



Top Tips when managing the Renal Transplant Patient

Key Article

Darmon M, Canet E, et al. Ten tips to manage renal transplant recipients. *Critical Care*. 2019, 45:380-383.

Introduction

- Renal transplant (RT) is one of the most common types of organ transplants performed across the globe
- In 2015, nearly 85,000 renal transplants were performed.
- There are many challenges when managing these patients clinically in the ED, as they are immunocompromised, often have residual renal dysfunction, cardiovascular comorbidities and high risk for critical illness.
- Renal transplant patients will often present with a new acute kidney injury, that can be caused by acute rejection, surgical or urological complications, side effects from immunosuppressive medications, or opportunistic infections.
- In most patients, it's important to be in touch with the patient's renal transplant team early, along with your clinical pharmacist as many of their chronic medications may need to be adjusted or even discontinued during critical illness.

Search for bacterial infection promptly

- Sepsis remains the most common cause for ICU admission of the RT patient
- The most frequent source is **bacterial graft pyelonephritis**, caused by residual indwelling urinary catheters, ureteral stents, as well as other usual causes. Bacterial pneumonia is the second most common cause of sepsis, along with surgical site infections and bacteremia.
- Renal imaging is recommended in all transplanted renal patients, to rule out not only urinary tract obstruction, but also renal abscess, or free fluid (anastomotic urinary leakage).
- Viral and fungal infections are also common
 - **Cytomegalovirus (CMV)** can cause life-threatening CMV viremia and organ dysfunction
 - **Influenza** and other respiratory viruses (**RSV, adenovirus**, etc.) may be benign in the immunocompetent patient, but can cause severe viral pneumonias in transplant patients. Critically ill transplant patients with respiratory infections should all receive a respiratory viral panel in addition to the usual sputum cultures.
 - **BK Polyomavirus**: may reactivate in immunocompromised patients – causing nephritis, ureteral stenosis, and hemorrhagic cystitis.
 - **Pneumocystis (PCP) pneumonia** is the most common fungal infection in patients without PCP prophylaxis (can occur after discontinuation).
 - **Bactrim** is the treatment of choice, but unlike in HIV patients, steroids remain controversial in the transplanted patient.
 - **Candida or aspergillus** infections are uncommon, but can lead to mycotic aneurysms of the vascular anastomosis of the transplant, and life-threatening intra-abdominal hemorrhage.

Challenges in managing anti-rejection drugs during critical illness

- Immunosuppression management depends on multiple factors, including baseline graft function, immunological risks, and type of critical illness.
- Common immunosuppression meds include:
 - Tacrolimus, Cyclosporin, Sirolimus: Calcineurin inhibitors, T & B-cell activation inhibitors
 - Mycophenolate: T & B-cell inhibition
 - Steroids
- Drug toxicities are important to consider in the ED, but are challenging to diagnose clinically because they often present mimicking other common ED diagnoses.
 - *Immunosuppression medication levels can be particularly helpful toward making these diagnoses*
 - Common toxicity complications include:
 - **Hematologic:** Neutropenia, Thrombotic microangiopathy
 - **Pulmonary:** Sirolimus-associated pneumonitis (pneumonia mimic)
 - **Neurologic:** Posterior reversibly encephalopathy syndrome (PRESS) – AMS or acute stroke mimic
- The ED physician should also be aware of common medication interactions that may arise in critically ill RT patients
 - Azole and macrolide antibiotics can inhibit metabolism, increasing risk of toxicity
 - Beware the use of calcium channel blockers (diltiazem) in patients taking tacrolimus with afib with RVR, as it can also precipitate tac toxicity

Vascular access and complications in patients after renal transplant

- Renal transplant anatomy is important
 - Renal grafts are often implanted in the lower abdomen
 - Vascular anastomoses are usually made with the internal or external iliac artery and vein. The ureter is usually a short connection, directly to the patient's native bladder.
 - As a result of this new anatomy, renal transplant patients are at particular risk for both symptomatic and asymptomatic VTE. Incidence has been reported as high as 10% within the first 2 years of implantation, and nearly half were asymptomatic DVTs!
 - Renal artery stenosis is also another important consideration for a new AKI
 - Transplant ultrasound will include evaluation of the graft's vasculature, doppler blood flow, and look for signs of transplant hydronephrosis.
- Patients will often keep AV fistulas after transplant surgery, as ligation can actually cause systemic complications. In fact, closure or thrombosis of a functional AVF can lead to:
 - reduced transplant function
 - compromise of ipsilateral vessels for future vascular access if long dialysis is again needed
- Central venous access pearls for the renal transplant patient
 - AVOID subclavian central lines as this could lead to subclavian stenosis, making it impossible to use that limb as a future HD site if needed
 - AVOID femoral access on the same side of the renal transplant

Other Important complications and considerations

- **Cardiovascular disease** is the leading cause of mortality accounting for 40-50% of deaths after the first year following renal transplant
- **Hyperparathyroidism** persists after transplantation, leading to an increased risk of orthopedic fractures 2/2 osteoporosis
- **Thrombotic microangiopathy** is one of the most devastating and feared sequelae after renal transplantation
 - **Rare complication** (~1% of patients), but carries a 50% mortality rate at 3-years
 - **Presentation:** Similar to hemolytic uremic syndrome
 - **Classic triad:** Thrombocytopenia, microangiopathic hemolytic anemia, and acute kidney injury.
 - **Lab features:** Elevated LDH, new anemia, decreased haptoglobin with schistocytes on a peripheral blood smear
 - **Causes:** A variety of different causes including
 - Genetic: Unrecognized ADAMTS13 activity
 - Infection: Shiga toxin-producing E. Coli, pneumococcal infection
 - Medication: Calcineurin inhibitor (Cyclosporin A, Tacrolimus) induced
 - **Treatment:**
 - Hold giving patient calcineurin inhibitor until discussed with transplant team.
 - Emergent plasmapheresis or IVIG has been found to be highly successful, but only in small studies.

Take home points

- The differential diagnosis for AKI in the renal transplant patient should include new infection, medication related, or hematologic complications.
- Renal transplant patients are at high risk for spontaneous VTE. Transplant anatomy can lead to mechanical vascular complications, including both symptomatic and asymptomatic venous thromboembolism.
- Avoid subclavian central venous access, along with femoral access on the same side as the patient's renal graft as this may cause future graft and vascular access complications
- Immunosuppression medication toxicity is common, but can present with a myriad of clinical symptoms.