Renal Transplant for the Primary Care Physician

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Disclosures

- Study participant for:
  - APOLLO (NIH)
  - KOAR (CareDx)
  - Mercury (Medeor Therapeutics)

- Currently employed by Loyola University Medical Center (2018-Current)

- Previously employed at the University of Illinois at Chicago (2015-2018)
Objectives

- Understand the reasons for early referral for kidney transplant
- Identify risk factors in patients seeking kidney transplants
- Understand the work-up for kidney transplant
- Know common side effects from transplant medications including medication interactions
- Realize the risk of malignancies post-transplant and surveillance for them
- When to refer the patient back to the transplant center
- Discuss new innovations in transplantation
Renal Transplant

- Dialysis only performs a fraction of the work that a functioning kidney does

- Preemptive kidney transplant patients live an average of 10-15 years longer than if they remained on dialysis

- Even adults as old as age 75 gain an average of four more years after transplant than if they stayed on dialysis
Recipients of a Kidney Transplant Have a Longer Life Expectancy Than Patients Who Remain on Dialysis

Based on estimates from 2012, recipients of a kidney transplant had about 2.5 times more remaining years of life than patients on dialysis

Increase access to available organ transplants
Expand reimbursement for living organ donors
Encourage development of artificial kidneys
Launch awareness initiative for the disease
Development of payment model that creates incentives for kidney transplants and home dialysis for Medicare beneficiaries

Spending on a dialysis patient is more than $89k/year vs. $35k/year for a transplant patient
I do sympathize with you, sir, but I'm afraid it cannot be viewed as 'carry on' luggage.
Early Referral

- Preemptive transplant associated with a reduced risk of death
- Avoidance of the morbidity associated with dialysis
- Some centers report increased graft survival with preemptive transplant
  - North American Pediatric Renal Transplant Cooperative Study Group

Early Referral


- 13.2% of the patients were preemptive transplants.
  - Most of them were s/p living donor transplants.
  - 38.6% were s/p deceased donor transplants.

Early Referral

- Preemptive transplant was associated with improved patient and graft survival regardless of donor status
- Lower rate of Delayed Graft Function (DGF) with preemptive transplants
  - DDKT—8.4% v. 25.6%; P < 0.001
  - LDKT—2.6% v. 6.1%; P < 0.001

How does the transplant process begin?

The Process of transplant begins when a CKD patient:

1. Expected to start renal replacement therapy in the next 12 months
2. Patient with kidney function < 20% (GFR < 20 mL/min) and not on dialysis
3. Patients on dialysis: ASAP or when medical condition stabilizes if they have one.

Early referral is important since graft outcome is determined by duration of dialysis

* Five and 10 yr Graft outcome based on dialysis duration
Early Referral

- Less likely to be referred early for kidney transplant:
  - Ethnic minorities
  - Lower socioeconomic status
  - Patients disadvantaged with their geographic location


Early Referral

- Consider referral to transplant center at an eGFR < 25-30 mL/min

- This benefits those that have a rapid decline in their kidney function

- This is advantageous to those who might require extra time for work-up
  - Obese and needs to lose weight for renal transplant
  - Has a malignancy that requires a waiting period before the patient can be active on the waitlist. Oftentimes, these malignancies are found during work-up.

- Insurance issues/financial issues

- Other psychosocial issues
Early Referral -- Obesity

- Obesity—no magic number for BMI and kidney transplant—center specific
- Overall, for all obese patients, there is a survival advantage to kidney transplant
  - Krishnan et al – UK Renal Registry from Jan 2004-Dec 2010 comparing survival between transplanted patients and those who remained on waitlist in 17,681 patients.
  - 1- and 5-year survival was significantly better in all BMI bands (P < 0.0001) from BMI less than 18.5 to BMI over 40
  - Possible selection bias?
- Analysis of 27,377 patients from the UNOS database showed that a BMI > 35 kg/m^2 is independently associated with an increased risk of DGF, prolonged hospitalization, acute rejection and decreased overall graft survival

Early Referral – Malignancy

- Malignancy

- 53% of recurrences occur in patients transplanted within 2 years of their cancer treatment

- 34% of recurrences if the interval is between 2-5 years

- 13% recurrence if the interval between treatment for malignancy and transplant is over 5 years

Penn I. The effect of immunosuppression on pre-existing cancers. Transplantation 1993; 55: 742-747
Early Referral – Malignancy

- Low Risk of Recurrence (< 10%)
  - Testicular
  - Thyroid
  - Uterine/cervix
  - Lymphoma

- Intermediate Risk of Recurrence (11-25%)
  - Colon
  - Breast
  - Prostate

- High Risk of Recurrence (> 25%)
  - Melanoma
  - Invasive urothelial
  - Multiple myeloma
  - sarcoma

Early Referral – Malignancy

- Liver CA – transplant not recommended w/o liver transplant
- Multiple Myeloma – transplant not recommended
- 5-year wait recommended
  - Malignant melanoma
  - Breast cancer
  - Cervical/uterine cancer

Risks Ahead
Risk Factors for Potential Kidney Transplant Recipients

- Time on dialysis
- Obesity
- Patients with a history of malignancy
- Cardiovascular disease
- Diabetes
- Peripheral Vascular Disease
- Race
- Age
- Multi-Parity
- Patients who have received blood transfusions
- Social factors including education, socioeconomic status and support at home
- NON-ADHERENCE
"I'VE BEEN HERE SO LONG I DON'T REMEMBER WHAT I DID, BUT IT HAD SOMETHING TO DO WITH NON-COMPLIANCE."
Risk Factors for Potential Kidney Transplant Recipients

- Time on dialysis
- 2014 allocation policy guidelines
- For those patients who were listed after their dialysis start date, their wait time is backdated to the date of dialysis initiation
Risk Factors for Potential Kidney Transplant Recipients

- CONTRAINDICATIONS:
  - Disseminated or untreated CA
  - Severe psychiatric disease
  - Unresolved psychosocial problems
  - Persistent substance abuse
  - Severe coronary artery disease or refractory CHF
Risk Factors for Potential Kidney Transplant Recipients

- Relative Contraindications:
  - Structural GU abnormality
  - Recurrent UTIs or other recurrent infections
  - EF of less than 30% (¿ Heart-kidney?)
  - Severe pulmonary hypertension
  - Advanced PVD
Risk Factors for Potential Kidney Transplant Recipients

- No longer a contraindication:
  - Hepatitis C
  - HIV

UP TO 30% OF PEOPLE LIVING WITH HIV HAVE ABNORMAL KIDNEY FUNCTION. UNTREATED KIDNEY PROBLEMS CAN BE FATAL.
Work-up

Candidate Selection
- Advanced CKD; as evidenced by the need for renal replacement therapy
- GFR ≤ 20 ml/min: required for deceased donor listing only
- Ability to provide fully informed consent for evaluation and surgery
- Ability to comply with post-transplant regimen
- Age – center specific
- Social support/Caregiver support
Work-up

- Financial Coordinator
- Social worker
- Nutritionist
- Transplant Coordinator
- Transplant Surgeon
- Transplant Nephrologist
- Psychologist – if indicated
- Other specialists – if indicated
Work-up

- Dental Clearance
- Includes age-appropriate cancer screening
  - PSA for prostate CA – males over age 40
  - PAP Smears
  - Mammograms – females over age 40
  - Colonoscopy
Work-up

- **Special Tests:**
  - Blood Group
  - Crossmatch (compatibility with donor)
  - Human Leukocyte Antigen (HLA) typing
  - Panel Reactive Antibodies (PRA)
    - PRA score is a percentage up to 100%
    - Represents the proportion of the population to which the person being tested will react via pre-existing antibodies that will target HLA.
Work-up – Infectious Disease Tests

- CMV IgG
- EBV IgG
- HIV I/II
- HTLV I/II
- Hepatitis A, B, C
- RPR- Syphilis
- VZV IgG

- HSV I/II Ab
- Mumps IgG
- Rubella IgG
- Rubeola IgG
- Quantiferon Gold
Work-up – Vaccines

- Hepatitis A & B
- HPV if applicable
- MMR
- VZV/Shingles
- Pneumonia
- Flu shot
"Do you mean just everyday living isn't enough of a stress test?"
Work-up – Cardiac Testing

- Cardiology consult (when indicated)
- EKG
- 2D-ECHO with EF and Pulmonary artery pressure reading

- Stress ECHO or Nuclear Stress
  - High risk patients $\geq 45$ y/o
  - All patients with DM
  - All patients with ESKD $> 2$ years
  - When indicated
Work-up – Imaging

- CXR
- CT Abdomen without contrast
- Dopplers of legs if needed
- Brain imaging if PCKD

- Carotid u/s
  - Bruit
  - Stent
  - Endarterectomy
  - h/o CVA/TIA
Antigen-presenting cell

"Cascade" of events activating:
- T-helper cells
- Natural Killer T cells
- Macrophages
- B cells & Ab production

Death of foreign cell type

T cell (being activated)

- Foreign antigenic peptide
- T cell Receptor
- ITAMs
- Calcineurin
- NFAT (inactive) → NFAT (active)
- mTOR
- IL-2
- IL-2 Receptor

T cell proliferation

Cell Cycle:
- G1
- S
- M
- G2

Nuclear transcription of cytokine genes

IL-2 mRNA

http://tmedweb.tulane.edu/pharmwiki/doku.php/organ_transplantation
Principles of Immunosuppression

- Immune Reactivity and Likelihood of Rejection are highest initially
- Use low doses of several drugs with non-overlapping toxicities
- Fine balance to avoid
  - Under-suppression → rejection
  - Over-suppression → infections and malignancy
Post Kidney Transplant

Medications:

- Induction agent
  - T-cell depleting agent – thymoglobulin
  - Cell mediated lysis - alemtuzumab
  - IL-2 receptor antibody – basiliximab – blocks IL-2 from binding to lymphocytes and inhibiting proliferation of T-cells.

- Maintenance immunosuppression
  - Calcineurin Inhibitors – tacrolimus or cyclosporine
  - Antimetabolite – mycophenolate, azathioprine
  - mTOR (mammalian target of rapamycin) inhibitor – sirolimus or everolimus
  - Corticosteroid – prednisone
  - Other agents: belatacept – anti-CD28 – blocks B7 ligands on APCs which are essential for costimulation in T-cell activation
Costimulation is the critical second signal.

Signal 1:
- Antigen triggers T-cell receptor

Signal 2:
- Costimulation

Activated T cell:
- Proliferation
- Cytokine production

No costimulation:
- No cell division
- No cytokine production
- Anergy
- Apoptosis

Source: Kidney Int © 2012 International Society of Nephrology
Toxicity Profiles of Immunosuppressive Meds

- **Corticosteroids**
  - Mild-moderate adverse effect
  - PTDM/NODAT (new onset diabetes after transplant)
  - Dyslipidemia
  - Moderate-severe adverse effect
  - Osteopenia
  - HTN

- **mTORi**
  - Mild-moderate adverse effect
  - PTDM/NODAT
  - Anemia & leucopenia
  - Delayed wound healing
  - Moderate-severe adverse effect
  - Dyslipidemia
  - Proteinuria
Toxicity Profiles of Immunosuppressive Meds

- **Cyclosporine**
  - Mild-moderate
    - NODAT
    - Dyslipidemia
    - Osteopenia
    - Decreased GFR
  - Moderate-severe
    - HTN

- **Tacrolimus**
  - Mild-moderate
    - HTN
    - Diarrhea/Nausea/Vomiting
    - Decreased GFR
  - Moderate-severe
    - NODAT
Toxicity Profiles of Immunosuppressive Meds

- **Mycophenolate**
  - Mild-moderate
  - Anemia & leucopenia
  - Moderate-severe
  - Diarrhea, n/v
  - Teratogenic—must educate patients about this and discuss birth control

- **Azathioprine**
  - Mild-moderate
  - Anemia & leucopenia
  - Caution—do not prescribe allopurinol with azathioprine
Drug Interactions with CNIs

- **Decreased concentrations:**
  - Phenytoin
  - Carbamazepine
  - Rifampin
  - St. John’s Wort

- **Increased concentrations:**
  - Macrolides except Azithromycin
  - Non-dihydropyridine CCBs
  - Triazole antifungals
  - Protease inhibitors
  - Grapefruit juice
PTDM Risk Factors

- Older age
- Higher body mass index (30)
- African American and Hispanics
- Family history of diabetes
- Education
- Transplant era (after 1995)
- Tacrolimus use
- Acute rejection
- Pre-transplant IFG
## Recommendations for Screening of Malignancies among Kidney Transplant Recipients

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>Mode</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTLD</td>
<td>H &amp; P to evaluate organ involvement, imaging as needed</td>
<td>Q 3months x 1 year and then annually</td>
</tr>
<tr>
<td>Skin &amp; Lip</td>
<td>Physical, refer to dermatology as needed</td>
<td>Every 6 months for high-risk patients, o/w annually</td>
</tr>
<tr>
<td>Genital/ Cervical</td>
<td>Physical + Pap smear</td>
<td>Annually</td>
</tr>
<tr>
<td>Bladder</td>
<td>Cystoscopy for de novo hematuria</td>
<td>As needed</td>
</tr>
<tr>
<td>Kidney</td>
<td>Ultrasound of native kidney</td>
<td>Biennially (for patients with acquired cystic kidney disease)</td>
</tr>
<tr>
<td>Liver (HBV and HCV)</td>
<td>AFP</td>
<td>Annually</td>
</tr>
<tr>
<td>Breast</td>
<td>Physical, mammogram</td>
<td>Annually</td>
</tr>
<tr>
<td>Prostate</td>
<td>Rectal exam, PSA</td>
<td>Annually</td>
</tr>
<tr>
<td>Colon</td>
<td>Age &gt; 50 year, FOBT or colonoscopy</td>
<td>Annual FOBT or colonoscopy q 5-10 years</td>
</tr>
</tbody>
</table>
Viruses and Post-transplant Malignancies

- EBV—lymphoma
- HPV—cervix and vulva
- HPV 8, 19—non-melanomatous skin cancer
- HBV, HCV—hepatobiliary
Other conditions to monitor for

- Depression & Anxiety
- Gout—increased in kidney transplant recipients
- Tertiary hyperparathyroidism—look for hypercalcemia
- Osteopenia/osteoporosis
Post-Transplant Vaccinations

- Recommended Vaccines
  - TDaP
  - Haemophilus influenza B
  - HAV
  - HBV
  - Pneumovax (consider booster q 3-5 years)
  - Prevnar
  - Inactivated polio
  - Influenza A & B annually (not intranasal)
  - Meningococcus (administer if recipient is high risk)
  - Typhoid Vi
  - Shingrix
Contraindicated Post-Transplant Vaccinations

- Contraindicated Vaccines
  - VZV/ Zostavax
  - BCG
  - Smallpox
  - Intranasal influenza
  - Live oral typhoid Ty21a and other newer vaccines
  - Measles (except during an outbreak)
  - Mumps
  - Rubella
  - Oral polio
  - Live Japanese B encephalitis vaccine
  - Yellow fever
When do you refer the patient back to the transplant center?

- Rise in creatinine
- Proteinuria—new or increasing
- Change in urinary habits/output
- Adverse medication effects
- Persistent new symptoms—i.e. diarrhea
- Persistent leucopenia
- Unrelenting infections
- Any patient who is considering pregnancy
- Call for any questions/concerns
Cell-free DNA testing

- Allosure – CareDx
- Prospera – Natera (new to market)
- TRAK – Viracor
What is cell-free DNA?

- Cell-free DNA refers to fragments of DNA in the bloodstream that originate from cells undergoing cell injury and death.

- DNA degrades into nucleosomal units consisting of ~166 bases.

- cfDNA is cleared from the blood by the liver and kidney, and has a half-life of ~30 minutes.
AlloSure: Validated dd-cfDNA test for identifying kidney injury

AlloSure Validation in DART, a Prospective, Multicenter Study

The Circulating Donor-Derived Cell-Free DNA in Blood for Diagnosing Acute Rejection in Kidney Transplant Recipients (DART) is the clinical validation study for AlloSure.

Key messages from DART

- AlloSure discriminates **Active Rejection** (Acute/active ABMR; Chronic, active ABMR; or TCMR) from **No Active Rejection** with high accuracy*

- AlloSure is more accurate than **Serum Creatinine** in diagnosis of **Active Rejection***

- AlloSure is highly sensitive in distinguishing **ABMR** from **No ABMR***

- AlloSure levels decrease following successful **Rejection Treatment**

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* In patients with clinical suspicion of active rejection, the most common cause for the clinical suspicion of active rejection was elevated serum creatinine

APOL1

- G1 and G2 gene variants that are associated with CKD and progression to ESRD in African ancestry.
- Protective against African sleeping sickness.
- 13% prevalence of high risk variants (2 risk alleles) in the black population.
- ~40% prevalence of 1 risk variant.
- High risk variants are 1.5 fold increased risk for CKD and 1.9 fold increased risk for ESRD.
- While risk is higher, CKD and ESRD rates are relatively low – approximately 1 in 12 and 1 in 16, respectively.
**APOL1 Genotype and Renal Function of African American Live Donors**

**METHODS**
Retrospective cohort
African American donors
Genotyped for APOL1

**OUTCOME** 12 years post-donation renal function

**CONCLUSION** APOL1 high-risk genotype in African American live kidney donors is associated lower pre- and post-donation renal function.

Mona D. Doshi et al. JASN 2018;29:1309-1316

doi: 10.1681/ASN.2017060658
Lower pre- and post-donation eGFR in donors with high-risk APOL1 genotype than low-risk APOL1 genotype.

Mona D. Doshi et al. JASN 2018;29:1309-1316
APOLLO Study

- APOL1 Long-term Kidney Transplant Outcome Network
- Observational study designed to assess the impact of APOL1 gene variants on functional outcomes of kidneys transplanted from living and deceased donors of African ancestry.
- Thirteen networks with over 260 transplant centers around the US and 58 OPOs
APOLLO Objectives

- **Primary Objective**
  - Determine whether the presence of APOL1 risk variants in a kidney donor shortens death-censored graft survival.

- **Secondary Objectives**
  - Define whether the presence of APOL1 risk variants is associated with worse renal function or proteinuria after transplant.
  - Defined whether the presence of APOL1 risk variants is associated with worse renal outcomes in living kidney donors after nephrectomy.
  - Define modifying factors that increase susceptibility of those with APOL1 risk variants.
Organ procurement organization (OPO) will collect blood and urine samples from all deceased donors of African ancestry whose family members consent to the study.
- Includes kidney, en bloc, dual kidneys, and multi-organ transplants.

Study centers will collect blood and urine samples from all living donors of African ancestry who consents to the study.

Recipients consent for data collection along with blood and urine specimens for future study.
New Initiatives at LUMC

- HCV (+) \( \rightarrow \) HCV (–) transplantation
- HOPE in ACTION
  - Prospective Multicenter, Clinical Trial of Deceased HIVD+ Kidney Transplants for HIV+ Recipients
Hepatitis C Donors

Annals of Internal Medicine

Original Research

Twelve-Month Outcomes After Transplant of Hepatitis C-Infected Kidneys Into Uninfected Recipients
A Single-Group Trial

Peter P. Reese, MD, MSCE; Peter L. Abt, MD; Emily A. Blumberg, MD; Vivianna M. Van Deerlin, MD, PhD; Roy D. Bloom, MD; Vishnu S. Potluri, MD, MPH; Matthew Levine, MD, PhD; Paige Porrett, MD, PhD; Deirdre Sawinski, MD; Susanna M. Nazarian, MD, PhD; Ali Naji, MD, PhD; Richard Hasz, BS, MFS; Lawrence Suplee, MS; Jennifer Trofe-Clark, PharmD; Anna Sicilia, BS; Maureen McCauley, BA; Caren Gentile, MS; Jennifer Smith, BS; Bijan A. Niknam, BS, BA; Melissa Bleicher, MD; K. Rajender Reddy, MD; and David S. Goldberg, MD, MSCE
Hepatitis C Donors - cont

- Why would I do this?
- Nearly everyone gets Hepatitis C from the donor.
- But Hepatitis C treatment has come a long way and is almost 100% curable.
Hepatitis C Donors – cont

- Median wait-time from enrolling in the study to transplant was 57 days.
- So wait-time was cut from 6-8 years to under 1.5 years.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Mean age at consent (SD), y</td>
<td>56.3 (6.7)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>8 (40)</td>
</tr>
<tr>
<td>Cause of end-stage renal disease, n (%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>3 (15)</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Congenital obstructive nephropathy</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Chronic interstitial nephritis</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Secondary focal and segmental glomerulosclerosis</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Blood type, n (%)</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>6 (30)</td>
</tr>
<tr>
<td>B</td>
<td>1 (5)</td>
</tr>
<tr>
<td>O</td>
<td>13 (65)</td>
</tr>
<tr>
<td>Median calculated panel reactive antibody level (range)</td>
<td>0 (0-48)</td>
</tr>
<tr>
<td>History of diabetes, n (%)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>Prior transplant, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Median time receiving dialysis at enrollment (IQR), d</td>
<td>352.5 (252-403)</td>
</tr>
<tr>
<td>Median weight (IQR), kg</td>
<td>86.2 (77.6-90.9)</td>
</tr>
<tr>
<td>Highest education level, n (%)</td>
<td></td>
</tr>
<tr>
<td>High school diploma</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Some college/trade school</td>
<td>4 (20)</td>
</tr>
<tr>
<td>College degree</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Master’s degree or higher</td>
<td>4 (20)</td>
</tr>
</tbody>
</table>

IQR = interquartile range; THINKER = Transplanting Hepatitis C kidneys Into Negative Kidney Recipients.
Kidney function was stable after the first year.

All patients were cured of their Hepatitis C infection by week 4 after being treated.
Team Members

- Surgery

- Medicine
### Transplant Rates (Deceased and Living Donor)
**BETWEEN JANUARY 2017 AND DECEMBER 2018**

<table>
<thead>
<tr>
<th>Rate</th>
<th>Detail</th>
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</thead>
<tbody>
<tr>
<td>30.1</td>
<td>People are transplanted per 100 years of waiting at this hospital</td>
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<tr>
<td>20.1</td>
<td>People are transplanted per 100 years of waiting nationally</td>
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</tbody>
</table>

### Deceased-Donor Transplant Rates
**BETWEEN JANUARY 2017 AND DECEMBER 2018**

<table>
<thead>
<tr>
<th>Rate</th>
<th>Detail</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.5</td>
<td>People are transplanted per 100 years of waiting at this hospital</td>
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<tr>
<td>14.1</td>
<td>People are transplanted per 100 years of waiting nationally</td>
</tr>
</tbody>
</table>
Illinois Transplant Fund

- Work to transplant patients who are underserved/undocumented
- Accept ACA insurance
- Partnership with Gift of Hope
- Require insurance with secondary as well as savings ($\approx 7,500)
  - Yearly savings
- Coverage at this time is up to 3 years
References

- Penn I. The effect of immunosuppression on pre-existing cancers. Transplantation 1993; 55: 742-7
- http://tmedweb.tulane.edu/pharmwiki/doku.php/organ_transplantation
Artificial Kidneys

<table>
<thead>
<tr>
<th></th>
<th>AWAK</th>
<th>WAK</th>
<th>IAK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>&lt;2 kg</td>
<td>&lt;5 kg</td>
<td>~500 g</td>
</tr>
<tr>
<td>Power requirements</td>
<td>Battery operated</td>
<td>Battery operated</td>
<td>None, uses cardiovascular pressure and chemical energy of cellular metabolism</td>
</tr>
<tr>
<td>Fluid requirements</td>
<td>~2 L dialysate/treatment</td>
<td>6 L dialysate/treatment</td>
<td>No dialysate, patients drink an electrolyte-rich fluid to keep up with losses</td>
</tr>
<tr>
<td>Stage of development</td>
<td>Trials in human</td>
<td>FDA clinical trials</td>
<td>Animal models</td>
</tr>
<tr>
<td>Strengths</td>
<td>Bloodless, easily portable, high clearances</td>
<td>Portable, low UF rate, electrolyte balance seen in clinical use</td>
<td>Low burden to patient, minimal waste generation</td>
</tr>
<tr>
<td>Limitations</td>
<td>Frequent exchange of cartridges (every 7 h)</td>
<td>Clotting and bleeding issues</td>
<td>May require repeated invasive procedures</td>
</tr>
</tbody>
</table>