6th Spotlight on The Nebraska Medical Center

Extraordinary Innovations in Transplantation and Oncology conference

July 8-9, 2014

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Living Kidney donation

Ketki Tendulkar, MD
Assistant Professor, Division of Nephrology
Department of Internal Medicine, UNMC

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Burden of Kidney Disease

- 20 million Americans have kidney disease
  - 8th leading cause of death
  - 27% of Medicare expenditures
- 570,000+ patients have End Stage Renal Disease (ESRD)
- Two management options for ESRD
  - Dialysis (different modalities)
  - Transplantation (deceased and living donor)

Major Risk: Time on Dialysis

- For eligible candidates, transplantation is optimal treatment
  - Far less resource intensive
  - Improved survival
  - Higher quality of life compared to dialysis
- Severe shortage in the number of organs available for donation

- Kidney waiting list (5/30/14)
  - National: 100,764
  - Nebraska: 196
- Kidney transplants 2013
  - National
    - 11,162 deceased donor
    - 5,732 living donor
  - Nebraska
    - 139 deceased donor
    - 25 living donor

Baseline estimates of costs
(in 2010 Canadian dollars)

	Age 18 - 50	Age 51 - 65
Mean Annual cost of dialysis	70,448	79,829
Mean first year cost of deceased donor transplant	95,502	104,964
Mean cost of deceased donor transplant (Years 2-20)	21,374	23,504
Mean first year cost of living donor transplant	100,115	102,860
Mean cost of living donor transplant (Years 2-20)	21,000	18,661

Barneih L et al CJASN 8: 2165-2173, 2013; Lee H, et al Am J Kidney Dis 40: 611–622, 2002
Barnieh L et al. Am J Transplant 11: 478–488, 2011

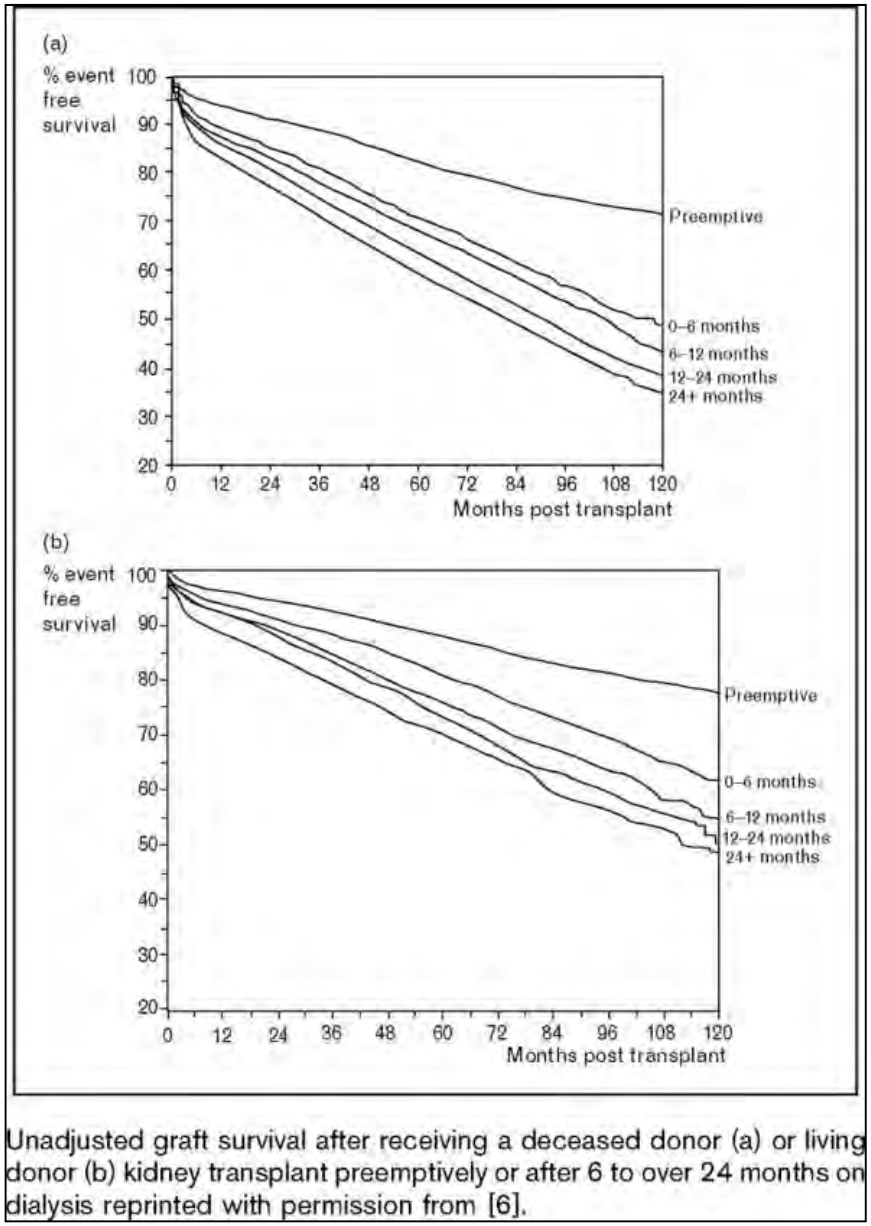
History of living donor transplants

- First successful kidney transplant performed between identical twins in 1954.
- Survival rates are comparable to people who never donate
- More than 6000 are performed every year in USA
- Death during and related to procedure
  - extremely rare
- Approximately 30-40 living donor kidney transplants every year at UNMC
  - Numbers are decreasing with
    - Rising BMI and
    - Medical co-morbidites

Why donate??

- Organ and tissue donation helps by giving patients a second chance at ‘good quality life’.
- Preemptive transplantation
  - Improved graft survival compared to those who undergo a period of dialysis before transplantation

- Living donation - higher success rate since it can be a planned surgery even before or soon after dialysis is needed
  - Decreases the wait time on dialysis
  - Significant graft survival advantage
  - Improved probability of immediate graft function
  - Increases the chances of recipient's long term health

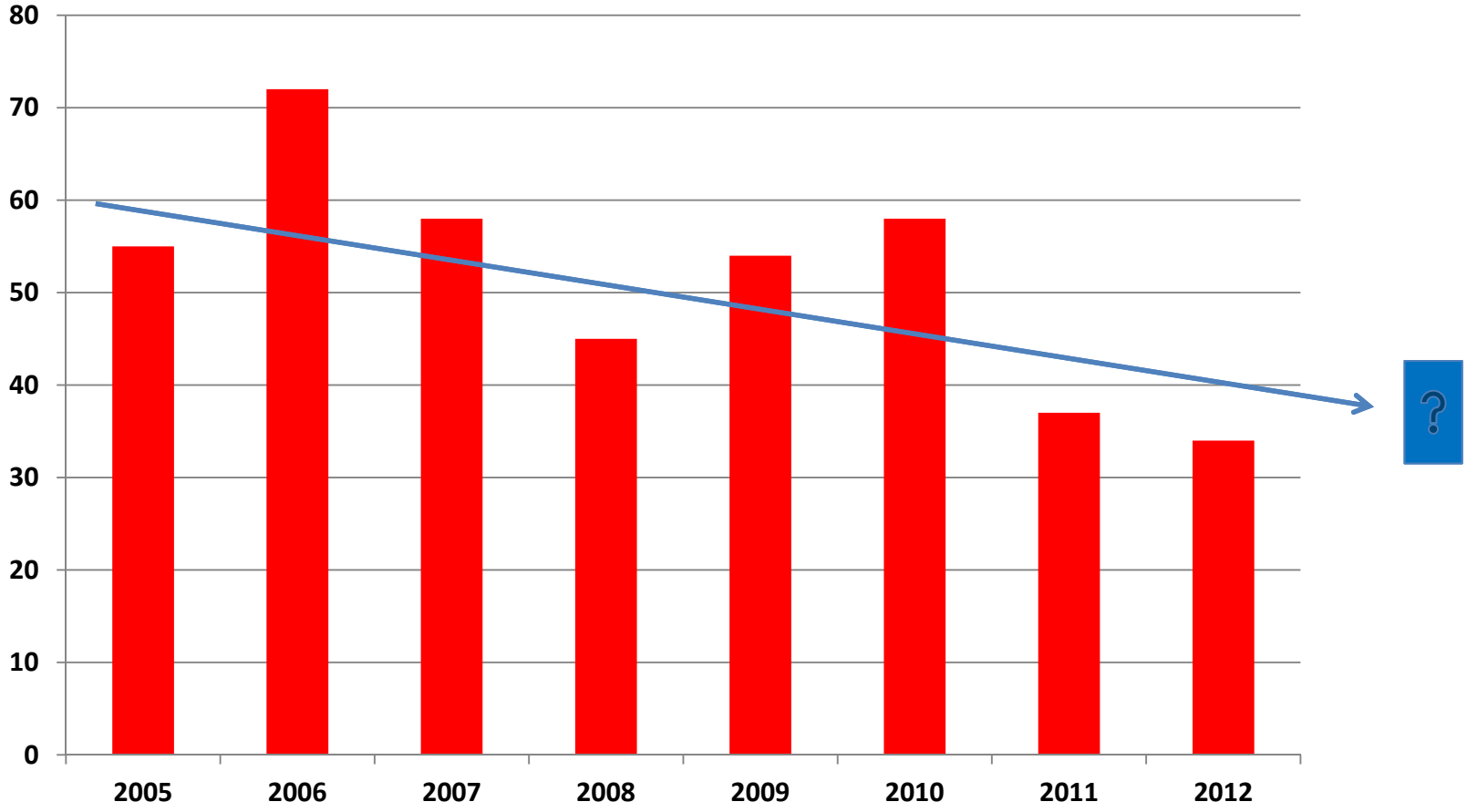


Unadjusted graft survival after receiving a deceased donor (a) or living donor (b) kidney transplant preemptively or after 6 to over 24 months on dialysis reprinted with permission from [6].

Recipients do better after a living donor transplant compared to cadaveric transplant

Davis C, et al. Curr Opin Nephrol Hypertension. 19(6):592-597, 2010.

Living Donor Kidney Transplants
(TNMC)



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Donor evaluation

- Assessment of blood groups and a cross-match between recipient and donor
- Medical, surgical, and psychosocial evaluation
- Donor selection Conference
  - Kidney donor may be
    - Accepted
    - Excluded
    - Require additional assessment

Absolute contraindications

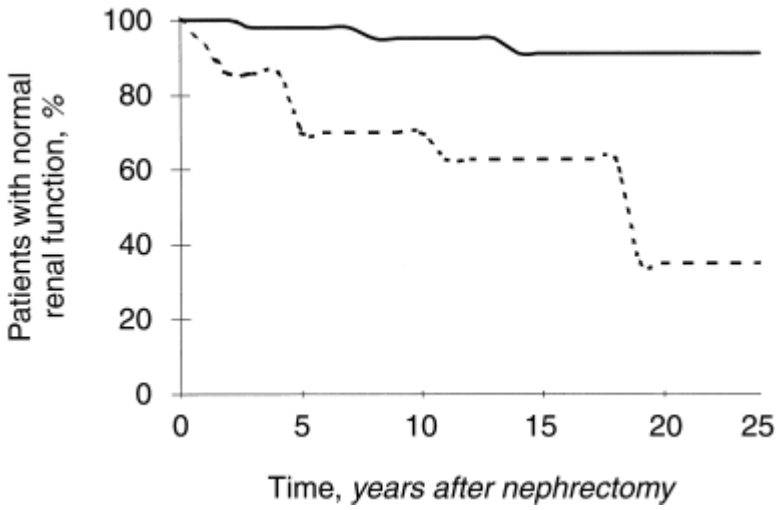
- Age <18 yrs
- Proteinuria
- GFR <80 mL/min/1.73 m^2
- Pregnancy
- Urologic and renal vascular abnormalities
- Active infection
- Chronic active viral infection (HIV, HTLV, Hepatitis B or C)
- Active malignancy

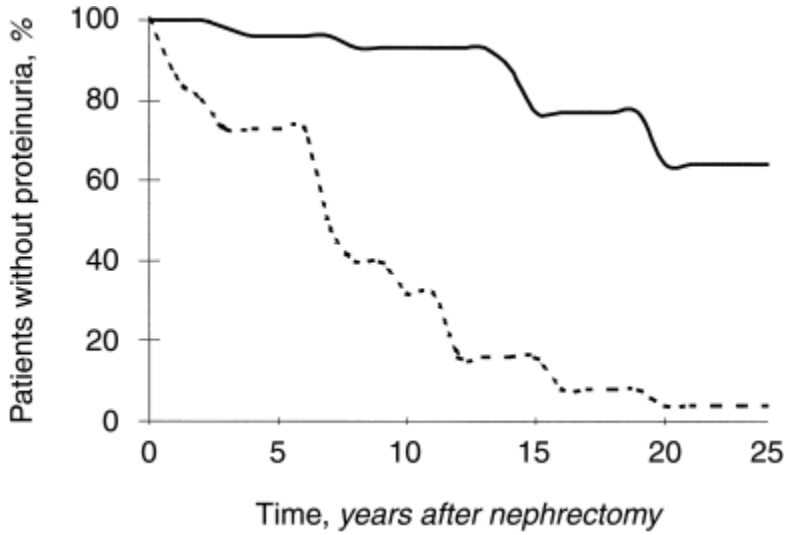
A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. Transplantation 2005.

Absolute Contraindications

- Chronic illness
  - Pulmonary, liver, autoimmune, neurologic, or cardiac disease, hypertension with end organ damage, diabetes mellitus
- Nephrocalcinosis, existent bilateral kidney stones
- Active substance abuse
- Disorders requiring chronic anticoagulation
- Psychological instability or coercion
- BMI >35 kg/m^2

Obesity is a risk factor for proteinuria and chronic renal failure after unilateral nephrectomy.





Probability of negative proteinuria and normal renal function in obese (dashed line) and nonobese (solid line) patients (log-rank test, $P < 0.001$).

Praga M, Rodicio JL et al Kidney International (2000) 58, 2111–2118

Donor Nephrectomy - Immediate Risks

- Pneumonia
  - Advocate smoking cessation
- Urinary tract infection
  - Check urinalysis prior to procedure
- Wound complications
- DVT with or without PE
  - Discontinue hormonal contraception or hormone replacement six weeks prior to surgery
- Death
  - Surgical mortality - 3.1 per 10,000 donors

Segev DL, Muzaale AD et al JAMA. 2010;303(10):959

Kidney Donation - Long-Term Consequences

- Single center study; 152 donors followed for approximately 11 years
  - Increase in blood pressure (from 125/79 to 134/81 mmHg)
  - Albuminuria – 10%
  - Reduction in GFR ≈25 percent
  - Changes - largely attributed to aging, possible effect of nephrectomy on GFR

Gossmann J et al Am J Transplant. 2005;5(10):

- 3700 kidney donors over 44 years
- Older age and a higher BMI - associated with lower GFR and HTN
- Hypertension and albuminuria in kidney donors - similar to matched controls

Ibrahim et al NEJM 2009;360:459-69.

- ESRD - 180 cases/million persons/year
  - General population - 268/million/year in the general population
- Survival of kidney donors – similar matched controls
- Quality-of-life scores better in donors than population norms

- Chronic Kidney Disease after donation
  - Hereditary factors
  - Living donors should undergo an annual assessment of renal function, including screening for proteinuria
- Follow-up
  - Mandatory - 6 months, 1 year and 2 years
  - Annually thereafter

Fehrman-Ekholm I et al Transplantation. 2001;72(3):444
Shohaib S Nephron. 1995;71(4):468
Ladefoged J Lancet. 1992;339(8785):124

- 96,000 kidney donors (median follow-up 15 years) compared to more than 20,000 people with two kidneys
- Overall risk of ESRD lower than general population
  - 90 per 10,000 among donors vs. 326 per 10,000 among controls
- Risk of kidney failure among donors by race
  - 51/10,000 among black vs. 23/10,000 among whites

Muzaale AD, et al JAMA. 2014;311.

Long term Outcomes - Racial Differences

- 39 African-American living donors completed a post-donation evaluation at University of Maryland General Clinical Research Center. Consisted of a health questionnaire and measurement of height, weight, three blood pressures readings, determination of albuminuria and Serum Creatinine.
  - Hypertension - 41%
  - 29% decline in GFR compared to baseline
    - Decline was even higher in donors with BMI greater than 35kg/m2

Nogueira JM et al Transplantation. 2009;88(12):1371.

- Compared with whites, black donors had increased risk of
  - Hypertension
  - Diabetes mellitus needing medical therapy
  - CKD
- Compared to NHANES data
  - Risk similar to black individuals in the general population
  - Donor nephrectomy – no increased risk of diabetes, hypertension and CKD
- Hispanic donors - similar outcomes as blacks

Gaston RS, Young CJ Am J Transplant. 2010;10(12):2574.

Pregnancy in donors

- Potential young female donors, must be aware of possibility of increased risks with pregnancy after donation
- Adherence to high level of surveillance and monitoring
- No clear evidence to guide the timing of pregnancies after donation
- Delay pregnancy at least a year after nephrectomy to allow recovery
  - Emotionally and medically (stabilize renal function)

Buszta C et al Transplantation. 1985;40(6):651
Wrenshall LE et al Transplantation.1996;62(12):1934
Ibrahim HN et al Am J Transplant. 2009;9(4):825.
Jones JW et al Transplant Proc. 1993;25(6):3082.
Reisaeter AV et al Am J Transplant. 2009;9(4):820.
Nevis IF et al Am J Transplant. 2009;9(4):661.

Economic considerations

- Donors incur many types of costs attributable to kidney donation and the total costs maybe higher than reported.
- The system covers only the direct consequences of organ removal, and recoups the costs of related medical services from the transplant recipient's health insurance provider.
- The system forces transplant programs to differentiate between health services that are, or are not directly attributable to donation
  - may compromise pre-transplant evaluation, postoperative care and long-term care of living donors.
- The system is particularly problematic in the United States, where a significant proportion of donors may not have medical insurance.
- The requirement to assign donor costs to a particular recipient is poorly suited to facilitate advances in living donation
  - non-directed donors and living-donor paired exchange programs.
- Basic medical insurance becomes a necessity for living donation.
- System of attributing donor costs to the recipient's insurance is insufficient.

Ommena ES, Gill JS Am J Transplantation 2010; 10: 747–750
Clarke KS, Garg AX Nephrol Dial Transplant. 2006 Jul;21(7):1952-60.

- Donating a kidney is a very personal decision and carries some risk.
- By accepting this potential small risk to themselves, donors are offering a profound benefit to another human being.
- Small number of kidney donors who do suffer kidney failure are given high priority on kidney transplant waiting lists.

How many Faces do you see?

What if you are not a match for your intended recipient – there is hope !!!

- Desensitization protocol includes
  - Rituximab, therapeutic plasma exchange and
  - High-dose intravenous immunoglobulin (IVIG)

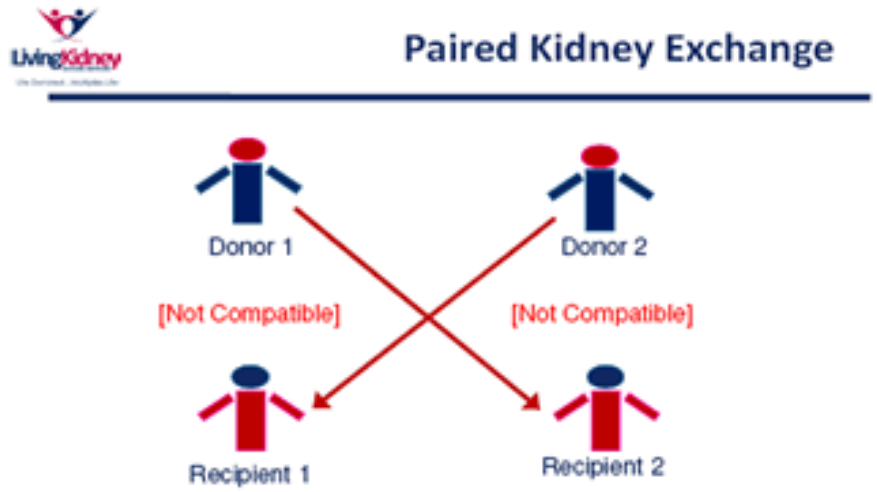
- Paired exchange
  - Potential to help more than one recipient
  - Relatively less complications after transplantation.

- For living donor transplants, there is no advantage to a genetically related donor versus an unrelated donor unless the related donor is HLA identical

Haririan A, Cooper M et al: Longer-term outcomes. AJT 9: 536–542, 2009
Sharif A, Alachkar N, Kraus E: QJM 105: 1141–1150, 2012

Paired Kidney Donation

- Positive crossmatch means that a donor and recipient are **not** compatible.

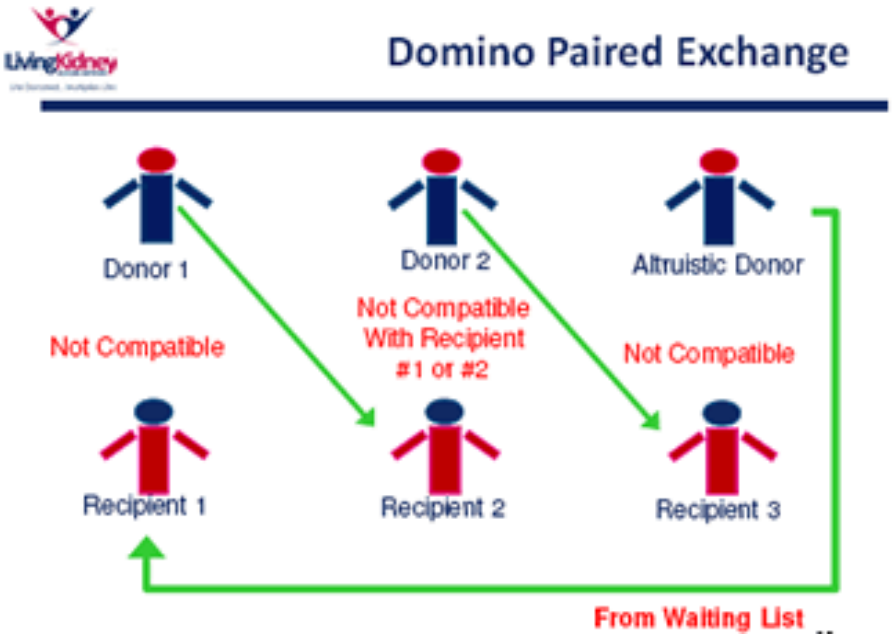


Kidney paired donation (KPD)

- Donor chain process
  - Donor who is incompatible with a designated recipient agrees to donate his or her kidney to a stranger, the designated recipient will receive a kidney from another stranger
  - Computerized database allows transplant centers and organ recovery agencies in the US to match cases in which the donor in each pair is incompatible with their respective recipient
  - By exchanging the donors in two or more pairs, a compatible match for multiple recipients can be found.

Anonymous Donation

- A domino kidney paired exchange starts with a non-directed or altruistic donor - allows many incompatible pairs to be transplanted.
- Donor #2 is not compatible with recipient #1 or #2.
- The altruistic donor allows the other pairs to be exchanged, and have the domino effect in saving many lives.



- National pool of potential matching pairs or chains - easier to find compatible donors
  - Hardest-to-match patients (previous transplant) or high antibody levels.
- Anonymous donor
  - Can also start a donor-recipient chain which could have the domino effect to save many lives.

Summary of The Living Donation Process at The Nebraska Medical Center

Regina Rau, RN, BSN

Nurse Coordinator

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Our Donor Process

- Voluntary phone call from Donor
- Education and Documentation
- Immunology Screen
  - Blood type
  - HLA
  - Crossmatch
- The Living Donor Evaluation
- Donor Surgery
- Donor Follow-up

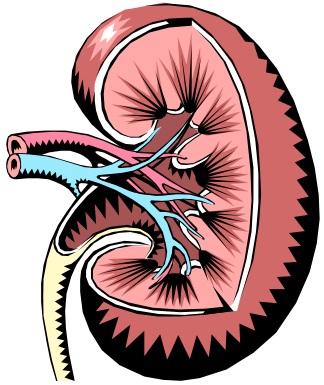
Initial Diagnostic tests

- CBC with diff, platelets, and coagulation profile.
- CMP, Lipid profile, liver function test
- Viral Testing
  - HIV, CMV, EBV, RPR, WNV, Hepatitis B and Hepatitis C
- UA with micro/macro and colony count
- 24 hour urine for CrCl, protein and albumin
- Drug screen
- TSH, T4
- Glucose tolerance test with HgBA1c

- Age appropriate malignancy screening
- EKG
- Chest x-ray
- CT angiogram
- More tests - depending on results of previous studies

Multidisciplinary Team

- Transplant Surgeon
- Donor Nephrologist
- Social Worker
- Psychologist
- Donor Coordinators
- Independent Donor Advocate



Role of the Independent Donor Advocate

- IDA role is independent and separate from the recipient team
- IDA protects and promotes the interest and rights of the living donor
- Confidentiality of the donor is maintained throughout the process
- Donor team respects the decision of the living donor
- IDA will ensure that donor understands the organ donation process
- Ensure the donor understands the short and long term risks
- Looks after the safety, education and interests of the potential donor
- Ensure the decision to become a living donor includes the emotional and psychological aspects of donation

Role of the IDA

- Ensure the donor knows that there are other options for the recipient
- Ensure the donor knows that they can back out at anytime and for any reason
- Ensure that the decision to donate is informed and free from coercion
- Ensure the living donor medical history is reviewed and determined medical suitability for donation
- Inform the potential donor of the UNOS requirements for living donor follow up at 6months, 1 year and two years
- Discuss the financial aspects of living donation
- Represent and advise the living donor throughout the process

The Donor Surgery

- Laparoscopic Nephrectomy
  - Two to three small incisions close to the umbilicus and one midline incision, through which the kidney is removed.
  - Laparoscopic donors require shorter hospitalization
- Open Nephrectomy
  - Flank incision using the retroperitoneal approach
  - Technique is safe with low mortality
  - Incision may result in discomfort and recovery maybe longer.

The Post-op Course

Admit to SOTU

- Will have IV fluids, PCA pump, Foley catheter
- Day 1-2, walk 3 x day, decrease IV fluids, discontinue pain pump and start oral pain medications, discontinue Foley catheter and advance diet as tolerated
- Typically discharged two days after surgery with pain medications and bowel regimen
- Follow-up with surgeon two weeks post donation
- Lifting restriction of less than 10 lbs for 6 weeks

Perioperative risks

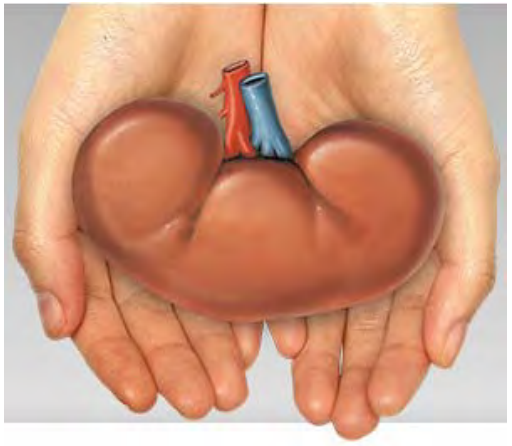
- Small bowel obstruction
- Shoulder pain
- Bleeding
- Pneumonia
- Urinary tract infection
- Wound infection
- Hernia
- Blood clots/pulmonary embolism
- Death-low risk 3.1 per 10,000 donors

Living Donor Follow Up

- UNOS requires all transplant programs to submit data on all living donors at 6 months, one year and two years.
- All donors sign and agree prior to donation to follow up with their primary care physician. Check weight, blood pressure. Also test Urine for protein and check Serum Creatinine.
- A functional status questionnaire is filled out by the donor.

Living Donor Options
at The Nebraska Medical Center

- Direct Donation
- Anonymous donation
- ABO incompatible donation
  - Kidney Paired Donation
  - Internal exchange



There is always Hope!

- **ABO incompatible transplants**
  - 2006 onwards TNMC has performed 14 transplants
- **Internal two-way exchanges**
  - 2004-2012 we have performed 8 of these exchanges
- **Two-way exchange**
  - 1 through the Paired Donor Network in 2010
- **Three-way exchange**
  - 1 through the KPD program in 2014
- **A chain that started with our Anonymous donor**
  - 1 through the KPD program in 2014

Summary

- So far this year, we have done 17 living donor transplants.
- Major goal is to expedite transplantation
  - limit time on dialysis.
- Reverse the downward trend in living donation.
- Spread the message for different options regarding living donation.
- Establish regular health care follow up for the living donor per OPTN/UNOS guidelines.
- Thank you.

Call us at **402-559-5000**. We welcome your call and questions

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