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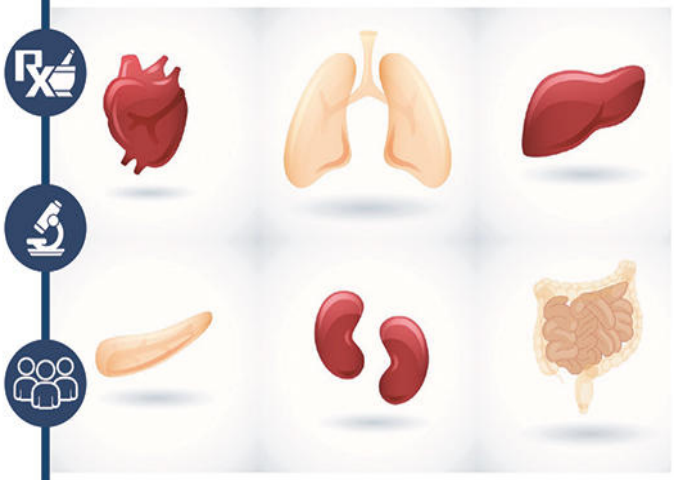

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Intra-abdominal infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

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Abstract

This new guideline from the AST IDCOP reviews intra-abdominal infections (IAI), which cause substantial morbidity and mortality among abdominal SOT recipients. Each transplant type carries unique risks for IAI, though peritonitis occurs in all abdominal transplant recipients. Biliary infections, bilomas, and intraabdominal and intrahepatic abscesses are common after liver transplantation and are associated with the type of biliary anastomosis, the presence of vascular thrombosis or ischemia, and biliary leaks or strictures. IAI after kidney transplantation include renal and perinephric abscesses and graft-site candidiasis, which is uncommon but may require allograft nephrectomy. Among pancreas transplant recipients, duodenal anastomotic leaks can have catastrophic consequences, and polymicrobial abscesses can lead to graft loss and death. Intestinal transplant recipients are at the highest risk for sepsis, infection due to multidrug-resistant organisms, and death from IAI, as the transplanted intestine is a contaminated, highly immunological, pathogen-rich organ. Source control and antibiotics are the cornerstone of the management of IAIs. Empiric antimicrobial regimens should be tailored to local susceptibility patterns and pathogens which the patient is known to be colonized, with subsequent optimization once the results of cultures are reported.

Introduction

The abdominal transplant procedures, which include kidney, liver, pancreas, and intestinal transplants, have evolved from experimental procedures to treatments of choice for end-stage organ failure. Despite improvements in patient and graft outcomes over the past several decades, infection remains a leading cause of morbidity and mortality in solid organ transplant (SOT) recipients[1]. While all abdominal organ transplant recipients share some risk factors for certain common infections (e.g. incisional infections and peritonitis), technical

issues arising from graft-specific surgical procedures are the major causes of graft-specific infectious syndromes. Herein, we review the surgical techniques, technical complications, and intra-abdominal infections (IAI) specific to recipients of liver, kidney, pancreas and intestinal transplants and provide guidance on the evaluation and management of these infections. Where possible, recommendations are evidence-based, although robust data are lacking. Where appropriate, alignment with published guidelines on IAIs by the Infectious Diseases Society of America was sought although their recommendations may not fully apply to immunosuppressed transplant recipients, who may have persistent technical complications resulting in unique challenges in treatment and an increased risk of relapse of infection upon discontinuation of antibiotics. While community-onset abdominal infections that are encountered in normal hosts such as diverticulitis, appendicitis, and cholecystitis do occur in SOT recipients, they will not be discussed here. Surgical site infections and abdominal infections related to ventricular assist devices are discussed in separate sections of these guidelines [2,3].

General principles of IAI in abdominal transplant recipients

All abdominal organ transplant recipients share common risks for incisional infections, with an increased risk for wound infections if mesh is used as part of wound closure. In contrast, technical complications uniquely encountered in each of the abdominal organ transplant procedures are associated with organ-specific infectious complications, typically within or in proximity to the transplanted allograft. In the absence of correction of these technical issues (e.g. hepatic artery thrombosis or biliary stricture), patients are at risk for delayed response to treatment and/or recurrences of these infections. Accordingly, the identification of organ-specific infectious complications should prompt evaluation for the presence and, where possible, correction of the technical problem(s) associated with the development of that infection. Successful completion of these efforts and optimal outcomes

of these patients requires the active involvement of a multidisciplinary team of transplant surgeons and physicians, diagnostic and interventional radiologists, and transplant infectious disease specialists.

General management principles

Empiric therapy

Empiric treatment of IAIs in SOT recipients should generally consist of Gram-positive and broad-spectrum aerobic and anaerobic Gram-negative coverage, though the exact agents will depend on the scenario and severity of illness. Specific empiric regimens should be individualized and tailored to the pathogens with which the patient is known to be colonized, potential side effect profile, drug-drug interactions, the hospital antibiogram, and the unit-specific antibiogram (when available). Most decisions on empiric therapy should follow local protocols, which presumably reflect local microbiology, combined with patient-specific factors[4]. Infection with multidrug-resistant (MDR) bacteria is common in transplant patients, including infections due to extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae (CRE), MDR *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant enterococci (VRE)[5-7].

The high incidence of MDR organisms in SOT recipients puts the clinician in a precarious situation, balancing the need for preventing the emergence of antimicrobial resistance on one hand and avoiding the high mortality rates risk associated with using inappropriately narrow-spectrum antibiotics on the other[8]. Indeed, there is little guidance in the literature regarding which patients would benefit from empiric antibiotics targeting these MDR pathogens. Empiric therapy for MDR Gram-negative organisms can be considered for patients with known colonization, those with septic shock who are hospitalized at institutions

with high rates of these organisms, or in the setting of an active outbreak. Administration of an empiric anti-VRE agent may be considered in patients with VRE colonization and hemodynamic instability, particularly liver transplant recipients[9-11]. Finally, there are limited data to support the use of empiric antifungal therapy though this can also be considered on a case by cases basis, especially in patients with bowel leaks, perforations, and septic shock of unclear origin[4,12]. In this setting, an echinocandin may be used empirically, with step-down to an azole if susceptible *Candida* species are isolated[13].

Source control

In general, the management of IAIs after transplantation is extrapolated from data in the non-transplant setting, with both drainage and antibiotics being the cornerstones of therapy[4]. For single, small abscesses, both needle aspiration and percutaneous drainage with catheter placement have been shown to be effective[14-16]. The choice of procedure is determined by operator experience, anatomical consideration, surgical preference, and the judgment of the treating clinician. However, this may not always be feasible due to critical illness, coagulopathy, and anatomy. Larger solitary abscesses should generally be treated with percutaneous drainage[16]. Drainage catheters should generally remain in place until drainage is minimal, as long as they are still in the correct position. Laparotomy with surgical resection may be necessary in patients who do not respond to appropriate drainage and antibiotics[17]. The optimal management of patients with multiple abscesses should be made on an individual basis, based on the size, number, and location of the lesions, as well as institutional factors (experience of surgeons and radiologists). Multiple percutaneous interventions may be necessary[17], but it is crucial to repeat aspirate cultures to ensure that no resistant organisms have emerged. Fluid samples should be sent for aerobic, anaerobic, and fungal cultures. Culturing for unusual pathogens such as *Nocardia* and mycobacteria can be

considered on a case by case basis. Culturing the contents of indwelling catheters should not be performed, as this usually simply represents drainage catheter colonization[18].

Duration of therapy

To our knowledge, the optimal duration of antibiotics for abdominal infections occurring after SOT has not been established and is largely arbitrarily chosen based on local custom. A recent trial of short-course antimicrobial therapy for IAI ("STOP-IT" trial) showed that in patients who had adequate source-control, the outcomes after approximately four days of antibiotics were similar to those after a longer course of antibiotics (approximately eight days)[19]. However, transplant patients were excluded, and thus the relevance of these findings to immunosuppressed patients with concomitant technical complications of their transplant procedures is not known. Accordingly, most transplant teams follow center-specific protocols for empiric therapies and duration of treatment, which can be modified based on patient-specific factors. While many clinicians may opt to treat transplant patients for longer than immunocompetent hosts, good quality data supporting this approach are lacking.

Our recommendations and principles regarding the initial approach to IAIs and empiric antibiotic coverage are summarized below. Suggested empiric regimens are listed in **Table 1**. **Figure 1** outlines a general algorithm that can be followed when caring for SOT recipients with intra-abdominal infections.

Recommendations on empiric antimicrobial therapy and initial approach to IAI:

1. Transplant centers should develop syndrome-specific protocols for empiric antimicrobial therapy based on local prevalence of antimicrobial resistant bacteria for each organ-specific intra-abdominal infectious syndrome (strong, low).

2. Diagnostic imaging with computed tomography (CT), ultrasound or magnetic resonance imaging (MRI) of the abdomen should be performed in all patients with suspected IAIs (strong, low).
3. Transplant recipients with abdominal infections, sepsis, and/or intra-abdominal catastrophes (perforations and leaks) should be given antibiotics as soon as possible after blood cultures are drawn (strong, high). For patients who are clinically stable, antibiotics may be withheld, pending the collection of appropriate abdominal cultures (strong, low).
4. Source control via either percutaneous sampling of collections or surgical exploration should be achieved (strong, moderate).
5. Direct aspiration of potentially infected fluid collections is the most reliable method of obtaining specimens for culture. Indwelling catheters should not be cultured (strong, very low).
6. Fluid samples should be sent for aerobic, anaerobic, and fungal cultures (weak, low).
7. Empiric Gram-negative coverage should consist of an antipseudomonal β-lactam, which would also cover most abdominal streptococci and Enterobacteriaceae **(Table 1)** (strong, high).
8. If the β-lactam of choice does not have obligate anaerobic coverage, the addition of metronidazole may not always be necessary, but is strongly recommended in cases of distal small bowel, appendiceal, or colonic infections, as well as gastrointestinal perforations (strong, high).
9. When aztreonam is used for Gram-negative coverage, an agent effective against Gram-positive cocci (such as vancomycin) should be added (strong, low).

10. Empiric therapy against ampicillin- and vancomycin-susceptible enterococci is recommended (strong, moderate).
11. Empiric antifungal coverage is not recommended in most settings (strong, moderate). Antifungal therapy can be considered on a case by case basis among SOT recipients with bowel leaks and perforations, and with septic shock of unclear etiology in the early post-transplant setting, particularly for adult liver transplant recipients (strong, moderate).
12. Antifungal therapy is recommended if *Candida* species are isolated from culture specimens. Initial use of an echinocandin is preferred. Step-down therapy to an azole is recommended if the organism is susceptible. The clinician must be cognizant of the drug-drug interactions between azoles and immunosuppressants (strong, low).
13. Empiric coverage for ESBL-producing Enterobacteriaceae, CRE, MDR *P. aeruginosa*, and other MDR Gram-negative bacteria should be reserved for patients known to be colonized with these pathogens; those who are hemodynamically unstable in transplant centers with a high prevalence of these pathogens; or those being cared for in a hospital unit experiencing an outbreak with these pathogens (weak, low).
14. Empiric therapy against VRE is not recommended except in hemodynamically unstable patients who are colonized with VRE or those who fail to improve despite otherwise broad-spectrum antibiotic therapy, particularly liver transplant recipients (weak, very low).
15. Empiric therapy against MRSA should be given to patients who are colonized with MRSA or those with septic shock and hemodynamic instability (strong,

moderate). Clinicians should be cognizant of the increased risk of nephrotoxicity associated with vancomycin and piperacillin-tazobactam combination therapy.

16. Empiric use of quinolones or ampicillin-sulbactam to treat IAIs is not recommended due to the high rates of resistance to these agents among Enterobacteriaceae (strong, moderate).
17. The empiric use of aminoglycosides and clindamycin is not recommended due to the risk of renal and ototoxicity and *C. difficile* infection, respectively. However, aminoglycosides may be used empirically in patients who have severe allergies to β-lactams due to potential high rates of resistance to alternatives (e.g. aztreonam, quinolones) (strong, moderate).
18. Empiric therapy with tigecycline should be avoided due to poor plasma concentrations, gastrointestinal adverse effects (nausea and vomiting), lack of antipseudomonal activity, and increased mortality in post-marketing surveillance (strong, moderate).
19. Abdominal transplant patients who are coming from the community and have neither been hospitalized nor treated for rejection or infections for several years may be given regimens similar to those given to non-immunosuppressed patients with community-onset abdominal infections (weak, very low).
20. Treatment against opportunistic and unusual pathogens (such as molds, mycobacteria, and *Nocardia*) should only be provided in cases of confirmed infection (strong, low).
21. Antibiotic durations for abdominal infections should be continued until resolution of signs/symptoms of sepsis (e.g. fever, leukocytosis), sterilization of blood cultures if positive, and source control (often determined radiographically) (weak, low).

Abdominal infections common to all abdominal transplants (Figure 1)

Incisional infections should be suspected in transplant recipients presenting with pain, erythema, drainage, and/or dehiscence of the surgical wound. Incisional infections typically present within the first 30 days after transplant[20] and can be caused by both Gram-negative and Gram-positive organisms, including VRE, CRE, ESBL-producing Enterobacteriaceae, and *P. aeruginosa*[9,21]. Incisional infections are covered in greater detail elsewhere[3] .

Peritonitis should be suspected in transplant recipients with peritoneal signs and usually signifies the presence of a surgical emergency, such as a perforation or an anastomotic leak[22]. Diagnosis is clinical with physical exam being the most helpful tool. However, for some patients, the exam may be subtle and non-specific, particularly in those receiving steroids. Accordingly, the possibility of peritonitis must be considered in all abdominal recipients presenting with fever in the first few months after transplant even in the absence of typical findings. Risk factors include prolonged surgery, bleeding, bowel leaks, and return to surgery. Microbiology is often polymicrobial. Gram-negative bacilli, Gram-positive cocci, and MDR organisms are frequently isolated on culture. Recovery of *Candida* species can be seen, particularly after bowel leaks and perforations.

For both these conditions, empiric antibiotic regimens are outlined in **Table 1**. Definitive therapy should be individualized, and treatment should be tailored to the results of microbiology. There are insufficient data to inform the optimal scenarios where the empiric use of antifungals in patients with bowel perforations and anastomotic leaks is required, but they can be considered on a case by case basis[12].

Intra-abdominal infectious syndromes by transplanted organ

Liver transplantation (Figure 1)

From the surgical perspective, liver transplantation remains a technically challenging procedure. Despite improvements in graft and patient survival, the risk of infection after liver transplantation remains higher than those of other organ transplants, with one-year overall infection rates approaching 80%[23]. Rates of bacterial infections of 33 to 70% have been reported for pediatric liver recipients with the vast majority of these typically presenting in the first 30 days after transplant[24]. Risk factors for IAIs in liver recipients include bile leak, prolonged operative time, blood loss, hypothermia, tissue hypoperfusion, renal failure, and exposure to microbiological contaminants. Intraoperative blood product transfusion volume reflects the complexity of the surgery and is a surrogate for tissue hypoxia, bleeding, and the formation of hematomas, which can become infected[25]. In a study of 331 adult liver transplant recipients at the University of Pittsburgh, culture-proven deep surgical site infections occurred in 15% of patients at a median of 13 days post-transplant and were associated with increased 90-day mortality[9]. These infections were characterized as abscesses/bilomas (58%), peritonitis (28%), deep incisional infections (8%), and cholangitis (6%). Enterobacteriaceae (42%), *Enterococcus* (24%), and *Candida* (15%) were predominant pathogens. Fifty-three percent of bacteria were MDR, including 95% of *Enterococcus faecium* (VRE) and 55% of Enterobacteriaceae (CRE and ESBL-producing organisms). Eighty two percent of deep infections were caused by bacteria resistant to antimicrobials used for prophylaxis, and 58% of patients were treated with an inactive empiric regimen. Similar types of infections, pathogens and antibiotic profiles would also be expected amongst pediatric liver recipients.

Surgical technique and complications

An important determinant of infection in the early post-liver transplant period is the surgical approach for bile duct reconstruction. The two most common forms of biliary reconstruction are choledochocholedochostomy (duct-to-duct anastomosis) and Roux-en-Y hepaticojejunostomy[26]. Essentially all pediatric recipients undergo Roux-en-Y hepaticojejunostomy as the small size of the bile ducts precludes a duct-to-duct anastomosis. For adult recipients, duct-to-duct anastomosis is the most common and preferred approach. It is more physiologic, preserves the Sphincter of Oddi, and is associated with a reduced risk of ascending cholangitis. However, the choice of one procedure over the other also depends on donor and recipient factors as well as surgeon preference.

Vascular complications

The development of vascular anastomotic complications is another important determinant of IAI in liver recipients. Hepatic artery thrombosis (HAT) is the most common vascular complication after liver transplant, occurring in 3-5% of adults with higher rates (2-20%) reported amongst pediatric liver recipients. The presence of HAT can be associated with extensive necrosis, hepatic abscesses, polymicrobial bloodstream infections, and sepsis. HAT can also result in bile duct ischemia (as the donor bile duct receives its blood supply from the hepatic artery) resulting in biliary strictures and leaks, which can in turn predispose to bilomas and abscesses [17,27]. Portal vein thrombosis presents similarly as HAT but is less common, occurring in 2% of adult and 2-5% of pediatric liver transplant recipients, respectively.

Biliary complications

Biliary complications occur in 10-15% of adult and 10-30% of pediatric liver transplant recipients. They may result from devascularization of the bile duct at the hilar dissection, failure to recognize anomalies of the biliary tree, technically challenging biliary reconstruction, and vascular complications[28]. Donation after cardiac death (DCD)-liver transplants are associated with high rates of ischemic cholangiopathy due to the second period of warm ischemia time (from circulatory arrest until start of preservation) compared to livers procured from brain dead donors[29]. Biliary strictures, which can be anastomotic or non-anastomotic, occur within the first year after transplant, account for one-third of biliary complications, and are associated with the development of recurrent episodes of cholangitis[28,30]. Bile leaks develop in 2-25% of patients after liver transplantation and are most common in the first 30 days after transplant, though they may present later when associated with HAT or indwelling drainage catheters[26,31]. Predisposing factors include technical issues related to the duct anastomosis and ischemia due to HAT or other causes[31]. Leaks typically occur at the site of the anastomosis, T-tube exit site (if used), and the site of the cystic duct remnant[31]. The presence of a bile leak can lead to peritonitis, which is frequently polymicrobial.

Complications after living donor or split liver transplantation

The most common factor limiting living donor liver transplants (LDLT) is the "small for size syndrome," which is of multifactorial etiology (due to donor and recipient factors) and manifests as early coagulopathy, cholestasis, encephalopathy and ascites after the exclusion of other causes[32]. Vascular complications such as HAT have been described in around 5% of patients[33,34] . Biliary complications are more common after LDLT compared to deceased-donor liver transplant, as the biliary reconstruction often involves multiple small

bile ducts. There is also a risk of bile leak not only from the anastomosis but also from the cut surface of the liver itself[35]. In general, similar concerns are observed when using split or reduced liver allografts from a deceased donor.

General Principles: Duration and Route of Therapy

There are no randomized controlled trials evaluating antibiotic route, regimens or duration of therapy for liver abscesses, bilomas or other abdominal infections after liver transplantation. Empiric antimicrobial therapy is listed in **Table 1**. Intravenous antibiotics are generally used (even for directed therapy) though there are no direct data comparing intravenous versus oral antibiotics in these settings. Antibiotics should be tailored to the results of cultures, particularly if cultures were obtained prior to the administration of antibiotics. However, narrow-spectrum Gram-negative coverage for Enterobacteriaceae and anaerobes may be continued in most situations regardless of results of cultures though there are no good data to support this approach. Patients with negative cultures are challenging and should be managed on a case by case basis, accounting for prior antibiotic use and esoteric exposures, while avoiding unnecessarily broad-spectrum, empiric therapy.

Antibiotic duration should be individualized, based on clinical and radiographic responses and the ability to achieve source control. There has been a marked variability in the durations of antibiotics used in the published studies of liver transplant recipients. For instance, while an average of six weeks of antibiotics was used in one study[36], another reported durations between 70 and 125 days[17]. In the current era in which shorter durations of antibiotics appear to be safer and as effective as long durations[37], the optimal length of therapy needs to be re-evaluated. Serial CT imaging can be considered to assess response to treatment in the post-transplant setting[36]. Patients who have demonstrated a robust clinical response to antibiotic therapy but who have small, residual lesions on imaging may be transitioned to an oral step-down regimen if their isolates are susceptible[4,38] **(Table 1).** This

approach can also be considered in patients with no positive cultures, on a case-by-case basis. Refractory cases may require re-transplantation[38], particularly if they are due to hepatic artery thrombosis (see below).

Liver-transplant-specific infections

Bilomas

Bilomas occur in around 11% and 8-16% of patients after adult and pediatric liver transplant, respectively, and form because of bile extravasation into the liver parenchyma or abdominal cavity[31,39-41]. Extravasation occurs when biliary ischemia results in bile duct injury, leading to leakage of bile from damaged intrahepatic ducts and formation of collections. Bilomas are associated with high rates of hospitalization, graft loss, and mortality[31,40,42]. In patients whose bile is already colonized with micro-organisms, the bilomas are infected upon formation. Otherwise, initially sterile bilomas may eventually become infected, either due to reflux cholangitis, anastomotic leaks, or secondary seeding from bacteremias[41].

Signs and symptoms of bilomas are non-specific. In a single-center, prospective study of 57 adult liver transplant recipients with post-transplantation bilomas, 35% of patients were asymptomatic and were identified solely because of unexplained elevations in hepatic enzymes[42]. Fever (44%) and abdominal pain (40%) were the most common symptoms, and 79% of patients had elevated hepatic enzymes. Hyperbilirubinemia was infrequent (28%), and leukocytosis and leukopenia had little correlation with fever or sepsis. The median interval from transplantation to the diagnosis of biloma was 9.1 weeks (range 2–377 weeks); 95% of the cases were identified in the first year after transplantation.

CT, ultrasound, or MRI of the abdomen are the diagnostic modalities of choice, and the diagnosis can be confirmed with aspiration of the collections. Bilomas invariably become infected, with a predominance of enterococci (37%, including VRE, which comprised 48% of enterococci in one study), followed by Gram-negative bacilli (16%, including *Pseudomonas aeruginosa*), *Candida*, and anaerobes[42]. The microbiology of bilomas therefore appears to differ from that of liver abscesses in which Gram-negative bacilli predominate. Whether this is due to antibiotic practices at the institution from which these data were reported or biloma-specific factors is unknown. Superinfection with multidrug-resistant organisms (such as ESBL-producing Enterobacteriaceae and *Stenotrophomonas maltophilia*) is common. Bacteremia has been described in about 16% of patients with bilomas[41].

Small bilomas, particularly those communicating with the biliary tree, may resolve spontaneously. While early re-transplantation was historically considered the preferred approach for larger hepatic bilomas, select patients with bilomas can be successfully treated with percutaneous drainage, stent placement, and prolonged antimicrobial therapy in case of infection[42]. Indeed, in patients without HAT, *Candida* infection, or enterococcal infection, non-surgical management appears to be effective with drainage (endoscopic or percutaneous) and prolonged antibiotic therapy ($\geq$ 4 weeks)[42]. If HAT is present however, then the likelihood of successful resolution of a biloma with nonsurgical management is much poorer, and re-transplantation may be necessary in up to two thirds of patients. In addition, patients should be referred for re-transplantation if there is no clinical improvement or if there is worsening of graft function on medical therapy[41,42].

Liver abscesses

Liver abscesses form in up to 58% of patients after liver transplant and cause significant mortality (33 to 42%)[9,17,36,38]. These can be difficult to distinguish from infected bilomas. About half of these develop within the first year, but time of onset is variable, with a median duration of approximately 200 days post-transplant (range from 30 days to over 4000 days)[17,36,38]. Roux-en-Y hepaticojejunostomy, HAT, ascending cholangitis, biliary strictures and liver biopsies are predisposing factors. Symptoms are similar to those of non-transplant recipients: fevers, chills, malaise, abdominal pain, nausea, vomiting, leukocytosis, elevated liver function tests, and less commonly jaundice. However, none of these findings are specific for liver abscesses, and abdominal CT or MRI are required to make the diagnosis.

A wide variety of offending pathogens have been reported. Causative organisms include streptococci, Gram-negative bacilli (including MDR isolates), MRSA, enterococci (including VRE), and less commonly *Candida* spp[9,17,36,38]. However, polymicrobial abscesses occur in up to 40% of patients[17]. Abscesses can occur simultaneously with bacteremia, but organisms recovered in the blood may not reflect all infecting pathogens within the abscess[17]. Thus, it is imperative to establish the microbiological diagnosis by abscess drainage, which has a diagnostic and therapeutic advantage. As is the case with bilomas and other abdominal fluid collections, in the absence of sepsis or hemodynamic instability, withholding antibiotics pending results of aspirated specimens is reasonable.

Ascending cholangitis

There are no studies specifically addressing ascending cholangitis after liver transplantation, which accounts for 6-7% of infections in both adult and pediatric liver transplant recipients[9,24,28]. Biliary strictures, biliary leaks, and Roux-en-Y

hepaticojejunostomy are well-established risk factors[43]. Presenting features are non-specific and include fever, abdominal pain, and chemical cholestasis. It is nearly impossible to distinguish ascending cholangitis from acute rejection, non-infectious biliary complications (leaks and strictures), and other liver-transplant-associated infections (abscesses, bilomas) on clinical grounds alone. Abdominal CT or magnetic resonance cholangiopancreatography (MRCP) are valuable in the evaluation and treatment of strictures. Similarly to other intra-abdominal infections, empiric antibiotics should target Gram-negative pathogens and enterococci. Blood cultures, if positive, can help tailor the antibiotic regimen, which may generally be given for 7-14 days. As previously mentioned however, robust data on antibiotic durations are lacking.

Bacteremia in the setting of a retained TIPS

Transjugular Intrahepatic Portosystemic Shunts (TIPS) are well-established as effective measures in the treatment of portal hypertension[44]. While TIPS can be removed during orthotopic liver transplantation, this is not always done. Liver transplant recipients with a retained TIPS who develop bacteremia are at risk of seeding the TIPS. TIPS infections are difficult to diagnose and should be considered in liver transplant recipients with sustained bacteremia and retained TIPS, particularly when there is no other source and the results of appropriate imaging studies and cardiac echocardiography are negative[45-47]. Data on the treatment of this entity are sparse though the use of prolonged antibiotics for an endovascular infection has been proposed. Chronic antibiotic suppression can be considered on a case by case basis[48] depending on the availability of oral options, cost, and toxicities.

Summary and key recommendations:

1. Vascular and biliary complications, liver-transplant related infections (abscesses, cholangitis, bilomas), and acute rejection have overlapping symptoms, and a definitive diagnosis should be aggressively pursued by appropriate diagnostic imaging (strong, low).
2. Empiric antibiotics for IAI after liver transplant should consist of broad-spectrum Gram-negative, anaerobic, and enterococcal coverage, and should be guided by local resistance patterns (strong, high).
3. Empiric therapy against VRE is not recommended except in septic patients who are colonized with VRE or those who fail to improve despite otherwise broad-spectrum antibiotic therapy (weak, very low).
4. Empiric therapy against MRSA should be given to patients who are colonized with MRSA or those with septic shock and hemodynamic instability (strong, moderate).
5. Antibiotics should be de-escalated when pathogens are identified (strong, low quality).
6. Liver abscesses and bilomas should be aspirated and samples sent for culture (strong recommendation, low quality evidence).
7. Prolonged treatment courses (≥ 4-week of antibiotics) are recommended with the results of follow-up imaging used to determine the final duration of therapy (strong, low).
8. Where feasible, the use of surgical resection is recommended for abscesses and bilomas that do not respond to antibiotics (strong, low).

9. In liver transplant recipients with retained TIPS and sustained bacteremia, treatment for a presumed endovascular infection is recommended (weak, low). Chronic suppression can be considered on a case-by-case basis (weak, very low).
10. The use of long-term prophylactic antibiotics for patients with biliary leaks, in the absence of an established infection, is not recommended (strong, low).

Kidney transplantation (Figure 1)

Outcomes of kidney transplant recipients have improved over the past decades, and the rate of complications including infection is much lower than in other abdominal transplants. In this section, we discuss surgical complications of kidney transplantation with a focus on intra-abdominal infection. Urinary tract infections are discussed in a separate specific Section of the Guidelines (UTI)[49] .

Surgical procedure and complications

Kidney transplantation is a heterotopic procedure[50] in which the kidney is placed extraperitoneally in the iliac fossa. The donor renal vein is anastomosed end-to-side to the external iliac vein, and the donor renal artery is anastomosed end-to-side to the external iliac artery. The donor ureter is attached to the bladder mucosa, often with the placement of a ureteral stent (to maintain the patency of the anastomosis), which is removed six weeks after transplantation.

Early vascular complications include hemorrhage, hematomas, and thrombosis. Arterial and venous thrombosis can present with severe pain along the site of the allograft, which can mimic wound infections, acute rejection, and allograft pyelonephritis. Lymphoceles occur within 2-3 months after kidney transplantation and are due to leakage from recipient lymphatics dissected at the time of surgery. Ureteral leaks are also early complications and arise as a consequence of surgical technique, ischemia, rejection, or

recipient bladder pathology. Leaks present with fever, allograft pain, urinomas, fluid leakage from the wound, and persistent drain output. Ureteral obstruction occurs in 1-8% of kidney transplant recipients and can predispose to allograft pyelonephritis[50]. Urinomas, lymphoceles, and hematomas can rarely become infected. Urinary tract infections are discussed elsewhere.[49]

Renal and perinephric abscesses

Data on the management of renal and perinephric abscesses after kidney transplant are largely limited to case reports and case series published in the 1970s and 1980s[51-53]. The largest study was a multicenter evaluation of 1945 kidney transplant recipients from four centers[51]. Only seven cases were found (with a prevalence of 0.3%), two of which were associated with lymphoceles. Abscesses occurred between two weeks and 52 months after transplant, though some cases were documented years later. Risk factors included wound infection, hematoma, reoperation, urinary tract infection, ureteral leak and urinoma, and excessive bleeding. Predominant pathogens included staphylococci, Gram-negative bacilli, enterococci, and rarely *Candida* (see below). Unusual organisms like *Nocardia* and *Mycoplasma hominis* have also been reported[54,55]. Donor-derived infection should be considered in cases where uncommon pathogens are isolated within the first four weeks of transplant[56].

Abscesses manifest with fever, allograft tenderness, and swelling, symptoms that are frequently observed in acute rejection, allograft pyelonephritis, and ureteral leaks. Blood and urine cultures are inconsistently positive. Thus, abdominal imaging with ultrasound or CT, and appropriate renal or perinephric fluid cultures, are required to make the diagnosis. Biopsies may be necessary as infection and rejection can coexist[51]. Given the dearth of data in kidney transplantation specifically, management is extrapolated from studies in non-transplant patients. Small renal and perinephric abscesses (≤ 5 cm) may be treated with

antibiotics alone, targeting Enterobacteriaceae and enterococci, but larger abscesses usually require drainage[4,57,58] . The need for obligate anaerobic coverage is uncertain. Antibiotics should be tailored to the pathogens isolated on culture. Durations should be individualized to clinical and radiographic improvement. Surgical resection and even transplant nephrectomy may be required in extreme cases.

Graft-site candidiasis

Graft-site candidiasis uniquely affects kidney transplant recipients, occurring within the first three months after transplant with an incidence of 1 in 1000[59]. It is thought to represent contamination of the organ in the preservation fluid during recovery from the donor. Most patients are febrile and have fungal arteritis and arterial aneurysms, while some develop urinomas, graft site abscesses, and incisional infections. Diagnosis of aneurysms is made via Doppler ultrasound, CT angiography, or conventional angiography. Optimal management includes urgent surgical drainage or nephrectomies; aneurysms should be surgically repaired. In one study, 3 of 18 kidney transplant recipients died, and 9 (50%) had their grafts surgically removed[59].

Duration of antifungal therapy is unknown though prolonged courses (one month to two years) have been given. Existing guidelines recommend that in patients who develop clinical or microbiologic evidence of infection, imaging studies should be repeated and therapy should be given for 4–6 weeks depending upon repeat imaging, cultures and clinical data[60]. Fluconazole is the drug of choice for susceptible organisms [12]. Although the triazoles (e.g., itraconazole, voriconazole, and posaconazole) have been used to treat renal parenchymal infections, they are not recommended for urinary tract candidiasis. Despite poor urinary penetration of echinocandins, these drugs may have a role in treating complicated *Candida* urinary tract infections[61]. Overall however, due to the poor urinary penetration of antifungals other than fluconazole and amphotericin B deoxycholate, the management of

graft-site candidiasis due to fluconazole-resistant *Candida* species should be considered on a case by case basis[12]. Pre-emptive antifungal therapy (with fluconazole if the isolate is susceptible) should be considered in kidney transplant recipients with *Candida* isolated in the preservation fluid, as should surveillance Doppler ultrasonography of the transplanted kidney. In the absence of documented infection, empiric antifungal therapy targeting *Candida* in the preservation fluid may be discontinued after two weeks[60]

Summary and key recommendations:

1. Management of renal and perinephric abscesses after kidney transplant consists of antibiotics and drainage of collections (strong, low).
2. Graft-site candidiasis usually represents contamination of graft preservation solution and should be treated with 4-6 weeks of antifungals (weak, low).
3. In the absence of infection, two weeks of antifungals should be given if the preservation fluid cultures grow *Candida* (weak, low).

Pancreas transplantation (Figure 1)

Three different procedures for pancreas transplantation exist: simultaneous pancreas-kidney transplant (SPK) (most common), pancreas after kidney transplant (PAK), and pancreas transplantation alone (PTA) (least common)[62]. Intra-abdominal infections account for 9.2 – 15% percent of technical failures after pancreatic transplantation and are still a major cause of death[63,64].

Surgical technique and complications

There are several techniques for implanting the pancreatic allograft, with no standard procedure used by all programs. [65]. The pancreas from the deceased donor is removed en bloc with the duodenum and spleen with eventual removal of the donor spleen and trimming of the donor duodenum. Handling the exocrine drainage of the pancreas is the most challenging aspect of the procedure and has direct implications on the risk of infection. This may be accomplished by anastomosing the duodenal segment of the pancreatic allograft to the recipient's bladder (bladder drainage) or to the recipient's small intestine (enteric drainage). Enteric drainage is the most common procedure and is associated with a lower risk of urinary tract infection than seen with bladder drainage though the risk of IAIs including intra-abdominal candidiasis may be higher[63,66]. In either case (bladder or enteric drainage), the donor duodenum is the site of the anastomosis.

Post-operative complications of pancreas transplantation include vascular thrombosis, transplant pancreatitis, and in the cases of bladder drainage, urinary tract infections, sterile cystitis, urethritis, and balanitis due to the daily elimination of high volumes of bicarbonate and pancreatic-enzyme-rich fluid into the bladder.

Intra-abdominal infections after pancreas transplantation

The risk of infection is highest within the first 1-3 months after pancreas transplant but does not seem to differ by the specific transplant type (SPK, PAK, or PTA)[67,68]. Graft loss or dysfunction occurs in up to 25% of patients with pancreatic infection[69], and mortality is substantial, ranging from 27% to 40%[70,71]. The incidence of IAIs in pancreas transplant recipients has decreased over time, from 30% in the 1980s[71] to 5-10% in the current era[72]. While the precise reason behind this is unclear, it is likely multifactorial with an interplay of improved surgical techniques, medical care, and immunosuppression strategies. Nevertheless, IAIs are still a major problem and are the second most common cause of graft loss after

vascular thrombosis[73]. This is in part because of contamination from the donor duodenum (which is part of both enteric and bladder anastomoses), which is opened during the transplant procedure. Indeed, leakage of contents from the donor duodenum occurs in 5-15% of pancreas transplant recipients and results in the spillage of pancreatic enzymes with either enteric material rich in bacteria and fungi or with urine[74]. Risk factors for duodenal leaks are ischemia, impaired wound healing, and high bladder pressure leading to anastomotic stress (in cases of bladder anastomoses). Duodenal leaks present with generalized peritonitis in cases of enteric anastomosis, or mild abdominal pain with elevated amylase levels in patients with bladder anastomoses (which improve with urethral catheter placement). Diagnosis of leaks is made on clinical and radiographic grounds (CT, CT cystogram, or fluoroscopic cystogram).

In addition to duodenal leaks, surgical re-exploration, blood transfusion, pulse steroids, lymphopenia, and post-operative dialysis are also risk factors for IAIs[67,69,70,75]. Donor factors can also increase the risk for rejection; indeed, the use of an organ from an obese donor (due to higher rates of ischemia-reperfusion injury) or an older donor (over 40 years of age) were significantly associated with abdominal infections[74,75]. Prolonged pre-transplant dialysis was associated with an increased risk of graft loss after SPK, though there was no difference in the infection rate based on modality of dialysis (peritoneal vs hemodialysis)[76]. Thus, in candidates for SPK transplants, pre-emptive (pre-dialysis) transplants may be considered. Acute rejection was independently associated with surgical site infection in one study, possibly due to intra-abdominal inflammation resulting in fluid collections around the graft, and the immune augmentation required to treat rejection[77].

Abdominal infections and pancreatic abscesses due to fungi portend a poor prognosis and are associated with a three-fold increased risk of mortality as well as a higher risk of graft dysfunction compared to bacterial pancreatic allograft abscesses[63,69]. Fungi can also cause

infectious arteritis and mycotic aneurysms[64]. Risk factors for *Candida* infections include enteric drainage, vascular thrombosis, and post-perfusion pancreatitis[66]. Thus, pancreatectomy should be strongly considered if fungi are isolated on pancreas abscess cultures.

Intra-abdominal infection after pancreas transplantation should be suspected in patients who present with fever, abdominal pain, and leukocytosis in the early post-operative course. Dedicated abdominal imaging (e.g. CT) should be performed. Generalized peritonitis after pancreatic transplant is usually due an intra-abdominal catastrophe such as perforation or duodenal leakage with spillage of urine or enteric contents into the peritoneum. Infections are polymicrobial with a predominance of Gram-negative bacilli (including anaerobes), streptococci, enterococci, anaerobes, and *Candida*. Percutaneous drainage should be performed if the abscess is anatomically amenable. Surgical exploration is often necessary both for source control and repair of the leak. The decision to remove the graft or take the patient back to the operating room for repeated "wash outs" needs to be made on an individualized basis based on the degree of the leak and extent of the infection. In recalcitrant cases where the infection does not respond to percutaneous or surgical drainage and antibiotics or in the setting of mycotic aneurysms at the site of the anastomosis, allograft pancreatectomy may be required for cure[63,78].

Patients who undergo allograft pancreatectomies for IAIs are at an increased risk of IAI after subsequent re-transplantation[79]. These were demonstrated to be due to the same micro-organism as the initial infection in most cases. While antibiotic prophylaxis targeting the prior organism at the time of the subsequent transplant appears rational, robust data are lacking.

Summary and key recommendations

1. Percutaneous aspiration of collections is required for microbiologic diagnosis and source control although surgical exploration and even allograft pancreatectomy (refractory cases) may be necessary (strong, moderate).
2. In patients with suboptimal surgical source control, antibiotic durations should be individualized and based on clinical and radiographic responses (strong, very low).
3. If the pancreas is removed and source control has been achieved, a short course (e.g. 7-days) of antibiotics is recommended in the stable patient (weak, very low).
4. In addition to antifungal therapy, allograft pancreatectomy should be strongly considered in all patients with fungal infections of the pancreas allograft, particularly those who do not respond to antifungal therapy and all those with mold infections (strong, low).

Intestinal transplants (Figure 1)

Intestinal transplantation is performed in patients with intestinal failure and long-term parenteral nutritional therapy[80]. Unlike other transplants, graft and patient survival of intestinal transplantation have not improved over the past decade, and case volumes have declined[81]. In addition, graft-versus-host disease is a unique complication of intestinal transplantation due to the large number of donor-derived lymphocytes. There are four major types of intestinal transplants, and the choice of the procedure depends on the state of the native organs, the presence of liver disease, and prior abdominal surgeries[80,82]. The four types are:

1. Isolated small bowel transplant,
2. Liver-small bowel transplants. The presence of the liver allograft has been linked with better graft outcomes[83].
3. Multivisceral transplants in which the liver, pancreaticoduodenal complex, and small bowel, with or without the stomach or colon can be transplanted.
4. Modified multivisceral transplant, which is a variant of multivisceral transplant performed in patients with preserved liver function that does not include the liver.

In this section, we discuss abdominal infections encountered after intestinal transplantation with a special emphasis on bloodstream infection. Diarrheal illnesses following intestinal transplantation are beyond the scope of this article and are discussed elsewhere[84].

The "nonsterile" environment of the intestine defines the epidemiology of bacterial infections before and after transplantation. Many of these patients have a history of catheter-related bloodstream infections and have had recurrent exposure to broad-spectrum antimicrobial agents leading to colonization and subsequent infection with MDR bacteria and to the overgrowth of fungi[85]. Moreover, intestinal transplantation is by definition a contaminated procedure, and although intestinal decontamination formulas are given to the deceased donor, effective mechanical cleansing is impossible. Donor gastrointestinal flora in the lumen of the intestinal allograft may result in bacterial infections if significant damage to the mucosa of the allograft occurs due to ischemia-reperfusion injury. Subsequently, a similar breakdown of mucosal integrity may occur as a result of rejection, graft-versus-host disease, or viral enteritis, which can also lead to bloodstream infections.

Rates of infection are highest within the first month after transplant[85,86]. Risk factors for abdominal infections after intestinal transplant include re-transplantation, older recipient age, presence of surgical mesh, requirement of renal replacement therapy, recent

hospitalization after transplant, use of mycophenolate mofetil, and induction with daclizumab (which is no longer available in the United States)[86,87]. Technical complications occur in 7.6% of intestinal transplant surgeries[83]; these include intestinal anastomotic leaks resulting in infectious peritonitis, vascular complications such as arterial thrombosis with consequent graft ischemia, and intestinal volvulus. Allograft ischemia due primarily to donor factors (cardiac arrest and subsequent hemodynamic instability of the cadaveric brain-dead donor) also confers an increased risk of infection[85].

It is not surprising that sepsis remains the most common cause of death after intestinal transplantation accounting for over half of cases[81,82]. Bacterial bloodstream infections occur in 66 to 92% of intestinal transplant recipients within the first year and arise from central venous catheters or abdominal sources (abscesses, wound infections, cholangitis, and peritonitis) in 30-50% and 17-33% of patients, respectively[88,89]. As expected, bloodstream infections arising from abdominal sources are due to colonizing gastrointestinal flora including Gram-negative aerobic and anaerobic bacilli, enterococci, staphylococci, and *Candida*. Polymicrobial bacteremia is also common[89]. Most ominously, intestinal transplant recipients appear to be at a particularly increased risk for infection with MDR bacteria[90]. Indeed, in a multicenter study of all intestinal transplants performed over a nine-year period in Spain, 65% of *P. aeruginosa*, 50% of *E. coli*, and 100% of *Acinetobacter baumannii* isolates following intestinal transplantation were considered MDR[86]. In another study, 47% of infections were caused by drug-resistant pathogens: 31% of *E. coli* and *Klebsiella* species were ESBL-producing, 36% of *P. aeruginosa* were MDR, 75% of enterococci were vancomycin resistant, and 100% of *S. aureus* isolates were methicillin resistant[90].

The predominance of MDR bacteria in this patient population is likely due to a combination of factors including pre-transplant antibiotics for recurrent bloodstream infections, pre-transplant colonization, frequent hospitalizations, as well as the institution-

specific practice of maintaining antibiotic prophylaxis until surveillance enterostomy demonstrates integrity of the intestinal allograft[86,91]. It should be noted that targeted prophylaxis does not appear to mitigate the risk of abdominal infections and bacteremia[90]. Thus, while a thorough knowledge of the patient's colonizing organisms is of paramount importance to devise appropriate empiric antibiotic regimens, of equal importance is the need to define optimal, standardized prophylactic antibiotic regimens and durations.

Invasive fungal infections occur in 22-59% of patients after intestinal transplantation at a median of 9 days after transplant, with IAIs accounting for one third of cases and *Candida* representing the overwhelming majority of isolates[92,93]. Most intra-abdominal fungal infections are diagnosed in the first month, likely due to the underlying disease, contaminated nature of the surgical procedure, loss of intestinal mucosal integrity, higher degree of immunosuppression, and selective pressure after multiple or prolonged courses of antibiotics[86,93]. In addition, other established risk factors for invasive fungal infections, such as high intraoperative blood product requirements, hyperglycemia, malnourishment, use of total parenteral nutrition, and renal replacement therapy are common after intestinal transplant. Multivisceral transplantation appears to have a protective effect, possibly due to the immunomodulation conferred by the liver[92].

Lastly, it should be noted that acute rejection, which affects up to 45% of patients with intestinal transplants, can be indistinguishable from infection on clinical grounds alone[80,81]. Features include fever, vomiting, abdominal pain, distention, and increased stoma output. Frequent and early endoscopies are therefore recommended in this setting. As the mucosal barrier is broken with immunologic injury, clinical sepsis can also accompany severe rejection, which should be considered as a potential etiology of any bacteremia with enteric organisms. However, the true incidence of this is unknown and may be lower than previously believed. In one study, even though bloodstream infections occurred in all patients

with acute cellular rejection, the presence of rejection was not significantly associated with bloodstream infection, occurring in only 1 out of 68 patients with bacteremias or fungemias[88].

Summary and key recommendations

1. Both CT of the abdomen and frequent endoscopies with biopsies are the diagnostic procedures of choice in intestinal transplant patients with fever, vomiting, abdominal pain, and increased stoma output (strong, low).
2. A thorough knowledge of the patient's microbiological history is essential to ensure appropriate empiric antibiotic coverage (weak, low).

Future directions and research

Abdominal infections following SOT continue to be associated with graft loss and mortality, and significant knowledge gaps persist. Contemporary data are required to better define the clinical characteristics and management of hepatic and renal abscesses after liver and kidney transplantation. Indications for surgical allograft removal in the setting of infection need to be prospectively validated. There is a need for randomized trials to determine the optimal antibiotic duration for abdominal infections in transplant recipients who have undergone appropriate source control. Indications for empiric antifungal and anti-VRE therapy should be better defined.

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Scenario	Antimicrobials	Notes	
No known colonization with MDRO: target nosocomial Gram-negatives (including *Pseudomonas aeruginosa* and Enterobacteriaceae) and susceptible enterococci	Piperacillin-tazobactam Cefepime or ceftazidime PLUS vancomycin, with or without metronidazole	If cephalosporin is used: • Add vancomycin** for enterococci. • Metronidazole should be given in cases of distal small bowel, appendiceal, or colonic infections, as well as gastrointestinal perforations	
		Severe β-lactam allergy	Aztreonam or antipseudomonal quinolones can be used in cases of severe beta-lactam allergies. These regimens should include vancomycin. Due to the high risk of resistance to these agents, an intravenous aminoglycoside can be considered on an individualized basis, based on severity of illness, and hospital, unit, and patient-specific antibiograms
Colonization with ESBL-producing Enterobacteriaceae	Meropenem, imipenem, or doripenem	Ertapenem lacks antipseudomonal activity and should generally not be used empirically	
Colonization with CRE	Ceftazidime-avibactam PLUS vancomycin with or without metronidazole* OR meropenem-vaborbactam*	Options limited, empiric treatment discouraged except in severe illness and known colonization Meropenem-vaborbactam should only be used if carbapenem resistance is mediated via KPC If ceftazidime-avibactam used: add vancomycin for enterococci. Indications for metronidazole listed above.	
Colonization with MDR *Pseudomonas aeruginosa*	Ceftolozane-tazobactam* or ceftazidime-avibactam PLUS vancomycin, with or without metronidazone	Options limited. Both have activity but may be unreliable against extensively drug-resistant isolates[94,95]. Rely on patient-specific antibiogram.	
Colonization with MRSA	Vancomycin	Daptomycin, linezolid, ceftaroline, tedizolid* are alternatives	
Colonization with VRE	Daptomycin, linezolid, tedizolid*, tigecycline.	Consider on a case by case basis. Liver transplant recipients with VRE colonization at highest risk.	

		Tigecycline associated with poor outcomes and adverse effects and should only be used as a last resort agent[96]	
Antifungal coverage	Caspofungin, micafungin, or anidulafungin	Generally not recommended empirically but can be considered in cases of bowel perforations or intestinal/pancreatic anastomotic leaks	
Low risk for nosocomial pathogens (community onset, no hospitalizations, immune augmentation for rejection, or infections in several years, good graft function, no antibiotic exposure except for prophylaxis)	C Non-pseudomonal 2nd or 3rd generation cephalosporin with metronidazole can be considered	Enterococcal coverage may not be necessary. Empiric use of ampicillin-sulbactam and quinolone-based regimens should be avoided, due to resistance among Enterobacteriaceae	
		Severe β-lactam allergy	Tigecycline, with the same caveats as above.
Step-down oral regimens (usually not empiric)	C (Oral 2nd or 3rd generation cephalosporin and metronidazole, amoxicillin-clavulanate, ciprofloxacin and metronidazole can be considered	To be used after response to appropriate intravenous therapy. Use if offending pathogens are susceptible. However, no randomized controlled trials have directly compared intravenous versus oral therapy in these situations.	

Table 1. Suggested empiric antimicrobial regimens in abdominal transplant recipients with intra-abdominal infections. MDRO, multidrug-resistant organism, defined as ESBL-producing Enterobacteriaceae, vancomycin-resistant Enterococcus faecium (VRE), MRSA, CRE, or MDR *Pseudomonas aeruginosa*. KPC, *Klebsiella pneumoniae carbapenemase*.

***For these novel agents, pediatric FDA approval and specific dosing recommendations are unavailable.**

****Emerging data suggest that vancomycin and piperacillin-tazobactam combination therapy is associated with an increased risk of acute kidney injury[97]. Clinicians should be vigilant of this association when using these antibiotics together.**

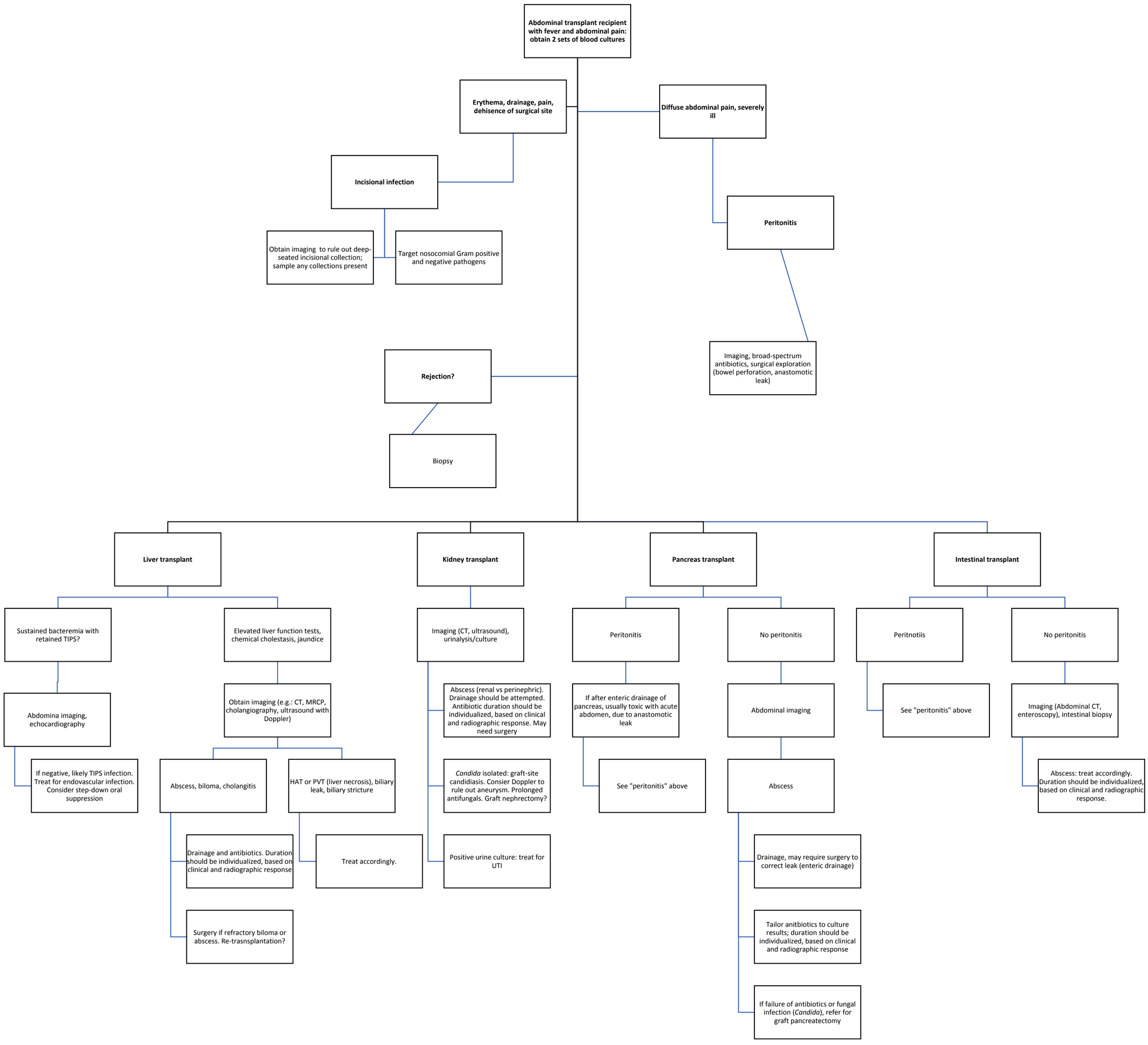

Figure 1. Algorithm for fever and abdominal pain after abdominal organ transplantation. CT, computed tomography; HAT, hepatic artery thrombosis; MRCP, magnetic resonance cholangiopancreatography; PVT, portal vein thrombosis; TIPS, transjugular intrahepatic portosystemic shunt; UTI, urinary tract infection.