Factors Affecting Outcomes for Kidney Transplant Recipients

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I have nothing to disclose

Objectives

• Introduce basic concepts of kidney transplantation
• Review impact of recipient clinical characteristics on patient and graft survival
• Outline donor factors that affect transplant outcomes
  • KDRI calculation
• Provide overview of post-transplant clinical events that affect patient outcomes
Kidney Allografts Are Different Than Native Kidneys

- Heterotopic position
- Short ureter, no nerves, no valve
- Single kidney (almost always)
- Allogenic tissue (almost always)

Anatomy of a Heterotopic Renal Allograft
Successful Kidney Transplantation Has Huge Positive Impact on Recipients

- Increased lifespan
- Less hospitalizations
- Improved quality of life
- Lower costs to society and to insurers
  - Much lower health care costs over long term
  - Can often return to work
  - Often able to have children

Successful Kidney Transplantation Dramatically Improves Survival

Adjusted Relative Risk of Death among 23,275 Recipients of a First Kidney Transplant
Kidney Transplantation Is Largely Successful
(OPTN/SRTR 2012 Annual Data Report)

Half-life of Kidney Transplants
(OPTN/SRTR 2012 Annual Data Report)
Recipient Characteristics Strongly Impact Outcomes

- Diabetes
- CAD
- PVD
- HIV
- Hepatitis C
- Compliance

- Drug use
- Lung disease (and smoking)
- Obesity
- Nutrition
- Vintage of dialysis

Estimated Post-Transplant Survival (EPTS)

- UNOS/OPTN calculator used to help allocate kidneys
- Utilizes four variables:
  - Age of recipient
  - Diabetes status at time of transplant
  - Number of prior solid organ transplants
  - Length of time on dialysis
The Longer You Wait On Dialysis
The Worse the Outcomes


Predicting Coronary Heart Disease after Kidney Transplantation:
(PORT) Study

American Journal of Transplantation
Donor Quality Is Highly Variable and Highly Important

• Age
• Kidney size and volume
• Preexisting kidney disease in donor
• Hypertension
• Diabetes
• Hepatitis C
• Smoking?
• Drug use

KDRI Allows Some Quantification of Donor Impact on Allograft Survival

• Reported with all kidney offers
• 0-100%
• Takes into account clinical factors:
  • Serum creatinine
  • Age
  • Donor size (height and weight)
  • Hepatitis C serostatus
  • DCD donor
  • Donor diabetes and HTN
  • Donor race
New Allocation Rules Are About to Take Effect

- Kidneys traditionally allocated based on time (and to some extent immunology)
- First effort to maximize life years gained from individual grafts
- Sensitization is weighed more heavily
- Wait time will be calculated from time of start of dialysis

Peri-operative Events Matter

- Cold ischemia time
- Warm ischemia time/DCD
- Ischemic-reperfusion injury
- Delayed graft function (DGF)
- Compromised allograft blood flow
- Compromised urodynamics
- Medication toxicity
Immunosuppression is Wonderful and Terrible

- Toxicity is the rule:
  - Immune-related
  - Non-immune related
- Calcineurin inhibitors have dramatic long-term nephrotoxicity but deliver excellent short- and intermediate-term results
- Newer agents being tried, unclear impact on long term patient and graft survival

Individual Immunosuppressive Drugs and Sites of Action in the Three-Signal Model

Post-transplant Events That Affect Outcomes

- NODAT
- Rejection (cellular, humoral, mixed)
- Development of donor-specific antibody
- BK viremia and nephropathy
- Recurrent disease
- Cardiovascular disease progression
- Infection
- Malignancy

Malignancy After Transplant

- Differential risk depending on type of malignancy
- PTLD
- Dermatologic malignancies
- Renal cell carcinoma (native kidneys)
- Donor-derived malignancy
- Others
Graft Function Closely Tracks with Outcomes

- Serum creatinine at 1 year
- eGFR, GFR, slope in 1/creatinine
- Proteinuria
- Biopsy findings
  - IFTA
  - Transplant glomerulopathy
  - Footprints of humoral response
    - C4D, peritubular capillaritis
    - Recurrent glomerulopathy

Graft Function Directly Relates to Patient Survival

- In a sense all kidney transplant recipients have a form of CKD
- More grafts are lost with death of patient than rejection
- Cardiovascular risks dominate– blood vessel health is key
  - Framingham and non-Framingham risk factors
  - CVD risk tracks with kidney function measures
Patient Compliance is the Key to Good Outcomes

- Missed meds track with diminished graft survival
- Challenges with changing insurance
  - Young adults on and off parents’ insurance
  - Loss of Medicare coverage
  - Loss of dialysis-supported secondary insurance
- Challenges with different caregivers and institutions
- Awareness of impact of side effects of medications on patients’ lives

Combined and Sequential Transplantation

- Combined solid organ transplants not uncommon, especially kidney-liver
- Sequential transplants have worse outcomes
- Repeat kidney transplants
  - Increasingly common
  - Carry elevated immunological and operative risk
Contact me

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