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Recommendations for intra-abdominal infections consensus report

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ABSTRACT

Guidelines include the recommendations of experts from various specialties within a topic in consideration of data specific to each country. However, to date there has not been a guideline standardizing the nomenclature and offering recommendations for intra-abdominal infections (IAIs) in Turkey. This is mainly due to the paucity of laboratory studies regarding the clinical diagnosis and treatment of IAIs or the sensitivity of microorganisms isolated from patients with IAIs. However, due to the diversification of host characteristics and advancements in technological treatment methods, it has become imperative to 'speak a common language'. For this purpose May 2015, a group of 15 experts in intra-abdominal infections, under the leadership of the Infectious Diseases and Clinical Microbiology Specialty Society of Turkey (EKMUD) and with representatives from the Turkish Surgical Association, Turkish Society of Colon and Rectal Surgery, Hernia Society, Turkish Society of Hepato-pancreato-biliary Surgery, and the Turkish Society of Hospital Infections and Control, was formed to analyze relevant studies in the literature. Ultimately, the suggestions for adults found in this consensus report were developed using available data from Turkey, referring predominantly to the 2010 guidelines for diagnosing and managing complicated IAIs in adults and children by the Infectious Diseases Society of America (IDSA) and the Surgical Infection Society. The recommendations are presented in two sections, from the initial diagnostic evaluation of patients to the treatment approach for IAI. This Consensus Report was presented at the EKMUD 2016 Congress in Antalya and was subsequently opened for suggestions on the official websites of the Infectious Diseases and Clinical Microbiology Specialty Society of Turkey and Turkish Surgical Association for one month. The manuscript was revised according to the feedback received.

Keywords: Diagnosis, guide, intra-abdominal infection, management, recommendations

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INTRODUCTION

Why these guidelines were created:

Guidelines include the recommendations of experts from various specialties within a topic in consideration of data specific to each country. However, to date there has not been a guideline standardizing the nomenclature and offering recommendations for intra-abdominal infections (IAIs) in Turkey. This is mainly due to the paucity of laboratory studies regarding the clinical diagnosis and treatment of IAIs or the sensitivity of microorganisms isolated from patients with IAIs (1, 2). In some laboratory-based microorganism susceptibility studies, a portion of total isolates have been reported as organisms associated with IAI (3, 4). However, due to the diversification of host characteristics and advancements in technological treatment methods, it has become imperative to 'speak a common language'. Therefore, despite insufficient national data for preparing a guideline, this consensus report was developed in order to raise awareness of this issue and compile the available national data.

The purpose of this Consensus Report:

This consensus report was prepared in order to create a standard clinical pathway for the diagnosis and treatment of patients with IAIs.

Who this Consensus Report is for:

They were designed to provide guidance to all physicians who are involved in the diagnosis and management of IAIs.

Which organizations were represented in the committee?

Under the leadership of the Infectious Diseases and Clinical Microbiology Specialty Society of Turkey (EKMUD), the committee consisted of 15 experts in IAI from the Turkish Surgical Association, Turkish Society of Colon and Rectal Surgery, Hernia Society, Turkish Society of Hepato-pancreato-biliary Surgery, and the Turkish Society of Hospital Infections and Control.

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This Consensus Report was prepared by a group of 15 experts from the Infectious Diseases and Clinical Microbiology Specialty Society of Turkey (EKMUD), Turkish Society of Hospital Infections and Control, Turkish Surgical Association, Turkish Society of Colon and Rectal Surgery, Hernia Society, and Turkish Society of Hepato-pancreato-biliary Surgery.

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The process of creating the guidelines/consensus report:

Preparation of the consensus report began with an initial meeting in May 2015. At this meeting, the participants primarily shared and determined the state of their issues and common practices. The participants decided to delegate the subareas amongst themselves and screen the relevant literature. Due to the particular lack of data regarding the agents of community-acquired IAI, a questionnaire was prepared to determine the reasons for not taking microbiologic samples. The questionnaire, entitled 'Questionnaire to assess surgeons' attitude and ability regarding microbiologic sampling in the diagnosis of intra-abdominal infections', was placed on the Turkish Surgical Association's website, and an e-mail notification was sent to all of the association's members. The questionnaire remained on the website for approximately six weeks, during which the members were sent several reminders via e-mail. The results of this survey were evaluated in the consensus report. The participants continued to correspond through e-mail. The consensus report was developed over the course of one year, with a total of four meetings held at the EKMUD headquarters in Ankara.

No additional patients were recruited for this report.

What databases and key words were used in the literature search?

The Ulakbim Turkish Medicine Index, Turkey Citation Index, and Turkish Medline databases were searched using the keyword terms intraabdominal/intra-abdominal infeksiyon and/or Türkiye; PubMed, EBSCOhost research databases, Proquest Health and Medical Package, Scopus and Web of Knowledge databases were searched using the keyword terms intraabdominal/intra-abdominal infection, and/or Turkey. The pages of European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) dating from 2010 to present were searched using the same keyword terms.

Evaluation criteria for the evidence/conclusions reached from the available data:

There were no prospective randomized-controlled studies which primarily examined the medical and surgical treatment of IAI in Turkey. The suggestions found in this consensus report for adults were developed based on the criteria for recommendation strength and evidence quality specified in Table 1. However, all guidelines do not use the same evidence strength table. Therefore, only the evidence grades which were consistent, recommended in both of these guidelines and were also considered appropriate by our expert panel were included in this consensus report with references to the relevant guidelines. Suggestions for which an evidence grade is not specified are the consensus of the panel. Ultimately, the guidelines were developed using available data from Turkey, and referring predominantly to the 2010 guidelines for diagnosing and managing complicated IAIs in adults and children by the Infectious Diseases Society of America (IDSA) and the Surgical Infection Society (5), as well as the guidelines listed below.

Table 1. Strength of recommendation and quality of evidence (5, 6)

Evaluation	Type of evidence
Strength of recommendation	
Grade A	Good evidence supporting a recommendation for use
Grade B	Moderate evidence supporting a recommendation for use
Grade C	Poor evidence supporting a recommendation
Quality of evidence	
Level I	Evidence from at least one well-designed randomized, controlled trial
Level II	Evidence from at least one non-randomized clinical trial
Level III	Evidence from opinions of respected authorities, based on clinical studies, descriptive studies, or reports from expert committees

- The Canadian Surgical Society and Association of Medical Microbiology and Infectious Diseases (AMMI) 2010 practice guidelines for surgical intra-abdominal infections (6).
- The World Society of Emergency Surgery (WSES) 2103 guidelines for management of intra-abdominal infections (7).
- The French Anesthesiology and Reanimation Society [Société Française d'Anesthésie et de Réanimation (SFAR)] 2015 guidelines for management of intra-abdominal infections (8).
- The German Society for Gastroenterology, Digestive and Metabolic Diseases and German Society for General and Visceral Surgery 2014 diverticular diseases guidelines (9).
- The Italian Society of Intensive Care and International Society of Chemotherapy consensus report that can be applied in the management of intra-abdominal candidiasis in adults (10).

- IDSA 2016 revised clinical practice guideline for the management of candidiasis (11).
- American College of Gastroenterology 2013 guideline for management of acute pancreatitis (12).

The expected outcomes of publishing and disseminating this guideline/consensus report:
This consensus report was developed with the aim of making a positive contribution to the diagnostic and treatment practices of all physicians involved with IAIs. It is expected to assist physicians in various areas by guiding their approaches to diagnostic evaluation (microorganismic, host, and surgical risk factors; severity of illness; diagnostic tests), treatment (source control; fluid therapy; empiric and agent-specific antibiotic therapy and monitoring of community-acquired and healthcare-associated IAIs) and patient follow-up.

Will this guideline/consensus report be revised?
All guidelines and consensus reports are intended as guides. However, due to the inherent contextual and temporal limitations of consensus reports, they must be reviewed and updated at regular intervals. We hope that this consensus report will be periodically reviewed and improved as its weaknesses become evident with practical application and as new data become available. We envision that this process will be furthered through bringing attention to the topic and with the support of scientific associations, and especially with data obtained from randomized controlled studies conducted in Turkey.

Legal status
This is first consensus report developed in Turkey, and the recommendations herein were designed as a guide.

Structure of this guideline/consensus report
The recommendations are divided into two sections, diagnostic evaluation starting from the IAI patient's initial presentation (microorganismic, host, and surgical risk factors; severity of illness; diagnostic tests) and treatment approaches (source control; fluid therapy; empiric and agent-specific antibiotic therapy and monitoring of community-acquired and healthcare-associated IAIs).

DIAGNOSTIC EVALUATION

I. Introduction
IAIs encompass various clinical entities ranging from uncomplicated appendicitis to fecal peritonitis.

Uncomplicated IAIs include intramural inflammation of the gastrointestinal tract.

Complicated IAIs describe clinical conditions in which infection has extended beyond the hollow organ into the peritoneal cavity, resulting in abscess or peritonitis. These terms are not intended to describe the severity or anatomic location of the infection. Complicated IAIs are a widespread problem and are the second most common cause of infection-related mortality in intensive care units. The incidence and mortality rates of IAIs in specific patient populations vary according to whether operative interventions were performed after trauma, etc. and the anatomic location and duration of surgical procedures performed. The reported mortality rate after appendectomy is 1.3-3.1%, with that rate increasing to over 10% in small intestine or colon surgery (6). Therefore, appropriate diagnostic evaluation should be a priority. Advances in diagnostic assessment and imaging, intensive care support, minimally invasive interventions, and antimicrobial therapy have led to substantial improvements in the accurate treatment of IAIs.

Patient history, physical examination and laboratory analyses are sufficient to identify most patients with a suspected IAI who require further treatment (IDSA, A-II) (5). For patients with compromised immunity associated with disease or therapy and selected patients with unreliable physical examination findings, such as those with altered mental state or spinal cord injury, IAI should be considered upon presentation with signs of an infection of undetermined origin (IDSA, B-III) (5).

The determination of host, microorganismic and surgical risk factors will facilitate the identification of high-risk patients.

II. Microbial risk factors
Organisms associated with IAIs in different locations and risk factors for multidrug-resistant microorganisms and specific drug-resistant microorganisms are shown in Tables 2-4 (13-16).

III. Host risk factors
Patients should be evaluated for the presence or history of malnutrition, diabetes mellitus (DM), malignancy, radiotherapy, 6-12 cycles of chemotherapy, selected chemotherapeutic agents, high American Society of Anesthesiologists (ASA) score (III-IV), high Acute Physiology and Chronic Health Evaluation II (APACHE-II) score (>15), delay in initial intervention (more than 24-48 hours), treatment failure, immunosuppression, and elevated inflammatory response (Table 5). The German guidelines for diverticular disease specify an ASA score of III-IV, DM, heart failure, chronic obstructive pulmonary disease (COPD), renal insufficiency, autoimmune vasculitis, gout, immunosuppression, hypoalbuminemia and steroid use as risk factors for increased mortality and morbidity in surgery for diverticular diseases (9). All patients should be evaluated for the presence of DM, severe cardiopulmonary disease, immunosuppression, and any of the following within the 3 months prior to presentation: 5 days or longer inpatient status and/or more than 2 days antibiotic use and/or an abdominal procedure (AMMI, A-II) (6). Patients with a history of hospitalization and/or antibiotic use and/or abdominal surgery should be considered to have healthcare-associated IAI (AMMI, A-II) (6).

IV. Surgical risk factors
Risk factors associated with surgery include inadequate source control, gastrointestinal system (GIS) location, division of integrity of GIS with other systems (e.g. opening in the GIS and urogenital system or iatrogenic/inadvertent violation of a space in malignancy), use of intra-abdominal foreign bodies, repeated operative procedures, level of experience and expertise among the surgical team, and techniques used.

V. Severity of illness
Severity of illness should be evaluated with APACHE-II score. Patients with scores of 15 and over should be considered as having severe infection and those with scores under 15 as having mild to moderate infection.

Sartelli et al. (17) developed a new, practical sepsis severity scoring system for patients with complicated IAIs and applied it to 4,652 patients with complicated IAI (excluding

Table 2. Intra-abdominal Infections and Organisms by Location (13-16)

Infection	Agent
Primary bacterial peritonitis	Gram-negative Enterobacteriaceae *Streptococcus spp.*
Secondary bacterial peritonitis	Polymicrobial infection (gram-negative Enterobacteriaceae, gram-positive *Enterococci, Staphylococci and anaerobes)*
Tertiary peritonitis	Polymicrobial infection (resistant microorganisms)
Organ	**Agent**
Gastroduodenal	*Streptococcus spp.* *Escherichia coli*
Gallbladder	*Enterococcus spp.* *E. coli* *Klebsiella* *Bacteroides spp.* *Clostridium spp.*
Small and large intestine	*E. coli* *Klebsiella spp.* *Proteus spp.* *Bacteroides spp.* *Clostridium spp.*
Appendicitis	*E. coli* *Klebsiella* *Bacteroides spp.* *Clostridium spp.*
Liver	*Enterococcus spp.* *E. coli* *Klebsiella spp.* *Bacteroides spp.*
Spleen	*Streptococcus spp.* *Staphylococcus spp.*

Table 3. Risk factors for multidrug resistant microorganisms (13-16)

High APACHE II score (≥15)
Prolonged hospitalization preoperatively
Hospital-acquired infection
Prior antibiotic use
Prolonged antibiotic use in the postoperative period
Prolonged hospitalization in the postoperative period

pancreatitis and primary peritonitis) 18 years of age or older who underwent surgery or invasive radiology with drainage in 132 centers in 54 countries, including 10 centers in Turkey. Of these patients, 3,966 (87.5%) had community-acquired IAI and the most common source of infection was the appendix, with 1,553 patients (34.2%). The criteria used in this scoring system are clinical findings at presentation, risk factors (age, immunosuppression), whether the IAI is healthcare-associated or community-acquired, infection localization and delayed source control (Table 6). The authors reported high sensitivity and specificity of the scoring system and determined that it could be utilized globally in the management of IAIs. According to these criteria, mortality rates were 0.63% for patients with scores of 0-3, 6.3% at scores of 4-6, and 41.7% at scores ≥7. For scores ≥13 the reported mortality rate was 80.9%.

Table 4. Risk factors for specific multidrug-resistant microorganisms (13-16)

Agent	Risk Factors
Vancomycin-resistant enterococcus (VRE)	• Previous antibiotic use (esp. vancomycin and 3rd generation cephalosporin) • Prolonged hospitalization • Staying in an intensive care unit • Severe underlying disease
Methicillin-resistant *Staphylococcus* aureus (MRSA)	• Presence of colonization
Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae	• Antibiotic use (cephalosporins and quinolones) • Prolonged hospitalization • Severe underlying disease • Invasive procedures such as insertion of nasogastric tubes, gastrostomy or jejunostomy tubes and arterial catheters • Total parenteral nutrition • Recent operations • Hemodialysis • Pressure sores • Malnutrition
***Candida* species**	• Broad-spectrum antibiotic use • Central venous catheter use • Total parenteral nutrition • Renal replacement therapy in an intensive care unit • Neutropenia • Use of immunosuppressive agents (glucocorticosteroids, chemotherapeutics and immunomodulators) • Recurrent gastrointestinal perforations • Repeated surgical procedures • Anastomotic leakage • Pancreatic infections treated surgically

VI. Diagnostic tests

Biochemical analyses: Studies evaluating the efficacy of biochemical assays like procalcitonin, C-reactive protein (CRP), and serum amyloid A in the diagnosis and follow-up of IAIs have yielded contradictory results (8, 9, 18-22). The SFAR 2015 IAI management guidelines stated that these markers may not be usable in diagnosis and that in previous studies none had value in determining the duration of antibiotic treatment. Bhangu et al. (22) reported that no single biomarker was sufficient in cases of acute appendicitis. In Turkey, Kaya et al. (23) prospectively evaluated CRP, procalcitonin and D-dimer levels in acute appendicitis patients and reported that CRP alone was not sufficient for a diagnosis, but may serve as an indicator of flegmonous appendicitis and perforated appendicitis. They also emphasized that D-dimer and procalcitonin are not superior to CRP as markers. In a prospective study by Okuş et al. (24) evaluating medical treatment and the value of CRP in the management of acute appendicitis, elevated CRP levels of 80 mg/L and over were determined to be a significant indica-

Table 5. Approach to patients with complicated intra-abdominal infection

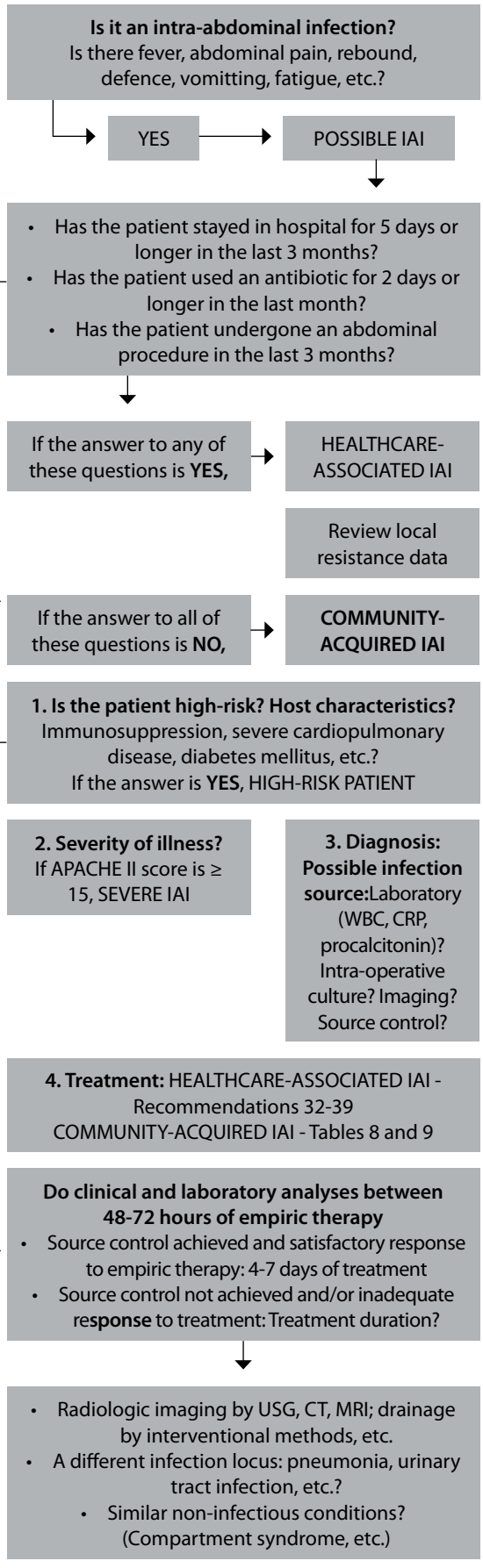

Table 6. WSES sepsis severity score for patients with complicated IAI (Score 0-18) (17)

Risk Factors	
Age (70 years and older)	2
Immunosuppression (corticosteroid, chemotherapy, etc.)	3
Clinical signs at time of presentation	
Severe sepsis (acute organ dysfunction)	3
Septic shock (requiring vasopressor therapy)	5
Healthcare-associated infection	2
Location of IAI	
Colon (non-diverticular) perforation peritonitis	2
Small intenstine perforation peritonitis	3
Diverticular diffuse peritonitis	2
Postoperative diffuse peritonitis	2
Delayed source control	
Preoperative peritonitis duration (24 hours or more)	3

tor of inadequate response to medical treatment. Pehlivanlı et al. (25) reported that CRP, interleukin-6, leptin, cortisol and caspase-3 did not have an effect on the decision to terminate planned abdominal repair in moderate and severe secondary peritonitis. The German diverticular diseases guidelines recommend monitoring CRP and white blood cell count in addition to clinical findings, and reported that CRP levels were associated with complications and/or perforation. Despite the above-mentioned studies investigating different aspects of IAIs, randomized controlled studies on this topic have not been conducted. Considering the conditions in Turkey and data from previous studies, it is advisable to evaluate white blood cell, CRP, procalcitonin, serum bilirubin levels, and liver and kidney function at the time of IAI diagnosis and during follow-up. These values are also necessary to be able to determine the pharmacokinetic efficacy of antibiotic regimens.

Microbiologic evaluation: The microflora of the gastrointestinal system comprises a complex ecological community including both facultative and anaerobic bacteria. The bacterial composition of the normal flora varies depending on anatomic location. The fewest bacteria are found in the stomach (0-a few *Lactobacillus spp.)*, and their density increases moving from the duodenum to the ileum. Bacterial density is highest in the colon (10^9-10^{11} CFU/g). Despite the presence of bacteria in high numbers in the natural gastrointestinal ecosystem, this does not translate into greater pathogenicity or clinical significance. Although *B. fragilis* and *E. coli* comprise less than 5% of the colonic microflora, they are among the organisms most commonly isolated in IAIs. For this reason, highly virulent bacteria present in the inoculum at low densities may be overlooked in mixed cultures. Considering the phenomenon of polymicrobial suppression of virulent pathogens, the Canadian practical guidelines for surgical IAIs describe 'core' pathogens (6). These include the anaerobes *B. fragilis* and other *Bacteroides*, *Fusobacterium*, *Clostridium*, *Peptostreptococcus*, *Veillonella*, and *Lactobacillus* species, the facultative isolates *Streptococcus* species, and from the Enterobacteriaceae family *E. coli, and Klebsiella*, *Enterobacter*, *Proteus* and *Serratia* species.

These pathogens should be considered first in all patients with suspected IAI, including community-acquired IAI (Table 2).

1. Routine aerobic and anaerobic cultures are considered optional in low-risk patients with community-acquired IAI. However, these cultures may be important in the detection of epidemiologic shifts in the resistance patterns of pathogens associated with community-acquired IAI and in the determination of oral treatment regimens during follow-up (B-II). In Turkey, aerobic and anaerobic cultures should be done to facilitate the detection of epidemiologic changes in the resistance patterns of IAI-associated pathogens. They may be especially important in terms of identifying quinolone/cephalosporin resistance in *E. coli* strains, monitoring metronidazole resistance in *B. fragilis*, and switching to empiric therapy and oral follow-up therapy. Cultures should be routinely taken from the infection area in healthcare-associated IAIs in high-risk patients (particularly patients more likely to carry resistant pathogens, such as elderly nursing home residents and patients with a history of frequent hospitalization, and patients who used antibiotics within the previous 1-3 months (A-II).

2. Blood cultures do not yield additional clinically significant information in patients with community-acquired IAI and are therefore not recommended routinely in these patients. However, understanding whether bacteremia is present in toxic-appearing or immunosuppressed patients is beneficial in deciding the duration of antibiotic therapy (IDSA, B-III).

3. Anaerobic cultures are not necessary in patients with community-required IAI if they are under empiric antimicrobial therapy against common anaerobic pathogens (IDSA, B-III).

4. Samples taken from the focus of the IAI should be representative of the material associated with the clinical infection (IDSA, B-III). There is no proven value of routine Gram staining of infectious material in community-acquired infections. Gram staining may be beneficial in detecting the presence of yeast in healthcare-associated infections (IDSA, C-III).

5. Cultures should be prepared from patient samples, provided they are of sufficient volume (at least 1 mL fluid or tissue, preferably more) and are conveyed to a laboratory by an appropriate transport system. For optimal yield of aerobic bacteria, 1-10 mL of fluid should be added directly to aerobic blood culture tubes. In addition, 0.5 mL of fluid should be sent to the laboratory for Gram staining and fungal cultures if indicated. If anaerobic cultures are ordered, at least 0.5 mL of fluid or 0.5 g of tissue should be conveyed in an anaerobic transport tube. Alternatively, 1-10 mL of fluid can be added directly to an anaerobic blood culture bottle in order to recover anaerobic bacteria (IDSA, A-I).

6. If a strain commonly isolated in the community (e.g. *Escherichia coli*) shows significant resistance (10-20%) to a broad-spectrum antimicrobial regimen in local use, routine cultures and sensitivity studies should be performed in cases of perforated appendicitis and community-acquired IAI (IDSA, B-III). Sensitivity tests should be performed for *Pseudomonas* sp, *Proteus* sp, *Acinetobacter* sp, *Staphylococcus aureus* and Enterobacteriaceae showing heavy growth because these varieties are more likely than others to develop resistance (IDSA, A-III).

Considering the resistance rates of organisms found in the community and commonly isolated in IAIs in Turkey, routine cultures and sensitivity studies should be performed in perforated appendicitis and community-acquired IAI. There are very few studies regarding the resistance rates of organisms associated with community-acquired IAIs in Turkey. In a study evaluating community-acquired IAIs in which intraoperative cultures were taken at 3 centers from 81 patients with no history of hospitalization or surgical interventions in the previous 3 months, the ESBL positivity rate was 9.9% for *E. coli* and 1.2% for *Klebsiella* species; resistance rates in *E. coli* were 14.5% for ceftriaxone and 22.2% for quinolone (26). A 49% rate of ESBL-positive *E. coli* was reported in healthcare-associated IAI (1). Reasons for the lack of studies on this topic in Turkey include failure to adequately raise surgeons' awareness of the importance of intraoperative sampling, surgeons not feeling the need to take cultures, insufficient technical infrastructure and organizational problems. One Turkish study reported that of 233 cases of community-acquired IAI (56 diagnosed as complicated IAI) operated by general surgeons in an emergency surgery clinic over a period of 5 months, cultures were requested in only 12 cases (5.1%). Six of these cultures yielded isolates, 3 of which were found to be ceftriaxone-resistant (27).

The consensus group prepared a questionnaire entitled 'Questionnaire to assess surgeons' attitudes and skills regarding microbiological sampling in the diagnosis of intra-abdominal infections' which was posted on the Turkish Surgical Association website and announced to all members via e-mail. The questionnaire remained on the society's website for about 6 weeks and the members were reminded several times via e-mail. A total of 136 people responded to the questionnaire.

According to the results of the questionnaire, the mean age of the respondents was 44.82±9.16 years, the mean duration of practice was 14.80±9.93 years (1-39 years), and the majority (67, 49.3%) comprised surgeons at state hospitals. Eighty-two respondents (60.3%) stated that they requested cultures. Of the 54 surgeons (39.7%) who did not request cultures in community-acquired IAIs, 43 (79.6%) believed that culture results did not guide treatment and that taking cultures was unnecessary. However, the reported rate of culturing varied with operation type. Thirteen (9.6%) of the respondents reported collecting samples during appendectomies, 10 (7.4%) in gallbladder surgeries, 69 (50.7%) in stomach/colorectal perforation surgeries, and 129 (94.7%) in intra-abdominal abscess surgeries or invasive procedures. Among the reasons stated for not collecting samples, "laboratories of state hospitals do not accept microbiological cultures out of working hours" (p=0.012) and at private hospitals, "the guidelines do not recommend culturing in community-acquired

infections" (p=0.047) were found statistically significant. These results emphasize the need for a national consensus report. Dissemination of the report to relevant physicians will provide greater consistency in the approach to patients with IAIs. Until epidemiologic data are obtained and organisms associated with IAIs are identified, cultures should also be performed at all hospitals in cases of community-acquired IAI.

VII. Imaging techniques: For patients with obvious signs of diffuse peritonitis and patients who will undergo immediate surgical intervention, the decision to conduct more advanced diagnostic imaging should be made based on the conditions of the healthcare facility and the physician's assessment. In adult patients not indicated for immediate laparotomy, computed tomography (CT) screening is the preferred imaging method for determining the source of IAI (IDSA, A-II).

MANAGING INTRA-ABDOMINAL INFECTIONS

I. SOURCE CONTROL

7. An appropriate source control procedure to immediately drain the locus of infection, control ongoing peritoneal contamination with radical resection (with or without diversion), and restore anatomic and physiologic function to the degree possible is recommended in nearly all patients with IAI (IDSA, B-II). Adequate source control is essential for managing IAIs and control cannot be achieved with antimicrobial therapy alone (IDSA, A-II). Factors leading to source control failure are shown in Table 7. These factors should be warning signs for anastomotic leakage, development of enterocutaneous fistula and/or recurrent/refractory IAI.

8. An immediate surgical procedure should be performed in cases of diffuse bacterial peritonitis (IDSA, B-II). However, with appropriate antimicrobial therapy and careful clinical monitoring, the procedure may be delayed until the patient's condition is suitable for surgery (e.g., there is no source of ongoing intraperitoneal infectious contamination such as a perforation, etc.) (IDSA, B-II). The length of this delay can vary depending on circumstances related to the patient, institution and surgeon.

9. Whenever possible, percutaneous drainage of abscesses and localized fluid collections is preferable to surgical drainage, especially in high-risk patients (IDSA, B-II). Drainage for intra-abdominal collections placed using invasive radiology is reported to be effective in 70-90% of cases (28, 29). Antimicrobial therapy without drainage may be sufficient for abscesses smaller than 3 cm in size (IDSA, B-II). However, a collection diameter less than 5 cm and the presence of biliary or intestinal fistula are significant risk factors for the failure of percutaneous drainage (8).

10. Randomized controlled studies have demonstrated that in patients with acute cholecystitis, early laparoscopic cholecystectomy (within the first 72 hours) shortens hospitalization times, speeds recovery, reduces costs, and lowers open cholecystectomy rates (30, 31). Guidelines also state that endoscopic drainage of the biliary tract is safer and more effective than surgical drainage (IDSA, A-I) (5, 6). Determining the severity of acute cholecystitis is important. Patients with mild acute cholecystitis are suitable for early laparoscopic cholecystectomy. However, considering the patient's overall condition, the diagnosis should be confirmed by USG and if necessary by imaging modalities such as CT or magnetic resonance cholangiopancreatography (MRCP), and the timing of surgical interventions for patients with acute cholecystitis should be planned in light of these data (32, 33). For cases of moderate acute cholecystitis, local inflammation may make cholecystectomy difficult (33). Therefore, open cholecystectomy should not be delayed (34). Cases of severe acute cholecystitis with accompanying issues like organ failure or deterioration of overall condition can be initially treated by percutaneous cholecystostomy (33). Percutaneous cholecystostomy should be performed within the shortest time possible (<72 hours) after diagnosis of acute cholecystitis (35). After the patient comes out of critical condition following percutaneous cholecystostomy and if no postsurgical complications develop, cholecystectomy can be performed in the early period (32). The most important step in treating acute cholangitis is determining severity of illness. Treatment of acute cholangitis consists of eliminating the underlying cause with antimicrobial therapy and biliary drainage (36). The treatment for acute suppurative cholangitis is an appropriate antibiotic, fluid therapy and biliary decompression (IDSA, A-I).

Table 7. Clinical factors predicting source control failure in intra-abdominal infection (5)

Delay in initial intervention (>24 hours)
High severity of illness (APACHE II score ≥15)
Advanced age
Co-morbidity and extent of organ dysfunction
Low albumin level
Poor nutritional status
Extent of peritoneal involvement diffuse peritonitis
Failure to achieve adequate debridement or drainage control
Presence of malignancy

11. Perforated appendicitis patients should undergo immediate surgery to achieve adequate source control (IDSA, B-III). Selected patients presenting several days after the development of inflammation with periappendiceal phlegmon (plastron) or small abscess preventing percutaneous drainage may be treated in hospital with antimicrobial therapy under close monitoring (IDSA, B-II). Patients with well-circumscribed periappendiceal abscess can be treated with percutaneous or operative drainage when necessary. Appendectomy may be performed in these patients or the abscess may be drained. Interval appendectomy after percutaneous drainage or non-operative management of perforated appendicitis patients is controversial and may not be necessary (IDSA, A-II). Each hospital should develop a step-by-step clinical approach to standardize diagnosis, inpatient interventions, discharge, and outpatient management (IDSA, B-II). These approaches should be designed by the entire medical

staff collaborating in and responsible for the care of these patients, including surgeons, infectious diseases specialists, primary care practitioners, emergency medicine physicians, radiologists, nursing providers and pharmacists. Clinical approaches should reflect local resources and standards of care (IDSA, B-II).

12. Perforated diverticulitis can be managed with laparoscopic lavage and drainage in selected patients (IDSA, C-II). In perforated diverticulitis, it is essential to differentiate patients with signs of peritonitis in physical examination from patients with evident perforation on CT but no signs of objective toxicity. The conventional treatment for perforated diverticulitis with purulent or fecal peritonitis is the Hartmann procedure (resection and proximal stoma). However, this procedure seems likely to change due to the application of current imaging techniques, antibiotic therapy, endoscopic techniques and laparoscopic lavage. Management by resectionless laparoscopic lavage is controversial. Guidelines published by international laparoscopic and surgical associations state that although colon resection is the gold standard, laparoscopic lavage may be performed in selected patients (37). The laparoscopic lavage approach is not recommended for unstable patients with obvious signs of peritonitis or patients with accompanying severe concomitant diseases.

13. In complicated acute pancreatitis, inflammation and subsequent necrosis occur within the first 2 weeks. Week 3 is the infection phase, in which clinical signs of local and systemic inflammatory syndromes emerge. It is difficult to clinically distinguish between sterile and infected pancreatic necrosis. Pancreatic abscess may develop in the late phase (week 4 and later). Acute pancreatitis with 3 consecutive days of organ failure is considered severe pancreatitis. Severe pancreatitis is frequently complicated by systemic inflammatory response syndrome (SIRS), multiple organ failure and sepsis syndrome. Determining whether pancreatic necrosis is sterile or infected is a priority. The presence of extraluminal gas on abdominal CT is pathognomonic. In the absence of this finding, a CT-guided aspiration biopsy should be obtained. Surgical interventions are usually only performed in cases of acute pancreatitis which, despite optimal treatment, exhibit progressive organ dysfunction and/or develop local complications such as infected necrosis, infected collections, abscess or fistula (12).

14. Emergency surgery should be performed in these patients unless there is hemodynamic disturbance of a severity which precludes surgical intervention. Surgical intervention should be considered for the following conditions and situations:

- Collections which are not accessible or cannot be drained percutaneously,
- Acute or diffuse peritonitis,
- Septic syndrome could not be managed by percutaneous drainage,
- When removal of the abscess wall is necessary for treatment,
- If the patient is in uncompensated septic shock,
- Drainage of acute cholangitis by two methods (biliary decompression with medical treatment and endoscopic drainage) was unsuccessful,
- When not technically possible (e.g. after distal gastrectomy), open surgical approaches should be utilized (IDSA, C-II).

15. There are three possible approaches for risky patients who are physiologically unstable and may result in source control failure: planned laparotomy, on-demand laparotomy, and standard open abdomen surgery (38). Relaparotomy, which may systematically disrupt physiology, should not be planned if surgical intervention is believed to have ensured adequate source control (8).

II. FLUID THERAPY

16. Patients with IAI should be administered intravascular fluid replacement and additional measures should be taken to ensure physiological stability. Intravenous fluid therapy should be initiated at the first suspicion of IAI, even if the patient shows no signs of reduced intravascular volume (IDSA, B-III).

17. Sepsis and septic shock is a complex process influenced by multiple factors requiring early hemodynamic support, effective source control and appropriate antibiotic use (IDSA, A-I). Fluid replacement should be initiated immediately upon the detection of hypotension in patients in septic shock (IDSA, A-II). Regardless of which system is the septic source, the general principles of sepsis and septic shock management should be followed and hemodynamic support should be provided. Achieving early and adequate source control should be the primary goal in the active treatment of abdominal sepsis (39, 40).

III. ANTIMICROBIAL REGIMENS

18. Antimicrobials and the antimicrobial combinations specified in Tables 8 and 9 are accepted as adequate for the empiric treatment of community-acquired IAI. However, antibiotics must be used at optimal dosages to minimize antimicrobial resistance, thereby guaranteeing maximum efficacy and minimal toxicity (Table 10) (IDSA, B-II) (5).

    Timing of Initiation of Antimicrobial Therapy: Antimicrobial therapy must be initiated *as soon as possible* in patients with severe sepsis/septic shock due to IAI (IDSA, A-III). For patients without signs of sepsis, antimicrobial therapy should be initiated *without delay* once a patient is diagnosed with complicated IAI or such a diagnosis is suspected.

Managing community-acquired intra-abdominal infections of mild to moderate severity in adults

19. Antibiotics used in empiric therapy should be effective against enteric gram-negative aerobic and facultative bacilli and enteric gram-positive streptococci. Empiric therapy must include agents with extended spectra activity against anaerobic bacilli for infections originating in the distal small intestine, appendix and colon and perforations in the presence of obstruction or paralytic ileus (IDSA, A-I) (5).

20. For adult patients with mild to moderate IAI in Turkey, the use of ertapenem, moxifloxacin or tigecycline monotherapy or combinations of metronidazole with cefazolin,

Table 8. Agents and regimens that may be used for the initial empiric treatment of extra-biliary complicated intra-abdominal infections (5)

	Community-acquired infection in adults	
Regimen	Mild to moderate infection	Severe infection
	Perforated or abscessed appendicitis and other infections	High-risk or serious physiologic disturbance, advanced age or immunocompromised state
Single agent	Ertapenem Moxifloxacin Tigecycline	Piperacillin-tazobactam Imipenem-cilastatin Meropenem
Combination	Cefazolin Cefuroxime Ceftriaxone Cefotaxime Ciprofloxacin or Levofloxacin[a] + Metronidazole	Cefepime, Ceftazidime Ciprofloxacin or Levofloxacin[a] + Metronidazole

[a]Due to increasing resistance to fluoroquinolones in Escherichia coli, local susceptibility profiles and, if available, strain sensitivity should be investigated.

Table 9. Agents and regimens that may be used for the initial empiric treatment of biliary infections in adults (5)

Infection	Regimen
Community-acquired mild to moderate acute cholecystitis	Cefazolin, Cefuroxime or Ceftriaxone
Serious physiologic disturbance caused by community-acquired acute cholecystitis, advanced age or immunocompromised state	Imipenem-cilastatin, Meropenem, Piperacillin-tazobactam,
Acute cholangitis of any severity following bilio-enteric anastomosis	Ciprofloxacin, Levofloxacin or Cefepime
Healthcare-associated infection of any severity	+ Metronidazole

Table 10. Initial intravenous antibiotic dosages in empiric treatment of complicated intra-abdominal infections in adults (5)

Antibiotic	Adult dosage[a]
ß-lactam/ß-lactamase inhibitor combination	
Piperacillin-tazobactam[b]	3.375 g every 6 h
Carbapenems	
Ertapenem	1 g every 24 h
Imipenem-cilastatin	500 mg every 6 h or 1 g every 8 h
Meropenem	1 g every 8 h
Cephalosporins	
Cefazolin	1-2 g every 8 h
Cefuroxime	1.5 g every 8 h
Ceftriaxone	1 g every 12 h
Cefotaxime	1-2 g every 6-8 h
Ceftazidime	2 g every 8 h
Cefepime	2 g every 8-12 h
Tigecycline	**100 mg initial dose followed by 50 mg every 12 h**
Fluoroquinolones	
Ciprofloxacin	400 mg every 12 h
Levofloxacin	750 mg every 24 h
Moxifloxacin	400 mg every 24 h
Metronidazole	**500 mg every 6-8 h or 1,500 mg every 24 h**
Aminoglicosides	
Gentamicin or tobramycin	3–7 mg/kg every 24 hours[c]
Amikacin	15–20 mg/kg every 24 hours[c]
Vancomycin	**15–20 mg/kg every 12 hours[d]**

Notes: FDA, United States Food and Drug Administration
[a]Dosages based on normal renal and hepatic function. [b]Dosage can be increased to 3.375 g every 4 h or 4.5 g every 6 h for Pseudomonas aeruginosa infection. [c]Initial dosage regimens for aminoglicosides should be adjusted according to body weight. [d]Serum-drug concentration should be considered for dosage individualization Initial dosage regimens for vancomycin should be based on total body weight.

cefuroxime, ceftriaxone, cefotaxime, levofloxacin or ciprofloxacin are preferable to regimens with anti-pseudomonal activity (Tables 8 and 9) (IDSA, A-I). Because data are scarce concerning the ESBL positivity rate of organisms involved in community-acquired IAIs in Turkey, empiric antibiotics should be selected on an individual hospital basis according to the ESBL rate in local epidemiologic data (10% or higher) or the ESBL risk factors described in Table 4. Furthermore, although *Pseudomonas* species are isolated in approximately 8% of IAIs, they are less likely to be the causative agent (41).

In a Turkish study investigating carbapenem and metronidazole resistance profiles of *Bacteroides* species, 39% of the total 66 strains evaluated were of intra-abdominal origin, and none showed metronidazole resistance. However, 5 of the strains were resistant to meropenem, and one of those meropenem-resistant strains was also resistant to imipenem. The same center reported the first imipenem-resistant *B. fragilis* in 1999 and the incidence

has since increased from 2% to 6%. It was also stressed that the metallobetalactamase gene was found at a much higher rate in strains of *B. fragilis* in Turkey (27%) compared to strains in other countries (2-9%) (42).

Clindamycin use is also not recommended in these patients because of the growing resistance of *B. fragilis* (IDSA, B-II). A study conducted in Turkey evaluating antibiotic susceptibility in anaerobic bacteria isolated from clinical specimens revealed the highest rate of clindamycin resistance in *Bacteroides* isolates (53%) (43).

The use of ampicillin-sulbactam is not recommended due to the high rates of resistance to this agent in community-acquired *E. coli* (IDSA, B-II). In a Turkish susceptibility study of 823 *E. coli* isolates from various patient specimens, including peritoneal fluid, only 386 (47%) of the *E. coli* isolates were sensitive to ampicillin/sulbactam. In the same study, amoxicillin/clavulanic acid susceptibility was found in 418 (51%) of the isolates (44).

Aminoglycosides are not routinely recommended for adults with IAI (IDSA, B-II). There are alternative agents which have been shown to be at least as effective and are less toxic.

Agents recommended for use in severe community-acquired or healthcare-associated infections are not recommended for community-acquired infections of mild to moderate severity because these regimens carry a higher risk of toxicity and facilitate infection with more resistant organisms (IDSA, B-II).

For mild to moderate IAIs including biliary infections, empiric antibiotic treatment against enterococci (IDSA, A-I) and empiric antifungal treatment against Candida species (IDSA, B-II) are not recommended.

21. In patients with mild to moderate IAIs including acute diverticulitis and the various forms of appendicitis who will not undergo a source control procedure, managing the infection with parenteral or early oral antibiotic therapy is recommended (IDSA, B-III). The German guidelines for diverticular diseases do not recommend antibiotic therapy for uncomplicated diverticulitis patients who do not have risk factors such as immunosuppression, and states that these patients can be monitored without inpatient treatment. Cases of complicated diverticulitis should be admitted for inpatient treatment including antibiotic therapy and surgical interventions, if necessary (9).

22. Ultrasonography is the first imaging technique for patients with suspected acute cholecystitis or cholangitis (IDSA, A-I). For patients undergoing cholecystectomy for acute cholecystitis, antimicrobial therapy should be discontinued within 24 hours unless there is evidence of infection beyond the walls of the gallbladder (B-II). Patients with suspected acute cholecystitis or cholangitis should receive the antimicrobial therapies recommended in Table 9. However, there is no indication for treatment against anaerobic organisms in the absence of biliary-enteric anastomosis (IDSA, B-II) (5, 30, 34).

23. In patients with acute pancreatitis (12):

- Cholangitis, catheter-related infections, bacteremia, urinary tract infections and extrapancreatic infections like pneumonia should be treated with antibiotics.
- Routine prophylactic antibiotic use is not recommended for patients with severe acute pancreatitis.
- Antibiotic use is not recommended to prevent sterile necrosis from developing into infected necrosis.
- Infected necrosis should be suspected in patients with pancreatic or extrapancreatic necrosis that worsens or fails to resolve despite 7-10 days of inpatient treatment. For these patients, it is recommended to (i) perform a CT-guided fine needle aspiration biopsy for Gram staining and cultures to aid the selection of an appropriate antibiotic, or (ii) use empiric antibiotic therapy without performing a fine needle aspiration biopsy.
- Interventional radiology procedures or surgical interventions may be performed once a patient is diagnosed with infected pancreatic necrosis. For patients with infected necrosis, antibiotics which can penetrate into the necrotic pancreatic tissue, such as carbapenems, quinolones and metronidazole, may be beneficial in reducing morbidity and mortality in situations where surgical intervention is deferred or delayed.
- The routine prophylactic or therapeutic use of antifungal agents is not recommended.

24. In appendicitis, although clinical signs are not sufficient for a definite diagnosis, the presence of findings such as characteristic abdominal pain, localized abdominal sensitivity, and laboratory evidence of acute inflammation will generally identify most patients with suspected appendicitis (IDSA, A-II). Patients with suspected appendicitis which could neither be confirmed nor excluded with diagnostic imaging should be closely monitored. Patients with a high index of suspicion should be monitored on an inpatient basis (IDSA, A-III). The recommended radiologic method for patients with suspected appendicitis is abdominal and pelvic CT imaging with contrast substance delivered by intravenous (not oral or rectal) route (IDSA, B-II). All patients diagnosed with appendicitis should be given antibiotic therapy (IDSA, A-II) (Table 8).

25. Operative intervention for acute non-perforated appendicitis should be performed as soon as possible, providing the procedure can be done appropriately (IDSA, B-II).

Managing high-risk community-acquired intra-abdominal infection in adults

26. The empiric use of antimicrobial regimens with broad-spectrum activity against gram-negative organisms is recommended for the treatment of patients with high-risk IAIs as defined by an APACHE II score $\geq$15 or the presence of other factors listed in Table 7. These agents include meropenem, imipenem-cilastatin, piperacillin-tazobactam, and ceftazidime as single agents or combinations of metronidazole with cefepime, ciprofloxacin or levofloxacin (IDSA, A-I).

27. In high-risk patients, antimicrobial regimens should be planned according to culture and susceptibility reports in order to ensure activity against predominant pathogens isolated from the cultures (IDSA, A-III).

28. Quinolone-resistant *E. coli* have become common in some communities. Therefore, quinolones should not be used unless local *E. coli* show more than 90% susceptibility to quinolones (IDSA, A-II). In Turkey, quinolone sensitivity of *E. coli* isolates from IAI patients is reported as 54% (1), demonstrating that quinolones should not be considered as a first choice for empiric treatment.

29. The empiric use of agents effective against enterococci is recommended (IDSA, B-II). Nearly all enterococci in community-acquired infections are *E. faecalis*, which are susceptible to ampicillin, piperacillin, and glycopeptides.

30. The use of agents effective against methicillin-resistant *Staphylococcus aureus* (MRSA) and yeast are not recommended in the absence of evidence that the infection is a result of these organisms (IDSA, B-III).

31. The routine use of an aminoglycoside with a second agent effective against gram-negative facultative and aerobic bacilli is not recommended in adults in the absence of evidence that resistant organisms are involved in the infection (IDSA, A-I).

Managing healthcare-associated intra-abdominal infection in adults

32. Empiric therapy for this type of infection should be based on local microbiologic results (IDSA, A-II).

33. To achieve empiric efficacy against likely pathogens, multi-drug regimens including broad-spectrum agents with coverage against gram-negative aerobic and facultative bacilli. If local data indicate a resistance rate under 20%, infections caused by *P. aeruginosa*, *Acinetobacter* species, ESBL(+) Enterobacteriaceae and other multidrug-resistant gram-negative bacteria can be treated with combinations of metronidazole with ceftazidime or cefepime, piperacillin-tazobactam, meropenem and imipenem. Treatment choices are more limited if the resistance rate exceeds 20%. In such cases imipenem, meropenem, piperacillin-tazobaktam and aminoglicosides are used in initial treatment. Colistin combined with carbapenem or tigecycline is an alternative in the treatment of infections with strains resistant to carbapenem, quinolone and aminoglycoside. Broad-spectrum antimicrobial therapy should be planned after culture and susceptibility reports are obtained (IDSA, B-III).

    In the IDSA guideline, tigecycline is recommended for community-acquired IAIs only, whereas in the WSES 2013 guidelines for managing IAIs it is also recommended for the treatment of stabile, noncritical healthcare-associated IAI (5, 7). The Canadian 2010 AMMI guidelines also state that the pharmacokinetic and pharmacodynamic properties of tigecycline are appropriate for the treatment of healthcare-associated infections, but specify that it must be combined with ciprofloxacin for coverage of *P. aeruginosa* (6). In centers in Turkey for which *P. aeruginosa* is not among the first organisms listed in local resistance data, tigecycline treatment can be started in empiric therapy to manage mild to moderate healthcare-associated IAIs in order to limit the use of carbapenem. In a study conducted at a center in which ESBL(+) *E. coli* was the most common organism in IAIs, tigecycline monotherapy was found to yield a 72.3% cure rate in patients with malignancy and complicated IAI (2).

34. Empiric therapy covering enterococci is particularly recommended for patients with postoperative infection, patients who used other selected antimicrobial agents which may select for enterococci, such as cefalosporins, within the previous 3 months, immune-deficient patients, and patients with valvular heart disease or intravascular prosthetic materials (IDSA, B-II). Antimicrobial therapy against enterococci should be administered if enterococci are isolated from patients with healthcare-associated IAI (IDSA, B-III). Initial empiric therapy should target *Enterococcus faecalis.* Antibiotics that can potentially be used against this organism are ampicillin, piperacillin-tazobactam, teicoplanin and vancomycin. Empiric therapy against vancomycin-resistant *E. faecium* is not recommended so long as the infection with this organism does not pose a high risk (IDSA, B-III). Empiric therapy against vancomycin-resistant *E. faecium* is recommended for liver transplant recipients with IAI originating in the hepatobiliary system and patients known to be colonized with vancomycin-resistant *E. faecium* (IDSA, B-III).

35. Empiric anti-MRSA therapy should be given to IAI patients known to be colonized by this organism or those with previous treatment failure who are at risk of infection by this bacteria (IDSA, B-II). Vancomycin is the recommended treatment for suspected or proven IAI due to MRSA (IDSA, A-III).

    In Turkey, teicoplanin is also an option for treating MRSA in IAI. In the WSES 2013 IAI management guidelines, teicoplanin is recommended in combination with carbapenem for the treatment of healthcare-associated critical extra-biliary complicated IAI (7).

36. In the IDSA guidelines, antifungal therapy is recommended if *Candida* species are isolated from intra-abdominal cultures taken intraoperatively (IDSA, B-II). The Italian guidelines recommend antifungal therapy if cultures taken intraoperatively or within 24 h of external drainage produce *Candida*, but do not recommend treatment based on positive cultures taken from drains which have been in place longer than 24 h (10).

    The consensus report prepared by the Italian Society of Intensive Care and International Society of Chemotherapy states that the pathogenesis of intra-abdominal candidiasis is different and gives recommendations for the management of surgical peritonitis and abscesses in patients without neutropenia (10). The report highlighted the fact that intra-abdominal candidiasis in Europe was predominantly due to *C. albicans* (65-82%) and mortality ranged from 25 to 60%. The specific and nonspecific risk factors for intra-abdominal *Candida* infections identified in that report are presented in Table 11. The report recommended the use of empiric antifungal treatment for IAI patients with at least one specific risk factor (IDSA, C-III) (10, 11) and patients positive for mannan/antimannan, beta D-glucan or PCR, with or without risk factors (IDSA, B-II) (10).

Table 11. Specific and non-specific risk factors for intra-abdominal Candida infection (10)

Specific risk factors	Non-specific risk factors
• Surgical interventions including laparoscopy	• Acute renal failure
• Perforations including those of the upper gastrointestinal tract which are not treated within 24 hours or are recurrent	• Presence of central venous catheter
	• Feeding with parenteral nutrition
	• Severe sepsis
	• Diabetes mellitus
	• Immunosuppression
	• Prolonged broad-spectrum antibiotic use or hospitalization in intensive care
• Leakage from gastrointestinal anastomoses including the esophagus, especially gastroduodenal surgical anastomosis	

In a Turkish study evaluating risk factors in liver transplant patients with candidemia, it was determined that meticulous surgical technique, starting with preparation of the patient pre-transplantation, and use of a biologic graft instead of a synthetic graft reduced the risk of candidemia. All of the patients who developed candidemia were found to have anastomotic leakage and/or reoperation/retransplantation and/or use of a vascular graft and/or presence of biliary complication. The most commonly isolated organism was *C. albicans* (45). Furthermore, *C. albicans* was reported as the most commonly isolated organism and was associated with the highest mortality in the intensive care unit of a university hospital, with 30-day crude mortality rate of 43.9% (46). In light of these data, empiric antifungal therapy must be considered, especially in cases of IAI with risk factors.

37. Fluconazole is an appropriate choice in *C. albicans* is isolated from properly obtained samples (IDSA, B-II) (5). For fluconazole-resistant *Candida* species, treatment with an echinocandin (capsofungin, micafungin or anidulafungin) is appropriate (IDSA, B-III). For critically ill patients, initial treatment with an echinocandin instead of a triazole is recommended (IDSA, B-III). Amphotericin B is not recommended as an initial treatment due to toxicity (IDSA, B-II) (5). However, in a 2016 updated clinical practice guideline for the management of candidiasis, echinocandin is recommended for initial treatment (11). In a Turkish study evaluating the use of antifungals in a general surgery department, it was reported that *C. albicans* was the organism most commonly isolated from IAI patients, fluconazole was the most used antifungal agent, and that antifungal therapy was administered more to immunosuppressed patients, regardless of culture positivity (47). In such cases, fluconazole or echinocandin should be preferred, taking into consideration patient's characteristics, risk factors, and local fluconazole resistance.

38. Prophylactic fluconazole may be considered for patients with anastomotic leakage related to a previous operation and/or recurrent gastrointestinal perforations (IDSA, B-I). Echinocandins may be used when there is high azole resistance (IDSA, C-II) (5). However, Knitsch et al. (48) conducted a randomized, placebo-controlled trial of preemptive antifungal therapy to prevent invasive candidiasis after gastrointestinal surgery at 53 centers in 17 countries (including 1 center from Turkey) and found that the preemptive use of echinocandins had no effect. Currently, antifungal prophylaxis is not routinely recommended in IAI.

39. In the repair of abdominal wall hernias, different repair techniques using various synthetic (polyester, polypropylene, polytetrafluoroethylene (PTFE), etc.) and biologic meshes are used (49). Factors reported to increase the risk of infection in these patients include cigarette use, multiple recurrence (presence of subclinical dormant microorganisms), presence of cutaneous draining sinus, the accompanying opening of any kind of stoma, open procedures, ASA > 3, poor technique, and coexisting disease (especially diabetes, malignancy, COPD or atherosclerotic heart disease). Because permanent synthetic meshes are susceptible to infection, they cannot be used in contaminated areas. Because all polyester- and polypropylene-based meshes induce severe, widespread adhesion formation, they generally should not be applied to surfaces which will directly contact the intestines unless absolutely necessary.

    In cases where infection is proven, 70% of the polypropylene-based meshes and 100% of the PFTE meshes are removed. In very urgent circumstances, the contaminated or infective abdominal wall may remain as 'partially or completely open abdomen' in patients who developed acute/subacute compartment syndrome and the intra-abdominal infective pathology could not be controlled/managed at any stage (damage control approach). In such cases, an absorbent synthetic mesh should be used to temporarily close the abdominal wall and contain the organs. After repairing complex abdominal wall defects, antibiotherapy covering core organisms should be given to immunosuppressed cancer patients with prolonged chemotherapy and/or radiotherapy exposure if there are serious risk factors, in the presence of multiple predisposing factors for the development of infection, or in the presence of mesh protrusion with or without enterocutaneous/enteroatmospheric fistulization ('complicated failure'). If there is infection of the surgical site, gram-positive bacteria should also be considered, particularly *S. aureus*.

Monitoring antimicrobial therapy in patients with intra-abdominal infection

Clinical monitoring: Antimicrobial treatment of proven infection should be limited to 4-7 days, provided adequate source control is achieved. No association has been demonstrated between longer treatment durations and improved outcome (B-III). Source control is the most important step determining treatment duration. Continued antibiotic therapy is not necessary for patients whose signs and symptoms of infection have resolved (B-III). Oral therapy can be used as primary medica-

tion or step-down therapy following initial intravenous antimicrobial therapy (IDSA, B-III). During the recovery period, amoxicillin-clavulanic acid and oral quinolone (moxifloxacin, ciprofloxacin, levofloxacin) or oral cefalosporins in combination with metronidazole can be used for patients able to accept oral medications and whose infections are due to bacteria susceptible to such agents (IDSA, B-II). Because of the lack of studies on this issue in Turkey, for antibiotics with satisfactory response to parenteral administration, treatment should be completed with the most appropriate oral form.

Microbiologic monitoring: For lower-risk patients with community-acquired IAI, if source control and initial therapy result in satisfactory clinical response, no change in treatment is necessary even if follow-up cultures recover unsuspected pathogens not included in the treatment spectrum. If resistant bacteria are detected in cultures taken during the first intervention and there are persistent signs of infection, treatment against those organisms is recommended (IDSA, B-III). Organisms recovered from blood cultures should be considered significant if they are of pathogenic potential or are isolated from at least 2 blood cultures (IDSA, A-I). Patients with positive blood cultures should be treated for at least 10 days. Follow-up cultures should be taken between 48-72 h of their antibiotic therapy, regardless of level of fever, and negative blood cultures should be demonstrated.

Treatment failure: Patients with persistent or recurrent clinical signs of infection following 4-7 days of antimicrobial therapy should undergo appropriate diagnostic imaging tests (CT, MRI or USG). Antimicrobial therapy against the organisms initially identified should be continued (IDSA, A-III). However, if initial empiric antimicrobial therapy does not result in a satisfactory clinical response, investigation into extra-abdominal sources of infection (pneumonia, urinary tract infection, bloodstream infection, etc.) and non-infectious inflammatory conditions is recommended (IDSA, A-II). Furthermore, the role of intra-abdominal hypertension and abdominal compartment syndrome in source control should be evaluated. For patients who do not show initial treatment response and for whom a focus of infection remains, an aspiration or tissue sample of sufficient volume (at least 1.0 mL fluid or tissue) should be obtained, sent to the laboratory in a transport system suitable for anaerobics, and used for both aerobic and anaerobic cultures (IDSA, C-III).

In the CIAOW study (complicated intra-abdominal infections worldwide observational study) conducted in 68 medical centers (including 10 in Turkey), the average mortality rate was reported as 10.5% (15). Patient's age, small intestine perforation, delay in surgical intervention, hospitalization in intensive care and immunosuppression were identified as factors affecting mortality. A thorough evaluation of all aspects, taking into account patients' risk factors, will decrease the mortality rate.

In conclusion, all guidelines and consensus reports are intended as guides. This consensus report was also prepared to facilitate diagnosis and treatment for all physicians dealing with IAIs. Because of the lack of relevant randomized, controlled trials, insufficient microbiologic sampling and few studies conducted on this topic in Turkey, the data available in the literature were evaluated. According to these data, it is apparent that epidemiologic data for each region, and in fact each hospital, is necessary in order to develop optimal protocols for patient follow-up. The first priority for Turkey is to collect intraoperative cultures from IAI patients to determine microorganism susceptibility and record the patients' characteristics. This report, which we believe will serve to raise awareness of this issue, is the start of a multidisciplinary approach to IAIs. Due to the inherent contextual and temporal limitations of consensus reports, they must be reviewed and updated at regular intervals. We hope that this consensus report will be periodically reviewed and improved as its weaknesses become evident with practical application and as new data become available. It should never be forgotten that we physicians attempt to calculate the risks, but it is the patients who assume the total risk incurred.

In reports to follow, we hope that the multidisciplinary collaboration will continue in many other topics such as the effects of probiotic use, the influence of rifaximin use in ulcerative colitis/diverticulitis on the distribution of intra-abdominal microbes, and the effect of prolonged ciprofloxacin+metronidazole use in inflammatory bowel disease on IAI treatment.

A brief summary of the main messages

DIAGNOSTIC EVALUATION OF INTRA-ABDOMINAL INFECTIONS

- Monitoring of patients with IAIs should be multidisciplinary.
- Microorganismic, host and surgical risk factors should be evaluated separately.
- Potential infections should be identified as healthcare-associated or community-acquired. Patients with hospitalization lasting five days or longer and/or more than two days antibiotic use and/or an abdominal procedure within the three months prior to presentation should be considered healthcare-associated IAI.
- Severity of the infection should be evaluated using APACHE-II score. Multicenter studies have shown that mortality increases with higher score.
- **Biochemical tests**: Considering the conditions in Turkey and data from previous studies, it is advisable to evaluate white blood cell, CRP, procalcitonin, serum bilirubin levels, and liver and kidney function at the time of IAI diagnosis and during follow-up. These values are also necessary to be able to determine the pharmacokinetic efficacy of antibiotic regimens.
- **Microbiologic evaluation:** In Turkey, intraoperative routine aerobic and anaerobic culturing is recommended, even for low-risk community-acquired IAI patients. In Turkey, aerobic and anaerobic cultures should be done to facilitate the detection of epidemiologic changes in the resistance patterns of IAI-associated pathogens.
- **Imaging**: For patients with obvious signs of diffuse peritonitis and those who will undergo immediate surgical intervention, the decision to conduct more advanced diagnostic imaging should be made based on the healthcare facility and the physician's assessment.

TREATMENT OF INTRA-ABDOMINAL INFECTIONS

- Adequate source control is essential for managing IAIs and control cannot be achieved with antimicrobial therapy alone.
- Sepsis and septic shock is a complex process influenced by multiple factors requiring early hemodynamic support,

effective source control and appropriate antibiotic use. Achieving early and adequate source control should be the primary goal in the active treatment of abdominal sepsis. Antibiotherapy should be initiated as soon as possible.

- For adult patients with mild to moderate community-acquired IAI in Turkey, the use of ertapenem, moxifloxacin or tigecycline monotherapy or combinations of metronidazole with cefazolin, cefuroxime, ceftriaxone, cefotaxime, levofloxacin or ciprofloxacin are preferable to regimens with anti-pseudomonal activity. Empiric antibiotics should be selected on an individual hospital basis according to the ESBL rate in local epidemiologic data (10% or higher) or the ESBL risk factors described in this consensus report.
- Routine prophylactic antibiotic use is not recommended for patients with severe acute necrotizing pancreatitis or sterile necrosis. Infected necrosis should be suspected in patients with pancreatic or extrapancreatic necrosis that worsens or fails to resolve despite 7-10 days of inpatient treatment. For these patients, it is recommended to take a sample for culturing, if possible, and use empiric antibiotic therapy.
- For patients with high-risk community-acquired IAI or healthcare-associated IAI, the empiric use of piperacillin-tazobactam, ceftazidime, meropenem, imipenem-cilastatin as single agents or combinations of metronidazole with cefepime, ciprofloxacin or levofloxacin is recommended. In Turkey, quinolone sensitivity of *E. coli* isolates from IAI patients is reported as 54% (1), demonstrating that quinolones should not be considered as a first choice for empiric treatment.
- Antimicrobial/antifungal therapy is recommended for patients with community-acquired high-risk IAI or healthcare-associated IAI in the presence of risk factors for or evidence of infection with resistant gram-positive bacteria or candida.
- Empiric therapy for healthcare-associated IAI should be based on local microbiologic results. Broad-spectrum antibiotic therapy initiated empirically should be adjusted according to culture and sensitivity results. In centers in Turkey for which *P. aeruginosa* is not among the first organisms listed in local resistance data, tigecycline treatment can be started in empiric therapy to manage mild to moderate healthcare-associated IAIs in order to limit the use of carbapenem.
- In abdominal wall hernia repair, different repair techniques with various synthetic (polyester, polypropylene, polytetrafluoroethylene (PTFE), etc.) and biologic meshes are used. In cases where infection is proven, 70% of the polypropylene-based meshes and 100% of the PFTE meshes are removed. In the presence of multiple predisposing factors for the development of infection, or in the presence of mesh protrusion with or without enterocutaneous/enteroatmospheric fistulization ('complicated failure'), antibiotherapy especially targeting the core organisms is initiated. If there is infection of the surgical site, gram-positive bacteria should also be considered, particularly *S. aureus*.
- Antimicrobial treatment of proven infection should be limited to four to seven days, provided adequate source control is achieved. Longer treatment duration has not been associated with further improvement. Source control is the most important step determining treatment duration.
- If there is persistent or recurrent infection after antimicrobial therapy of four to seven days or if initial empiric antimicrobial therapy does not result in a satisfactory clinical response, investigation into extra-abdominal sources of infection (pneumonia, urinary tract infection, bloodstream infection, etc.) and noninfectious inflammatory conditions is recommended. The role of intra-abdominal hypertension and abdominal compartment syndrome in source control should also be evaluated.
- Table 5 serves as a summary of the consesus report.

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