

Acute Kidney Injury in Kidney Transplants

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CASE STUDY

Case study

- 66 - year - old man
- Hemodialysis therapy for 2 years
- Receiving a deceased donor transplant
- He developed AKI requiring dialysis during septic shock following an incarcerated hernia
- His eGFR was normal before this episode
- His kidney failure was attributed to acute tubular necrosis.

Case study

- His medical history was also notable for
- HCV infection Hypertension Monoclonal gammopathy
- Six months following transplantation, he was seen in the clinic and was found to have an elevated serum creatinine level.
- immunosuppression regimen of prednisone, tacrolimus, and mycophenolate mofetil.
- Laboratory testing in the clinic had demonstrated AKI
- he was treated with intravenous pulse methylprednisolone

Case study

- Following treatment for this rejection episode, the patient developed a bilateral pruritic rash on the lower extremities, buttocks, back, abdomen, and upper extremities
- Laboratory data demonstrated AKI, with an elevation in serum creatinine level to 2.65 mg/dL



Clinical Approach

- What is the diagnosis for AKI in this patient with an extensive skin rash following kidney transplantation?
- What is the most likely cause of the patient's kidney injury and what treatment options are available?

Clinical Approach

- What is the differential diagnosis for AKI in this patient with an extensive skin rash following kidney transplantation?
 - Result of an undertreated rejection
 - Sequela of over immunosuppression
 - De novo glomerulonephritis associated with systemic vasculitis.

Clinical Approach

- What is the most likely cause of the patient's kidney injury and what treatment options are available?
- The patient's kidney biopsy specimen is consistent with GN caused by cryoglobulin deposition.

AKI in transplant

- Transplantation of a deceased donor kidney is associated with a significantly higher risk of acute kidney injury (AKI) following implantation and reperfusion.
- Dialysis treatment of the kidney transplant recipient (KTR) in the first 7 days of transplantation is termed “delayed allograft function” (DGF). DGF is associated with higher rates of allograft loss and rejection
- No regulatory-approved therapies

AKI in transplant

- Opportunities include
 - Donor intervention and management
 - Recipient intervention and management

Clinical Stabilization

- Perioperative period to minimize hemodynamic dysfunction that worsens ischemic injury.
 - Volume expansion
 - Pretransplant dialysis for electrolyte correction
 - Pressor support
 - Dopamine: effect in terms of minimizing DGF?
 - Choice of immunosuppression
 - ATG - calcineurin inhibitor

Injury and Inflammation

- Innate immune activation pathways are critical to mediating injury
 - Complement activation
 - Adhesion molecule expression
 - Pathogen-associated molecular
 - Pro-coagulant microenvironment

Injury and Inflammation

- PROTECT” trial : Eculizumab (anti-C5 antibody) or placebo
- incidence of DGF ,death , graft loss to follow-up at 7 days post transplant
- 35.9% on treatment, compared to 41.7% for patients receiving placebo ($p = 0.398$)

Effects of AKI on Graft Survival in Renal Transplantation

- Kidney transplantation recipients have various risk factors for AKI
 - Immunosuppressive state
 - Calcineurin inhibitors
 - CKD with a single kidney
 - Ischaemia -reperfusion injury
 - Surgical complications
 - Urinary diversion

Effects of AKI on Graft Survival in Renal Transplantation

- Prolonged cold ischemia time is highly associated with (DGF)
- Every 6 h of cold ischemia = 23% increase in the risk of DGF
- AKI was a risk factor for graft survival independent of the incidence of acute rejection.
- The most common etiology of AKI
 - Urinary tract infection
 - Other Infectious
 - Pneumocystis pneumonia associated with worse outcomes

Summary of the AKI studies during the maintenance phase of kidney transplantation.

| | The study by Nakamura et al. [26] | The study by Mehrotra et al. [28] |
|---|---------------------------------------|-----------------------------------|
| Patient number | 289 | 27,232 |
| Institute | Single | Multiple |
| Donor type | Living only | Living (24%) and deceased (76%) |
| Observation period | 4 years | 3 years |
| AKI identification method | RIFLE criteria | ICD-9-CM codes |
| AKI occurrence rate (%) | 20.4 | 11.3 |
| Hazard ratio for graft failure | hazard ratio for graft failure | |
| ^a Mild AKI | 2.28 | 2.74 |
| ^b Severe AKI | 3.95 | 7.35 |
| ^a AKI Risk in the study by Nakamura et al., and AKI without dialysis in the study by Mehrotra et al. [28] | | |
| ^b AKI Injury/Failure in the study by Nakamura et al., and AKI with dialysis in the study by Mehrotra et al. [28] | | |

Effects of AKI on Graft Survival in Renal Transplantation

- Importantly, both of these studies suggest that sepsis is an important factor in the pathogenesis of AKI during the maintenance phase of kidney transplantation
- The incidence of AKI is very high in severe sepsis and shock, resulting in high mortality

Biological Effects of AKI

- AKI has long-term biological effects.
- RIFLE criteria (Risk, Injury, Failure, Loss and End-stage Kidney) predicting
 - Full renal recovery
 - Dialysis requirement
 - Length of hospitalization
 - In-hospital mortality
- Episodes of AKI may be a risk factor for the progression of renal disease

Non-Renal Transplantation

Effects of AKI on Graft Survival in Non-Renal Transplantation

- ARF is associated with extra renal organ system failure
- These patients usually had three or four failed organ systems
- Increased rates of graft failure and mortality after non-renal transplantation

Factors for AKI and CKD in Non-Renal Transplantation

- Toxicity of calcineurin inhibitors
- Intraoperative hypoxemia
- Hypoperfusion due to diuretics overuse
- Use of antibiotics
- Inflammation

Inflammation

- Accumulated neutrophils in renal tissues may also play an important role in the development of AKI
- Antiinflammation strategies, such as glucocorticoid administration and miniature extracorporeal circuits were found to have **no positive** effects on the incidence of AKI

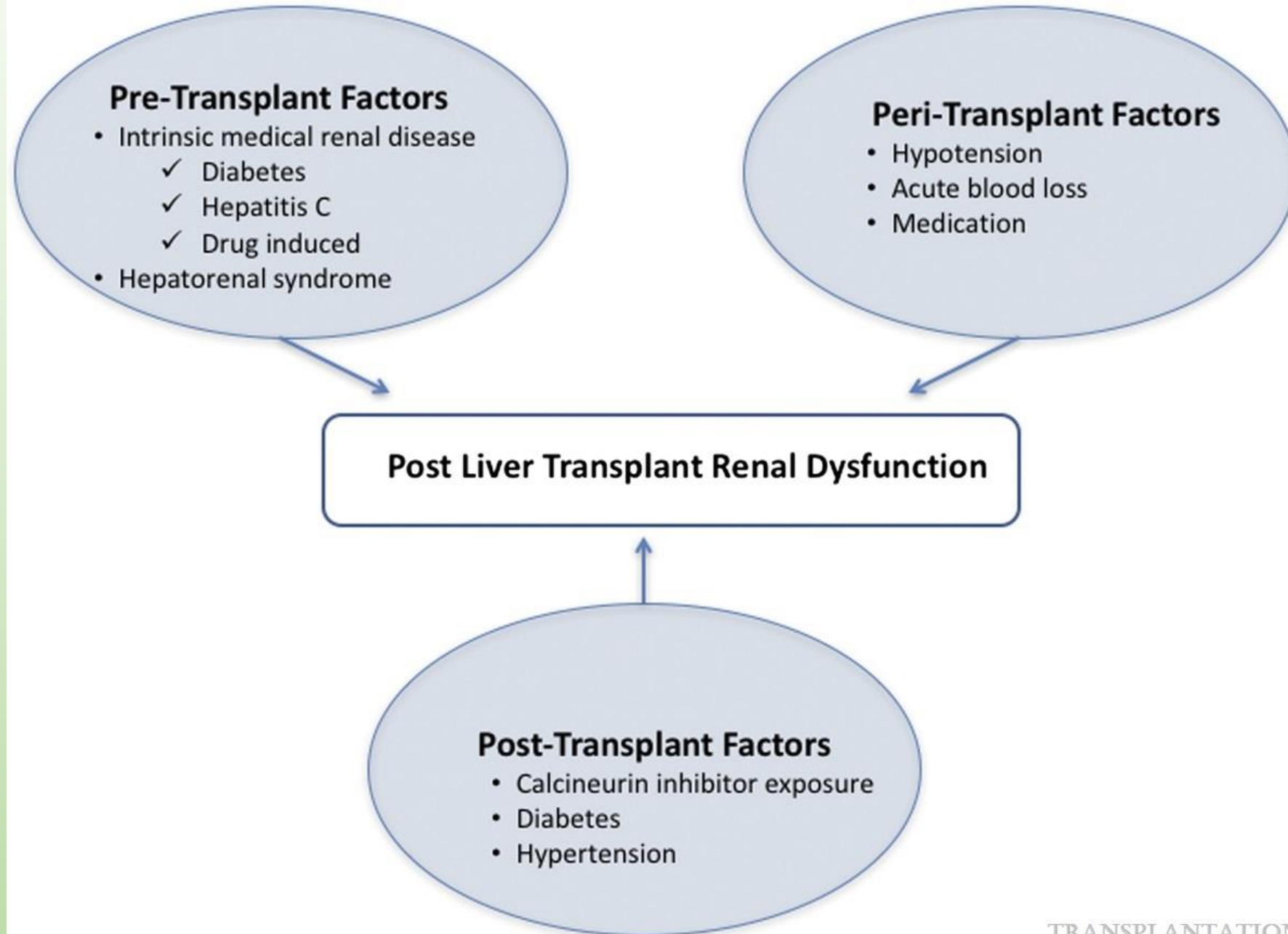
Lung transplantation

- Respiratory failure may experience renal ischemia
- likely to experience an episode of intraoperative hypoxemia
- Pre-transplantation mechanical ventilation
- Hypertension were associated with AKI after lung transplantation
- Capillary leakiness after lung transplantation may lead to the overuse of diuretics, which may also facilitate renal hypoperfusion

Acute Kidney Injury After Liver Transplantation

- Acute kidney injury (AKI) after liver transplantation (LT) is common with an incidence that exceeds 50% in some series
- In other series, about 15% of patients required transient renal replacement therapy (RRT) immediately after LT

Factors associated with development of post-LT AKI.



BIOMARKERS

- Scr is an imperfect marker for the early detection
- GFR may decrease significantly with only minimal effect on Scr
- IV fluid and massive transfusions lead to hemodilution of sCr
- Markers of acute tubular injury (neutrophil gelatinase-associated lipocalin [NGAL], kidney injury molecule-1, and interleukin-18
- Urinary NGAL either immediately pretransplantation, during surgery or early after the procedure predicts postoperative AKI.

In summary

- Post transplant AKI influence long and short term kidney function in kidney and non kidney transplant
- There are several cause of AKI in transplant recipient
- Infection and septic shock are the most common cause of AKI
- Severity of sepsis is related to kidney outcome

Thank for your attention