

The Evaluation of Kidney Transplant Candidates and Potential Living Donors

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Case #1

- 37 yo male, ESRD due to FSGS
- DD kidney transplant 5 years ago-
primary nonfunction
- Second DD kidney transplant 3 years
ago-massive proteinuria with **recurrent
FSGS** 2 months post-transplant
- Back on dialysis 18 months later
- Wants another transplant

Case #2

- **70 yo** Asian male, neuropsychiatrist, works full time
- ESRD due to FSGS, BMI 20.4
- HTN, CABGx5 vessel 10 years ago, on PD for 3 months, blood transfusion+, PRA: 40%
- **Prostate cancer**: diagnosed 8 months ago, Gleason score 7, treated with cryoablation, most recent PSA < 0.1
- Two potential donors: 58 yo friend and 24 yo grandson

Case #3

- 29 year old male, ESRD due to posterior urethral valves
- Kidney transplant from his mother at the age of 13- lasted 7 years
- DD kidney transplant at the age of 22- back on dialysis 14 months ago
- Multiple access surgeries- currently dialyzing via subclavian catheter
- Comes in for a 3rd transplant- 8 hospital admission in the last 12 months for **cocaine overdose and misses his dialysis treatments** 2-3 times per month

Kidney Transplantation

- The **best** treatment option for majority of patients with ESRD regardless of sex, race, age or cause of ESRD
 - Increase in life expectancy
 - Increase in quality of life
 - Decrease in healthcare costs
- No formal upper age limit
- The demand for kidney transplantation exceeds the supply of transplantable organs
- Waiting times are quite long

What Makes Your Patient a Kidney Transplant Candidate?

- Is there a reasonable life expectancy?
- Can perioperative risk be reasonably managed?
- Does the patient have any condition(s) that will be worsened by, or complicate:
 - ***Surgery***
 - ***Immunosuppression***
- Is the surgery technically feasible?

Purpose of the Transplant Evaluation

- Identify potentially suitable recipients
- Prepare patients for kidney transplantation
 - Education of patients and families
 - Risks and benefits
 - Transplant options
 - Optimize candidate's health
 - Help CKD planning for referring care-givers

Recipient Evaluation

- Referral for transplant evaluation-from nephrologists (majority) or self-referral (rare)
- Basic information gathering: insurance coverage, **patient's medical history**, family history (including potential living donors) and laboratory results
- Initial interview and exam

Recipient Evaluation

- Physical exam
- Chest x-ray, ECG-12 lead
- Dental evaluation
- Pap smear, mammogram, PPD
- Labs: Complete metabolic panel, eGFR, CBC, serologies (HIV, hepatitis B and C, CMV, and RPR), HLA typing, PRA , PSA, blood type

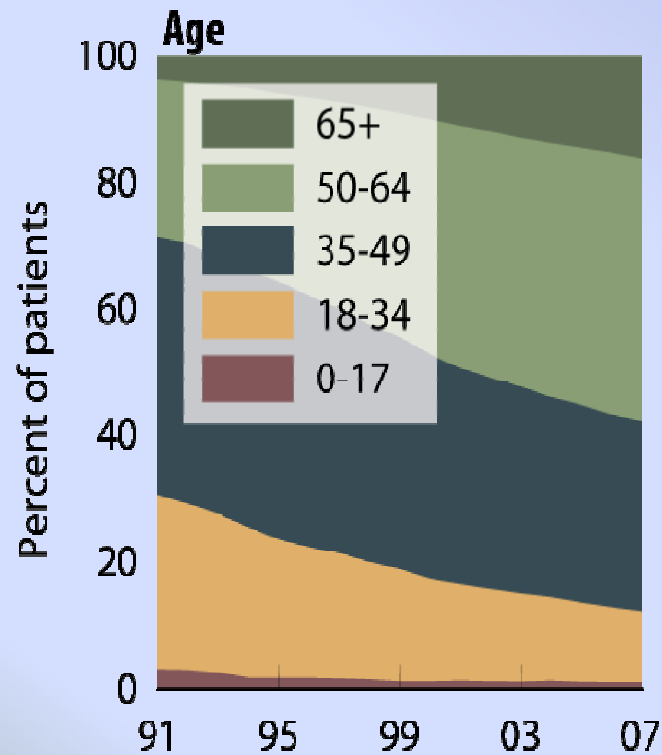
Physical Exam

- Carotid pulse/bruit
- Peripheral pulses, abdominal and femoral bruit
- Careful abdominal exam: previous surgeries/scars, organomegaly, large kidneys in patients with PKD
 - **Is there enough room for the graft?**
- Testicular exam, rectal exam
- Breast exam

Recipient Evaluation

- Stress test (dobutamine echo or thallium)/echo/cardiac catheterization
- Colonoscopy
- Arterial Doppler of carotids or lower extremities
- CT abdomen/CT pelvis
- Toxicology screen
- Pulmonary function tests
- Bladder function

Age and Kidney Transplantation



Age of patients on wait-list

USRDS Annual Report 2009

- Growing population
- Above 70
 - *Quality of life, NOT life expectancy*
- Functionality with age
- Ethical issues
 - *Organ shortage*
 - *Living donors*
 - *Age discrimination*
- Case-by-case basis
 - *Benefit vs risk of harm*

Medical History

- Recent diagnosis of cancer
- Active infection (catheter-related, endocarditis, osteomyelitis, etc.)
- Recent chest pain, heart attack, or arrhythmias
- Foot ulcers, GI bleeding, blood transfusion
- Malnutrition, morbid obesity

Medical History-Cancer

- Active or recent evidence of a malignancy, except for some skin cancer (basal cell): transplant is contraindicated
- Israel Penn International Transplant Tumor Registry (IPITTR)
- Waiting time: varies amongst different tumors
 - *Breast Ca: at least 2 years-up to 5 years in certain tumors (regional lymph node involvement, bilateral disease, inflammatory histopathology)

Recurrence Risk of Pre-existing Breast Cancer After Solid Organ Transplantation

Wait time	<2 yrs	2-5 yrs	>5 yrs
# Patients	10	30	51
% Recurrence	20	20	9.8
Died of disease	10	17	4

	Stage I (55)	Stage II (25)	Stage III (11)
Median wait (mo)	65.3	87.2	61.5
% Recurrence	5.4	8	63.6
% Died of disease	3.6	4	45
Survival (1,3,5 yrs)	95, 87, 73%	95, 88, 88%	100, 67, 14%

- **High mortality with less than 5-year waiting period**
- **No transplantation in stage III breast cancer patients**

Buell JF et al, abstract #518, AST 2003

Medical History-Cancer

- Prostate Ca: At least 2 years disease-free period followed by negative blind random biopsies
- Renal cell Ca: 2-year waiting time for asymptomatic >2 cm RCC, possibly shorter time <2 cm, at least 5 years for symptomatic RCC (recurrence risk is still $\sim 26\%$)
- Colorectal Ca: waiting period of 5 years for all Duke's classifications

Medical History-Infection-HIV

- Undetectable plasma HIV-1 RNA levels (viral load) for at least 3 months
- CD4+ T-cell count of more than 200 cells/microL
- No history of opportunistic infections or neoplasms (no AIDS-defining illness)
- Maintained on highly active antiretroviral therapy (HAART)
- Increased incidence of acute rejection after transplantation
- Close follow up – Infectious Diseases & Transplant Nephrology

Medical History-Infection

Hepatitis C

- The prevalence of the positive HCV antibody among HD patients in the US: average 9.3%, range: 6%-38% among dialysis centers
- Among the kidney transplant population, the prevalence of anti-HCV positivity range: 5%-46%, depending on the countries and/or centers
- Available data on kidney transplantation in this patient population suggest a survival advantage compared to remaining on hemodialysis

Medical History-Infection

Hepatitis C

- After transplantation, liver disease is more frequent in HCV-positive patients than in HCV-negative patients
- HCV-positive patients have a higher risk for developing proteinuria, diabetes and infections after transplantation
- Long-term patient and graft survival rates are lower in HCV-positive patients than in HCV-negative graft recipients

Medical History-Infection

Hepatitis C

- OPTN and SRTR database, Social Security Death Master File
- 75,629 HCV negative patients and 3,708 HCV positive patients, kidney transplant 1995-2004
- **Increased mortality risk for HCV-positive recipients vs HCV-negative recipients, particularly among younger age groups**
- **The use of induction therapy was not associated with an increased mortality risk, for either lymphocyte depleting or nondepleting antibodies**
- **The use of MMF was associated with reduced mortality risk among HCV-positive recipients**

Luan FL, et al. Transplantation 2008

Medical History-Infection

Hepatitis C

- All transplant candidates should be tested for HCV
- Serum transaminases may be normal even if the patient has advanced liver disease
- If HCV RNA is positive, proceed with liver biopsy
- Cirrhosis—consider combined liver/kidney transplant
- **HCV is not a contraindication for transplant**

Cardiovascular Disease

- Pre-transplant CVD is an important risk factor for post-transplant CVD
- High risk patients (diabetics, older patients, patients with 2 or more risk factors) should have a cardiac stress test/cardiac cath-if needed- before transplant
- Repeat screening every 1-2 years during waiting, every year for diabetics

Screening Diabetic Transplant Candidates for CAD

- Coronary angiography is recommended:
 - All Caucasian type I diabetics over age 45
 - Type I diabetics younger than age 45 with EKG changes (ST-T segment), smoking history (>5 pack/year), diabetes for at least 25 years

Sensitivity: 97%, negative predictive value: 96%

Manske CL et al, Kidney Int 44:617-621, 1993

Obesity and Transplantation

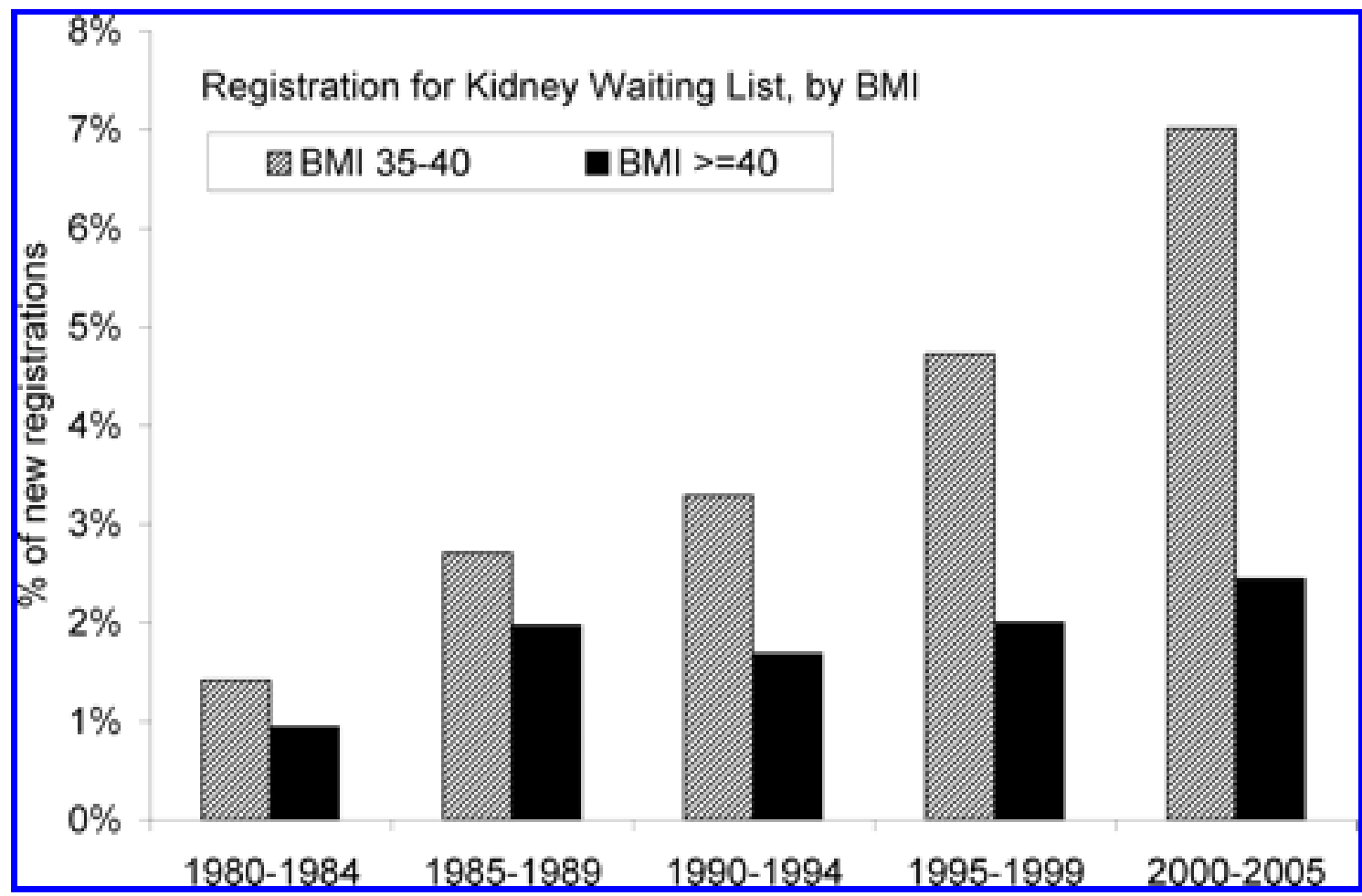
- The majority (60%) of subjects at time of transplantation currently are overweight or obese
- Between 1987 and 2001, the proportion of obese transplant recipients rose by 116% (grossly similar to that in the general population)
- The likelihood of being obese increased with age, female sex, NIDDM, black race, and the more recent the transplant year

Friedman AN et al, Am J Kidney Dis 2003

Obesity-Access to Kidney Transplantation

- 132,353 patients who were registered for kidney transplantation in the United States between 1995 and 2006
- Among all patients awaiting kidney transplantation, the likelihood of receiving a transplant decreased with increasing degree of obesity, categorized by ranges of BMI
- Similarly, the likelihood of being bypassed when an organ became available increased in a graded manner with category of obesity

Segev DL et al, JASN 2007



Segev DL et al, JASN 2007

Obesity and Transplantation

- More superficial wound breakdown, complete wound dehiscence, and wound infections
- Similar graft survival and patient survival
Johnson DW et al, Transplantation 2002
- UNOS data in obese (BMI 30-40) type 1 diabetic SPK recipients: increased DGF, 1-year kidney acute rejection, and pancreas graft thrombosis
- After adjusting for possible confounders, the odds ratios for overall transplant complications were 1.03 for overweight (BMI 25-29.9) and 1.38 for obese
- Obesity, but not overweight, was associated with patient death, pancreas graft loss, and kidney graft loss at 3 years

Sampaio MS et al, Transplantation 2010

Obesity and Transplantation

- Analysis of paired kidneys: obesity (BMI>30) is not a risk factor for DGF, acute rejection, and 1-year graft survival, but decreased long-term graft survival

Yamamoto S et al, Clin Transplant 2002

- Obese transplant (BMI >35) recipients have similar outcomes to nonobese patients, more posttransplant diabetes, more delayed graft function and more acute rejection at 6 months

Howard RJ et al, Transplantation 2002

Chang SH et al, Transplantation 2007

Obesity and Transplant Outcome

- UNOS database: 27,377 primary kidney-only transplants between 1997 and 1999
- Morbid obesity (BMI ≥ 35) was independently associated with increased risk of:
 - DGF (p < 0.001)
 - Prolonged hospitalization (p < 0.001)
 - Acute rejection (p = 0.006)
 - Decreased overall graft survival (p = 0.001)

Gore JL, et al. Am J Transplant 2006

Medical History-Other Risks

- Disease activity (lupus, vasculitis)
- Urologic disease, cystic disease
- Pre-transplant native kidney nephrectomy
- GI diseases (peptic ulcer, gallstones, pancreatitis)
- Medications (interactions)
- Psychosocial issues, alcohol and substance abuse
- Recurrent diseases (FSGS, MPGN, HUS, lupus)
- Ethical issues (noncompliance with medications, multiple transplants, transplant after recurrence)

What Can You Do to Help Your Patient's Transplant Candidacy

- Encourage optimal health maintenance
 - *Vaccinations*
 - *Exercise*
 - *Healthy eating*
 - *Adherence*
- Keep transplant center “in the loop”
 - *Records*
 - *Communication*
- Refer early
 - *Encourage pre-emptive transplant*

Live Donor Evaluation

Living Donors

- The annual number of available deceased donors will not resolve the ongoing shortage of organs
- The survival of a kidney transplanted from a live donor exceeds the results achieved from a deceased donor
- Success of live donor transplantation no longer necessitates the consideration of an HLA match unless there is possibility of a transplant from HLA identical sibling
- The survival rate of a kidney transplant from a genetically unrelated donor is excellent

Living Donors

- In 1954: Requiring an identical twin for success
- During the 1980's: Selection of an HLA-matched family member
- Current: any person (irrespective of the HLA match) can be a donor if they are medically and psychosocially suitable
- **It is illegal to buy or sell kidneys or coerce a donor**

Potential Live Donor

- Appropriate for donation from nephrologic standpoint – what is his//her renal risk?
- Healthy enough for surgery?
- Competent, willing to donate; free of coercion
- Medically and psychosocially suitable
- Fully informed of the risks and benefits of donation
- Fully informed of risks, benefits, and alternative treatment available to the recipient

Potential Advantages of Live Donation

- Better short-term and long-term results
- More consistent early function and ease of management
- Avoidance of long wait for cadaveric transplant
- Less delayed graft function
- Less aggressive immunosuppressive regimens
- Surgery can be planned ahead (medical and personal convenience)
- Emotional gain to donor
- Helps relieve stress on national cadaver donor supply

Potential Disadvantages of Live Donation

- Psychological stress to donor and family
- Inconvenience and risk of evaluation process (i.e. IV contrast)
- Operative mortality (0.03% or 1 in 2000 patients)
- Major perioperative complications (4.4%, range: 0.0 to 13.0%)
- Minor postoperative complications (up to 50%)
- Long-term morbidity
- Risk of traumatic injury to remaining kidney
- Risk for unrecognized chronic kidney disease

Long-Term Consequences of Kidney Donation

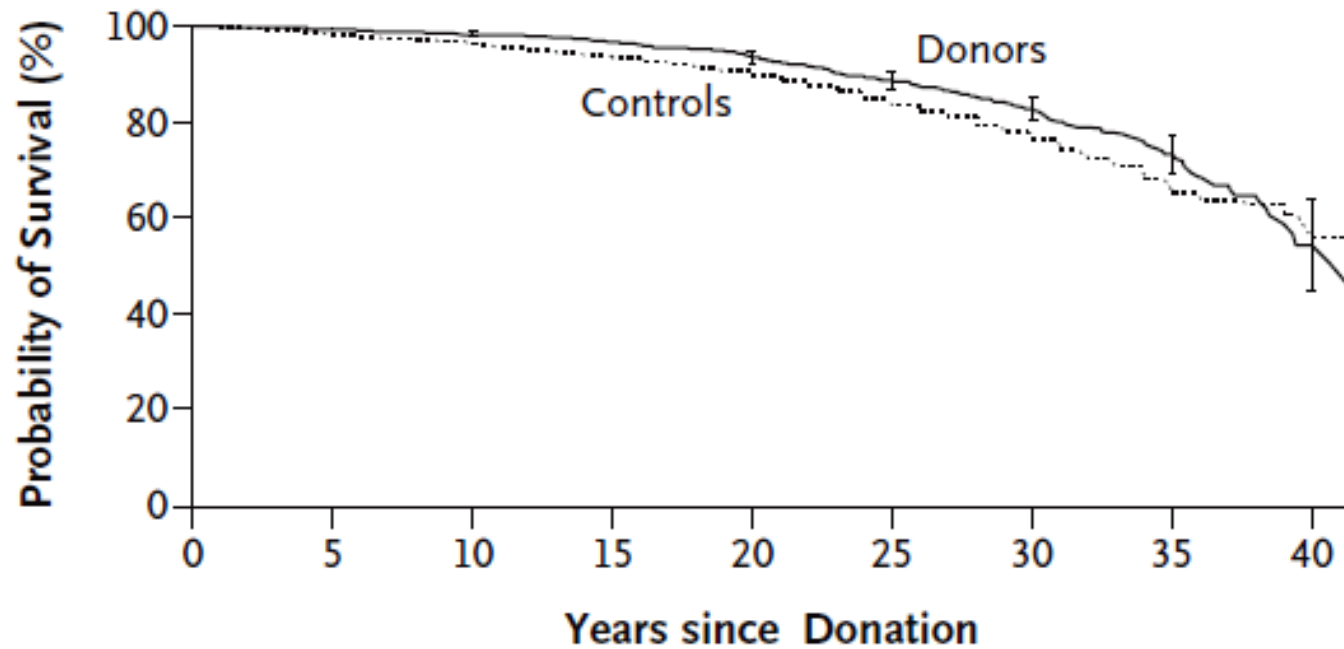
- 3698 kidney donors who donated kidneys during the period from 1963 through 2007
- From 2003 through 2007: glomerular filtration rate (GFR) and urinary albumin excretion were measured; the prevalence of hypertension, general health status, and quality of life were assessed in 255 donors

Ibrahim H, et al. NEJM 2009

Long-Term Consequences of Kidney Donation

- The survival of kidney donors: similar to that of controls-matched for age, sex, and race or ethnic group
- ESRD developed in 11 donors: rate of 180 cases/million persons/year, as compared with 268 per million/year in the general population
- At a mean of 12 ± 9 years after donation, 85.5% of the subgroup of 255 donors had a GFR of ≥ 60 ml/min, 32.1% had hypertension, and 12.7% had albuminuria
- Older age and higher BMI, but not a longer time since donation, were associated with both lower GFR (< 60 ml/min) and hypertension

Ibrahim H, et al. NEJM 2009



No. of Donors	3698	2716	2065	1575	1228	775	410	140	16
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Figure 1. Survival of Kidney Donors and Controls from the General Population.

I bars at 5-year intervals indicate 95% confidence intervals for the probability of survival among kidney donors.

Medical Follow-up of Living Kidney Donors by 1 Year After Nephrectomy

- In 2003, our program developed a policy recommending that donors receive medical follow-up by 1- year postnephrectomy
- A retrospective cohort study of 137 live kidney donors at UPenn
- Medically complex donors: hypertension, body mass index ≥ 30 , nephrolithiasis, age 65 years or older, creatinine clearance < 80 mL/min/1.73 m², or had a first-degree relative with diabetes mellitus
- Adequate follow-up: one visit with a nephrologist at our center, or blood pressure, serum creatinine, and urinalysis checked elsewhere

Reese P, et al. Transplant Proc 2009

Medical Follow-up of Living Kidney Donors by 1 Year After Nephrectomy

- Eighty-three donors (61%) had adequate follow-up, 42 did not, and 12 could not be contacted
- At multivariate logistic regression, donors with adequate follow-up were more likely to be medically complex and older than donors with inadequate follow-up
- A substantial minority of donors do not receive recommended care by 1 year after nephrectomy

Donor Evaluation

- Live kidney donor **must** receive a complete medical and psychosocial evaluation
- Blood typing: often the first test, relatively inexpensive
- Initial cross-match
- Preliminary medical evaluation

Donor Evaluation

- Complete history (*hereditary dz) and physical exam
- Labs (routine, serologies, OGTT)
- UA, urine culture, pregnancy test
- 24 hour urine for protein and creatinine
- GFR measurement (glofil-ideal)
- Chest x-ray, ECG, exercise stress test for patients older than 50 years of age
- CT angio or MRA of renal arteries
- Psychosocial evaluation
- Repeat crossmatch before transplantation

Hereditary Diseases

- Alport's syndrome
- Diabetes
- Polycystic kidney disease
- FSGS
- IgA nephropathy
- Hypertension
- HUS, SLE, and cystinosis

Alport Syndrome

- Defect in $\alpha 5$ subunit of type IV collagen in GBM
- Most cases X-linked recessive but in 15% are autosomal recessive
- Screen- urinalysis (UA), BP, hearing, eye exam
- Adult male with normal UA – can donate
- Adult female with normal UA – possible carrier
- Adult female with hematuria – definite carrier, cannot donate, 15% risk CKD
- Benign renal biopsy age >40, no HTN may consider them as donors

Diabetes

- Contraindication to donation
- Fasting plasma glucose >126mg/dl
- Fasting glucose 100-125mg/dl
 - Should have 2hr OGTT (>200 is c/w DM)
 - Consider for those with BMI>30, TG>250, HDL<35
- Family history of diabetes
 - 1st degree relative with DM – 25% risk of developing DM
 - 2 relatives with DM – 50% risk of developing DM
- Gestational diabetes requiring insulin
 - 50% risk of developing DM within the next 5 years

ADPKD

- Screen first degree relative donors with ultrasound
- Age specific ultrasound criteria for diagnosis
 - Age < 30 – 1 cyst in each kidney or 2 cysts in 1 kidney
 - Age 30-59 – 2 or more cysts in each kidney
 - Age > 60 – 4 or more cysts in each kidney
 - 100% reliable if donor > age 30
- DNA analysis is also available
- Use of MRI-change

Amsterdam Forum Guidelines

- A **GFR** < 80 ml/min or 2 SD below normal (based on age, gender, and BSA corrected to 1.73 per m²) generally preclude donation
- Patients with a **BP** > 140/90 mmHg by ABPM are generally not acceptable as donors
- Patients with a **BMI** > 35 kg/m² should be discouraged from donating
- **Dyslipidemia** alone does not exclude kidney donation (Keep an eye on “Metabolic Syndrome”)

Amsterdam Forum Guidelines

- A 24 h urine **protein** of >300 mg is a contraindication to donation
- Individuals with a history of **diabetes** or fasting blood glucose ≥ 126 mg/dl (7.0 mmol/l) on at least two occasions (or 2 h glucose with OGTT ≥ 200 mg/dl (11.1 mmol/l)) should not donate

Hematuria-Prospective Kidney Donors

- 512 consecutive prospective donors, 14 (2.7%) continued to have asymptomatic, microscopic hematuria over 1 month
- If the medical history, physical examination, and computerized tomographic angiography were unremarkable, and if they still wished to donate, a kidney biopsy was performed
- In two prospective donors, hematuria resolved after treatment for urinary tract infection
- Two others declined donation and were referred to their primary care provider

Koushik R, et al. Transplantation 2005

Hematuria-Pro prospective Kidney Donors

- Kidney biopsy in the remaining 10 showed: two normal; 4 thin basement membrane nephropathy (TBMN); one nonhomogeneous basement membrane abnormalities; one IgA nephropathy, one patient with 7 of 30 glomeruli globally sclerotic; and one TBMN and early hypertensive changes without systemic HTN
- Only 4 of the 10 who underwent kidney biopsy donated (two normal, two TBMN).

Koushik R, et al. Transplantation 2005

Persistent Microscopic Hematuria
Two or more positive dipstick urine tests on separate occasions over at least one-month period



Detailed family history	Need to undergo for TBMN, Alport's syndrome etc
Urine culture	to rule out infection
24 hour urine collection	to estimate protein, calcium, urate etc
Cytology	to look for malignancy
Cystoscopy	
Renal imaging:	
CT-Renal angiogram	to look for Nephrolithiasis, urothelial cancer
(or)	and also to assess anatomy of renal vasculature
Intravenous Pyelography	



If no urological cause found, then **Counseling** and **option for deferring donation**



Deferred donation
Further follow-up with PCP

For those willing to undergo further evaluation
Renal Biopsy should be performed

Causes of Persistent Microscopic Hematuria

- **Glomerular** bleeding (common causes, not associated with proteinuria or casts)
 - Thin basement membrane nephropathy (TBMN)
 - Alport Syndrome (early stage) or carrier state
 - IgA nephropathy

Causes of Persistent Microscopic Hematuria

- **Extraglomerular** bleeding
 - Stone disease
 - Hemoglobinopathy (SS/SA hemoglobin)
 - Polycystic kidney disease
 - Benign prostatic hyperplasia (elderly donors)
 - Malignancy (bladder, kidney, prostate)
 - Arteriovenous malformations and fistulas
 - Schistosomiasis (in endemic areas)
 - Hypercalciuria, hyperuricosuria, etc.

Amsterdam Forum Guidelines

- Asymptomatic potential donor+history of a **single stone** may be suitable if:
 - No hypercalcuria, hyperuricemia, or metabolic acidosis
 - No cystinuria or hyperoxaluria
 - No urinary tract infection
 - No evidence of multiple stones or nephrocalcinosis on CT scan

Amsterdam Forum Guidelines

- **Stone** formers who should not donate are:
 - Nephrocalcinosis on X ray or bilateral stone disease
 - Stone types with high recurrence rates, and are difficult to prevent

Amsterdam Forum Guidelines

- A prior history of the following **malignancies** usually excludes live kidney donation:
 - Melanoma
 - Testicular cancer
 - Renal cell carcinoma
 - Choriocarcinoma
 - Hematological malignancy
 - Bronchial cancer
 - Breast cancer
 - Monoclonal gammopathy

Psychosocial Evaluation of Living Kidney donors

- Sociodemographic history and current status
- Capacity to comprehend information
- Psychological status
- Relationship with transplant candidate
- Rationale and reasons for volunteering to donate
- Knowledge, understanding, and preparing for donation
- Social supports
- Financial status and suitability

New Strategies in Living Donation

- New techniques: Hand-assisted laparoscopic donor nephrectomy
- Desensitization and transplantation across the blood-type barrier
- Older living donors for older recipients
- Paired kidney exchange (PKE)
- Altruistic (nondirected) donation
- Altruistic donor chains (domino paired donations)
- List exchange programs
- Living Donor Paired Donation program: increased since 2006 **but** makes up only 1% of transplants performed in the US

Paired Kidney Exchange

- To obtain compatible donor transplants for two or more recipients with immunologically incompatible potential live kidney donors by exchanging donors
- 2-way exchange or 3-way exchange-using a computer program-usually performed simultaneously
- PKE programs now operate in the Netherlands, South Korea, Romania, the United Kingdom, US and Australia
- Isolated reports of PKE have been published from Switzerland, Israel and Canada
- Most single centers are unable to enroll enough pairs for efficient exchange on a permanent basis, and collaboration with other centers is essential

Paired Kidney Exchange

- Legal framework to allow the development of national programs for both altruistic nondirected donation and paired donation
- Allocation algorithm for matching
- Mandatory medical suitability criteria
- Listing in the deceased donor waiting list
- Donor travel versus shipping of organs

Donor Evaluation-Actual Cases

- Microscopic hematuria and renal mass (renal cell carcinoma)
- Unknown pregnancy
- Significant bilateral hydronephrosis
- Horseshoe kidney
- Unrecognized hypertension
- Slightly elevated liver enzymes, + HCV (previously unknown)
- Fibromuscular dysplasia
- EF < 20% on ECHO
- Proteinuria: kidney biopsy IgA nephropathy

The Declaration of Istanbul on Organ Trafficking and Transplant Tourism

- Organ trafficking and transplant tourism should be prohibited because they violate the principles of equity, justice, and respect for human dignity
- The Declaration is also clear regarding the consequences of transplant commercialism: “Because transplant commercialism targets impoverished and otherwise vulnerable donors, it leads inexorably to inequity and injustice and should also be prohibited”
- **The live donor cannot become the target source of kidney transplantation unless proper follow-up is provided, with the same emphasis of care that is afforded the recipient**

Transplantation 2008



An International Survey

- Sent out by Donor Nephrectomy Outcome Research (DONOR) Network investigators
- 203 health practitioners from 119 cities in 35 different countries responded to the survey
- Sixty-three percent of respondents nephrologists, 27% surgeons, 4% nurse practitioners and 6% other individuals involved in discussing risks with potential donors

Housawi AA, et al. Nephrol Dial Transplant 2007

Table 2. Long-term medical risks discussed with potential living kidney donors

	Proportion of health care providers ^a who discuss risk (with 95% confidence interval)
Hypertension	92 (87–95)%
Proteinuria	83 (77–87)%
Chronic kidney disease ^b	81 (75–86)%
Kidney failure requiring dialysis	86 (81–90)%
Premature cardiovascular disease	33 (27–40)%
Premature death not related to the surgery	34 (28–41)%

^aSurvey of 203 transplant professionals (predominantly nephrologists and surgeons) who were responsible for informing potential donors of risks prior to donation.

^bA glomerular filtration rate <60 ml/min.

Long-Term Morbidity

- 73 patients who had unilateral nephrectomy
- Normal kidney function, no proteinuria at the time of surgery
- Reasons for nephrectomy: stones in 29, renal mass in 14, hydronephrosis in 11, and renal tuberculosis in 5 patients
- Mean follow-up: 13.6 ± 8.6 years (18 months-35 years)
- 20 in 73 patients (27%) developed proteinuria/renal insufficiency

Praga M, et al. Kidney International 2000

Table 1. Clinical characteristics of patients at the time of unilateral nephrectomy

	Total (N = 73)	Patients who maintained normal renal function (Group I) (N = 53)	P value	Patients who later developed proteinuria/ renal insufficiency (Group II) (N = 20)
Age years	39.7 ± 14.7 (11–66)	39 ± 14 (11–65)	NS	41 ± 14 (11–66)
Gender	35 M; 38 F	24 M; 29 F	NS	11 M; 9 F
Mean arterial pressure mm Hg	94 ± 12 (70–140)	93 ± 12 (70–140)	NS	98 ± 12 (80–130)
Serum creatinine mg/dL	1 ± 0.1 (0.7–1.4)	0.9 ± 0.1 (0.7–1.3)	NS	1 ± 0.1 (0.9–1.4)
Proteinuria g/24 hours	0	0	NS	0
Body weight kg	68 ± 12 (40–99)	63.5 ± 8.9 (40–85)	<0.001	80.1 ± 12.1 (53–99)
Body mass index kg/m ²	26.2 ± 5.3 (18–41.4)	24.3 ± 3.7 (18–34)	<0.001	31.6 ± 5.6 (22–41.4)

In 14 obese patients (BMI>30 at the time of nephrectomy), 13 (92%) developed proteinuria/renal insufficiency.

Praga M, et al. Kidney International 2000

Long-term Morbidity

- Organ Procurement and Transplantation Network (OPTN) database
- A total of 56 previous living donors in 47,996 subsequently listed for cadaveric kidney transplantation (0.04%); 43 have received transplants; 36 currently have functioning grafts; One died after transplantation; Two candidates died while waiting
- 1999 adjusted incident rate for ESRD in the general U.S. population: 315 per million population, or 0.03%

Ellison MD et al, Transplantation 2002

Proteinuria and Reduced Kidney Function in Living Kidney Donors- A Meta-Analysis

- Forty-eight studies from 27 countries followed a total of 5048 donors
- Follow-up: average of 7 years (median 6, range 1–25 years)
- Published from 1973 to 2005
- 21% prospectively followed donors in time
- Four studies described the characteristics of donors lost to follow-up

Garg AX, et al. Kidney Int 2006

Long-Term Consequences of Live Kidney Donation

- Between 1973 and 2001, 152 living donor nephrectomies
- Seven of 152 donors had died from nonrenal diseases
- Of the remaining 145, data collection on 135 (93%) donors
- The mean time from nephrectomy to the current evaluation: 11 ± 7 (range 1–28) years

Long-Term Consequences of Live Kidney Donation

- A decrease in creatinine-clearance or GFR by 20–25%, but no correlation between residual renal function and blood pressure or the amount of proteinuria in this cohort
- Blood pressure in these donors were slightly higher but it remained lower than in the normal population
- An increase in urinary protein excretion, but pathological albuminuria was rare

Long-term Morbidity

- Information on 464 live donors (60%)
- 20-37 years of follow-up
- 84 had died and 380 were alive; 3 in 84 had kidney failure; Of the 380 still alive, three had abnormal kidney function and two had undergone transplantation
- The rate of proteinuria and hypertension was similar to the age-matched general population

Ramcharan T et al, Am J Transplant 2002

Obesity and Cardiac Risk after Kidney Transplantation

- BMI at the time of transplant and posttransplant cardiac risk
- Single center, 1102 recipients, transplanted 1991-2004
- High BMI: risk factor for posttransplant congestive heart failure and atrial fibrillation

Lentine K, et al. Transplantation 2008

Screening Asymptomatic Diabetic Patients for CAD

- 97 asymptomatic type 1 and 2 DM kidney and kidney-pancreas transplant candidates
- 33% of type 1 and 48% of type 2 DM patients had significant stenosis ($>$ or $=$ 70%) in 1 or more coronary arteries
- On multivariate logistic regression analysis, BMI $>$ 25 was significantly associated with CAD (relative risk = 4.8, $P = 0.002$), also age of the patient, and smoking history
- Young African American DM patients with no smoking history and a BMI \leq 25 are at reduced risk, and invasive tests may not be necessary in this group

Ramanathan V, Goral S, Transplantation 2005

Heart Disease-Evaluation

- 151 patients with IDDM, candidates for kidney transplantation without any chest pain, at University of Minnesota
- Routine arteriogram as part of the protocol
- 31 patients had significant stenosis
- 26/31 were randomized either to revascularization or medical treatment

Manske CL et al, Lancet 340:998-1002, 1992

Heart Disease-Evaluation

- 10/13 medically managed and 2/13 revascularized patients had a cardiovascular end-point 8.4 months (median) after arteriogram
- Revascularization decreased the frequency of cardiac events in this patient population
- **Conclusion:** Diabetic renal transplant candidates should be screened for silent CAD before transplantation

Manske CL et al, Lancet 340:998-1002, 1992

Cardiovascular Disease and Hypertension Risk in Living Kidney Donors

- A retrospective cohort from Ontario, Canada between the years 1993 and 2005
- 1278 living donors and 6359 healthy adults as controls
- Follow-up: a mean of 6.2 years (range, 1-13 years) after donation
- There was no significant difference in death or cardiovascular events between donors and controls (1.3% vs. 1.7)
- Donors were more frequently diagnosed with hypertension than controls (16.3% vs. 11.9) but were also seen more often by their primary care physicians

Garg AX, et al for the DONOR Network, Transplantation 2008

Long-Term Consequences of Kidney Donation

- Meta-analysis-48 studies from 27 countries followed a total of 5048 donors
- Follow-up: average of 7 years after donation (range 1–25 years); the average 24 h urine protein: 154 mg/day; the average GFR: 86 ml/min
- An initial decrement in GFR after donation was not accompanied by accelerated losses over that anticipated with normal aging (6 studies in 189 controls and 239 donors; controls 96 ml/min vs donors 84 ml/min)

Garg AX, et al. Kidney Int 2006

24 h urine protein

Source*	Donors, post-donation		Controls		24 h urine protein Mean difference (mg/day) 95% CI
	Years after donation,	24 h urine Protein (mg/day)	24 h urine Protein (mg/day)	24 h urine Protein (mg/day)	
	Mean (range)	N mean (s.d.)	N mean (s.d.)		
D'Almeida <i>et al.</i> ⁴⁵	7 (1–14)	59 151 (125)	28 96 (116)		54 (1, 108)
Williams <i>et al.</i> ⁵⁸	13 (10–18)	37 115 (135)	17 31 (125)		84 (10, 157)
Mathillas <i>et al.</i> ⁶⁰	15 (10–20)	33 306 (320)	14 212 (255)		94 (–79, 267)
Pooled estimate		129 147 (22)	59 83 (30)		66 (24, 108)

- The average 24 h urine protein was 154mg/day and the average GFR was 86 ml/min
- Kidney donation resulted in small increases in urinary albumin, which increased with time after donation

Proteinuria and Reduced Kidney Function in Living Kidney Donors- A Meta-Analysis

- Ten years after nephrectomy, donors had a GFR that was 10 ml/min lower compared to controls
- 12% of donors developed a GFR less than 60 ml/min during follow-up
- The pooled incidence of proteinuria: 12%

Case #4

- 48 yo woman, ESRD due to IgA nephropathy, on dialysis
- **Breast cancer** treated with surgery and radiation 16 months ago
- Her sister wants to donate a kidney to her (6 antigen match), family wants surgery in 1 month
- Can we transplant her now?

Amsterdam Forum Guidelines

Cardiovascular Risk Assessment

- The clinical predictors of an **increased perioperative risk** (for non-cardiac surgery) by the American College of Cardiology /American Hospital Association standards fall into three categories: major, intermediate, and minor
- **Major predictors:** unstable coronary syndromes, decompensated heart failure, significant arrhythmias and severe valvular disease-contraindications to live kidney donation

Amsterdam Forum Guidelines

Cardiovascular Risk Assessment

- Most of the **intermediate predictors**: mild angina, previous myocardial infarction, compensated or prior heart failure, and diabetes mellitus-contraindications to donation
- **Minor predictors**: older age, abnormal ECG, rhythm other than sinus, low cardiac functional capacity, history of stroke, or uncontrolled hypertension-warrant individual consideration

Recipient Evaluation

- Patients and their families should be well informed concerning the procedure as well as immunosuppression-related side effects and complications
- Informed decision and active participant