

Kidney transplantation in C3G: *Transplant or dialysis ?*

Christie P Thomas MD
Professor and Vice Chair, Faculty Advancement
Department of Internal Medicine
Medical Director, Kidney Transplant Program
University of Iowa Carver College of Medicine

Objectives

- To review the steps in preparing for a transplant
- To understand kidney transplant options like living donation including directed, non-directed and kidney exchange
- To learn about transplant outcomes for patients with C3G
- To appreciate when chronic dialysis might be considered

Steps in preparing for a transplant

- If > 18 yrs old, must have declining kidney function with an eGFR approaching ~ 20 ml/min/1.73m²
- If < 18 yrs old, should have declining kidney function and expected to need a transplant or dialysis eventually

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

Steps in preparing for a transplant -II

- Counseling about dialysis versus transplant for C3G
- Complete any additional visits, tests required (specialists, vaccinations)
- Ask about treatment options for disease recurrence
- Get placed on the transplant waitlist
- Maintain your hemoglobin around 10 gm/dl (avoid transfusion if possible)
- Encourage your living donors to contact transplant center
- Keep your contact information up to date with the transplant center
- Let the transplant center know if you get pregnant, fall sick or need surgery or will be unavailable for an extended period of time

To understand transplantation options like living donation including directed, non-directed and kidney exchange

Types of kidney donors

Deceased Donors

- Patients are listed with UNOS (United Network for Organ Sharing) and wait their turn.
- Waiting times vary based on a variety of factors including; likelihood of benefit (EPTS), time on waitlist, blood group, HLA match and where the donor organ is procured.

Living Donors

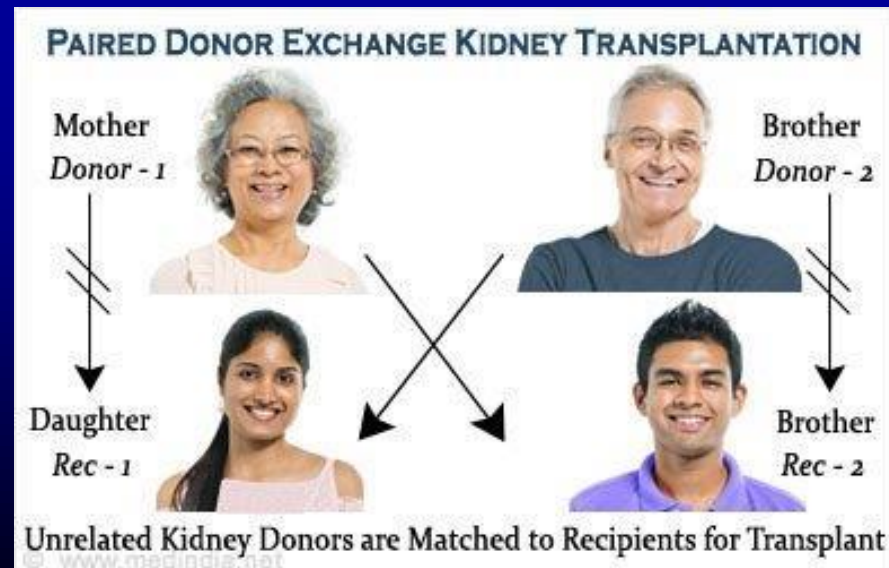
- Related (parent, child, sibling)
- Unrelated (spouse, friend, stranger, kidney exchange)

Benefits from a living kidney donor transplant:

- Surgery can be electively scheduled.
- Kidney usually works immediately and lasts longer than from a deceased donor.

Types of living donors

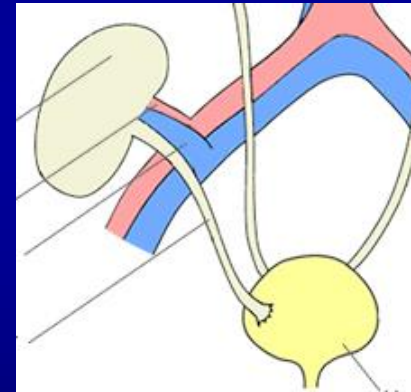
- Compatible (Blood type, HLA)
 - Related
 - Unrelated
- Incompatible (Blood type, HLA)
- Compatible but non-ideal (Age, size mismatch)



To learn about transplant outcomes for
patients with C3G

Risks of Kidney Transplant - General

- **Complications during or immediately after 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 (e.g. C3G)*

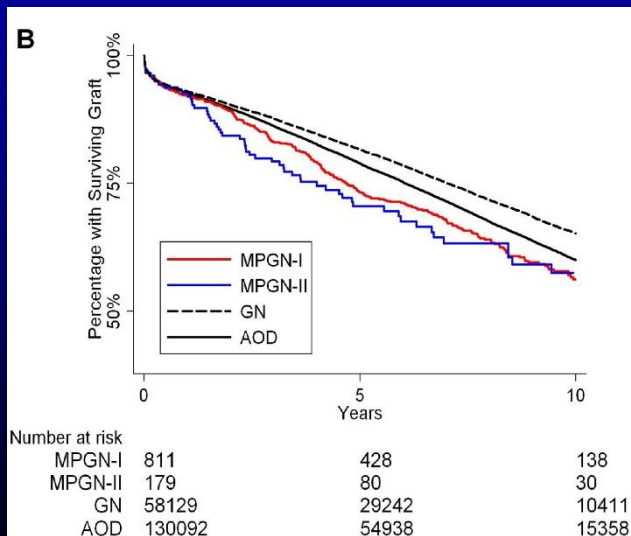


C3G (DDD) recurrence – I

- 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)

C3G – recurrence after transplant

Summary

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

Should patients with C3G be transplanted?

- Any patient who has previously not been transplanted should be considered a candidate for a transplant.
- Any patient who has been transplanted but not had early transplant failure from C3G recurrence should also 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.

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

- No FDA approved treatment
- 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)

- C5aR inhibition – Phase 2- Avacopan
- C3 inhibitor: Phase 2 - Pegcetacoplan
- Factor B inhibition-Phase 3 – Ipatocopan (LPN023) - MAP

[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

To appreciate when chronic dialysis
might be considered

Chronic dialysis

- While waiting for a kidney transplant
 - Blood group, lack of living donors, HLA antibodies
- If unable to find a willing transplant center
- If patient wants to wait for better therapy for possible C3G recurrence
 - If early recurrent kidney transplant failure

Summary

- Kidney transplantation is the preferred option for any patient with end stage kidney disease including from C3G
- Get all recommended vaccines prior to transplant if able
- Many vaccines including COVID19 are less effective after transplantation
- Although the risk of recurrent disease is high, it may not occur early or lead to early loss of kidney function
- Although no specific treatment for C3G after transplant is available, new treatments are in clinical trials
- If transplant is not an option or if the wait is expected to be long, consider home hemodialysis rather than center-based dialysis (if able)

Questions

ADDITIONAL MATERIAL

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

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.

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.**

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

Once You Are Listed

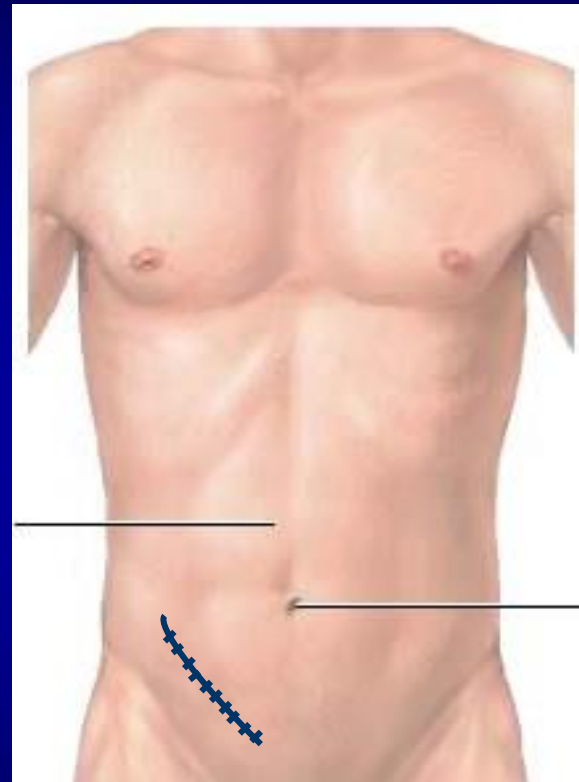
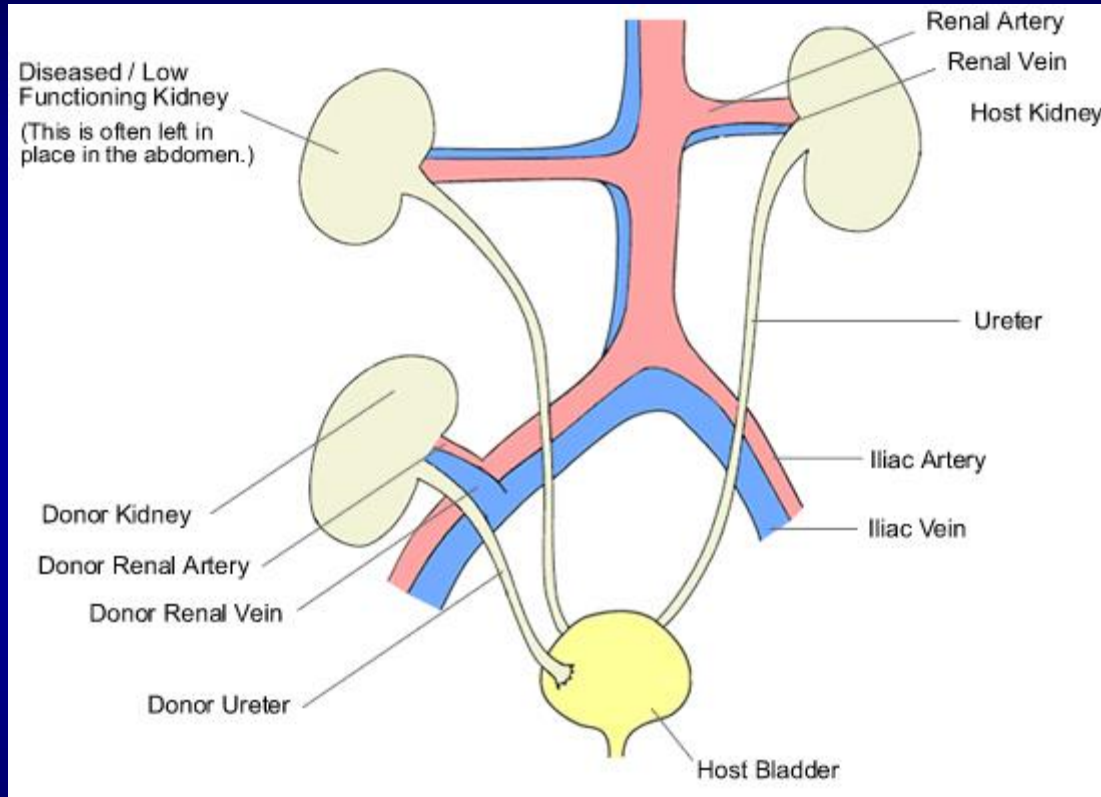


- ✓ **Stay in touch with your nurse coordinator.**
- ✓ **This nurse needs to know:**
 - ✓ How to reach you.
- ✓ **You need to let us know of changes in your insurance coverage.**
- ✓ **Any new test results (laboratory tests, heart tests, scans, etc...).**
- ✓ **If you become sick and need antibiotics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

Kidney Transplant



Immunosuppressive medications for life