Renal Transplant

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Summary of CNA Renal Transplant Competencies

- Potential contraindications to renal transplant.
- Assessment/selection of renal transplant recipient candidate.
- Assessment/selection of living donor.
- Pathophysiology, assessment and nursing interventions for preventing and managing the potential complications – post renal transplantation.
- Identifies and defines commonly administered renal transplant medications. Possible interactions.
- Options available for renal Tx candidate (deceased and living kidney, kidney-pancreas, and living paired exchange)
Potential Contraindications or Considerations related to Renal Transplantation (Renal Tx)

- Malignancy (without sufficient remission)
- Active Sepsis or Chronic infection.
- Severe cardiovascular disease or recent CVA
- Unstable Psychiatric Disorder
- Morbid Obesity is a risk – maybe acceptable unless BMI is greater than 40
- Non-Adherence
- Ongoing Substance Misuse
Potential Contraindications or Considerations related to Renal Transplantation (Renal Tx)

- Severe co-morbidities (extra-renal-pulmonary or cardiac)
- Uncorrectable lower urinary tract disease
- Persistent coagulation disorders
- Reproductive or renal anatomical or structural issues
- Over active or uncontrolled hyperparathyroidism
- Hepatitis B or C is a risk but acceptable if no progressive liver disease or cirrhosis
- HIV positive is a risk but if well is acceptable (good CD 4 count)
- Age is not consideration unless potential recipient candidate is over 70.
Client Survival After Kidney Transplantation versus Conventional Hemodialysis

- Annual mortality rates for patients undergoing dialysis range from 21%-25%, but <8% with cadaveric and <4% with living-related transplant recipients.
- Healthier patients generally are selected for transplantation.
- The benefit of transplantation is most notable in young people and in those with diabetes mellitus.

<table>
<thead>
<tr>
<th></th>
<th>Dialysis</th>
<th>Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non diabetic</td>
<td>20</td>
<td>31 years</td>
</tr>
<tr>
<td>Diabetic</td>
<td>8</td>
<td>25 years</td>
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</table>
Transplant Centers in BC

- Transplant centers in BC are at following hospitals:
- Saint Paul’s Hospital
- Vancouver General Hospital (BC Transplant Society)
- BC Children’s Hospital.
Referral Process:

- Referred by primary nephrologist
- Client must meet initial criteria for medical suitability
- Referral at GFR between 20-25
- Transplant team includes physician, social worker, pre-transplant clinical coordinator or nurse.
- Clinic appointments occur at transplant centers in lower mainland.
- Initial appointment with team is booked once pre-transplant assessment is done.
An adult donor kidney transplanted to the left iliac fossa of an adult recipient.
Types of Kidney Donor

- Living related.
- Living unrelated (emotionally motivated).
- Cadaveric (Brain-dead)
Living versus Deceased Donation

- Living Donor is Best!
  - minimal waiting time
  - minimal delayed graft function (less chance of rejection).
  - 1 year 96% and 5 year 91% graft survival
- Deceased Donor acceptable but not ideal
  - Waiting time 5 to 10 years depending on blood type
  - higher chance of rejection
  - 1 year 92% and 5 year 83% graft survival
Kidney Graft Survival Rates

Source: OPTN/SRTR as of May 1, 2008
CRITERIA FOR LIVING DONOR SELECTION

- Unrelated or related.
- ABO blood group-compatible.
- Negative Crossmatch – no immunological reaction.
- HLA-identical or haploidentical (good match).
- Normal renal function. No evidence of hypertension or stable hypertension managed by one agent.
CRITERIA FOR CADAVER DONOR SELECTION

- Irreversible brain damage.
- Normal renal function appropriate for age.
- No evidence of preexisting renal disease.
- No evidence of transmissible diseases.
- ABO blood group-compatible.
- Negative cross-match.
- Best HLA match possible.
Considerations in evaluating a prospective Living Kidney Donor

- Whether there is a medical condition that will put donor at increased risk for complications for general anesthesia or surgery.
- Whether the removal of one kidney will increase the donor’s risk for developing renal insufficiency.
**Assessment of Living Donor**

- CBC, Renal Function, Liver Function, CXR, EKG, MIBI, ECHO and Abdominal US.
- Assessment for proteinuria, underlying disease process and viral testing.
- Discussion with donor about benefits and risks
- Assessment of renal vessels with CT and/or MRI angiogram.

- ABO
- Crossmatch
- Panel Reactive Antibodies
- Human Leukocyte Antigen (HLA)
- Pap smear (females)
- Prostate exam/test (males)
- BMI
Pre-transplant Work-up/Assessment for Recipient

- Same work-up and assessment as donor but recipient has dental examination and check-up.
- Recipient will have work-up completed to assess candidacy.
- HLA and other immunological tests may be repeated throughout pre-transplant period.
Does Donation Of A Kidney Pose A Long-term Risk For The Donor?

- Following nephrectomy, compensatory hypertrophy and increase in GFR occur in the remaining kidney.
- Slight risk of proteinuria and hypertension.
- Meta-analysis of data from donors followed for >20y confirmed safety of kidney donation.
Matching between Recipient And Donor

A- Tissue typing

• Determined by 6 antigens located on cell surface encoded for by the HLA gen located on the short arm of chromosome 6.

• Class I antigens (HLA-A and HLA-B) are expressed on the surface of most nucleated cells.

• Class II antigen (HLA-DR) are expressed on surface of APC and activated lymphocytes.

• These 6 antigens are referred to as major transplant antigens.

• The match between donor and recipient can range from 0 to six.
Matching between Recipient And Donor

B- Cross matching

- A laboratory test that determines whether a potential transplant recipient has preformed antibodies against the HLA antigens of the potential donor. (Donor Lymphocytes + Recipient Serum). Negative crossmatch is desirable. This means no reaction or response.

- A Final CM is mandatory

C- Compatible ABO blood group.
Structure of the HLA class I and class II antigens.
Effect Of HLA Matching On The Graft Outcome

- Data from large registries indicate that, the better the HLA-match, the better the long-term survival of the allograft.
- The benefits of lesser degrees of matching have become less obvious with the use of newer and more potent immunosuppressive drugs.
- Matching for DR antigens are more favorable than others.
Transplant Surgery

- If pre-emptive transplant (before needing dialysis) surgery is generally booked when recipient GFR is 15 and under.
- Surgery is not booked until donor and recipient are approved and meet the criteria.
- The two types of donor incision: laparoscopic (minimal invasive surgery and open nephrectomy.
- Laparoscopic donor nephrectomy is available for most left sided donors and it allows quicker return to normal activities.
Transplant Surgery

- Donors may be discharged 2-5 days post-op
- Expected time off work is 6-8 weeks
- Donors follow up with transplant team and surgeon as well as family doctor.
- For recipients, hospital stay is 5-7 days depending on potential for complications/acute rejection.
- Recipient will stay in Vancouver for 3 months post-transplant. Recipient will go on anti-rejection drugs post-op and will be monitored closely –initial 3 months.
Kidney Transplant

- Diseased kidneys
- Inferior vena cava
- Aorta
- Ureters
- Transplanted kidney
- Transplanted ureter
- Bladder
Post-op management

- Monitor for post-op complications such as lymphocele or urine leaks.
- Monitor fluid input and output closely to avoid extracellular volume depletion.
- Monitor for signs of rejection
- Monitor hematologic and biochemical abnormalities (anemia and creatinine)
- Monitor for blood pressure- at risk for hypertension
- Delayed graft function (acute tubular necrosis)
Post-op Management

- Hyperlipidemia
- Central Venous Pressure (CVP)
- Steroid Induced complications such as hyperglycemia, diabetes, or psychosis.
- Educational needs
- Diagnostic tests such as renal biopsy of graft and ultra sound doppler.
- Post-nephrectomy
- Drug levels (Neoral)
- Medication Management-including initiation of immunosuppressive agents
Post Management - Other Issues

- Smoking
- Weight gain (can be caused by steroids)
- Blood sugars
- Substance Misuse
- Routine Malignancy Screening
- Bone Disease
- Reproductive Issues
Factors Influencing The Longevity Of Renal Allograft (Post-op)

- Age
- HLA matching
- Delayed graft function
- Ischemia time.
- Number of acute rejection episodes.
- Native kidney disease.
- Ethnicity.
- Others
Relative incidence of causes of allograft dysfunction during the year following transplantation.
What Are The Major Causes Of Long-Term Allograft Failure?

- Chronic rejection.
- Death with functioning graft.
What Are The Most Common causes Of Death After Kidney Transplantation?

- Cardiovascular disease.
- Infection.
Renal Allograft Rejection

1- Hyperacute.

2- Acute.

3- Chronic.
POST KIDNEY TRANSPLANT REJECTION SIGNS

HYPERACUTE...
- Onset with 48 hours
- Malaise, high fever
- Graft tenderness
- Organ must be removed to ↓ S & S

ACUTE...
- 1 Week to 2 Years
- Oliguria, Anuria
- ↑ Temp (>37.8°C - 100°F)
- ↑ BP
- Flank Tenderness
- Lethargy
- ↑ BUN, K, Creatinine
- Fluid Retention

CHRONIC...
- Gradual Over Months to Years
- ↑ In BUN, Creatinine
- Imbalances in Proteinuria Electrolytes
- Fatigue
Hyperacute Rejection

- Is mediated by preformed antibodies that recognize HLA antigens in donor organ.
- Usually these are formed as a consequence of blood transfusion, pregnancy, prior organ transplantation, autoimmune diseases.
- Fibrinoid necrosis lead to immediate graft loss.
- Delayed form may occur several days following transplantation.
- Plasmapheresis, dialysis, and pulse steroid may be used.
Hyperacute rejection.
Acute Renal Allograft Rejection

- IS mediated by activated T-lymphocytes.
- Activations of T-cells occur after recognition of graft antigen either directly or after being processed and presented by APC.
- This usually occur during the first 6 months.
- It manifest as increase in s. creatinine with or without oliguria.
How Common Is acute Rejection?

- At least one episode of acute rejection occurs in 62% in patients treated by immunosuppressive agents.
- With newer immunosuppressive drugs rates are less.
Treatment Of Acute Rejection

1. Pulse steroids
2. ATG, OKT3.
3. MMF, Tacrolimus.
4. IVIG.

More than 90% of acute rejection episodes occurring in the first 6 months can be reversed.
Chronic allograft Rejection

- Manifest clinically by a slow and gradual decline in renal function, usually more than 6 months after transplant and typically accompanied by moderate to heavy proteinuria.
- Histologically, characterized by glomerulo-sclerosis, interstitial fibrosis, and obliteration of arteriolar lumina.
- Treatment is unsatisfactory.
Chronic allograft Rejection VS Transplant glomerulopathy

- A- Immunologic
- B- Non-immunologic
  - hypertension
  - Hyperlipidemia
  - Drug toxicity (CsA, FK)
  - Ischaemic injury
  - Viral infection (CMV)
  - Others
- C4d deposits in peritubular capillaries as marker of ongoing immune injury
Management of Transplant glomerulopathy

- Switch from calcineurin inhibitor.
- ACEIs or ARBs.
- Statins.
- Increasing immunosuppression?
- Others
### Banff criteria for diagnosis of allograft rejection

<table>
<thead>
<tr>
<th>BANFF GRADE</th>
<th>HISTOLOGY</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Interstitial edema and tubulitis (i.e., lymphocytic invasion of tubular basement membranes.</td>
</tr>
<tr>
<td>II</td>
<td>More severe tubulitis with or without mild vasculitis characterized by intimal lymphocytic infiltrates</td>
</tr>
<tr>
<td>III</td>
<td>Severe vasculitis with fibrinoid necrosis.</td>
</tr>
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</table>
Principles underlying use of current immunosuppressive treatments and agents

1- The benefits of a successful transplant outweigh the risks of chronic immunosuppression.

2- Immunosuppressive therapy is required indefinitely.

3- Multidrug regimens are generally employed.

4- Large doses of immunosuppressant drugs are used in the early transplant period.
## Classes of Maintenance Immunosuppressive Drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Immunophilin-binding agents</td>
<td><strong>Calcineurin inhibitors</strong></td>
</tr>
<tr>
<td></td>
<td>Cyclosporine</td>
</tr>
<tr>
<td></td>
<td>Tacrolimus (FK506)</td>
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<tr>
<td></td>
<td><strong>Calcineurin-independent agents</strong></td>
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<tr>
<td></td>
<td>Sirolimus (rapamycin)</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Prednisone</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td><strong>Purine inhibitors: nonselective</strong></td>
</tr>
<tr>
<td></td>
<td>Azathioprine</td>
</tr>
<tr>
<td></td>
<td><strong>Purine inhibitors: lymphocyte selective</strong></td>
</tr>
<tr>
<td></td>
<td>Mycophenolate mofetil (RS-61443)</td>
</tr>
<tr>
<td></td>
<td>Mizoribine*</td>
</tr>
<tr>
<td></td>
<td><strong>Pyrimidine inhibitors</strong></td>
</tr>
<tr>
<td></td>
<td>Brequinar*</td>
</tr>
<tr>
<td>Poorly understood mechanisms</td>
<td>Deoxyspergualin*</td>
</tr>
<tr>
<td></td>
<td>Leflunomide*</td>
</tr>
</tbody>
</table>

*Experimental or not yet approved by Food and Drug Administration (FDA).*
Risks associated with chronic Immunosuppression

1- Malignancy
2- Infection
3- Side effects of different drugs (steroids, CsA, tacrolimus, MMF, .....)
Side Effects of Glucocorticoids

- Weight gain with cushingoid features
- Hypertension
- Hyperlipidemia
- Osteopenia
- Cataracts
- Dermatologic effects (acne, striae, easy bruising)
- Impaired growth
- Glucose intolerance
## Side Effects of Immunophilin-binding Agents

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Cyclosporine</th>
<th>Tacrolimus</th>
<th>Sirolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephrotoxicity</td>
<td>++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Neurotoxicity (tremor, seizures)</td>
<td>+</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gingival hyperplasia</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension</td>
<td>++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>++</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>Glucose intolerance</td>
<td>+</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Bone marrow suppression</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
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</table>
## Side Effects of Antimetabolites

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Azathioprine</th>
<th>Mycophenolate Mofetil</th>
</tr>
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<tbody>
<tr>
<td>Bone marrow suppression</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>
Induction Immunosuppressive therapy

- During the first 1-3 weeks post transplant.
- Usually refer to use of anti-T-cell antibodies
  - polyclonal (ATGAM, thymoglobin).
  - Monoclonal (Simulect, Zinapax, OKT3).
- Helpful to delay use of calcineurin drugs, may decrease acute rejection and improve graft outcome (debatable).
- Expensive, risk of infection and malignancy
- Better used in selected patients.
## Side Effects of Induction Antibodies

<table>
<thead>
<tr>
<th>Side effect</th>
<th>OKT3</th>
<th>Polyclonals</th>
<th>Anti-CD25 Agets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>+++</td>
<td>+</td>
<td>_</td>
</tr>
<tr>
<td>Headache</td>
<td>++</td>
<td>+</td>
<td>_</td>
</tr>
<tr>
<td>Myalgias</td>
<td>++</td>
<td>+</td>
<td>_</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>++</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>(diarrhea, nausea)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>+</td>
<td>+/-</td>
<td>_</td>
</tr>
</tbody>
</table>
Some commonly used combinations of maintenance immunosuppressive drugs

1- Prednisolone + Azathioprine
2- Prednisolone + cyclosporine (or tacrolimus)
3- Prednisolone + cyclosporine + Azathioprine
4- MMF (cell cept) may replace Azathioprine.
5- Sirolimus (Rapamimmune) may replace Azathioprine or cyclosporine
Common drug interactions

- Drugs acting on cytochrome $P_{450}$ affect the metabolism of CsA, tacrolimus, and sirolimus.

1- ↑ Metabolism $\rightarrow$ ↓ level
   • Anticonvulsants • Antituberculous

2- ↓ Metabolism $\rightarrow$ ↑ level
   • anti-fungus (ketoconazole..)
   • erythromycin and clarithromycin
   • calcium channel blockers
   • metoclopramide

- Azathioprine and allopurinol.
Other transplant options available to chronic kidney disease clients

- Kidney-pancreas transplant
- Living paired exchange anonymous donor program
Living Anonymous Donor Exchange

Paired Donation

Pair 1
- Donor 1
- Recipient 1

Pair 2
- Donor 2
- Recipient 2

Not compatible
Compatible
Compatible
Not compatible
Conclusions

• In general, renal transplantation should be recommended as the preferred mode of RRT for most patients with ESRD in whom surgery and subsequent treatment is safe and feasible. Special considerations should be taking for donors and recipients who are still growing or are of childbearing age.
Interesting Role Model!

Healthy Kidney Transplant Recipient