

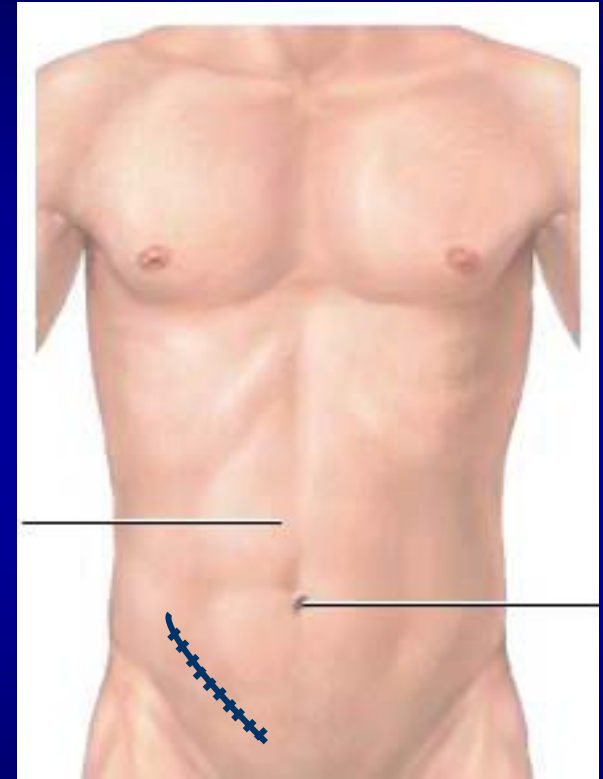
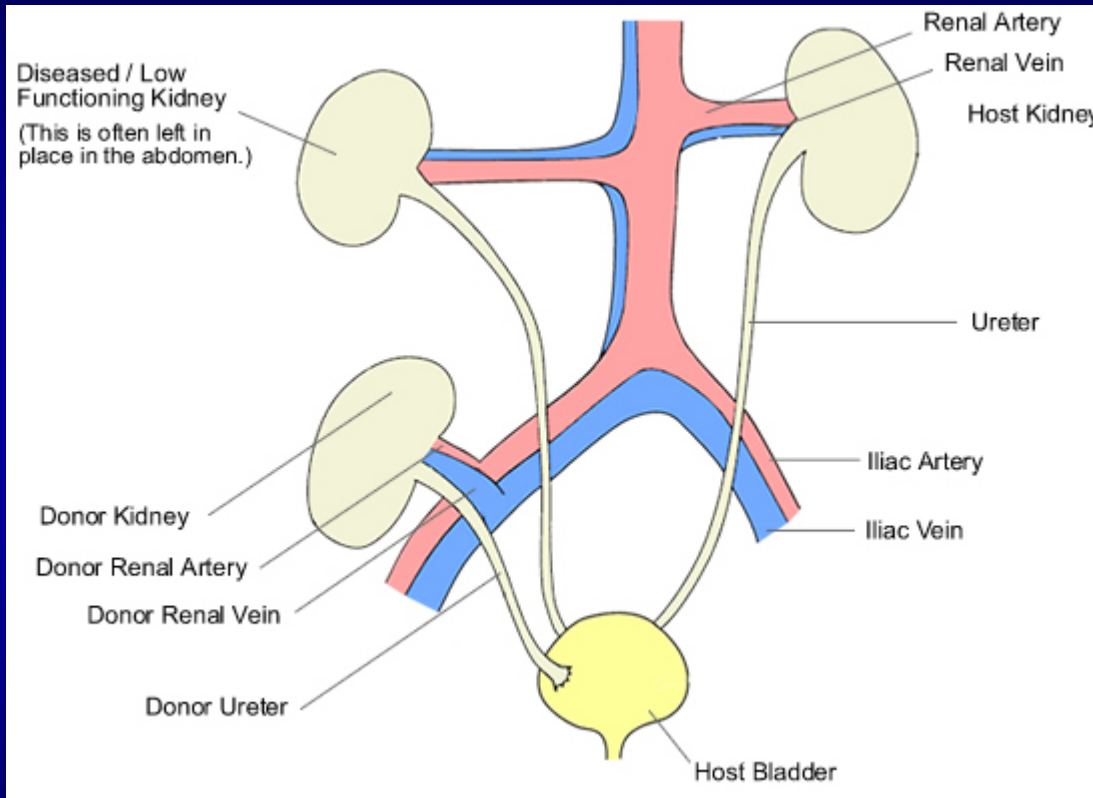
Kidney transplants for C3G: *What are the outcomes lately?*

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Objectives

- Kidney transplantation for C3G – how and when?
- Outcomes after kidney transplantation

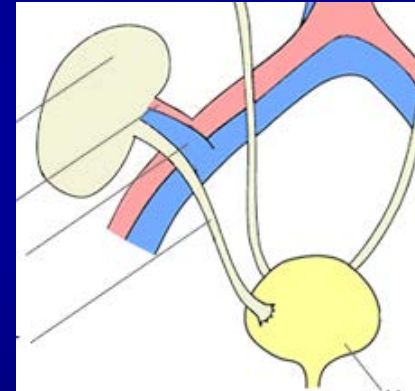
Kidney Transplant



Immunosuppressive medications for life

Risks of Kidney Transplant

- **Complications during the surgical procedure.**
 - Bleeding
 - Infection
 - Pneumonia, wound infection, urinary tract infection
 - Urine drainage complication
 - Urine leak
 - Narrowing of the connection between ureter and bladder
 - Inability to empty bladder.
 - Risk associated with any general surgical procedure
 - Blood clots.
 - Heart attack or stroke.
- **Complications after the surgical procedure**
 - Side effects of medications:diarrhea, headache, tremor
 - Infections
 - Rejection
 - Original kidney disease returns

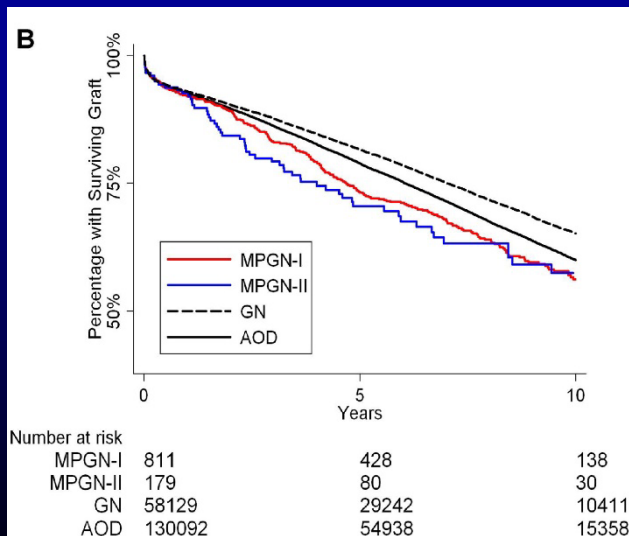


C3G (DDD) recurrence – I

- NAPRTCS database (national pediatric transplant database)
 - Retrospective review (1985-2002)
 - 75 patients with MPGN II (DDD): 44 were > 12 yrs old
 - 5 yr graft survival 50% +/- 7.5 in MPGN II vs 74.3% +/- 0.6 for other
 - Among MPGNII patients living donor 5 yr survival (65.9% +/- 10.7) better than deceased donor (34.1% +/- 9.8%) survival
 - Recurrent disease caused graft failure in 14.7% of patients
 - No correlation with prior or post transplant C3 concentration

C3G (DDD)-recurrence II

- UNOS database (US transplant database – all comers)
 - Retrospective review (1987-2007) - 189,211 patients
 - 179 patients with MPGN II (DDD) – 0.1%: Median age 27 yr
 - Median kidney survival 11.1 yr (other GN 14.3 yr)
 - 10 year kidney survival 57.5% in MPGN II (other GN 65.2 yr)
 - Recurrent disease caused graft failure in 29.5% of patients



Kidney survival in MPGNII compared to other (death censored)

C3G (C3GN) recurrence - III

- 21 patients at 1 institution with C3GN were transplanted
- Original disease diagnosed at a median age of 21 years
- 14 of 21 (66.7%) recurred after transplant; 6 of 8 had low C3 prior
- Median time to recurrence 28 months
- 3 of 14 had MGRS (Immunoglobulin or Ig excess from a process like myeloma)
- Kidney failure in 50% of those who developed recurrent disease
 - Median time 77 months
- Remaining 50% have functioning kidneys (median followup 73 months)

Should patients with C3G be transplanted?

- Any patient who has previously not been transplanted should be considered a candidate.
- Any patient who has been transplanted but not had early transplant failure from C3G recurrence should be considered a candidate
- Risk of recurrent disease may be influenced by
 - Sex, age, genetics, autoantibodies, complement activity
- Not all recurrent disease leads to premature kidney loss
- Consequence of early kidney loss
 - early kidney failure from C3G probably predicts recurrent early loss.
 - Exposure to donor kidney leads to development of antibodies to HLA antigens.

Sensitization (HLA antibodies) can make future transplants difficult.

Steps in preparing for a transplant

- Discuss with your nephrologist as early as possible
- Schedule a visit to a transplant center
- Take your support person (caregiver) with you
- Be prepared for a long visit (1-2 days to complete)

At the transplant center:

Meet with surgeon, nephrologist, social worker, nurse coordinator, dietician, pharmacist, financial counselor, blood tests, X-rays

Sometimes specialists, clinical psychologist, CT scan, stress test

When should patients with C3G be transplanted?

- Ideally when the disease appears inactive
 - patient not requiring immunosuppressive therapy
 - Urine testing shows no red cells (blood) or casts
 - Signs of complement activation have resolved
 - Normal C3,
 - undetectable C3 nephritic factor (if previously abnormal),
 - MORL assays: Normal CH50, Normal APFA, Normal hemolytic assay
- Adults with monoclonal Ig (MGRS) should first be treated for the plasma cell disease

How should C3G patients be transplanted?

- As with other transplants, a living donor is almost always preferable to a deceased donor transplant
- Immunosuppressive regimen should include standard therapy – tacrolimus, MMF (mycophenolate, cellcept) +/- prednisone
- No data to support pre-operative use of eculizumab
- No data to support pre-operative plasma exchange
- Transplant center should have a plan for monitoring for early transplant recurrence
 - Urine for blood (microscopic)
 - Urine protein or albumin

Treatment options for recurrence

- Eculizumab (C5 convertase inhibition) -
 - Has been effective in some C3G cases
 - Most cases prior to transplantation
 - Some required months of therapy prior to response

Publication bias may be a problem (More reviews than cases)

- Factor B inhibition-Phase 2 - LPN023
- C5aR inhibition – Phase 2- Avacopan
- Factor D inhibition – Phase 2 study – ACH-4771
- C3 inhibitor: Phase 2 - Pegcetacoplan

[Pediatr Nephrol.](#) 2014 Jun;29(6):1107-11. doi: 10.1007/s00467-013-2711-5. Epub 2014 Jan 10.

[Am J Kidney Dis.](#) 2015 Mar;65(3):484-9. doi: 10.1053/j.ajkd.2014.09.025. Epub 2014 Dec 17.

[Clin Kidney J.](#) 2015 Aug;8(4):445-8. doi: 10.1093/ckj/sfv044. Epub 2015 Jun 15.

[Pediatr Nephrol.](#) 2017 Jun;32(6):1023-1028. doi: 10.1007/s00467-017-3619-2. Epub 2017 Feb 24

[Clin J Am Soc Nephrol.](#) 2012 May;7(5):748-56. doi: 10.2215/CJN.12901211. Epub 2012 Mar 8.

Should plans for eculizumab be made preemptively?

Options

- Prophylactic use of eculizumab ahead of and following transplant – insufficient data
- Rescue therapy with eculizumab if recurrence occurs and cannot be controlled
 - Contingency planning - ideal
 - Insurance preapproval prior to transplant
 - Required vaccinations prior to transplant

C3G – recurrence after transplant

- probably universal by biopsy – but may not always impact kidney function
- clinically meaningful disease: 50-75% by 3-5 years
- kidney failure in 50% by 7-15 years

Issues to consider

Getting ready:

- Limit blood transfusions to the extent possible to reduce 'HLA' antibody production
- Get evaluated for a transplant as soon as possible at a center that is willing to transplant C3G (eGFR < 20).

Transplant decision:

- Decision complicated by risk of recurrence and lack of proven therapy.
- However, 10-year kidney survival may be > 50%
- If recurrence occurs, consider using eculizumab or entering a clinical trial

Questions

ADDITIONAL MATERIAL

Steps in preparing for a transplant

- Discuss with your nephrologist as early as possible
- Schedule a visit to a transplant center
- Take your support person (caregiver) with you
- Be prepared for a long visit (1-2 days to complete)

Meet with surgeon, nephrologist, social worker, nurse coordinator, dietician, pharmacist, financial counselor, blood tests, X-rays

Sometimes specialists, clinical psychologist, CT scan, stress test

Medical/Surgical Consultation

- **Transplant surgeons and nephrologists will will:**
 - Review your history
 - Perform a physical examination
 - Review your diagnostic tests
- **Goals:**
 - Ensure you need a transplant
 - Ensure a transplant is the right decision for you
 - Ensure there are no medical or surgical reasons not to do a transplant
 - Ensure you have the information you need about the transplant process

Social Work Consultation

- **To assess your:**
 - Ongoing caregiver support and transportation
 - Understanding of current medical condition and expectations of treatment
 - Medical compliance
 - Education and work history
 - Mental health and substance use history
- **To provide information about:**
 - Post transplant requirements and potential needs
 - Caregiver roles, responsibilities, and expectations
 - Living wills and power of attorney for healthcare
- ✓ **It is essential to your transplant success that your primary caregiver attend all appointments.**

Types of Kidney Donors

- **Deceased Donors**

- Patients are listed with UNOS (United Network for Organ Sharing).
- Wait times vary based on a variety of factors including; time on dialysis, location, age, blood/tissue type.

- **Living Donors**

- Related (parent, child, sibling)
- Unrelated (spouse, friend)

- **Benefits from a living kidney donor transplant:**

- Surgery can be electively scheduled.
- Organ usually lasts longer than from a deceased donor.

Once You Are Listed



- ✓ **Stay in touch with your nurse coordinator.**
- ✓ **This nurse needs to know:**
 - ✓ How to reach you.
- ✓ **You need to let us know of changes in your insurance coverage.**
- ✓ **Any new test results (laboratory tests, heart tests, scans, etc...).**
- ✓ **If you become sick and need antibiotics or hospital care.**

Responsibilities After Transplant

- You must learn about your **immunosuppression** medications and their side effects.
- You must take them as prescribed, daily, for the lifetime of your transplant.
- You must not stop these drugs unless directed to by a member of the transplant team.
- If your insurance affects your ability to get these drugs, let us know right away. **WE CAN HELP!**
- If your transplant is not performed at a Medicare approved facility, this may affect your ability to have immunosuppression paid for under Medicare Part B.