Kidney Transplantation

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Disclosure

• John Silkensen, MD has no financial relationships with commercial interest(s).
Learning Objective

• Explain referral and co-management strategies for kidney transplantation
Self Assessment Questions

1. Which of the following is not an absolute contraindication to kidney transplant?
   - Active substance abuse
   - Active malignancy
   - Life expectancy less than 2 years
   - GFR <20mL/min

2. A patient with progressive CKD is considering a kidney transplant. Which one of the following statements is correct?
   - CKD patients can be referred to a transplant center when their GFR is < 20 mL/min/1.73m²
   - Pre-emptive and living donor kidney transplants are associated with better graft survival
   - The most common cause of kidney transplant loss is death with a functional transplant
   - All of the above
Treatment Options for CKD/ESRD

• Hemodialysis
• Peritoneal dialysis
• Transplantation
History of Immunosuppression in Transplantation

• 1954: First organ transplant (kidney transplant between identical twins)
• 1960: Total lymphoid irradiation
• 1962: Azathioprine (AZA)
• 1963: AZA/steroid in combination
• 1967: Anti-lymphocyte globulin
• 1979: Cyclosporin A (CsA)
• Triple regimen of CsA, AZA, and steroid became the mainstay for years at many transplant centers
The Goal of Immunosuppression

• Achieve sufficient level to circumvent damage to the transplanted organ by the allogeneic response
• Provide low enough burden to allow recipient immune system to respond to infectious organisms and carry out surveillance for tumor cells
• Employ agents with complementary mechanisms of action to optimize efficacy of individual agents and reduce risk of toxicity associated with them
Achieving Balance in Transplantation
Principle of Kidney Transplantation

Iliac Fossa
Adjusted Relative Risk of Death among 23,275 Recipients of a 1st Deceased Donor Transplant

Key Concepts

• Transplanted patients have a healthier life, longer life and better quality of life
• Kidney transplantation is the most cost-effective modality of renal replacement
• Living donor kidney outcomes are superior to deceased donor kidney outcomes
• Early transplantation (either pre-emptive or within 1 year of dialysis initiation) yields the best results
• Early transplantation is more likely to occur in patients that are referred early to nephrologists
• Referral for transplant evaluation should occur when eGFR $\leq 20$ mL/min/1.73m$^2$
Key Concepts

• The most common cause of transplant loss is death with a functional transplant.
• The most common causes of death in a kidney transplant patient:
  o Heart disease +++
  o Infections
  o Malignancies
• Immunosuppressant medications are essential to prevent immunological loss of the transplant, but side effects can also lead to potential loss of transplant in addition to causing untoward side effects.
Eligibility

- Able to be evaluated once GFR < 20 mL/min
- Need just one test less than 20 mL/min to remain active on deceased donor kidney transplantation list
- With GFR 15-19 mL/min - can be transplanted if living donor or if six antigen match
- If GFR < 15 mL/min - open to all offers
- Why starting early - certain blood types have longer wait time, some potential recipients have no potential live donors, the wait-list is long
Contraindications to Kidney Transplantation

- Active malignancy
- Advanced lung disease
  - Chronic O2 needs
  - FEV$_1$ < 1
- Ongoing infection
- Life expectancy less than 2 years
- Active substance abuse
- Ischemic cardiac disease
  - Not amenable to revascularization
- Severe peripheral vascular disease
- Liver cirrhosis/primary oxalosis - unless combined liver/kidney
- Poorly controlled psychiatric illness
- Minimal rehabilitative potential
- Morbid obesity – BMI > 40
Trends in Transplantation

**Incident Transplant rates, unadjusted**

- % dialysis patients
- Transplant rate

**Wait List Counts**

- Counts: first listings
- Counts: subsequent listings
- Wait time: first listings
- Wait time: subsequent listings

**Total Transplants**

- Total
- Deceased donor
- Living donor

**Total functioning transplants**
Acute Rejection in the 1st Year Post-Transplant

Acute rejection rates during the first year post-transplant for recipients age 18 and older with a functioning graft at discharge. USRDS ADR 2014.
Causes of Death in Kidney Transplant Patients with a Functioning Graft 2010–2012

Mortality rate per 1,000 patient years

- Infection: 2.0
- Malignancy: 1.8
- CVD: 3.6
- Other: 3.1
- Unknown: 18.2

USRDS ADR 2014
Cardiovascular Disease

- CKD is a known cardiac risk factor
- Cardiac risk factors in the general population are likely operative in CKD patients
- Many patients with CKD have diabetes and hypertension
- Some factors unique to transplant patients may contribute to or increase the risk of cardiovascular disease
Post-Transplant Malignancy

- Risk is 4X to 100X compared to rates of malignancy in the general population (especially skin cancer)
- No comprehensive reporting system
- Available data suggests 2- to 3-fold under-reporting
- The precise rate is UNKNOWN
- Accounts for 10% of deaths in kidney transplant recipients with a functioning graft
- ➡ SCREENING is KEY!
  - Threshold for screening should be low.
Transplant Related Infections

• The majority of infections occur in the first month, often related to the GU tract
• In the first six months, infections associated with post-operative infections or enhanced immunosuppression are seen
• Long-term infectious complications often relate to the level of immunsuppression
## Immunization for Kidney Transplant Recipients

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Not Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Influenza types A and B (yearly)</td>
<td>• Varicella zoster</td>
</tr>
<tr>
<td>• Pneumovax (every 3-5 years)</td>
<td>• Intranasal influenza</td>
</tr>
<tr>
<td>• Diphtheria-Pertussis-Tetanus</td>
<td>• BCG</td>
</tr>
<tr>
<td>• Haemophilus influenza B</td>
<td>• Live oral typhoid</td>
</tr>
<tr>
<td>• Hepatitis A and B</td>
<td>• Measles, Mumps, Rubella</td>
</tr>
<tr>
<td>• Inactivated polio</td>
<td>• Oral polio</td>
</tr>
<tr>
<td>• Meningococcus</td>
<td>• Yellow fever</td>
</tr>
<tr>
<td></td>
<td>• Smallpox</td>
</tr>
<tr>
<td></td>
<td>• Live Japanese B encephalitis vaccine</td>
</tr>
</tbody>
</table>
Case Question

A 30 y/o man with diabetic nephropathy receives a living donor kidney transplant from his sister. He does well for the first 3 weeks, but then is seen in clinic with a fever and a creatinine elevation to 2.5 (from his baseline level of 1.4).

Which one of the following statements is correct?

A. The creatinine elevation could be related to volume depletion

B. The creatinine elevation may be related to a medication

C. The creatinine elevation could be a result of a urinary tract infection

D. All of the above
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D. All of the above—CORRECT!!!
Drugs the Effect CsA and Tacrolimus Levels

Induce P450 3A4 = increase metabolism and reduce levels

- Carbamazepine
- Phenobarbital
- Phenytoin
- Rifampin

Inhibit P450 3A4 = inhibit metabolism and increase levels

- Amiodarone
- Diltiazem
- Erythromycin
- Fluconazole
- Itraconazole
- Ketoconazole
Self Assessment Questions

1. Which of the following is not an absolute contraindication to kidney transplant?
   - Active substance abuse
   - Active malignancy
   - Life expectancy less than 2 years
   - *GFR <20mL/min*

   **Rationale:** GFR of <20mL/min is when patients should be referred for a consultation about renal transplant. All other answer choices are contraindications to transplant.

2. A patient with progressive CKD is considering a kidney transplant. Which one of the following statements is correct?
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   - Pre-emptive and living donor kidney transplants are associated with better graft survival
   - Most common cause of kidney transplant loss is death with a functional transplant
   - *All of the above*

   **Rationale:** All of the statements are correct regarding transplant.
Questions and Answers
Additional Resources

• Organ Procurement and Transplantation Network: http://optn.transplant.hrsa.gov

• United Network for Organ Sharing: http://www.unos.org