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REVIEW

Approach to the transplanted patient in acute care: a comprehensive update

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Abstract

Organ transplant patients present to emergency departments (EDs) for conditions often associated with transplantation due to changing anatomy, denervated allograft and immunosuppression. Infections and rejection are among the most feared problems in these patients. It is necessary to maintain a high index of suspicion. The process should be carried out in a multidisciplinary fashion with the transplantation team including specialists in infectious diseases. When evaluating these patients, conditions that are easily managed in other patients should be carefully investigated. Emergency care providers should recognize infections and other complications, obtain diagnostic work up, initiate empirical treatment and consider specialty consultation and inpatient admission. Even if these patients are referred to hospitals for reasons unrelated to transplantation, healthcare providers need to know their differences, the expected effects of the drugs to be administered, and to be aware of probable drug interactions while their treatment is being planned.

Keywords

Transplantation; Lung; Kidney; Infection; Immunosuppression; Heart; Liver; Rejection; Solid organ transplantation

1. Definitions and introduction

Worldwide, the first organ transplantation (TX) was performed in 1950 [1]. Its prevalence is increasing; in 2022, 42,800 organ transplants were performed only in the United States [2]. The kidney is the most transplanted solid organ (58%), followed by the liver (21%), the heart (8%), the lung (5%) and the pancreas (5%) [1, 3]. It is necessary to pay attention to their specific situation when transplanted patients present to the ED. In the evaluation of these patients, the physiological and anatomical differences should be recognized, and TX-associated infections, adverse effects of the drugs used, transplant rejection, graft-versus-host disease (GVHD) and post-surgical complications need to be considered.

Most patients with solid organ or hematopoietic cell TX present to the emergency departments (ED), especially in developing countries. Kidney transplantation (KTX) is the most common TX procedure among all and is a superior treatment option because of lower health expenditure in all age groups compared to dialysis in patients with chronic renal failure (CRF), and provision of longer life and higher quality of life.

2. General approach to patients

2.1 History

The history of these patients should be focused on the main complaint on presentation and extended in line with the characteristic properties unique to the given patients. First, detailed information should be obtained related to the TX process. The time of operation, and the source of the TX (cadaver or live donor) should be questioned, for it has been assumed that living donor transplantation grafts are superior to deceased donor transplantation grafts in terms of graft survival and a lesser recipients' morbidity [4]. In addition, the drugs used in the process and the recent changes in the use of these drugs should be evaluated, because each agent can produce a different array of effects and adverse outcomes to seek for. Of note, living donor transplantation grafts have potential risks. Therefore, a thorough history and investigation are carried out to search for significant diseases that can be transmitted to the recipient from the donor [5]. The history of possible infections should be expanded in line with the increased risk of infection in these patients; whether there is a fever or changes according to the basal state should be questioned. It should be evaluated whether there is a history of chronic infection (Cytomegalovirus (CMV), Epstein-Barr Virus (EBV), Hepatitis B, Hepatitis C and others). A recent history of acute infection and the treatments received for it should be evaluated [6]. Depending on the basal condition of the patient, changes may be a guide in the diagnosis of organ rejection. For example, an increase or decrease in the urine output in the patient with KTX, the exertion capacity of the heart transplant patient, jaundice in the liver transplant patient, or changes in skin color are among the important signs to be sought. Whether the

patient has a history of rejection before, how he or she has had and relieved after this attack, if any, should be questioned [6].

2.2 Physical examination

The physical examination should also be focused on the main complaint on presentation at first, as in the history taking. It should also be extended to TX procedures, medications used, and any suspected differential diagnoses in these patients. The risk of opportunistic infection is increased due to immunosuppression; therefore, a detailed examination of patients should be performed in this regard. Ear, nose and throat examination and meningeal signs take priority in terms of possible infections, progressing caudally.

A detailed cardiopulmonary examination may indicate pneumonia which is often encountered in transplanted patients. Findings suggestive of pericardial effusion and/or murmurs detected during a heart examination may also be harbingers of viral infections. Abdominal examination may suggest complicated urinary tract infections or peritonitis, especially in patients with KTX. If there is an indwelling peritoneal catheter placed in the patient, the evaluation of the patient in terms of peritonitis should gain priority [7]. Pain in the upper right quadrant, and tenderness may be indicative of infections such as hepatitis B and/or C, CMV and EBV. Skin examination helps in the diagnosis of viral syndromes, meningococcal meningitis (petechiae), and rashes of GVHD or drug reactions. Neurological examination in search of neck stiffness and altered mental status is a guide to the diagnosis of infections of the central nervous system.

3. Complications, presentations and survival

The risk of developing anemia, cardiovascular syndrome (CVS), vascular calcification, metabolic bone disease and mortality, is reduced in TX, compared to the patients not undergoing transplantation process; while the risks of infection, malignancy, side effects of immunosuppressive drugs, obesity, and diabetes are higher in the patient with TX. The most common causes for ED referral of these patients include infections (39%), non-infectious gastrointestinal and genitourinary pathologies (15%), dehydration (15%), electrolyte disorders (10%), cardiopulmonary conditions (10%), injuries (8%) and transplant rejection (6%) [3].

The mortality rates after TX processes show large variations between studies secondary to sampling criteria, geographic and sociodemographic features, technological advances, *etc.* Death rates from cardiovascular and infectious diseases among solid organ transplant (SOT) recipients have decreased due to improved screening and intervention methods [8].

Bloodstream infections are a leading cause of morbidity and mortality in this population, with mortality reaching 50% when associated with septic shock [9, 10]. Crude mortality was 15.4%–82.4% and was consistently higher than for non-multidrug resistant organism bloodstream infections (MDRO BSIs) [11].

In 2003, the Dialysis Outcomes and Practice Patterns Study (DOPPS) reported that the crude 1-year mortality rate was 21.7% in the United States for patients on dialysis [12]. On the other hand, patients with kidney transplantation (KTX) experience survival benefits at all age groups, with a 68% lower risk of death compared to patients remaining on dialysis awaiting transplantation [13]. They also experience on average an additional 11 extra years of life after KTX, even among elderly or diabetic patients [14]. Risk of mortality is initially worse with KTX compared with dialysis, with a relative risk of 2.84. However, by 3–4 months, the risks are equal and subsequently, there are long-term survival benefits to the transplantation [15].

3.1 Cardiovascular syndrome

Cardiovascular Syndrome (CVS) is a major risk factor affecting morbidity and mortality in SOT recipients. Patients with liver transplantation (LT) for nonalcoholic fatty liver disease (NAFLD) have been compared with those with hepatitis C virus (HCV) [16]. The authors reported that the median follow-up after LT was 5.6 years in patients with NAFLD *vs.* 13.5 years in patients with HCV ($p = 0.0009$). Five years after LT, cardiovascular morbidity was more frequent in the NAFLD group than in the HCV group (12.8% *vs.* 9.3%) ($p = 0.0256$). On the other hand, CRF is a well-known risk factor for CVS in KTX recipients, while impaired kidney function and albuminuria increase the risk of CVS by 2 to 4 times. The most common cause of death in the first 3 months after SOT and KTX is infection, and the 2nd is congestive heart failure and CVS.

In addition, cardiovascular diseases are the most important cause of death in KTX patients with diabetes mellitus (DM), whilst infection and malignancy have a greater share of the causes of death in patients without DM. Acute coronary syndromes, including acute myocardial infarction (AMI), are more common in the elderly and diabetic patients.

3.2 Malignancy

Malignancy is among the most common causes of death after SOT. A recent meta-analytic study reported that SOT recipients had a 2.06-fold increased cancer mortality risk (standardized mortality ratio (SMR), 2.06; 95% confidence interval (CI): [1.56–2.71]) than the population [8]. Risks were higher in kidney (SMR 1.92; 95% CI: [1.30–2.84]), liver (SMR 3.07; 95% CI: [1.80–5.24]) and lung/heart (SMR 4.87; 95% CI: [3.33–7.12]) transplants.

A significant correlation was found between a high albumin/creatinine ratio and the incidence of malignancy development. The risk of developing malignancy after KTX is 3–5 times higher than a patient receiving dialysis. The mortality rate caused by CVS and infection has decreased with frequent and detailed patient follow-up and antibiotic prophylaxis in recent years, while the mortality rate caused by malignancy is still high.

3.3 Infections after transplantation

Infections occur very commonly in transplanted patients (25%–80%) and are the most important cause of mortality [17]. One of the biggest causes of this is immunosuppressive

agents used against rejection phenomena. Due to the suppressed immune response in these patients, inflammation can sometimes also be suppressed and mask the classic signs and symptoms of infection in the early stages.

3.3.1 Clinical features of infections in the transplanted patient

Fever and related issues comprise the most common reason for SOT recipients to present to the ED. Of note, fever can be masked by various factors, such as immune-suppressing agents, uremia and hyperglycemia, and may be absent or subtle in half of the patients with the infection. In addition, fever may be due to factors other than infection, such as drug effects, hypersensitivity reaction, rejection or malignancy. Lower-than-expected fever and leukocyte values are detected, especially in patients treated with mycophenolate mofetil and azathioprine. Even a low-grade fever in a patient who has undergone SOT requires an aggressive investigation.

Of note, SOT recipients are at risk for developing infection with transfusion-associated pathogens. Patients undergoing transplantation during the winter months are often exposed nosocomially to viruses such as respiratory syncytial virus (RSV) and influenza [18].

Immunosuppressive drugs reduce rejection rates but increase the risk of infection. The signs and symptoms of infection depend on the type of infection and can be partly estimated based on the time frame that passes from TX (Table 1) [18, 19]. For example, in one month after TX, resistant organisms, surgical and hospitalization-related complications, and infections related to colonization of the transplanted organ are common. Pneumocystis jirovecii, viral infections, latent infections and opportunistic infections occur more often between one and six months. After six months, conventional factors and late viral infections come to the fore [17, 20].

3.3.2 Diagnosis and management

It is of vital importance for emergency physicians to recognize infections early on, obtain diagnostic workup, initiate empirical treatment, and consider specialty consultation and inpatient admission [21]. When evaluating these patients, conditions that are easily managed in other patients should be carefully investigated.

The assessment should include workup based on complaints, history and physical examination. Emergency physicians should consider the patient's past and current treatments, comorbid conditions, the presence of necrotic tissue and collection, metabolic diseases, infections with immunomodulatory activity (CMV, EBV, Human Immunodeficiency Virus (HIV)) in the management.

Leukopenia can indicate acute bacterial infection, and an increase in atypical lymphocytes, associated with leukopenia, is often suggestive of severe viral infections (especially CMV). Agents commonly isolated in lung infections include *Pneumocystis jirovecii*, *Nocardia*, *Legionella pneumophila* and *Aspergillus spp*, which require special staining techniques and tests for their definitive diagnosis. Treatment recommendations should be unique for each patient after carefully analyzing with respect to potential atypical infections that require specific coverage. Table 2 provides a stepwise approach to infection management after organ TX.

Rapid and careful evaluation should be performed whenever sepsis or septic shock is suspected, followed by initiation of intravenous (IV) fluid replacement and broad-spectrum antibiotics [1]. Imaging for the transplanted organ should also be planned along with examinations for the suspected focus of infection, while the gold standard is often a biopsy. In patients with KTX, bacteremia is most often manifested by urinary tract infection. A recent study pointed out that Enterobacteriaceae constitute and remain the prevalent etiological agents, multidrug resistant (MDR) germs are taking on an increasingly important role [22]. Table 3 summarizes a comprehensive list of diagnostic work up according to the type of infection [13].

Empirical antimicrobial therapy for transplant patients must be managed in a multidisciplinary fashion in cooperation with the infectious diseases and TX team (Fishman 2007). Empirical treatments that can be considered are given in Table 4 (Long 2019 [3], Cimino 2016 [23], Jorgenson 2019 [19]).

Viral infections: A systematic review of 25 studies explored clinical presentations, laboratory findings and outcomes

TABLE 1. Types and sources of infection that can ensue in line with the transplantation period.

Transplantation period	Time passed	Infection
Early	1 mon	Nosocomial/Surgical site: Aspiration pneumonia, wound site infection, urinary tract infection, graft tissue superinfection, vascular structure infection, C. Difficile colitis Donor organ infection: MRSA, VRE, TBC, Candida, Toxoplasmosis, Chagas disease
Intermediate	1–6 mon	Mostly opportunistic infections: Pneumocystis Jirovecii, Histoplasma, Coccidioides, Cryptococcus, Hepatitis B and/or C, Kaposi's Sarcoma, Cytomegalovirus (CMV), tuberculosis (TBC), Epstein-Barr Virus (EBV) Surgical site infection Reactivation of suppressed infection of the receiver: CMV, Herpes zoster virus (HZV), Herpes simplex virus (HSV), EBV
Late	>6 mon	Community-acquired infection: Respiratory viruses, Pneumococcus, Legionella, Listeria, Influenza, EBV

C. Difficile colitis: Clostridium; MRSA: Methicillin-resistant Staphylococcus Aureus; VRE: Vancomycin-resistant enterococcus.

TABLE 2. Infection management after organ transplantation.

Order of priority	Steps in the management
1.	Consider the different etiological agents/microorganisms.
2.	Because of impaired inflammatory responses, atypical clinical and radiological findings and unexpectedly subtle symptoms are common.
3.	The results of serological tests performed while the patient is in the ED should not be relied upon.
4.	The imaging threshold should be lowered as impaired anatomy can change signs of infection.
5.	A thorough and complex antimicrobial management is required due to drug interactions.
6.	Health care-related infections and those attributed to increased antimicrobial resistance are common.
7.	Surgical consultation may be required to intervene with local infections, such as abscess drainage and debridement.

ED: emergency department.

TABLE 3. Diagnostic tests in accord with the suspected focus of infection.

Suspected source	Diagnostic work up
Unknown source	• Urine culture, chest X-ray, blood culture, lactate, complete blood count with differentials, CMV PCR, Purified Protein Derivative or QuantiFERON test
Sepsis	• If the criteria for sepsis are met, a complete blood count with differentials, kidney functions, lactate and blood cultures should be taken, and patient-specific drug treatments are initiated • Imaging may be performed depending on the suspected area
Pulmonary	• Chest X-ray and computed thoracic tomography if pneumonia is suspected • Complete blood count with differentials • Blood culture • Legionella and pneumococcal antigen test in urine • Purified Protein Derivative • CMV PCR, Coccidioides serology • A biopsy may be obtained
Central nervous system	• Computed tomography (CT) of the brain, magnetic resonance (MRI) imaging without contrast if it is not visualized in the first CT • Lumbar puncture, cell count, glucose, protein, culture of acid-resistant bacilli, cryptococcal antigen, viral PCR to analyze cerebrospinal fluid samples • Biopsy may be requested in focal lesions
Urinary tract	• Urinalysis and culture • Kidney function panel and complete blood count • If sepsis criteria are met, complete blood count, kidney function panel and patient-specific drug treatments should be taken
Diarrhea	• Leukocyte counts, culture, clostridium difficile test, parasite and eggs and CMV PCR in stool samples

CMV: Cytomegalovirus; PCR: Polymerase Chain Reaction.

of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) in Iranian liver transplant patients [24]. The rate of mortality and high levels of C-reactive protein (CRP), Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) are similar to the non-immune suppressed patients. However, detection of high levels of serum CRP, ALT/AST, and ALP combined with a clinical COVID-19 symptom and the finding of CT scan may indicate the presence and severity of the disease.

CMV is the most common virus type in people who have received solid organ transplants. CMV is a major cause of illness and death during the first year after transplantation. In people who have received an SOT, giving antiviral medications reduces CMV disease and death from CMV disease, compared with placebo or no treatment. Longer periods of prophylaxis were found to be more effective than three months of therapy in kidney and lung transplant recipients.

Ganciclovir is more effective than acyclovir and as effective as valganciclovir which is currently the most used antiviral drug to prevent CMV disease in transplant recipients [25]. Low-dose valganciclovir was found as effective as the standard dose for preventing CMV in moderate-risk KTX recipients. Different doses of valganciclovir did not result in a difference in preventing CMV disease.

4. Delayed graft function and ED management

It occurs more often in dead donor recipients. In those with KTX, most kidney grafts that have poor function may have a delay in graft function. It is necessary to exclude in the case of unfunctional TX kidney first:

TABLE 4. Empirical antimicrobial therapy choices in transplanted patients.

Coverage	Preferred antimicrobial agents-notes
All patients	• All cases should be managed in conjunction with consultations with infectious diseases and the transplantation team
Neutropenic patients without an established source of infection	• 3rd generation cephalosporins or carbapenems and anti-MRSA agents
Suspected MRSA	• Vancomycin, Linezolid
Tuberculosis	• Rifampicin
Parasitic infections	• Trimethoprim sulfamethoxazole
Viral infections	• Often requires reduced doses of immunosuppressants
EBV	• -
CMV	• Ganciclovir or Valganciclovir
HSV and VZV	• Acyclovir (intravenous infusion is preferred in disseminated forms)
Fungal infections	• They are managed with consultations with infectious diseases and transplantation teams, depending on the risk level of *Aspergillus*, *candida albicans* and *cryptococcus neoformans*

EBV: Ebstein-Barr Virus; CMV: Cytomegalovirus; HSV: Herpes simplex virus; MRSA: methicillin-resistant staphylococcus aureus; VZV: Varicella zoster virus.

√ Arterial and venous occlusion,

√ Congestion and leakage in the urinary system.

To rule out these impairments, renal blood flow is evaluated with Doppler Ultrasonography (USG). Patients with surgical indication may require emergency surgery.

Graft thrombosis is one of the leading causes of graft failure. A Cochrane review has shown that no evidence can be derived from Randomized controlled trials (RCTs) to be used to guide anti-thrombotic strategies in liver, heart, lung or other SOTs [26]. Thrombotic process can act as a contributing factor to cardiac allograft vasculopathy (CAV) which is recognized with its hallmarks; endothelial inflammation, platelet activation, and thrombosis. Antiplatelet therapy may prevent the development of CAV. The management of CAV encompasses the use of statins, treatment of cytomegalovirus infection, and management of rejection [27, 28]. A systematic review and meta-analysis showed uncertain evidence that acetyl salicylic acid (ASA) may reduce the development of CAV [29]. Further studies are required for the comparison of anticoagulants and antiplatelets to placebo in SOT. Unfractionated heparin may increase the risk of bleeding following KTX, but this finding is of low certainty.

Advances in operational and anesthetic techniques and more effective organ preservation have paved the way to improved patient and graft survival rates in patients undergoing LT while addressing emergent issues, such as short-term complications and early allograft dysfunction [30]. Primary non-function caused by early allograft dysfunction in patients with LT is one of the most dangerous complications of LT [31]. Research reported the incidence of this phenomenon between 5% and 40% following LT [32].

Agostini *et al.* [33] indicated that duration of ischemia, variables of donors including elevated body mass index (BMI), steatosis and cause of death, are among the risk factors for early graft dysfunction. An elevated serum sodium level in the donor is also suggested to be linked to higher rates of early allograft dysfunction (EAD) [34], although conflicting findings on this assertion exist in the literature [35].

Remote ischemic conditioning (RIC) has been postulated to show advantages in protecting organs from ischemia-reperfusion injury. The findings of a meta-analysis showed that RIC did not reduce mortality in LT patients compared with controls (risk ratio (RR) 0.9, 95% confidence interval [0.31–2.66]) [36]. Remote ischemic modulation does not improve clinical outcomes in patients undergoing organ transplantation (heart, lung, liver and kidney).

Monitoring biomarkers is an important aid to herald subclinical rejection in patients who have undergone LT in most clinical settings and affects outcomes favorably. For example, research data proposed that serum C-X-C motif chemokine ligand 8 (CXCL8) concentration can be a highly accurate noninvasive marker of subclinical rejection after LT in children [37]. Some other data indicated that monitoring serological markers is recommended in managing patients who have undergone LT, aiding in selecting patients in whom immunosuppression can be safely withdrawn [38]. Likewise, T-cell mediated rejection has been associated with certain key genes which reflect mechanisms including chemotactic activity, antigen processing and T cell differentiation in research [39].

5. Side effects associated with medications used by transplantation patients

Transplantation patients including kidney recipients typically use extensive medications that contain immunosuppressive agents due to the risk of rejection [13, 19]. Table 5 provides a summary of immunosuppressive agents [13]. In early post-TX period, induction agents are used to prevent early acute rejection. Among the most used induction agents are basiliximab, antithymocyte globulin, alemtuzumab. Reactions to these drugs are common and are mostly associated with cytotoxicity. Patients often present to the ED with fever, tremor, headache, nausea, weakness, dizziness, general body aches leukopenia

TABLE 5. An overview of immunosuppressive agents.

Induction		Maintenance		Treatment of rejection	
T cell depleting agents	ATG Thymoglobulin Alemtuzumab	Calcineurin inhibitors	Cyclosporine Tacrolimus	Mild ACR rejections Corticosteroids	Prednisone Methylprednisolone
IL-2 receptor antagonist	Basiliximab	Antiproliferative agents	MPA Azathioprine	Moderate to severe ACR rejections T-cell depleting agents	ATG Thymoglobulin
			Sirolimus Everolimus	AMR	IVIG/PP Rituximab
		Corticosteroids	Prednisone Methylprednisolone		Bortezomib Eculizumab
		Costimulatory pathway blocker	Belatacept		

ACR: Acute cellular rejection; AMR: Antibody-mediated rejection; ATG: Anti-thymocyte globulin; IVIG/PP: Intravenous immunoglobulin/Plasmapheresis; IL: Interleukin; MPA: Mycophenolic acid.

and thrombocytopenia during this period.

Drugs and side effects used for this purpose are given in Table 6 (Cimino 2016 [23], Vincenti 2003 [40], Long 2016 [1]). In a national cohort of Australia between 1984 and 2006, Na *et al*. [41] pointed out that induction antibody and maintenance corticosteroids are used more commonly in heart and lung compared to liver recipients ($p < 0.001$), and antibody therapy for rejection more common in liver recipients ($p < 0.001$). Liver recipients were more likely to receive calcineurin inhibitor monotherapy compared to heart and lung recipients ($p < 0.001$). Liver recipients consistently received lower doses of azathioprine than heart and lung recipients ($p < 0.001$).

6. Transplantation rejection

The second complication feared after infection comprises the rejection of the graft, which is one of the immediate causes of allograft dysfunction. Although its incidence decreased with newly developed immunosuppressive protocols, they are still common [2].

CD4+ (Clusters of differentiation 4+) and CD8+ donor major histocompatibility complex (MHC)-restricted T cells are sufficient to reject allografts by a T-cell receptor-mediated direct ("cognate") interaction using a defined array of effector molecules [42]. Conversely, "noncognate" host MHC-restricted CD4+ T cells must interact with intermediate host-type antigen-presenting cells and so greatly amplify the response by triggering antibody and inflammatory responses.

Rejection is usually detected by routine screening procedures or by several special workups (endomyocardial biopsy, transbronchial biopsy, *etc.*) [23]. Therefore, it may not always be possible to perform these examinations in the ED. Clinical findings must be evaluated with consultations and advanced laboratory workup for decision-making process.

Acute cellular rejection (ACR) is defined by different degrees of interstitial and/or perivascular infiltrate with myocyte damage [43]. On the other hand, acute antibody-mediated (humoral) rejection (AMR) has a highly varied incidence for it needs to be diagnosed either histopathologically or immunologically, with only a weak consensus on clinical recognition.

It is well-reported following ABO-incompatible LT and mainly recognized with graft dysfunction within two weeks post-LT and is often associated with graft loss [44]. A study showed 16% mortality after developing AMR over a 5-year study period [45]. Another study by Everitt *et al*. [46] showed that pediatric recipients with severe AMR (pAMR3) have worse CV outcomes compared to those without AMR. Adult recipients with asymptomatic AMR or mixed rejection have increased CV mortality compared to those with ACR alone [47].

Rejection is mostly asymptomatic in KTX; thus, the diagnosis is established by a marked increase in serum creatinine. Other causes of serum creatinine elevation including increased calcineurin inhibitor blood concentrations, volume status, and surgical factors need to be ruled out. Suspicion of acute kidney rejection should be confirmed by biopsy. Table 7 depicts rejection processes divided into three phases in accordance with their timing [1, 48].

7. Organ specific approach to transplants

7.1 Kidney TX

KTX is the most common solid organ transplant, being the preferred treatment modality in end-stage renal disease (ESRD). The kidneys harvested from deceased, or heart-beating donors are often placed in the recipient's pelvis and anastomosed into the ureters and bladder [49]. The most common complications that can develop after KTX is infection which can be caused by the donor kidney or the recipient's kidneys and/or bladder. Patients with suspected infection should be investigated in detail early on with treatment [50]. Patients with rejection can be asymptomatic, as well as with a decrease in urine, fever, and resistant hypertension [51].

The level of serum creatinine is the most important marker used in the evaluation of graft function in the transplanted

TABLE 6. Side/adverse effects of the medications used in transplant patients.

Agent	Mechanism	Side/adverse effect
Cyclosporine (Sandimmun®)	Calcineurin inhibitor, suppresses T lymphocyte activity and Interleukin-2 (IL-2) functions	Acute/chronic nephrotoxicity, electrolyte disorders, gout, hemolytic uremic syndrome, gingival hyperplasia, hirsutism, hypertension, hyperlipidemia
Tacrolimus (Prograf®)	Calcineurin inhibitor, suppresses T lymphocyte activity and IL-2 functions	Similar to cyclosporine Neurotoxicity (headache, shaking chills, paresthesia, seizures), hair loss
Azathioprine (Imuran®)	Inhibits purine synthesis	Bone marrow suppression, macrocytosis, anemia, hepatotoxicity, pancreatitis
Mycofenolate mofetil (Cellcept®), Mycofenolic acid (Myfortic®)	Inhibits purine synthesis, cytostatic on B and T cells	Abdominal pain, poor oral intake, nausea/vomiting, diarrhea, anemia, leukopenia, thrombocytopenia
Corticosteroids	Inhibits phagocytic functions, Reduces production of proinflammatory mediators, Suppresses T lymphocyte activity Reduces cellular signal conduction	Weight gain, cataracts, acne, thinning of the skin, bruises, osteoporosis, gastrointestinal hemorrhage, hyperglycemia, hyperlipidemia, psychological involvement, cushingoid appearance
Sirolimus (Rapamune®), Everolimus (Afinitor®)	Inhibits mammalian target of rapamycin (mTOR) receptors and blocks immune cells' signal conduction Suppresses B and T lymphocyte activities	Dyslipidemia, hepatic artery thrombosis, bone marrow suppression, pulmonary fibrosis, rash, skin ulcers
Polyclonal antibodies	Antilymphocyte antibodies, Used for immunosuppression after cessation of the nephrotoxic agent Used in the treatment of rejection resistant to corticosteroids	Fever, serum sickness, anaphylaxis, anemia, thrombocytopenia
Monoclonal antibodies	Antilymphocyte antibodies, Used in the prophylaxis against rejection in the early phase Used for immunosuppression after cessation of the nephrotoxic agent Used in the treatment of rejection resistant to corticosteroids	Headache, aseptic meningitis, encephalopathy, seizures, nausea/vomiting, diarrhea pulmonary edema and nephrotoxicity can be noted within the first three days of the treatment period. IL-2 receptor antibodies can also trigger anaphylaxis rarely

TABLE 7. Rejection stages and their pathogenesis.

Stage	Pathogenesis	Period
Hyperacute	Antibodies against antibodies already present in the body, they lead to complement activation and thrombosis	The first minutes to hours
Acute	Acute cellular rejection due to activated lymphocytes Humoral rejection due to antidonor antibodies expressed after organ transplantation	Six months
Chronic	Antibody and cell-mediated rejection	Months to years

patient. In healthy patients, 50% increase in creatinine is interpreted to be in favor of acute renal failure, while in patients with KTX increases of 20% should be considered as such [52]. Urinalysis should be requested on suspicion of infection or rejection. Leukocytes in the urine do not always confirm urinary tract infection; the source of leukocytes may also represent the manifestation of organ rejection. The appearance of erythrocytes or proteinuria may indicate underlying glomerulonephritis, drug toxicity or graft nephropathy. The appearance of bacteria in the urine and/or the presence of nitrites is often associated with infection. Drug levels may indicate the effectiveness or patient compliance of the immunosuppressant used, and cooperation with the transplantation team may be helpful in this respect.

Some anatomical complications may occur due to KTX. Among them, the most common conditions are vascular throm-

bosis and stenosis. Patients often present with uncontrolled hypertension, peripheral edema and decreased urine output. Although Doppler ultrasound can show a decrease in blood flow, angiographic methods are the gold standard (Table 8).

The nephrotoxic effect of the contrast media should be consulted and discussed with the transplantation team, whenever planned to be used for radiological investigations. Magnetic resonance angiography may be more advantageous as it can be applied without contrast media or combined with gadolinium, which is less toxic than other agents. The decision must be made with the transplant team. After diagnosis, the preferred treatment modality is stent placement with interventional radiological procedures [1].

Consultation with the transplant specialists should be performed on suspicion of acute TX rejection. The first treatment for acute rejection is IV methylprednisolone. Methylprednisolone (500 mg IV daily for 3 days) is administered as soon as the rejection is diagnosed. If the patient responds, oral prednisone is switched to return to a baseline of 0.3 mg/kg per day on the fourth day.

Treatment of antibody-mediated rejection usually involves Therapeutic Plasma Exchange (TPE), IV Immunoglobulin (IVIG) and rituximab. All suspected acute KTX rejections should be confirmed by biopsy.

7.1.1 Anemia-leukopenia

Anemia is seen in 20% to 57% of the patients after KTX. Anemia developed after a well-functioning kidney allograft usually resolves within 3–6 months after KTX.

Leukopenia occurs commonly after KTX. Patients with leukocyte $<3 \times 10^9$/L need to be evaluated further. In the absence of infection (no signs of systemic infection, no CMV viral load), medications should be questioned. Mycophenolate, azathioprine and valganciclovir are the most common causes of leukopenia. Cotrimoxazole and many other drugs are also associated with low leukocyte counts.

If leukopenia is severe (absolute number of neutrophils is below 0.5×10^9/L) infection should be considered, and protective isolation, broad-spectrum antibiotics and granulocyte-colony stimulating factor (G-CSF) should be initiated. If leukopenia is attributed to CMV infection, ganciclovir or valganciclovir is initiated and supplemented with G-CSF.

7.1.2 Hypertension

Hypertension is a common problem after KTX. The first-choice agents in antihypertensive therapy consist of calcium channel blockers, beta-blockers or angiotensin-converting enzyme (ACE) inhibitors. ACE inhibitors and angiotensin II receptor blockers (ARBs) should not be used in the early post-KTX period because they can affect creatinine levels.

7.2 Liver transplantation

The most common reasons for liver transplant patients to present to EDs are fever and abdominal pain. Hepatosplenomegaly, ascites, malaise and weakness may also be seen after the rejection [51, 53]. Complications of transplantation include bleeding, rejection, and infection, as well as biliary, vascular, and operation site-related complications. When evaluating differential diagnoses in these patients, blood biochemistry including amylase and lipase, coagulation parameters, acute phase reactants, cultures from blood, urine and ascites fluids, and complete blood count are helpful [54]. Doppler USG can detect fluid collections, thrombosis in the hepatic artery or portal vein, and dilation of the biliary tract. Contrast-enhanced CT may be required for the diagnosis of vascular complications or gallbladder stenosis. Cholangiography is useful for detailed hepatobiliary evaluation. All these examinations may not be easy to apply in ED environments, in case of doubt, the patient should be evaluated with the transplantation team.

Overall in-hospital mortality in adult living donor liver transplantation (LDLT) performed between 1994 and 2007, 576 consecutive adult patients who underwent LDLT at a single medical center was 18.9% [55]. The most frequent cause of death was infection (62.5%), which was followed by rejection (15.7%) and nonseptic multiple-organ failure (8.9%). Factors associated with 1-year mortality include the requirement of a high volume of packed red blood cells, hyperlactatemia, and consistently elevated bilirubin [5, 56]. Ioannou *et al.* [57] indicated that infective endocarditis resulted in a mortality rate of 43.5% in patients with LT.

7.3 Lung transplantation

In a large series from France, the most common indications of lung transplantation included cystic fibrosis, chronic obstructive pulmonary disease/emphysema and infiltrative lung disease [58]. One to two-year mortality figures varied between 81% and 72.9% in accord with the patients' emergency or non-emergency status for transplantation.

Fever, cough and attacks of dyspnea are common causes of lung transplanted patients' admission to the EDs [59]. Im-

TABLE 8. Organ transplant rejection characteristics and management after KTX.

Organ	Signs and symptoms	Diagnosis and management issues
Kidney	Mostly no symptoms. Fever, malaise, oliguria, graft pain, tenderness in the area. Hypertension. Progressive impairment in kidney functions (high creatinine, low glomerular filtration rate).	Acute elevation in serum creatinine with electrolyte imbalances. Growth in size of graft on USG, erasure of corticomedullary distinction, and the appearance of pronounced hypoechoic pyramids. Renal Doppler studies may show a high resistance index. Usually, a biopsy is needed during follow-up in the hospital.

portant clinical features include respiratory rate, pulse oximetry, cyanosis, perspirations, the excessive use of accessory muscles, signs of congestive heart failure and adequacy of peripheral perfusion. Decreased breath sounds and/or rales can be remarkable during pulmonary examinations. Chest X-rays and/or CT, and arterial blood gas analysis should be obtained whenever there is a suspicion of the inadequacy of ventilation. Signs and symptoms of infection can often be confused with those of rejection, although their treatment modalities are very different from each other. Detailed examination of these patients includes histopathological examinations, culture tests, respiratory function tests and bronchoscopy, if necessary [60]. Treatment of both infection and rejection should be initiated simultaneously in case of clinical suspicion because it may take a long time before obtaining the results of these examinations.

Patients should be managed following consultations with the transplantation team in the early period. Corticosteroids are often preferred in cases of rejection. Infections can be caused by bacteria, fungi or viruses, as well as by colonized microorganisms linked to the patient's underlying disease (bronchiectasis, cystic fibrosis, *etc.*). The appropriate treatment in these patients should be planned with the TX team and consultation with infectious diseases.

7.4 Heart transplantation (HTX)

Heart transplants are performed for patients with end-stage heart failure who cannot be relieved with standard medical or surgical treatment. It is performed in a wide spectrum of patients, from newborns to the elderly [61]. The sympathetic and parasympathetic nerves are not connected to the transplanted heart. Therefore, the transplanted heart has no vagal tonus [62]. The denervated heart has a normal sinus rhythm with a heart rate between 90 and 100 bpm.

Denervation results in the absence of centrally mediated tachycardia initially in response to stress or exercise, but the heart continues to respond to circulating catecholamines. With proper conditioning, patients can return to normal activity levels, including intense exercise after a transplant [3].

The donor's sinus node is implanted to maintain normal atrioventricular conduction while the donor's heart is being transplanted. If the patient's sinoatrial node is not removed, the two sinus nodes are electrically isolated and remain active. For this reason, two different P waves are often seen in electrocardiograms (ECGs).

Two surgical techniques have been used for orthotopic HTX, biatrial and bicaval approach. During biatrial TX, recipients retain the right and left atrial cuffs which facilitate the transplantation of the donor graft. After HTX the recipients have two sinoatrial (SA) nodes which are electrically isolated and active. For this reason, two different P waves are often seen in the ECG. The sinus node of the donor heart is easily identified due to the constant 1:1 relationship with the QRS complex, while the patient's P wave can be seen in the ECG irrespective of donor heart rhythm. This P wave can cause confusion; it can masquerade atrial flutter, early atrial complexes or sinoatrial blocks [3]. Currently in adults, HTX is typically performed using bicaval technique in which only posterior part of the left atrium with pulmonary veins is left in situ, and subsequently, there is one sinoatrial node only (from donor graft) with one P wave in the ECG.

A systematic review of around 7200 pediatric HTXs performed until 2019 showed that biatrial anastomosis was used in 62.2% (95% CI: 52.8–70.6) of the patients [63]. The bicaval technique was performed in the remaining 37.8% (95% CI: 29.4–47.1). Sinus node dysfunction was the most frequent indication for pacemaker implantation (54.4%; 95% CI: 42.6–65.7) followed by atrioventricular block (45.6%; 95% CI: 34.3–57.3). In a meta-analytic study, authors indicated that bicaval orthotopic HTX results in more favorable early and late outcomes for patients who underwent a bicaval HTX compared with a biatrial orthotopic HTX [64].

Clinical evaluation is based on the main reason for the ED visit. Patients may present with various symptoms such as shortness of breath, orthopnea, syncope and edema in the case of rejection, but chest pain due to denervation is not typically present [65]. Chest X-ray, ECG, and further evaluation are based on probable cardiac complications. Cardiac biomarkers are elevated in case of rejection, and findings indicative of cardiac failure may be seen in chest X-ray.

Echocardiography plays a crucial role in evaluating the extent and severity of acute cellular rejection (ACR) in patients with HTX. Recently, strain echocardiography has been suggested to be used with reasonable sensitivity to detect HTX rejection [66]. Resting and stress echocardiography can be combined with modern techniques such as myocardial contrast echocardiography to diagnose and prognosticate cardiac allograft vasculopathy. Recent studies also showed that the myocardial strain measured by speckle tracking echocardiography is affected in ACR and could be used to identify early rejection as a rule-out strategy [67]. The authors concluded that left and right ventricular global longitudinal strain can be used as a marker for ACR and reduce the need for endomyocardial biopsy.

Examination methods using point-of-care ultrasound (POCUS) and/or echocardiography employ specific protocols like Focus-assessed transthoracic echocardiography (FATE) in emergency situations and expedite patient evaluation and decision-making. FATE represents an abbreviated transthoracic echocardiography (TTE) protocol, which is an effective supplementary tool [68]. In critically ill patients, it is an easily learned systematic approach to the echocardiographic examination [69]. The fundamentals scanned are the chamber dimensions, wall thickness, ventricular function, pleura and obvious pathology [70]. The information is used analogously to the clinical context to improve patient management.

7.5 Corneal transplantation (CTX)

CTX is the most common and successful allogeneic transplant worldwide. Considering that the deterioration caused by corneal damage is very serious, it represents an effective method of restoring visual functions [71].

In corneal graft rejection, sudden onset edema accompanied by anterior chamber inflammatory manifestations of the graft is observed. The inflammatory process begins at the edge of the graft, which is closest to the most proximal blood vessels, and then proceeds to the center, finally covering the entire graft.

Patients present with eye pain, photophobia, corneal or scleral stinging, and decreased visual acuity. Treatment is often oral administration of 1 mg/kg prednisone [72]. Patients with CTX should be consulted with the ophthalmology department emergently when they experience a decrease in visual acuity or present to the ED with any ocular symptoms and/or findings.

8. Conclusions

For most failing organs and systems including kidneys, lungs, liver and heart, TX represents a superb mode of treatment for the patient regarding both survival rate and life quality. Iatrogenic immunosuppression and T-cell dysfunction put transplant recipients at increased risk for both common infections and opportunistic infections. On the other hand, the risk of graft rejection is a significant concern despite the widespread and regular use of immunosuppressive agents in vulnerable patients. It is of vital importance to recognize infections early on, obtain diagnostic workup, initiate empirical treatment, and consider specialty consultation and inpatient admission.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

CA and OK—conceptualization, methodology, validation, writing–original draft preparation, writing–review and editing, project administration. CA—software, formal analysis, resources, data curation. OK—investigation, visualization, supervision. Both authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study is exempted from informed consent or ethical approval as the research does not involve any intervention to patients or analysis of individual data.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Ozgur KARCIOGLU is serving as one of the Editorial Board members of this journal. We declare that Ozgur KARCIOGLU had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to NR.

REFERENCES

[1] Long B, Koyfman A. The emergency medicine approach to transplant complications. The American Journal of Emergency Medicine. 2016; 34: 2200–2208.

[2] Israni AK, Zaun DA, Gauntt K, Schaffhausen CR, Lozano C, McKinney WT, *et al*. OPTN/SRTR 2022 annual data report: deceased organ donation. American Journal of Transplantation. 2024; 24: S457–S488.

[3] Long B. The transplant patient. In Tintinalli JE (ed.) Tintinalli's emergency medicine: a comprehensive study guide (pp. 1984–1994). 9th edn. McGraw Hill: New York, USA. 2019.

[4] Simforoosh N, Gooran S, Tabibi A, Bassiri A, Ghraati MR. Cadaver transplantation in recent era: is cadaveric graft survival similar to living kidney transplantation? International Journal of Organ Transplantation Medicine. 2011; 2: 167–170.

[5] Puri P, Kumar A, Qaleem M. Donor evaluation protocol for live and deceased donors. Journal of Clinical and Experimental Hepatology. 2024; 14: 101217.

[6] Chhabra D. Assessment and management of the kidney transplant patient. 2022. Available at: https://emedicine.medscape.com/article/429314-overview#a1 (Accessed: 30 November 2024).

[7] Humar A, Matas AJ. Surgical complications after kidney transplantation. Seminars in Dialysis. 2005; 18: 505–510.

[8] Wang Z, Deng L, Hou W, Liu S, Zhang Y, Sheng C, *et al*. Cancer mortality among solid organ transplant recipients: a systematic review and meta-analysis. Preventive Medicine. 2024; 189: 108161.

[9] Adelman MW, Connor AA, Hsu E, Saharia A, Mobley CM, Victor DW III, *et al*. Bloodstream infections after solid organ transplantation: clinical epidemiology and antimicrobial resistance (2016–21). JAC-Antimicrobial Resistance. 2024; 6: dlad158.

[10] Gavaldà J, Aguado JM, Manuel O, Grossi P, Hirsch HH; ESCMID Study Group of Infection in Compromised Hosts. A special issue on infections in solid organ transplant recipients. Clinical Microbiology and Infection. 2014; 20: 1–3.

[11] Liu AJ, Dennis ASM, Fariha Z, Pai Mangalore R, Macesic N. Multidrug-resistant organism bloodstream infections in solid organ transplant recipients and impact on mortality: a systematic review. JAC-Antimicrobial Resistance. 2024; 6: dlae152.

[12] Goodkin DA, Bragg-Gresham JL, Koenig KG, Wolfe RA, Akiba T, Andreucci VE, *et al*. Association of comorbid conditions and mortality in hemodialysis patients in Europe, Japan, and the United States: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Journal of the American Society of Nephrology. 2003; 14: 3270–3277.

[13] Parajuli S, Clark DF, Djamali A. Is kidney transplantation a better state of CKD? Impact on diagnosis and management. Advances in Chronic Kidney Disease. 2016; 23: 287–294.

[14] Pesavento TE. Kidney transplantation in the context of renal replacement therapy. Clinical Journal of the American Society of Nephrology. 2009; 4: 2035–2039.

[15] Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, *et al*. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. The New England Journal of Medicine. 1999; 341: 1725–1730.

[16] Van Herck J, Verbeek J, van Malenstein H, Laleman W, Cassiman D, Verslype C, *et al*. Liver-related and cardiovascular outcome of patients transplanted for nonalcoholic fatty liver disease: a European single-center study. Transplantation Proceedings. 2021; 53: 1674–1681.

[17] Fishman JA. Infection in solid-organ transplant recipients. The New England Journal of Medicine. 2007; 357: 2601–2614.

[18] Green M. Introduction: infections in solid organ transplantation. American Journal of Transplantation. 2013; 13: 3–8.

[19] Jorgenson MR, Descourouez JL, Saddler CM, Smith JA. Post kidney transplant: infectious complication. In Parajuli S, Aziz F (eds.) Kidney Transplant Management (pp. 73–93). Springer: Cham. 2019.

[20] Fishman JA. Infection in organ transplantation. American Journal of Transplantation. 2017; 17: 856–879.

[21] Zhong D, Liang SY. Approach to transplant infectious diseases in the emergency department. Emergency Medicine Clinics of North America. 2018; 36: 811–822.

[22] Pinchera B, Trucillo E, D'Agostino A, Gentile I. Urinary tract infections in kidney transplant patients: an open challenge-update on epidemiology, risk factors and management. Microorganisms. 2024; 12: 2217.

[23] Cimino FM, Snyder KA. Primary care of the solid organ transplant recipient. American Academy of Family Physicians. 2016; 93: 203–210.

[24] Samidoust P, Nikoupour H, Hemmati H, Samidoust A. Clinical manifestations and characterization of COVID-19 in liver transplant recipients: a systematic review of case reports and case series. Ethiopian Journal of Health Sciences. 2021; 31: 429–438.

[25] Vernooij RW, Michael M, Ladhani M, Webster AC, Strippoli GF, Craig JC, *et al*. Antiviral medications for preventing cytomegalovirus disease in solid organ transplant recipients. Cochrane Database of Systematic Reviews. 2024; 5: CD003774.

[26] Surianarayanan V, Hoather TJ, Tingle SJ, Thompson ER, Hanley J, Wilson CH. Interventions for preventing thrombosis in solid organ transplant recipients. Cochrane Database of Systematic Reviews. 2021; 3: CD011557.

[27] Kobashigawa JA, Pauly DF, Starling RC, Eisen H, Ross H, Wang SS, *et al*. Cardiac allograft vasculopathy by intravascular ultrasound in heart transplant patients: substudy from the Everolimus versus mycophenolate mofetil randomized, multicenter trial. JACC: Heart Failure. 2014; 1: 389–399.

[28] Eisen HJ, Kobashigawa J, Starling RC, Pauly DF, Kfoury A, Ross H, *et al*. Everolimus versus mycophenolate mofetil in heart transplantation: a randomized, multicenter trial. American Journal of Transplantation. 2013; 13: 1203–1216.

[29] Aleksova N, Brahmbhatt DH, Kiamanesh O, Petropoulos JA, Chang Y, Guyatt G, *et al*. The effect of antiplatelet therapy on survival and cardiac allograft vasculopathy following heart transplantation: a systematic review and meta-analysis. Clinical Transplantation. 2021; 35: e14125.

[30] Gadour E. Lesson learnt from 60 years of liver transplantation: advancements, challenges, and future directions. World Journal of Transplantation. 2025; 15: 93253.

[31] Chen XB, Xu MQ. Primary graft dysfunction after liver transplantation. Hepatobiliary and Pancreatic Diseases International. 2014; 13: 125–137.

[32] Agopian VG, Harlander-Locke MP, Markovic D, Dumronggittigule W, Xia V, Kaldas FM, *et al*. Evaluation of early allograft function using the liver graft assessment following transplantation risk score model. JAMA Surgery. 2018; 153: 436–444.

[33] Agostini C, Buccianti S, Risaliti M, Fortuna L, Tirloni L, Tucci R, *et al*. Complications in post-liver transplant patients. Journal of Clinical Medicine. 2023; 12: 6173.

[34] Bastos-Neves D, Salvalaggio PRO, Almeida MD. Risk factors, surgical complications and graft survival in liver transplant recipients with early allograft dysfunction. Hepatobiliary & Pancreatic Diseases International. 2019; 18: 423–429.

[35] Ramirez CGB. Orthotopic liver transplantation: complications. In Doria C (ed.) Contemporary Liver Transplantation (pp. 1–13). 1st edn. Springer: Cham. 2016.

[36] Zhang M, Ma X, Wang X, Zhang C, Zheng M, Ma W, *et al*. Effect of remote ischemic conditioning on organ transplantation: a meta-analysis of randomized controlled trials. Transplantation Proceedings. 2024; 56: 1457–1468.

[37] Zhang Z, Wang Z, Dong C, Sun C, Zheng W, Wang K, *et al*. Serum CXCL8 concentration can be used as a noninvasive marker of subclinical rejection after pediatric liver transplantation. Transplantation. 2023; 107: 1999–2008.

[38] Pérez-Escobar J, Jimenez JV, Rodríguez-Aguilar EF, Servín-Rojas M, Ruiz-Manriquez J, Safar-Boueri L, *et al*. Immunotolerance in liver transplantation: a primer for the clinician. Annals of Hepatology. 2023; 28: 100760.

[39] Shao W, Ding H, Wang Y, Shi Z, Zhang H, Meng F, *et al*. Key genes and immune pathways in T-cell mediated rejection post-liver transplantation identified via integrated RNA-seq and machine learning. Scientific Reports. 2024; 14: 24315.

[40] Vincenti F. Immunosuppression minimization: current and future trends in transplant immunosuppression. Journal of the American Society of Nephrology. 2003; 14: 1940–1948.

[41] Na R, Laaksonen MA, Grulich AE, Webster AC, Meagher NS, McCaughan GW, *et al*. Longitudinal dose and type of immunosuppression in a national cohort of Australian liver, heart, and lung transplant recipients, 1984–2006. Clinical Transplantation. 2015; 29: 978–990.

[42] Lin CM, Gill RG. Direct and indirect allograft recognition: pathways dictating graft rejection mechanisms. Current Opinion in Organ Transplantation. 2016; 21: 40–44.

[43] Stewart S, Winters GL, Fishbein MC, Tazelaar HD, Kobashigawa J, Abrams J, *et al*. Revision of the 1990 working formulation for the standardization of nomenclature in the diagnosis of heart rejection. The Journal of Heart and Lung Transplantation. 2005; 24: 1710–1720.

[44] Wozniak LJ, Naini BV, Hickey MJ, Bhattacharyya S, Reed EF, Busuttil RW, *et al*. Acute antibody-mediated rejection in ABO-compatible pediatric liver transplant recipients: case series and review of the literature. Pediatric Transplantation. 2017; 1: e12791.

[45] Thrush PT, Pahl E, Naftel DC, Pruitt E, Everitt MD, Missler H, *et al*. A multi-institutional evaluation of antibody-mediated rejection utilizing the Pediatric Heart Transplant Study database: incidence, therapy and outcomes. The Journal of Heart and Lung Transplantation. 2016; 35: 1497–1504.

[46] Everitt MD, Hammond ME, Snow GL, Stehlik J, Revelo MP, Miller DV, *et al*. Biopsy-diagnosed antibody-mediated rejection on the proposed International Society for Heart and Lung Transplantation working formulation is associated with adverse cardiovascular outcomes after pediatric heart transplant. The Journal of Heart and Lung Transplantation. 2012; 31: 686–693.

[47] Kfoury AG, Hammond ME, Snow GL, Drakos SG, Stehlik J, Fisher PW, *et al*. Cardiovascular mortality among heart transplant recipients with asymptomatic antibody-mediated or stable mixed cellular and antibody-mediated rejection. The Journal of Heart and Lung Transplantation. 2009; 28: 781–784.

[48] Cozzi E, Colpo A, De Silvestro G. The mechanisms of rejection in solid organ transplantation. Transfusion and Apheresis Science. 2017; 56: 498–505.

[49] Suthanthiran M, Strom TB. Renal transplantation. The New England Journal of Medicine. 1994; 331: 365–376.

[50] Venkat K, Venkat A. Care of the renal transplant recipient in the emergency department. Annals of Emergency Medicine. 2004; 44: 330–341.

[51] Unterman S, Zimmerman M, Tyo C, Sterk E, Gehm L, Edison M, *et al*. A descriptive analysis of 1251 solid organ transplant visits to the emergency department. Western Journal of Emergency Medicine. 2009; 10: 48.

[52] Chapman JR, O'Connell PJ, Nankivell BJ. Chronic renal allograft dysfunction. Journal of the American Society of Nephrology. 2005; 16: 3015–3026.

[53] Savitsky EA, Votey SR, Mebust DP, Schwartz E, Uner AB, McCain S. A descriptive analysis of 290 liver transplant patient visits to an emergency department. Academic Emergency Medicine. 2000; 7: 898–905.

[54] Gür A, Oguzturk H, Köse A, Turtay MG, Ersan V, Bayindir Y, *et al*. Prognostic value of procalcitonin, CRP, serum amyloid A, lactate and IL-6 markers in liver transplant patients admitted to ED with suspected infection. In Vivo. 2017; 31: 1179–1185.

[55] Kaido T, Egawa H, Tsuji H, Ashihara E, Maekawa T, Uemoto S. In-hospital mortality in adult recipients of living donor liver transplantation: experience of 576 consecutive cases at a single center. Liver Transplantation. 2009; 15: 1420–1425.

[56] Safi K, Pawlicka AJ, Pradhan B, Sobieraj J, Zhylko A, Struga M, *et al*. Perspectives and tools in liver graft assessment: a transformative era in liver transplantation. Biomedicines. 2025; 13: 494.

[57] Ioannou P, Alexakis K, Kofteridis DP. Endocarditis in liver transplant recipients: a systematic review. Journal of Clinical Medicine. 2021; 10: 2660.

[58] Roux A, Beaumont-Azuar L, Hamid AM, De Miranda S, Grenet D, Briend G, *et al*.; FOCH lung transplant group. High emergency lung transplantation: dramatic decrease of waiting list death rate without relevant higher post-transplant mortality. Transplant International. 2015; 28: 1092–1101.

[59] Mohseni MM, Li Z, Simon LV. Emergency department visits among lung transplant patients: a 4-year experience. The Journal of Emergency Medicine. 2021; 60: 150–157.

[60] Dabbs ADV, Hoffman LA, Iacono AT, Zullo TG, McCurry KR, Dauber JH. Are symptom reports useful for differentiating between acute

rejection and pulmonary infection after lung transplantation? Heart & Lung. 2004; 33: 372–380.

[61] Mancini D, Lietz K. Selection of cardiac transplantation candidates in 2010. Circulation. 2010; 122: 173–183.

[62] Awad M, Czer LS, Hou M, Golshani SS, Goltche M, De Robertis M, *et al*. Early denervation and later reinnervation of the heart following cardiac transplantation: a review. Journal of the American Heart Association. 2016; 5: e004070.

[63] Mylonas KS, Repanas T, Athanasiadis DI, Voulgaridou A, Sfyridis PG, Bakoyiannis C, *et al*. Permanent pacemaker implantation in pediatric heart transplant recipients: a systematic review and evidence quality assessment. Pediatric Transplantation. 2020; 24: e13698.

[64] Zijderhand CF, Veen KM, Caliskan K, Schoonen T, Mokhles MM, Bekkers JA, *et al*. Biatrial versus bicaval orthotopic heart transplantation: a systematic review and meta-analysis. The Annals of Thoracic Surgery. 2020; 110: 684–691.

[65] McCartney SL, Patel C, Del Rio JM. Long-term outcomes and management of the heart transplant recipient. Best Practice & Research Clinical Anaesthesiology. 2017; 31: 237–248.

[66] Karatasakis A, Kiamanesh O, Cheng RK, Kirkpatrick JN, Dudzinski DM. Echocardiographic evaluation of the post-heart transplant patient. Current Cardiology Reports. 2025; 27: 63.

[67] Xourgia E, Brignoli K, Linder O, Neagoe AM, Capek L, Bruno J, *et al*. Speckle-tracking echocardiography of left and right ventricle and acute cellular rejection in orthotropic heart transplantation: a systematic review and meta-analysis. The International Journal of Cardiovascular Imaging. 2025; 41: 669–679.

[68] Holm JH, Frederiksen CA, Juhl-Olsen P, Sloth E. Perioperative use of focus assessed transthoracic echocardiography (FATE). Anesthesia & Analgesia. 2012; 115: 1029–1032.

[69] Macas A, Maciuliene A, Ovsianas J, Juodviroyte G, Bakoyte G. Focus assessed echocardiography performed by inexperienced examiners in a cardiac intensive care unit. Proceedings of the Latvian Academy of Sciences, Section B. 2014; 68: 242–246.

[70] Nagre AS. Focus-assessed transthoracic echocardiography: implications in perioperative and intensive care. Annals of Cardiac Anaesthesia. 2019; 22: 302–308.

[71] Singh R, Gupta N, Vanathi M, Tandon R. Corneal transplantation in the modern era. Indian Journal of Medical Research. 2019; 150: 7.

[72] Azevedo Magalhaes O, Shalaby Bardan A, Zarei-Ghanavati M, Liu C. Literature review and suggested protocol for prevention and treatment of corneal graft rejection. Eye. 2020; 34: 442–450.

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