versus Gram-positive bacteremia: what is more alarming? Crit Care. 2010;14:161.
2. Barkhausen T, Tschernig T, Rosenstiel P, et al. Selective blockade of interleukin-6 trans-signalling improves survival in a murine polymicrobial sepsis model. Crit Care Med. 2011;39(6):1407-13.
3. Baron RM, Baron MJ, Perrella MA. Pathobiology of sepsis: are we still asking the same questions? Am J Respir Cell Mol Biol. 2006;34:129–34.
4. Georgescu AM, Szederjesi J, Voidazan S, et al. Soluble urokinase-type plasminogen activator receptor (suPAR) – a possible biomarker for bacteremia in sepsis. Rev Romana Med Lab. 2015;23(1):59-73.
5. Fodor RŞ, Georgescu AM, Cioc AD et al. Time- and dose-dependent severity of lung injury in a rat model of sepsis. Rom J Morphol Embryol. 2015;56(4):1329-37.
6. Marginean CO, Melit LE, Chincesan M, et al. Communication skills in pediatrics – the relationship between pediatrician and child. Medicine. 2017;96(43):e8399.
7. Sartelli M, Chichom-Mefire A, Labricciosa FM. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intraabdominal infections. World J Emerg Surg. 2017;12:1-34
8. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med. 2003;31:1250–6.
9. Sartelli M. A focus on intra-abdominal infections. World J Emerg Surg. 2010;5:9.
10. Bouali K, Magotteaux P, Jadot A, et al. Percutaneous catheter drainage of abdominal abscess after abdominal surgery: results in 121 cases. J Belg Radiol. 1993;76:11–4.
11. VanSonnenberg E, Mueller PR, Ferrucci Jr JT. Percutaneous drainage of 250 abdominal abscesses and fluid collections. I. Results, failures and complications. Radiology. 1984;151:337–41.
12. Jaffe TA, Nelson RC, DeLong D, Paulson EK. Practice patterns in percutaneous image-guided intra-abdominal abscess drainage: survey of academic and private practice centres. Radiology. 2004;233:750–6.

13. Agresta F, Ciardo LF, Mazzarolo G, et al. Peritonitis: laparoscopic approach. World J Emerg Surg. 2006;24:1–9.
14. Bedada AG, Hsiao M, Bakanisi B, Motsumi M, Azzie G. Establishing a contextually appropriate laparoscopic program in resource-restricted environments: experience in Botswana. 15. Sartelli M. A focus on intra-abdominal infections. World J Emerg Surg. 2010;5:9.
16. Montravers P, Dufour G, Guglielminotti J, et al. Dynamic changes of microbial flora and therapeutic consequences in persistent peritonitis. Crit Care. 2015;19:7.
17. Lamme B, Mahler CW, van Ruler O, Gouma DJ, Reitsma JB, Boermeester MA. Clinical predictors of ongoing infection in secondary peritonitis: a systematic review. World J Surg. 2006;30:2170–81.
18. Vincent JL, De Backer D. Circulatory shock. N Engl J Med. 2013;369:1726–34.
19. Sartelli M, Abu-Zidan FM, Catena F, et al. Global validation of the WSES Sepsis Severity Score for patients with complicated intraabdominal infections: a prospective multicenter study (WISS Study). World J Emerg Surg. 2015;10:61
20. Calandra T, Cohen J. The international sepsis forum consensus conference on definitions of infection in the intensive care unit. Crit Care Med. 2005;33(7):1538–48.
21. Hawser SP, Bouchillon SK, Hoban DJ, Badal RE. In vitro susceptibilities of aerobic and facultatively anaerobic gram-negative bacilli from patients with intra-abdominal infections worldwide from 2005–2007: results from the SMART study. Int J Antimicrob Agents. 2009;34:585–8.
22. Morrissey I, Hackel M, Badal R, Bouchillon S, Hawser S, Biedenbach D. A review of ten years of the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 2002 to 2011. Pharmaceuticals (Basel). 2013;6:1335–46.
23. Sartelli M, Weber DG, Ruppé E, et al. Antimicrobials: a global alliance for optimizing their rational use in intraabdominal infections (AGORA). World J Emerg Surg. 2016;11:33.
24. Kong VY, Sartorius B, Clarke DL. Acute appendicitis in the developing world is a morbid disease. Ann R Coll Surg Engl. 2015;97:390–5.
25. Andersen JC, Bundgaard L, Elbrønd H, Laurberg S, Walker LR, Støvring J. Danish national guidelines for treatment of diverticular disease. Dan Med J. 2012;59: C4453.
26. Cirocchi R, Trastulli S, Desiderio J, et al. Treatment of Hinchey stage III-IV diverticulitis: a systematic review and meta-analysis. Int J Colorectal Dis. 2013;28:447–57.
27. Meyer F, Marusch F, Koch A, et al. Emergency operation in carcinomas of the left colon: the value of Hartmann's procedure. Tech Coloproctol. 2004;8 Suppl 1:s226–9.
28. Shin DK, Shin SY, Park CY,et al. Optimal methods for the management of iatrogenic colonoscopic perforation. Clin Endosc. 2016;49:282–8.
29. An SB, Shin DW, Kim JY, Park SG, Lee BH, Kim JW. Decision-making in the management of colonoscopic perforation: a multicentre retrospective study. Surg Endosc. 2016;30:2914–21.
30. Søreide K, Thorsen K, Søreide JA. Predicting outcomes in patients with perforated gastroduodenal ulcers: artificial neural network modelling indicates a highly complex disease. Eur J Trauma Emerg Surg. 2015;41:91–8.
31. Sanabria A, Villegas MI, Morales Uribe CH. Laparoscopic repair for perforated peptic ulcer disease. Cochrane Database Syst Rev. 2013;2:CD004778.
32. Ayite A, Dosseh DE, Tekou HA, James K. Surgical treatment of single non-traumatic perforation of the small bowel: excision-suture or resection anastomosis. Ann Chir. 2005;131:91–5.
33. Ara C, Sogutlu G, Yildiz R, et al. Spontaneous small bowel perforations due to intestinal tuberculosis should not be repaired by simple closure. J Gastrointest Surg. 2005;9:514–7.
34. Ansaloni L, Pisano M, Coccolini F, et al. 2016 WSES guidelines on acute calculous cholecystitis. World J Emerg Surg. 2016;11:25.
35. Lee JG. Diagnosis and management of acute cholangitis. Nat Rev Gastroenterol Hepatol. 2009;6:533–41,
36. Bin OY, Zeng KW, Hua HW, Zhang XQ, Chen FL. Endoscopic nasobiliary drainage and percutaneous transhepatic biliary drainage for the treatment of acute obstructive suppurative cholangitis: a retrospective study of 37 cases. Hepatogastroenterology. 2012;59:2454–6.
37. Daams F, Luyer M, Lange JF. Colorectal anastomotic leakage: aspects of prevention, detection and treatment. World J Gastroenterol. 2013;9:2293–7.
38. Mitchell C, Prabhu M. Pelvic inflammatory disease: current concepts in pathogenesis, diagnosis and treatment. Infect Dis Clin North Am. 2013;27:793–809.
39. Garbin O, Verdon R, Fauconnier A. Treatment of the tubo-ovarian abscesses. J Gynecol Obstet Biol Reprod. 2012;41:875–85.
40. Weinberg JA, Griffin RL, Vandromme MJ, et al. Management of colon wounds in the setting of damage control laparotomy: a cautionary tale. J Trauma. 2009;67:929–35.
41. Miller PR, Chang MC, Hoth JJ, Holmes JH, Meredith JW. Colonic resection in the setting of damage control laparotomy: is delayed anastomosis safe? Am Surg. 2007;73:606–9.
42. Mureşan M, Bancu S, Bara T, Bancu L, Turcu M, Mureşan S. Local recurrence after the sphincter –saving operation and abdominal perineal resection in rectal cancer. Chirurgia. 2009;104(4):23-25.
43. Duggan S, Leonhardt I, Hünniger K, Kurzai O. Host response to Candida albicans bloodstream infection and sepsis. Virulence. 2015;6(4):316-26.
44. Auma MA, Siedner MJ, Nyehangane D, et al. Malaria is an uncommon cause of adult sepsis in south-western Uganda. Malaria Journal. 2013;12:146.
45. Stearns-Kurosawa DJ1, Osuchowski MF, Valentine C, Kurosawa S, Remick DG. The pathogenesis of sepsis. Annu Rev Pathol. 2011;6:19-48.

46. Remick DG. Pathophysiology of sepsis. Am J Pathol. 2007; 170:1435–44.

47. Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med. 2008;34:17–60.

48. Muresan M, Muresan S, Bara T, et al. The intraabdominal pressure: A real indicator of the tension-free principle during anterior wall repair procedure after incisional hernias. Ann Ital Chir. 2015;86(5):421-26.

49. Muresan M, Muresan S, Brinzaniuc K, et al. How much does decompressive laparotomy reduce the mortality rate in primary abdominal compartment syndrome? A single-centre prospective study on 66 patients. Medicine. 2017; 96(5):e6006.

50. Oberhoffer M, Karzai W, Meier-Hellmann A, Bogel D, Fassbinder J, Reinhart K. Sensitivity and specificity of various markers of inflammation for the prediction of tumor necrosis factor-alpha and interleukin-6 in patients with sepsis. Crit Care Med. 1999;27:1814–8.

51. Rose-John S, Scheller J, Elson G, Jones SA. Interleukin-6 biology is coordinated by membrane-bound and soluble receptors: role in inflammation and cancer. J Leukoc Biol. 2006;80:227–36.

52. Mima T, Nishimoto N. Clinical value of blocking IL-6 receptor. Curr Opin Rheumatol. 2009;21(3):224-30