Kidney Transplant Fundamentals: Evaluation, Selection, and Surgical Considerations

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Kidney Transplant Fundamentals: Evaluation, Selection, and Surgical Considerations

Learning Objectives

By the end of this module, students will be able to:

1. Evaluate potential kidney transplant recipients using current guidelines and contraindication frameworks
2. Differentiate between living and deceased donor evaluation and procurement strategies
3. Explain HLA matching, crossmatching techniques, and the clinical significance of donor-specific antibodies (DSA)
4. Assess patient sensitization using panel reactive antibody (PRA) calculations
5. Describe the surgical technique of renal transplantation and immediate post-operative management
6. Discuss ABO-incompatible transplantation protocols and outcomes
7. Evaluate the impact of kidney donor profile index (KDPI) and estimated post-transplant survival (EPTS) scoring on allocation decisions
8. Explain paired kidney exchange programs and their impact on waitlist dynamics

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I. TRANSPLANT RECIPIENT EVALUATION

A. General Principles

Kidney transplantation is the renal replacement therapy of choice for eligible ESRD patients, offering superior survival and quality of life compared to dialysis. Comprehensive pretransplant evaluation addresses both transplant candidacy and pretransplant comorbidity optimization.

Key Timeline: Average time from referral to transplantation is 3-6 months for living-related donors, 6-12 months for living unrelated donors, and variable for deceased donors (average wait time now exceeds 5 years nationally in the US).

B. Absolute Contraindications (Relative Assessments Required)

Contraindication	Rationale	Current Perspective
Active malignancy	Immunosuppression increases recurrence risk	Transplant most solid malignancies 2-5 years post-cure; some advocate earlier (>2 yr) with close monitoring
Active untreated infection	Risk of dissemination on immunosuppression	May proceed if documented sustained negative cultures (e.g., TB)
Severe cardiac disease (NYHA IV, uncontrolled arrhythmia)	High perioperative and early graft loss	Cardiac optimization essential; LVEF >30% generally required
Expected survival <5 years (non-renal)	Transplant benefit predicated on allograft survival	Individual assessment; many >60 yr successfully transplanted
Psychosocial inability to comply	Immunosuppression adherence critical	Pre-transplant psychosocial evaluation and support essential
Active substance abuse	Compliance and allograft injury risk	Minimum 6-12 months sobriety generally required

C. Relative Contraindications and Optimization

Age: No absolute upper age limit; outcomes in carefully selected octogenarians are favorable.

Obesity: BMI >40 kg/m² carries increased surgical and metabolic morbidity. Pretransplant weight loss (goal: BMI <35) recommended.

Diabetes: Requires intensive glycemic control; HbA1c >8.5% warrants delay for optimization.

Cardiovascular disease: Stress testing (dobutamine echo or nuclear) recommended if >5 risk factors or prior events. Coronary angiography considered based on symptomatology and functional capacity.

Chronic infections: - **Hepatitis C:** Now may be transplanted with DAA therapy planned pre- or post-transplant - **Hepatitis B:** Vaccination or prophylaxis strategies deployed; HBsAg+ patients transplanted with antiviral therapy - **HIV:** CD4 >200 cells/μL, undetectable viral load, and ART adherence required

Renal disease recurrence: Patients with FSGS, IgA nephropathy, membranoproliferative GN, and hemolytic uremic syndrome (HUS) have variable recurrence but are generally not absolute contraindications.

II. DONOR EVALUATION AND SELECTION

A. Living Donor Evaluation

Living donor kidneys provide superior long-term outcomes compared to deceased donor kidneys, with 10-year graft survival rates of 60-70% vs. 45-55%.

Medical Evaluation Components:

1. **Renal function assessment:**
   - Serum creatinine and calculated GFR (KDIGO preferred)
   - Baseline proteinuria (<150 mg/day acceptable)
   - Absence of hypertension or controlled BP on ≤1 agent
2. **Cardiovascular screening:**
   - HTN, DM, CAD risk stratification
   - Stress testing if significant risk profile
   - Goal: preserve donor long-term health
3. **Metabolic assessment:**
   - Glucose tolerance; DM is contraindication
   - Lipid panel
   - Bone health (DEXA scan if risk factors)
4. **Infectious disease screening:**
   - HIV, HBsAg, anti-HBc, anti-HCV, RPR, CMV IgG, EBV IgG
   - Additional testing for endemic regions (Chagas, TB)
5. **Imaging:**
   - Renal ultrasound (assess size, exclude masses)
   - Renal artery duplex (multiple vessels increase surgical complexity)
   - Consider CT angiography for anatomic variants
6. **Psychological and social assessment:**
   - Verify informed consent, understand risks and life expectancy reduction
   - Screen for coercion, financial inducement
   - Ensure appropriate expectations regarding recipient outcomes

Living Donor Outcome Data: Donors have slightly elevated risk of ESRD (RR ~1.5-2.0 compared to general population) but maintain excellent quality of life with one kidney; lifespan unchanged.

B. Deceased Donor Evaluation

Standard Criteria Donors (SCD): Age <50 years, absence of significant HTN/DM, SCr <1.5 mg/dL.

Expanded Criteria Donors (ECD): Age ≥50 years OR (age 40-49 AND serum creatinine >1.5 mg/dL) OR history of hypertension or diabetes.

Donation After Cardiac Death (DCD): Donor support withdrawn after cardiac arrest; kidneys procured during ischemic time. Associated with higher delayed graft function (DGF) rates (~50%) but good long-term outcomes.

Donor Risk Assessment: - Donor age and comorbidities (HTN, DM, CVD history) - Cause of death (trauma, stroke, anoxia) - Donor renal reserve and biopsy findings (if obtained)

Key Laboratory Parameters: - Serum creatinine (baseline renal function proxy) - BUN, electrolytes - Liver function (assess organ integrity) - Blood cultures, serologies, toxicology

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III. IMMUNOLOGICAL COMPATIBILITY ASSESSMENT

A. ABO Blood Group

Basis: Natural IgM antibodies against incompatible blood group antigens present from infancy.

ABO Type	Can Donate To	Can Receive From
O	O, A, B, AB	O
A	A, AB	O, A
B	B, AB	O, B
AB	AB	O, A, B, AB

ABO-Identical transplantation offers superior outcomes; ABO-compatible grafts function well with modern immunosuppression.

B. HLA Typing and Matching

HLA System: Human leukocyte antigens (HLA) present on all nucleated cells; major targets of adaptive immune response against allograft.

HLA Loci Tested: HLA Class I (A, B, C) and Class II (DR, DQ, DP).

HLA Matching Grade:

Mismatch	Description	Impact
0-ABDR	Identical (rare)	Best outcomes; lowest rejection
1-2 ABDR	Well-matched	Excellent outcomes
5-6 ABDR	Fully mismatched	Acceptable with modern IS; requires close monitoring

Clinical Significance: With modern immunosuppression, HLA mismatch burden has diminished but remains relevant for long-term graft survival. Zero-mismatch grafts have superior 10-year survival.

C. Crossmatching

Complement-Dependent Cytotoxicity (CDC) Crossmatch: - Traditional method; detects recipient IgG antibodies binding donor lymphocytes - Positive crossmatch = contraindication to transplant in standard practice

Flow Cytometry Crossmatch: - More sensitive; detects weak IgG and IgM antibodies - Used to refine CDC-negative cases

Luminex Single Antigen (SAB) Beads: - Identifies specific HLA antibodies against donor antigens - Detects donor-specific antibodies (DSA) - Gold standard for contemporary pretransplant assessment

HLA Antibody Definitions:

Category	Significance
Donor-Specific Antibodies (DSA)	IgG antibodies targeting donor HLA antigens; major risk factor for rejection
Non-Donor-Specific Antibodies (non-DSA)	IgG to HLA antigens not on donor; lesser threat but may contribute to chronic inflammation
Class I DSA	Target HLA-A, -B, -C; associated with antibody-mediated rejection (AMR) and chronic AMR
Class II DSA	Target HLA-DR, -DQ, -DP; emerging evidence of independent risk for AMR and graft loss

D. Panel Reactive Antibody (PRA) and Sensitization

Definition: Percentage of population against which recipient has detectable IgG antibodies.

Calculation: - Percentage of panel cells bearing HLA antigens recognized by recipient serum - PRA >10-20% considered sensitized; impacts urgency allocation and transplant access

Clinical Impact: - Highly sensitized patients (PRA >80%) have limited compatible donors; spend extended time on waitlist - Sensitization from prior transplants, transfusions, pregnancy, or dialysis transfusions - Requires compatible or ABO-incompatible transplant protocols

Mean Fluorescence Intensity (MFI): - Quantifies DSA strength via Luminex - MFI >1000-2000 considered significant risk for hyperacute or acute rejection - Used to risk-stratify transplant candidates

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IV. SURGICAL TECHNIQUE AND IMMEDIATE POST-OPERATIVE MANAGEMENT

A. Surgical Approach

Standard Procedure: 1. **Incision:** Heterotopic placement in iliac fossa (Gibson incision), not replacing native kidneys 2. **Vascular anastomosis:** Donor renal artery to internal iliac (or external iliac) artery; renal vein to external iliac vein 3. **Ureteral anastomosis:** Ureteroureterostomy (to native ureter) or ureteroneocystostomy (to bladder); most commonly ureteroneocystostomy 4. **Native kidneys:** Left in place unless infected, causing hypertension, or polycystic disease

Surgical Considerations: - Ischemic time (cold ischemia time, CIT) impacts DGF risk; <20 hr ideal, <30 hr acceptable - Warm ischemia time during vascular anastomosis kept minimal - Arterial and venous complications (thrombosis, stenosis) occur in 1-3% of cases

B. Immediate Post-Operative Management (First 24-48 Hours)

Graft Function Monitoring: - Hourly urine output (expect 100-200+ mL/hr initially) - Serum creatinine decline (ideal: 10-25% daily drop if DGF not present) - Ultrasound with Doppler: assess perfusion, exclude fluid collections, evaluate ureter

Delayed Graft Function (DGF): - Defined as need for dialysis in first post-op week - Occurs in 15-25% of deceased donor, 5% of living donor transplants - Managed conservatively with fluid management and dialysis; does not necessarily indicate graft loss - Monitor for hyperkalemia, acidosis, volume overload

Immunosuppression Initiation: - Induction agents started intraoperatively or immediately post-op - Maintenance agents initiated (tacrolimus, mycophenolate, prednisone typically) - Dosing adjusted for renal function and drug levels

Fluid and Electrolyte Management: - Goal: euvolemia; CVP 5-10 cm H_2O - Aggressive hydration in first 24-48 hr supports urine output and graft perfusion - Monitor potassium, phosphate, magnesium closely - Acidosis correction if pH <7.2

Prophylaxis: - Antibiotic: single-dose prophylaxis (cephalosporin, fluoroquinolone) - CMV prophylaxis (valganciclovir) if donor/recipient mismatch (D+/R- highest risk) - PCP prophylaxis (TMP-SMX) started day 1 if sulfa-tolerant

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V. ABO-INCOMPATIBLE TRANSPLANTATION

A. Background and Rationale

ABO-incompatible (ABOi) transplantation overcomes blood group incompatibility through desensitization, expanding donor pool and reducing waitlist times. Living related ABOi grafts historically had ~50% 3-year survival; modern protocols achieve >90% 1-year and 70-80% 5-year graft survival.

B. Desensitization Strategies

Plasmapheresis-Based Protocols: - Plasma exchange to remove IgG isohemagglutinins (target: titer <1:4 or <1:8) - Performed 3-5 times in week preceding transplant - Goal: reduction of IgG to donor ABO antigen

Immunoadsorption Columns: - ABO antigen-coated columns selectively remove anti-ABO IgG - More efficient than plasmapheresis; allows same-day transplant in some protocols

Splenectomy: - Historically performed; rationale is to remove antibody-producing B cells - Current protocols often omit splenectomy; not essential with modern IS

Low-Titer Protocols: - Single-donor immunoglobulin (IVIG), rituximab, and minimalist plasmapheresis - Reducing procedural burden while maintaining excellent outcomes - Requires careful titer monitoring (target IgG <1:4 pre-op)

C. Post-Transplant Management

Monitoring: - ABO antibody titers at regular intervals post-op - Rejection surveillance with protocol biopsies in early period - Graft function trending

Prevention of Hyperacute Rejection: - Induction therapy with T-cell (ATG, thymoglobulin) or B-cell (rituximab) agents - Tacrolimus-based maintenance with goal trough 8-12 ng/mL - Mycophenolate and corticosteroids

Outcomes: Modern ABOi protocols achieve graft survival comparable to ABO-compatible grafts when desensitization is successful.

VI. PAIRED KIDNEY EXCHANGE PROGRAMS

A. Concept and Mechanics

Problem: Incompatible living donor-recipient pairs (ABO incompatible, crossmatch-positive, or HLA sensitized) previously had limited transplant options.

Solution: Paired kidney exchange (PKE) matches incompatible pairs with other incompatible pairs, creating mutually compatible swaps.

Example: - Pair 1: Recipient A (O blood type) with Donor B (AB blood type) — incompatible - Pair 2: Recipient B (AB blood type) with Donor A (O blood type) — incompatible - Solution: Swap donors; both recipients receive compatible kidneys

B. Extended Matching Chains

Desirable Donor (DD) Chain: Initiated by altruistic non-directed donor (NDD); chains of swaps continue until an incompatible pair "closes" the chain by providing a kidney to the national waiting list.

Bridge Donor Chain: Similarly initiated but require closure differently.

National Kidney Registry: Facilitates multi-center coordination; 6-way, 8-way, and larger exchanges documented.

C. Impact and Outcomes

Benefits: - Reduces waiting time for incompatible pairs - Increases access to living donor transplantation - Improves HLA matching opportunities (paradoxically, exchange participants often achieve zero mismatches) - Equivalent outcomes to standard living donor transplants

Logistics: Synchronized surgeries (often at multiple centers) ensure fairness and prevent exploitation.

Ethical Considerations: Strict non-coercion protocols; thorough informed consent; altruistic donation encouraged.

VII. KDPI AND EPTS SCORING

A. Kidney Donor Profile Index (KDPI)

Definition: Percentage likelihood that a deceased donor's kidney(s) will fail before a reference kidney from an average donor.

Formula: Incorporates donor age, height, weight, race/ethnicity, history of hypertension, history of diabetes, cause of death (cerebrovascular vs. other), and serum creatinine.

KDPI Range	Interpretation	Clinical Application
0-20%	Excellent donor	Allocated to younger recipients (EPTS <20%) in new allocation system
21-35%	Very good	Flexible allocation
36-50%	Good	Acceptable for most recipients
51-80%	Marginal	Expanded criteria donors; acceptable for older/sicker recipients
81-100%	Poor**	Very marginal; consider in highly sensitized or long-waitlist patients

Clinical Significance: KDPI is predictor of graft survival; lower KDPI (better donor quality) allocated preferentially to younger, healthier recipients expected to have longer life expectancy.

B. Estimated Post-Transplant Survival (EPTS)

Definition: Percentage likelihood that a recipient will survive for at least 20 years after transplantation.

Factors: Age, dialysis vintage, BMI, diabetes status, prior transplant history.

EPTS Range	Interpretation	Clinical Application
0-20%	Excellent survival expected	Prioritized to receive best-quality kidneys (KDPI <20%)
21-35%	Very good survival expected	Standard allocation
36-50%	Good survival expected	Flexible allocation
51-100%	Limited survival expected	Allocated marginal kidneys (KDPI >80%) or in-region priority

Allocation Impact: KDPI/EPTS matching system implemented 2015 by UNOS aims to maximize overall life-years gained from the donor pool by pairing best donors with longest-living recipients and marginal donors with shorter-living recipients.

Controversy: System benefits younger, healthier recipients; may disadvantage older/sicker dialysis patients but optimizes population-level outcomes.

VIII. CLINICAL PEARLS

1. **Pre-transplant optimization is essential:** Ensure excellent glycemic control (HbA1c <7%), blood pressure control, cardiac assessment, and dental care before transplantation.
2. **Living donor kidneys are superior:** Encourage living donation; develop a strong living donation education program in your practice.
3. **Crossmatch interpretation requires context:** CDC-negative/SAB-positive (donor-specific antibody with negative CDC crossmatch) may be acceptable in modern protocols with desensitization; discuss with immunology.
4. **DGF is common in deceased donor transplants but not catastrophic:** 80-90% of DGF kidneys achieve excellent long-term function; manage expectantly with dialysis support.
5. **ABO incompatibility is not absolute:** Modern desensitization protocols achieve excellent outcomes; expand donor pool when appropriate.
6. **KDPI/EPTS matching optimizes population-level outcomes:** Accept that marginal kidneys in older recipients may provide net benefit; discuss realistic expectations.
7. **Surgical anatomy varies:** Multiple renal arteries (20%), early branching, and retroaortic/circumaortic positioning require imaging review to minimize vascular complications.
8. **Native kidneys are retained:** Unless chronically infected, severely hypertensive, polycystic, or causing other complications.
9. **Transplant benefit begins at referral:** Shorter dialysis vintage correlates with superior outcomes; refer early (when GFR 15-20 mL/min/1.73 m^2).
10. **Transplant is superior to dialysis:** At any age, transplant offers superior survival, quality of life, and cost-effectiveness vs. long-term dialysis.

IX. PRACTICE QUESTIONS

Question 1: A 68-year-old man with ESRD from hypertensive nephrosclerosis presents for transplant evaluation. He has controlled hypertension on one agent, no diabetes, normal BMI, and recent normal stress test. His living brother (age 62) offers to donate. Pretransplant evaluation of the living donor reveals: - Serum creatinine 1.1 mg/dL, calculated GFR 65 mL/min/1.73 m^2 - BP 135/80 on no medications - No proteinuria - Normal imaging - Willing and psychologically cleared

Is this living donor appropriate?

A) No, because he is >60 years old
B) Yes, with counseling regarding his baseline renal function and age
C) No, because his GFR is <70 mL/min/1.73 m^2
D) Yes, but only if the recipient undergoes splenectomy

Answer: B. Age alone is not a contraindication; this donor meets criteria with acceptable renal function (GFR 65), normal BP on no medications, and no proteinuria. Counseling should address his baseline GFR and slight age-related renal function decline post-donation but is not prohibitive.

Question 2: A 35-year-old dialysis patient with prior failed transplant (failed 8 years ago from chronic rejection) is being reevaluated for transplant. Current sensitization: - Class I PRA 40%, Class II PRA 25% - Luminex SAB reveals multiple high-MFI class I and class II DSA from prior graft - Wants to move forward with transplant

Which statement is most accurate regarding this candidate's sensitization?

A) He should remain on dialysis indefinitely due to high sensitization
B) He is a candidate for desensitization and/or compatible paired exchange
C) He requires splenectomy before any transplant can be performed
D) His prior rejection history is an absolute contraindication to retransplantation

Answer: B. This patient is sensitized (PRA >30%) but not an absolute contraindication. Desensitization protocols (plasmapheresis, IVIG, rituximab) and/or paired kidney exchange programs can expand his donor pool. Prior transplant failure is not absolute contraindication to retransplant, especially with modern immunosuppression.

Question 3: A deceased donor kidney has KDPI 85%. The two potential recipients are: - Recipient A: 45 years old, EPTS 15%, 2 years on dialysis - Recipient B: 72 years old, EPTS 75%, 5 years on dialysis

According to current UNOS allocation policy, which recipient should receive priority?

A) Recipient A, because he is younger
B) Recipient B, because he is older and has fewer remaining years
C) The kidney should not be transplanted due to high KDPI
D) Recipient B, because KDPI/EPTS matching indicates marginal kidneys should go to recipients with limited survival

Answer: D. This high-KDPI (85%) marginal donor kidney should be allocated to the recipient with limited expected post-transplant survival (Recipient B, EPTS 75%) to maximize overall life-years gained. Recipient A with excellent EPTS (15%) should be reserved for better-quality kidneys (lower KDPI).

See Also

Related Student Handouts

- Transplant Complications
- Transplant Immunosuppression
- Dialysis Fundamentals
- CKD Complications

Clinical Content (01-Clinical-Medicine/Nephrology)

- Kidney Transplantation Hub
- Essential Renal Laboratory Tests

Butler-COM Resources

- Butler COM - Nephrology Deep Dive

X. REFERENCES

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Clinical Resources

- Clinical Review: Immunosuppression Transplant Review — Comprehensive clinical review with PubMed references