CHEST

The Critically Ill Kidney Transplant Recipient

A Narrative Review

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Kidney transplantation is the most common solid organ transplantation performed worldwide. Up to 6% of kidney transplant recipients experience a life-threatening complication that requires ICU admission, chiefly in the late posttransplantation period (≥ 6 months). Acute respiratory failure and septic shock are the main reasons for ICU admission. Cardiac pulmonary edema, bacterial pneumonia, acute graft pyelonephritis, and bloodstream infections account for the vast majority of diagnoses in the ICU. *Pneumocystis jirovecii* pneumonia is the most common opportunistic infection, and one-half of the patients so infected require mechanical ventilation. The incidence of cytomegalovirus visceral infections in the era of preemptive therapy has dramatically decreased. Drug-related neutropenia, sirolimus-related pneumonitis, and posterior reversible encephalopathy syndrome are among the most common immunosuppression-associated toxic effects. Importantly, the impact of critical illness on graft function is worrisome. Throughout the ICU stay, acute kidney injury is common, and about 40% of the recipients require renal replacement therapy. One-half of the patients are discharged alive and free from dialysis. Hospital mortality can reach 30% and correlates with acute illness severity and reason for ICU admission. Transplant characteristics are not predictors of short-term survival. Graft survival depends on pre-ICU graft function, disease severity, and renal toxicity of ICU investigations and treatments. CHEST 2016; 149(6):1546-1555

KEY WORDS: critical care; *Pneumocystis jirovecii*; renal transplants

Kidney transplantation is currently the best therapeutic option for patients with end-stage renal disease. Overall, kidney transplantation is cost-effective and associated with lower mortality compared with long-term dialysis,[1] providing patients with a better quality of life.[2] Over the past two decades, the release of new immunosuppressive drugs, improvement of the standard of care, and implementation of new protocols have increased graft survival.[3]

These advances have prompted the increased use of kidney transplantation, and in 2010 it was estimated that 180,000 patients in the United States were living with a functional renal allograft.[4] However, the mortality rate among kidney transplant recipients is significantly higher than that of the general

ABBREVIATIONS: AGPN = acute graft pyelonephritis; ARF = acute respiratory failure; ATG = anti-lymphocyte globulin; BSI = bloodstream infection; CMV = cytomegalovirus; CVD = cardiovascular disease; PRES = posterior reversible encephalopathy syndrome; RRT = renal replacement therapy; TMA = thrombotic microangiopathy

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population, suggesting the need to better identify targets for improvements.[5] Indeed, long-term exposure to induction and maintenance immunosuppressive therapy carries a risk of cardiovascular events, severe infections, drug-related toxicities, as well as immunosuppression-associated malignancies.[6-9] A sizeable proportion of these patients require treatment in the ICU.

This review article describes the most severe medical complications that lead to ICU admission following kidney transplantation. The complex issue of managing immunosuppression in patients with organ dysfunctions is discussed. Hospital mortality and graft survival after ICU admission are the outcome variables of interest.

Epidemiology

Over the last two decades, intensive care for kidney transplant recipients has decreased from 40% to less than 10%. However, several biases hamper any precise evaluation of the actual incidence of life-threatening complications leading to ICU admission. First, modalities of patient follow-up and ICU admission policies vary widely across centers. Second, although decreasing, in some centers, the ICU is used in the immediate posttransplantation period as a facility to secure and ease immediate homeostasis and monitoring. Third, the literature reports on different study periods, during which transplantation and supportive care practices have changed. Finally, prophylactic strategies have changed over time and still differ across centers.

The pioneer study by Sadaghdar et al[10] was conducted in the United States in 1995. They reported a high rate of ICU admission after kidney transplantation. Namely, of 178 recipients of kidney transplants performed in the center during the study period (August 1992-July 1993), 74 (41.6%) were admitted to the ICU. Excluding the 27 patients admitted for postoperative monitoring, 44 recipients (24.7%) were admitted to the ICU 23 ± 30 months after transplantation. However, three more recent studies report far lower use of the ICU in this setting. In 2011, we published a large observational study carried out in nine high-volume transplantation centers in France. Over an 8-year study period (January 2000-August 2008), 452 of 6,819 kidney transplant recipients (6.6%) required ICU admission in the participating ICUs.[11] Along this line, in a single-institution study performed in the United Kingdom, Arulkumaran et al[12] reported that 47 of 576 kidney recipients (8.1%) had been admitted to the ICU between 2006 and 2010. Finally, in a Greek study published by Mouloudi et al[13] in 2012, 61 of 1,355 kidney transplant recipients (4.1%) required ICU admission between 1992 and 2012.

Although not specifically sought, this decreased use of intensive care might be explained by advances and wide use of anti-infectious prophylactic strategies implemented in the posttransplantation period, which have significantly altered the incidence and severity of posttransplantation infections.[14] In addition, improved surgical procedures,[15] echography-guided kidney biopsies,[16] and advances in immunosuppression may have contributed to the observed decrease in ICU use.

In summary, 5% to 10% of kidney transplant recipients experience a life-threatening complication that warrants ICU admission (Table 1). Acute respiratory failure (ARF) and septic shock are consistently and steadily the main reasons for ICU referral.[10-13,17-25]

Cardiovascular Events

It is well known that end-stage renal disease is a major cardiovascular risk factor. In the HEMO (Hemodialysis) Study, about 80% of the patients requiring chronic hemodialysis had a cardiovascular disease (CVD), including congestive heart failure (40%), ischemic heart disease (39%), and arrhythmia (31%).[26] Although kidney transplantation reduces long-term cardiovascular mortality when compared with dialysis, one should keep in mind that CVD accounts for 30% of fatalities among recipients who die with a functioning transplant.[4] Special attention should be paid to a history of atrial fibrillation. In a large cohort study, Lenihan et al[27] reported that preexisting atrial fibrillation was experienced in 6% of kidney transplant recipients. Recipients with previous atrial fibrillation carried a significantly higher risk of posttransplantation death, graft failure, and ischemic stroke as compared with those without atrial fibrillation.

Two studies assessed the ability to predict unplanned ICU admission in the early posttransplantation period. In the first one, conducted in Japan, Higashi et al[28] reported that 5.8% of the recipients developed postoperative pulmonary edema. According to their experience, this complication was correlated with the presence of pretransplantation left ventricular diastolic dysfunction. Patients who developed pulmonary edema had a higher ratio of early transmitral flow velocity to averaged annular (septal and lateral) mitral velocity (E/E′; a marker of elevated pulmonary capillary wedge pressure) than those who did not (17.8 [14.1-22.5]

TABLE 1] Studies Reporting on ICU Admission After Kidney Transplantation

Study/Year	Country	Kidney Transplantations Over the Study Period, No.	Recipients Admitted to ICU, No. (%)	Hospital Mortality, No. (%)
de Carvalho et al[17]/2014	Brazil	NR	190 (NR)	73 (38.4)
Bige et al[18]/2014	France	2,650	220 (8.3)	17/83 (20.4)
Ting et al[19]/2013	United Kingdom	70	14 (20)	0 (0)
Mouloudi et al[13]/2012	Greece	1,335	61 (4.1)	26 (42.6)
Arulkumaran et al[12]/2012	Kingdom	576	47 (8.1)	24 (51)
Zrim et al[20]/2012	Australia	508	39 (7.7)	NR
Canet et al[11]/2011	France	6,819	452 (6.6)	45/200 (22.5)
Klouche et al[21]/2009	France	1,015	57 (5.6)	23 (40.3)
Candan et al[22]/2006	Turkey	1,130	34 (3)	20 (58.8)
Kirilov et al[23]/2003	Israel	871	27 (3.1)	10 (36.8)
Kogan et al[24]/1999	Israel	1,349	19 (1.4)	2 (10.5)
Sadaghdar et al[10]/1995	United States	178	71 (39.9)	8 (11.3)
Total		16,501	1,041 (6.3)	248 (30.9)

NR = not reported.

vs 11.1 [10.6-11.7]; $P < .01$) at pretransplantation transthoracic echocardiography. The second study, performed in the United Kingdom, sought to determine the ability of pretransplantation functional measures determined during cardiopulmonary exercise testing to predict posttransplantation ICU admission. Fourteen of the 70 recipients (20%) were finally admitted to the ICU. The best predictor of posttransplantation ICU admission was a reduced anaerobic threshold ($\dot{V}O_{2AT}$). In this study, standard pretransplantation echocardiographic parameters at rest failed to predict further need for ICU admission.[19]

ARF accounts for about one-half of patients admitted to the ICU after kidney transplantation.[11,18,21] In this setting, cardiogenic pulmonary edema is a common diagnosis and should be systematically discussed, especially when the patient is admitted in the early posttransplantation period (< 1 month). Indeed, it has been reported that up to 50% of the recipients admitted to the ICU for ARF within a month of the transplantation procedure had cardiogenic pulmonary edema.[11] In agreement with these data, a study conducted in the United Kingdom reported that hypervolemia was present in 30% of kidney recipients and was independently associated with elevated blood pressure.[29] Baseline kidney graft function must also be taken into account when assessing the probability of a cardiovascular event. In a post hoc analysis of the FAVORIT (Folic Acid for Vascular Outcome Reduction in Transplantation) Trial, an estimated glomerular filtration rate less than 45 mL/min per 1.73 m^2 was independently associated with the occurrence of cardiovascular events: CVD death, myocardial infarction, resuscitated sudden death, stroke, coronary revascularization, or peripheral, carotid, aortic, or renal artery procedures.[6] This condition is common among recipients admitted to the ICU, where most studies reported impaired renal function at baseline and at the time of ICU admission.

Pulmonary edema in kidney recipients is associated with hypertension and volume overload, usually in the context of kidney graft dysfunction. ICU management includes afterload reduction, diuretics, and noninvasive mechanical ventilation in the case of respiratory distress. Nevertheless, it has been reported that up to 30% of patients require intubation and mechanical ventilation, and the majority (55%) are treated with renal replacement therapy (RRT). Although the ICU mortality rate for kidney recipients with acute pulmonary edema is low (about 10%), the long-term renal prognosis is poor as reflected by a high rate of worsening graft function or dialysis dependence.[11]

Infections

Kidney transplant recipients are at high risk of infection. Severe sepsis and septic shock are the leading causes of ICU admission in this population.[11,17,18,21] Infections after solid organ transplantation can be challenging to diagnose and treat because of a great diversity of pathogens and unusual clinical patterns. Indeed, in the immunocompromised patient, symptoms of infection

are often diminished.[30] Nevertheless, in the ICU setting some clinical vignettes are typical and require increased awareness.

Perioperative Complications

A study conducted in Australia reported that 59% of kidney recipients experienced at least one surgical (fluid collection, bleeding), urological, or wound complication. However, only 6% required ICU admission.[18] Nevertheless, mycotic arteritis of the vascular anastomosis, a rare but potentially life-threatening invasive fungal infection, must be mentioned. Mycotic arteritis leads to anastomotic leaks, aneurysm, or wall rupture and results in hemorrhagic shock necessitating urgent nephrectomy. *Candida* and *Aspergillus* are the fungi commonly involved. Damage to the gut during surgery and contamination of the preservation fluid are occasionally reported. These complications usually occur in the first month posttransplantation and portend a poor prognosis (graft loss and death).[31]

Pneumonia

In the ICU setting, the lung is consistently the primary source of infection in kidney transplant recipients, accounting for 50% to 60% of cases.[11,12,17,18,22] Bacteria are the most common documented pathogens (about two-thirds of the microbiological identification), whatever the time from transplantation. A study has suggested an association between mycophenolate mofetil and the development of bronchiectasis.[32] Permanent dilatation and destruction of the bronchial walls promote *Pseudomonas aeruginosa* colonization. This should be considered when choosing the first-line antibiotic regimen. ICU treatment of bacterial pneumonia is characterized by the need for intubation and mechanical ventilation in up to 62% of patients, and vasopressors in 55%. Hospital mortality reaches 35%.[11]

Cytomegalovirus (CMV) was historically the leading virus identified in the severe forms of viral pneumonia.[33] In the current era, with prophylaxis and preemptive treatment strategies, CMV pneumonia is much less common. Indeed, in a study conducted in Finland and Germany among 1,129 kidney recipients screened over an 8-year study period, CMV pneumonia was confirmed in only three patients.[34] Data have underlined the role of influenza or respiratory syncytial virus infections in severe pneumonia (Fig 1A). As an example, during the pandemic influenza A H1N1 infection in 2009, 17.5% of infected kidney recipients required ICU admission, with a high rate of mechanical ventilation (66.6%) and death (37%). Factors associated with an adverse outcome included delayed antiviral therapy (after 48 h), diabetes mellitus, and abnormal chest imaging results at presentation.[35]

Pneumocystis jirovecii pneumonia is the most common opportunistic infection diagnosed in kidney recipients admitted to the ICU for ARF, most often in the late posttransplantation period (> 6 months) after trimethoprim-sulfamethoxazole prophylaxis has been stopped[11,17,18,36] (Fig 1B). Increased immunosuppression to treat acute rejection in the previous months is common. The median time from the onset of respiratory symptoms to ICU admission is about 5 to 10 days, which is significantly shorter than in patients with AIDS. Clinical features are characterized by severe hypoxemia, bilateral interstitial or alveolointerstitial opacities on chest radiographs, diffuse ground-glass opacities on CT scans, and the need for invasive mechanical ventilation in one-half of patients. Shock is reported in less than 10% of the patients and is associated with microbial superinfection. Fiber-optic bronchoscopy and BAL has a high diagnostic yield.[11,37] In deeply hypoxemic patients, unlike patients with AIDS, the benefit of newly implemented high-dose steroids is not established. Few studies are available and results are controversial.[38-40] Hospital mortality reaches 30% in kidney recipients admitted to the ICU for *Pneumocystis jirovecii* pneumonia.[11]

In a retrospective analysis of a large national registry, Shorr et al[41] found that the use of anti-lymphocyte globulin (ATG) to treat rejection was associated with an increased risk for ARDS in kidney transplant patients. Antibody induction agents have been associated with a cytokine release syndrome resulting in pulmonary edema.[42] However, the fact that patients who have experienced rejection and have been treated with ATG may be more severely ill and more prone to develop infections precludes any conclusion regarding a causal relationship between ATG and ARDS.

Acute Graft Pyelonephritis

Acute graft pyelonephritis (AGPN) is the most frequent infection in kidney transplant recipients. Among kidney recipients, 13% to 18.7% develop AGPN. AGPN has been reported to cause deteriorating renal graft function and even to cause graft loss when it occurred within 3 months posttransplantation.[43,44] In the ICU setting, AGPN is the second most common infection after

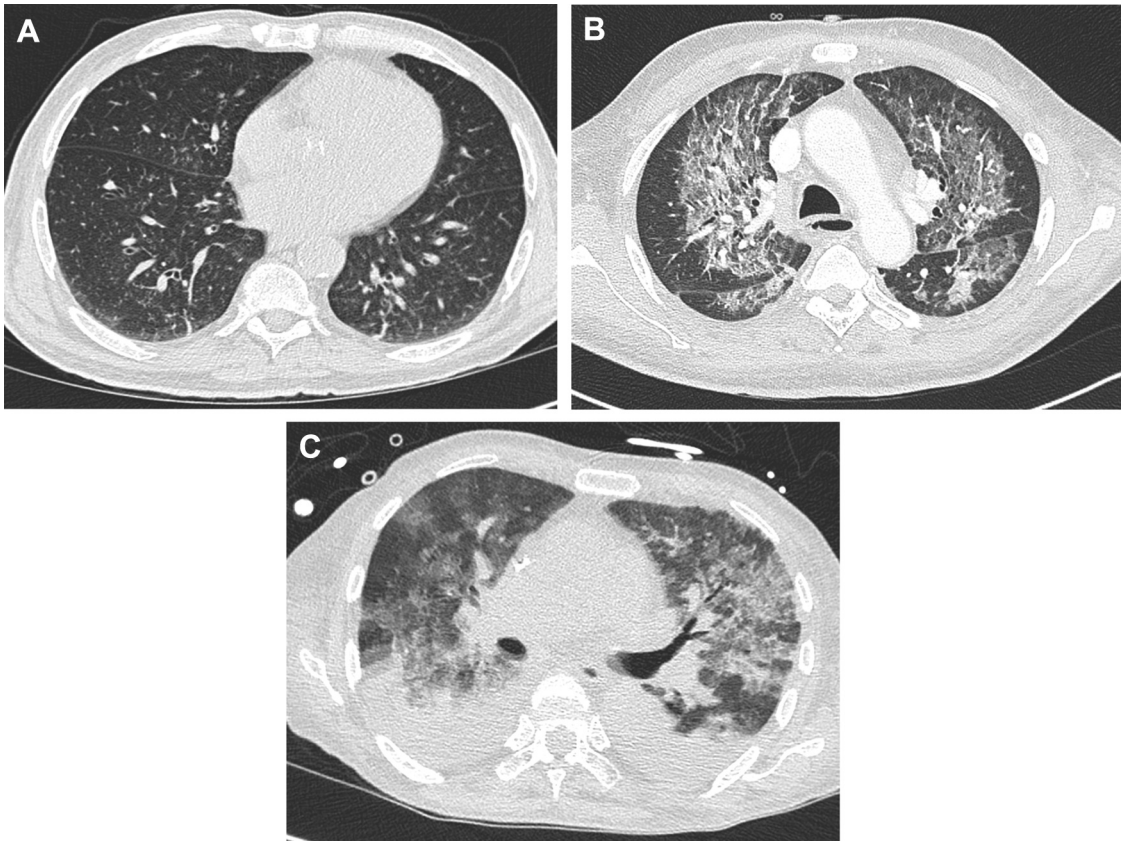

Figure 1 – *A, A 62-year-old woman was admitted to the ICU for respiratory distress 1 year after kidney transplantation. She had a history of cough and fever in the previous 5 days. A CT scan shows diffuse bilateral centrilobular micronodules. Diagnosis was achieved after an immunofluorescence test for influenza A virus, performed on bronchoalveolar lavage fluid, yielded a positive result. The patient required 4 days of noninvasive mechanical ventilation and fully recovered. B, Typical radiographic findings for* Pneumocystis jirovecii *pneumonia in a 67-year-old man 14 months after kidney transplantation. A CT scan shows diffuse bilateral alveolointerstitial and ground-glass opacities. Diagnosis was achieved after an immunofluorescence test, performed on bronchoalveolar lavage fluid, yielded a positive result. The patient required 10 days of invasive mechanical ventilation and fully recovered. C, A 59-year-old woman was admitted to the ICU for severe hypoxemia. She had a 2-month history of fatigue and dyspnea without fever, 7 years after kidney transplantation. A CT scan shows bilateral asymmetrical consolidations, ground-glass opacities, and bilateral pleural effusion. BAL microbiological evaluation produced negative results. Analysis of BAL cells showed intrapulmonary hemorrhage. Sirolimus-associated pneumonitis was suspected. Sirolimus therapy was discontinued and she received corticosteroids. The patient required 15 days of noninvasive mechanical ventilation and fully recovered.*

pneumonia among kidney recipients (17%-25% of the sepsis cases).[11,17,18] Most of the patients admitted for AGPN experience septic shock, and less frequently acute respiratory distress syndrome. RRT is implemented in more than one-half of patients throughout the ICU stay. Among ICU survivors, worsening graft function or dialysis dependence after discharge is common, notably among those with impaired baseline creatinine.[18]

Bloodstream Infection

In the ICU, 22% to 24% of kidney recipients admitted for sepsis develop bloodstream infections (BSIs).[11,17,18] Acute rejection, ureteric stent, deceased donor, and a Charlson score ≥ 3 have been reported to be independently associated with BSI. Gram-negative bacilli are consistently the main pathogens isolated (60%-71%), and *Candida* species are isolated in 5% to 6% of the patients. The urinary tract, catheters, and abdomen account for more than two-thirds of the primary sources of infection. In up to 25% of cases, BSI remains of unknown origin. In recipients with BSI, shock and invasive mechanical ventilation have been identified as independent risk factors for mortality.[45] Gram-negative BSI after kidney transplantation is associated with higher risks of allograft failure and all-cause mortality.[46,47]

Other Infections

Of course, the spectrum of pathogens encountered after kidney transplantation is wide. Nevertheless, it seems important to underline that those listed previously are the main pathogens likely to lead to ICU admission. Other

pathogens reported include the following: *Clostridium difficile* colitis, *Mycobacterium tuberculosis* (frequently disseminated or extrapulmonary tuberculosis), *Nocardia* (pneumonia, brain abscesses), *Cryptococcus* (meningitis or pneumonia), and *Toxoplasma gondii* (pneumonia, neurologic disorders, seizures, myocarditis).[48-50] These infections are frequently diagnosed in recipients with a high level of immunosuppression.

Management of Immunosuppressive Therapy During Sepsis

There is no consensus on the management of immunosuppressive drugs in the ICU during severe sepsis or septic shock. On the one hand, considering the recipient's life-threatening condition and the risk of dying of infection, it might be reasonable to discontinue immunosuppressive drugs to enhance sepsis recovery. Such a strategy has been reported by authors, sometimes with the continuation of steroids alone.[51] It should be kept in mind that the potential benefit of this strategy on mortality has not been demonstrated and that it carries a risk of allograft rejection. On the other hand, maintaining immunosuppressive drugs is challenging. First, it might delay sepsis recovery, and somewhat increase mortality. However, this is also unproven. Second, drug-drug interactions between antiinfective agents and immunosuppressive agents are numerous (eg, calcineurin or mTOR [mammalian target of rapamycin] inhibitors with macrolide antibiotics, rifamycin, or azole antifungal agents).[52] Third, shock resuscitation and acute kidney injury dramatically alter the pharmacokinetics and pharmacodynamics of immunosuppressive drugs, making it mandatory to closely monitor their levels.

Immunosuppressive therapy in the ICU setting should be managed jointly by nephrologists and intensivists, taking into account baseline graft function before ICU admittance, time from transplantation, immunological risk, severity of sepsis, and some difficult-to-treat pathogens.

Drug-related Toxicity

Drug-induced Neutropenia

Neutropenia occurs frequently in kidney transplant recipients and is associated with an increased incidence of bacterial, viral, and fungal infections. Heylen et al[53] recently demonstrated that kidney recipients with neutropenia had an OR of 2.34 (1.08-5.07) for the development of invasive aspergillosis. Zafrani et al[54] reported that 28% of kidney recipients experienced neutropenia 79 (16-365) days after transplantation. Several drugs used in kidney transplantation may induce neutropenia. In this study, the combination of mycophenolic acid with tacrolimus was associated with the highest risk of neutropenia as compared with other combinations. In addition to drug reduction or discontinuation, the successful use of granulocyte colony-stimulating factor has been reported.[54,55]

Sirolimus-associated Pneumonitis

Drug-related pulmonary toxicity has been reported in 11% of kidney recipients given sirolimus.[9] The severity is usually mild to moderate, and the common presenting symptoms are cough and fatigue. Usual radiographic findings are pulmonary infiltrates, patchy bilateral asymmetrical peripheral consolidations, and ground-glass opacities. BAL shows hypercellularity with lymphocytosis. In some rare cases, invasive mechanical ventilation may be required. Acute presentations of sirolimus-associated pneumonitis have been reported with respiratory distress, severe hypoxemia, extensive lung infiltration on chest radiograph, and intraalveolar hemorrhage on BAL (Fig 1C). In patients who develop severe symptoms, in addition to withdrawing sirolimus and supportive care, high-dose steroids could be considered.[56,57]

Posterior Reversible Encephalopathy Syndrome

The incidence of posterior reversible encephalopathy syndrome (PRES) after kidney transplantation is estimated to be 0.35%.[58] Impaired consciousness, seizures, and severe hypertension are the most common conditions that lead to ICU admission. PRES can occur a few days or many years after transplantation. Calcineurin inhibitors (particularly tacrolimus) and less frequently sirolimus are the leading causes of PRES. Neurotoxicity of immunosuppressive drugs may occur even at therapeutic levels. At presentation, blood pressure can be elevated or within the normal range. Magnetic resonance imaging is the most sensitive imaging test to confirm PRES (Fig 2). Most patients recover after the immunosuppressive agent has been withdrawn, blood pressure has been controlled, and supportive measures have been instituted.

Thrombotic Microangiopathy

Acute kidney injury and hypertension may be associated with thrombotic microangiopathy (TMA). TMA is defined by the association of microangiopathic hemolytic anemia, thrombocytopenia, and organ injury. The incidence of TMA after kidney transplantation

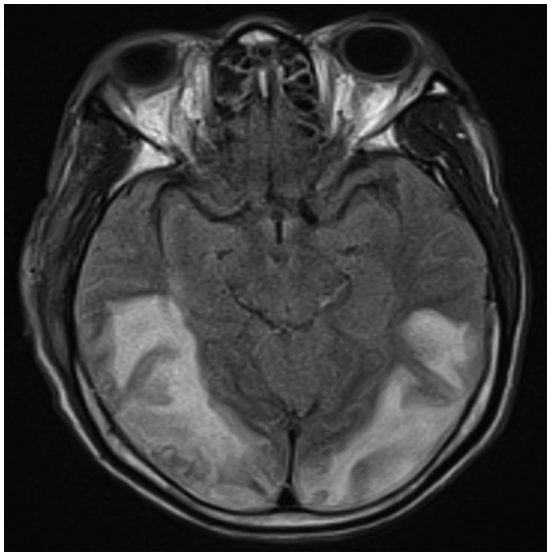

Figure 2 – *Typical findings consistent with posterior reversible encephalopathy syndrome (PRES) on magnetic resonance imaging. An axial magnetic resonance image (fluid-attenuated inversion recovery) demonstrates extensive vasogenic edema with bilateral involvement of the parietal and occipital lobes, consistent with PRES.*

ranges between 4% and 14%, usually in the early posttransplantation period, but it may also develop years after transplantation.[59] By far, drug-mediated TMA involving calcineurin inhibitors and sirolimus is the most common form of TMA. Other causes of TMA include posttransplantation recurrence of hemolytic-uremic syndrome, acute rejection, CMV infection, and malignancy. Rare cases of idiopathic thrombotic thrombocytopenic purpura are also reported. Therapeutic guidelines for posttransplantation TMA are not well defined and need a multidisciplinary approach. Withdrawal of the offending drug, treatment of hypertension, and supportive care are essential.

ICU Management and Outcome

ICU admission occurs mostly in the late posttransplantation period (≥ 6 months). In the study by de Carvalho et al,[17] median time from transplantation to ICU admission was 25.2 months, 21.9 months in the study by Bige et al,[18] and 17 months in the study by Canet et al.[48] The likely explanation might be the efficacy of current preventive strategies

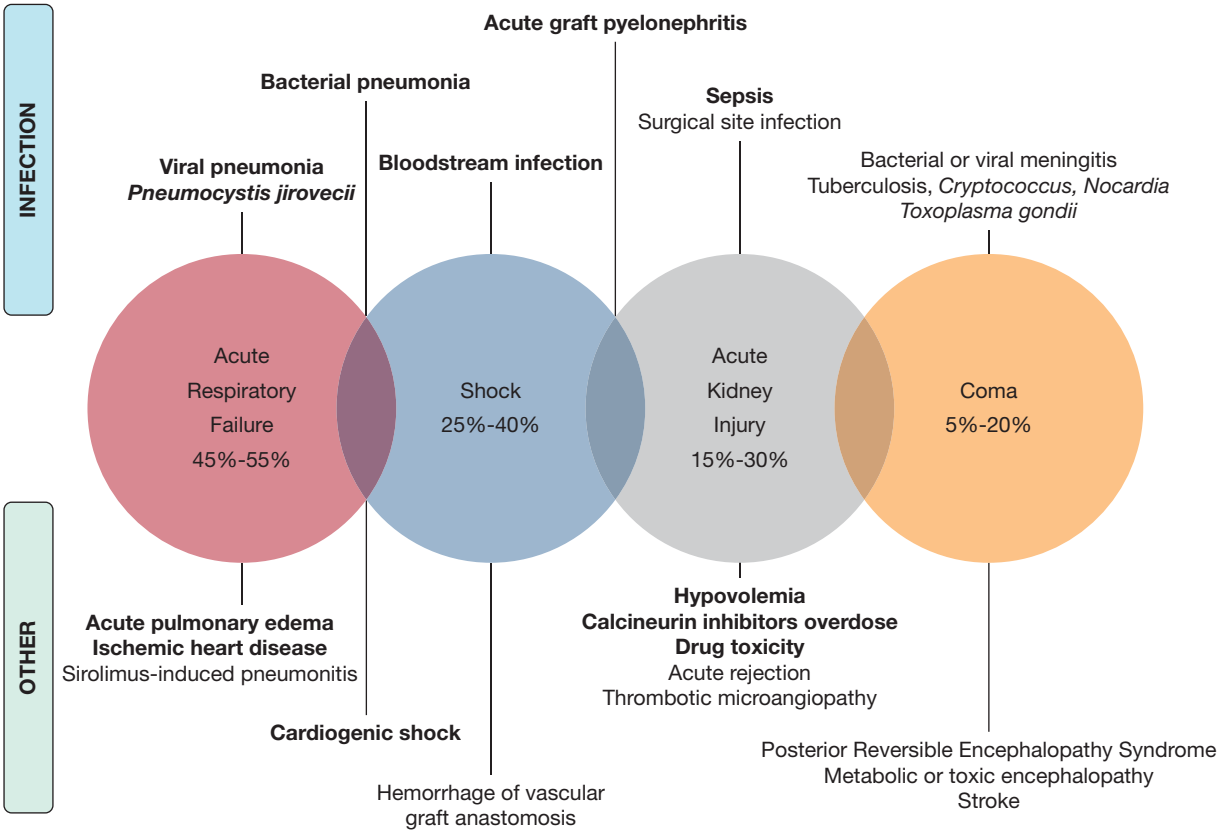

Figure 3 – *Admission diagnoses and corresponding etiologies in kidney recipients admitted to the ICU. Adapted from Sadaghdar et al,[10] Canet et al,[11] Arulkumaran et al,[12] Mouloudi et al,[13] Ooms et al,[15] Patel et al,[16] de Carvalho et al,[17] Bige et al,[18] Ting et al,[19] Zrim et al,[20] Klouche et al,[21] Candan et al,[22] and Kirilov et al.[23]*

implemented before transplantation and during the first 6 months (vaccination, prophylaxis, preemptive treatment). Interestingly, in these studies, an increase in immunosuppressive therapy to treat an acute rejection episode is reported in 20% to 30% of the kidney recipients in the months prior to ICU admission. Figure 3 depicts the diagnoses commonly reported in the ICU according to organ dysfunction. Some practical recommendations are listed in Table 2.

ICU Stay and Patient Outcome

During the ICU stay, about 40% of the recipients require RRT (Fig 4). This rate is much higher than the 5% to 10% usually reported in unselected critically ill patients.[60] Indeed, kidney recipients are at high risk for acute kidney injury throughout the ICU stay. In addition to several exposure factors (sepsis, shock, nephrotoxic drugs, radiocontrast agents), impaired baseline graft function before ICU admission is detrimental.[18]

Hospital mortality can be as high as 30%. Factors reported to be independently associated with mortality in critically ill kidney recipients are shock, invasive mechanical ventilation, the number of organ dysfunctions, bacterial infection, and opportunistic fungal infection. None of the transplant-related characteristics have been reported to be associated with ICU or hospital mortality.[11-13,17,18,21]

TABLE 2] Ten Practical Recommendations for ICU Treatment of Critically Ill Kidney Transplant Recipients

1. Do not delay admission to the ICU
2. Routinely assess cardiac function
3. Consider bacterial pneumonia, acute graft pyelonephritis, and bloodstream infections as being major reasons for ICU admission
4. Evaluate the risk for *Pneumocystis jirovecii* pneumonia (lack of prophylaxis) and discuss flexible fiber-optic bronchoscopy and bronchoalveolar lavage
5. Consider immunosuppressive drug-related toxicity
6. Avoid nephrotoxic drugs and contrast agents
7. Evaluate the kidney graft by Doppler sonography to investigate for a surgical complication (fluid collection, bleeding) or a thrombotic event in the renal vessels
8. Engage in close therapeutic drug monitoring of immunosuppressive therapy. Consider discontinuing temporarily some immunosuppressive drugs in patients with septic shock
9. Consider administering granulocyte colony-stimulating factor to severely neutropenic recipients
10. Provide full-code ICU management based on good short- and long-term outcomes

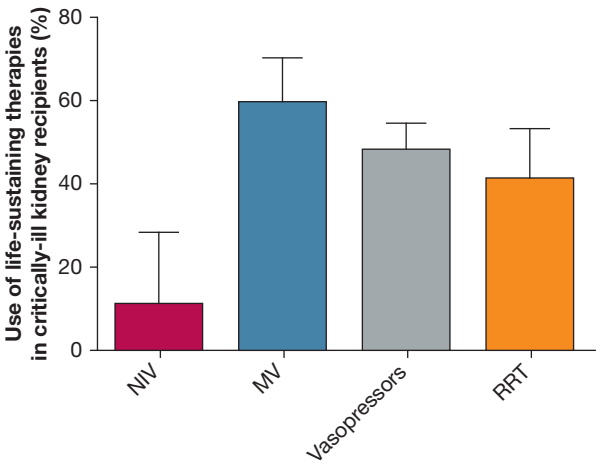

Figure 4 – *Proportion of critically ill kidney transplant recipients who require life-sustaining therapies. MV = mechanical ventilation; NIV = noninvasive mechanical ventilation; RRT = renal replacement therapy. Data are presented as medians with interquartile range. Adapted from Sadaghdar et al,[10] Canet et al,[11] Arulkumaran et al,[12] Mouloudi et al, [13] Ooms et al,[15] Patel et al,[16] Ting et al,[19] Zrim et al,[20] Klouche et al,[21] Candan et al,[22] and Kirilov et al.[23]*

Graft survival

The long-term effect of critical illness on renal allograft is poor. Indeed, less than one-half of kidney recipients admitted to the ICU will be discharged alive and free from dialysis. After ICU discharge, a decline in graft function is reported in 20% to 30% of patients, and graft loss in 8% to 20% of the critically ill kidney recipients.[11,12,18,21,25] Nevertheless, it should be kept in mind that the baseline graft function must be taken into account when considering these data. Indeed, some of the kidney recipients have experienced multiple complications before ICU admission. In this case, the critical illness acts as the ultimate injury to previously impaired graft function. Factors reported to decrease the likelihood of dialysis-free survival are acute kidney injury on admission, bacterial infection, delayed ICU admission, and hypoxemia.[11] In a retrospective study, a cyclosporine-based immunosuppressive regimen and a high baseline level of serum creatinine were independently associated with a lower probability of survival without graft function impairment on day 90 post-ICU discharge.[18]

Conclusion

In summary, 6% of kidney transplant recipients experience life-threatening complications that warrant ICU admission. Pneumonia, acute graft pyelonephritis, and bloodstream infection are the leading causes of ICU admission and are associated with decreased

transplantation survival. *Pneumocystis jirovecii* pneumonia is common and carries high mortality rates. Cardiogenic pulmonary edema occurs in the early posttransplantation period and in cases of advanced graft dysfunction. Overall mortality is about 30% and correlates with acute illness severity and the reason for ICU admission, not with transplant-related characteristics. Acute kidney injury and RRT are common in the ICU, and a complete recovery of graft function after discharge is uncertain. Immunosuppressive therapy throughout the ICU stay should be administered jointly by intensivists and nephrologists and reassessed regularly according to the patient's condition.

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