Recipient and Donor Outcomes

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St. Paul's Hospital
University of British Columbia

Transplant Nephrology Core Curriculum

Recipient Outcomes
- Historical Outcomes
- Current Outcomes
  - Short term
  - Long term
- Survival benefit of transplantation
- Waiting list
- Survival Factors
  - Donor Factors
  - Recipient Factors
- Causes of Graft Loss

Donor Outcomes
- Surgical Risk
- Long-term Outcomes
  - Normal vs Not Normal Donors
  - Survival
  - ESRD
  - Cardiovascular Disease
  - HTN
  - Proteinuria
  - Low GFR Progression
- Pregnancy
- Quality of Life

Conflict of Interest Disclosure
John S. Gill, MD
Employer: St. Paul’s Hospital; University of British Columbia
Consultancy Agreements: Astellas, BMS
Research Funding: Genzyme, Roche
Honoraria: Novartis, Roche

Historical Outcomes
Current Short Term Outcomes

Outcomes of Renal Allografts

One Year Unadjusted Patient Survival by Year, Living and Deceased Donor Kidney Transplants

One Year Unadjusted Graft Survival by Year, Living and Deceased Donor Kidney Transplants
Current Long-Term Outcomes


<table>
<thead>
<tr>
<th>Year of Transplant</th>
<th>Overall Graft Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>8</td>
</tr>
<tr>
<td>1989</td>
<td>6</td>
</tr>
<tr>
<td>1990</td>
<td>6</td>
</tr>
<tr>
<td>1991</td>
<td>6</td>
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<td>1992</td>
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<tr>
<td>1994</td>
<td>6</td>
</tr>
<tr>
<td>1995</td>
<td>6</td>
</tr>
</tbody>
</table>

Legend
- Projected Half-Life
- Kaplan-Meier Half-Life

** as published in NEJM (March, 2000)

*Am J Transplant. 2004 Aug;4(8):1289-95

Unadjusted Graft and Patient Survival SRTR (1997-2007)
Wolfe et al AJT, 2010

Kaplan-Meier Overall Graft Survival by Year of Transplant
First Deceased Donor Transplants 1988-1995

Year of Transplant | Years to Half-Life |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>7.5</td>
</tr>
<tr>
<td>1989</td>
<td>7.9</td>
</tr>
<tr>
<td>1990</td>
<td>7.9</td>
</tr>
<tr>
<td>1991</td>
<td>8.0</td>
</tr>
<tr>
<td>1992</td>
<td>7.7</td>
</tr>
<tr>
<td>1993</td>
<td>7.9</td>
</tr>
<tr>
<td>1994</td>
<td>7.9</td>
</tr>
<tr>
<td>1995</td>
<td>8.0</td>
</tr>
<tr>
<td>Tx</td>
<td>1-year (%)</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Kidney: deceased donor</td>
<td>89.0</td>
</tr>
<tr>
<td>Kidney: living donor</td>
<td>95.1</td>
</tr>
<tr>
<td>Liver: deceased donor</td>
<td>82.2</td>
</tr>
<tr>
<td>Liver: living donor</td>
<td>81.7</td>
</tr>
<tr>
<td>Pancreas alone</td>
<td>76.9</td>
</tr>
<tr>
<td>Heart</td>
<td>86.8</td>
</tr>
</tbody>
</table>

*Rates are unadjusted

**Graft survival**

OPTN/SRTR 2005 Annual Report

Survival Benefit of Transplantation

• INSERT SLIDES 14 – 19
UNCHANGED FROM EXISTING PRESENTATION

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Survival Benefit of Transplantation

Mortality RR* for 23,275 first cadaveric transplant versus 46,164 waitlisted (WL) dialysis patients

Projected years of life from WL by age group

Projected years of life from WL by diabetes mellitus (DM)
Waiting list for transplantation
**Number of ECD & DCD Kidney Donors by Year, 2000 - 2009**

- **Ten-Year Increase**
- +44%
- +70%

**Waitlist and Transplant Activity for Kidneys, 2000-2009**

**Probability of deceased donor transplantation among wait-listed patients by ABO and PRA**

<table>
<thead>
<tr>
<th>ABO</th>
<th>A</th>
<th>B</th>
<th>AB</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRA</td>
<td>0-29</td>
<td>30-79</td>
<td>&gt;80</td>
<td>0-29</td>
</tr>
<tr>
<td>1</td>
<td>0.41</td>
<td>0.26</td>
<td>0.23</td>
<td>0.24</td>
</tr>
<tr>
<td>3</td>
<td>0.75</td>
<td>0.59</td>
<td>0.48</td>
<td>0.54</td>
</tr>
<tr>
<td>5</td>
<td>0.88</td>
<td>0.76</td>
<td>0.61</td>
<td>0.76</td>
</tr>
<tr>
<td>7</td>
<td>0.92</td>
<td>0.84</td>
<td>0.69</td>
<td>0.87</td>
</tr>
</tbody>
</table>

Cumulative time on the wait list (yr)

1  | 0.41|0.26|0.23|0.24|0.12|0.10|0.56|0.34|0.26|
3  | 0.75|0.59|0.48|0.54|0.37|0.28|0.84|0.71|0.52|
5  | 0.88|0.76|0.61|0.76|0.59|0.42|0.92|0.84|0.62|
7  | 0.92|0.84|0.69|0.87|0.72|0.51|0.95|0.89|0.67|

*Start date is the earlier of dialysis initiation or wait-listing.

Gill et al unpublished data
Factors Impacting Long-term Outcome

• Donor Factors
  – Donor Age
  – Donor Co-morbidities
  – Cause of death
  – Kidney function
  – Race
  – Mechanism of Death

Insert slide 28 from existing presentation

Categories of deceased kidney donors

Significant “Donor” Risk Factors for Overall Graft Loss
45,850 first Transplants 1996-2002

Adjusted Relative Risk

Patients in whom brain death is confirmed, presumed or imminent

Indicators of organ quality
  • Age > 60 or < 19 yrs.
  • Cause of death (CVA or)
  • Degree of reperfusion
  • Delayed SN (1.5 mg/dL)

DBD = donation after brain death, DCD = donation after cardiac death, cDCD = controlled DCD, eDCD = extended cDCD, CVA = cardiovascular accident, SN = serum creatinine

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Figure III-3. SCD, ECD, and DCD Kidney Transplants, 1998-2007


Times to Equal Risk of Mortality and Equal Cumulative Mortality for Expanded Criteria Donor (ECD) Kidney Recipients vs Patients Receiving Standard Therapy

Patient and allograft survival of kidney transplantation with DCD and DBD organs.

Rao P S, Ojo A CJASN 2009;4:1827-1831

Rao P S, Ojo A CJASN 2009;4:1827-1831

Data from: 2007 OPTN/SRTR Annual Report, Tables 5.10a, b, c. *Death is included as an event.
Recipient Factors – Age

- Retain slide 39, 40, 42, 46, 47, 48 from previous presentation
Recipient factors - BMI

Gore et al AJT 2006 Feb;6(2):357-63

Allocation of kidneys from deceased donors (aged 50+) in the USA: 1990–2002

Patient survival for transplant recipients of kidneys from donors aged 15–50

Survival of grafts from younger donors
Recipient Factors - Race

<table>
<thead>
<tr>
<th>Race</th>
<th>Overall Graft Survival (%)</th>
<th>1-Year Graft Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>53.9</td>
<td>36.1</td>
</tr>
<tr>
<td>African American</td>
<td>53.2</td>
<td>32.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>52.9</td>
<td>32.7</td>
</tr>
<tr>
<td>Other</td>
<td>51.3</td>
<td>32.0</td>
</tr>
</tbody>
</table>

Note: Data from Gore et al AJT 2006 Feb;6(2):357-63

Recipient Factors - Race

Table 4: Multivariate Cox regression of factors associated with graft failure

- Body mass index (vs. normal)
  - Underweight: 1.21 (1.03-1.42) 0.02
  - Overweight: 0.98 (0.92-1.05) 0.61
  - Obese: 1.07 (0.98-1.17) 0.13
  - Morbidly obese: 1.22 (1.09-1.38) 0.001
- Recipient age: 1.00 (1.00-1.01) 0.01
- Recipient sex (vs. male)
  - Female: 1.03 (0.97-1.09) 0.29
- Race (vs. white)
  - African American: 1.49 (1.39-1.60) <0.001
  - Hispanic: 0.83 (0.76-0.90) <0.001
  - Other: 0.76 (0.67-0.89) <0.001
- Recipient comorbidities
  - Diabetes mellitus: 1.26 (1.19-1.35) <0.001
  - Coronary artery disease: 1.17 (1.07-1.28) <0.001
  - Peripheral vascular disease: 1.19 (1.04-1.38) <0.001
  - HLA 0 mismatch (vs. any mismatch): 0.76 (0.66-0.88) <0.001
  - Cold ischemia > 24 h (vs. > 24 h): 0.90 (0.84-0.97) <0.003
  - Living donor (vs. deceased): 0.65 (0.59-0.73) <0.001

HILA: human leukocyte antigen.
Recipient Factors – Dialysis Vintage

Recipient Factors – Transplant Failure

Dialysis exposure and post-transplant outcomes

Transitions Between Dialysis and Transplantation and Risk of Death

Gill et al., Kidney International 2007 Mar;71(5):442-7
### Recipient Factors – Repeat Transplantation

#### Kaplan-Meier Overall Graft Survival by Year of Transplant

<table>
<thead>
<tr>
<th>Deceased Donor Re-transplants 1988-1995</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year of Transplant</strong></td>
</tr>
<tr>
<td>1988</td>
</tr>
<tr>
<td>1989</td>
</tr>
<tr>
<td>1990</td>
</tr>
<tr>
<td>1991</td>
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<td>1992</td>
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<tr>
<td>1993</td>
</tr>
<tr>
<td>1994</td>
</tr>
<tr>
<td>1995</td>
</tr>
</tbody>
</table>

#### Kaplan-Meier Overall Graft Survival by Year of Transplant

- **Year of Transplant**
- **Years to Half Life**
  - 1988: 2.0
  - 1989: 2.6
  - 1990: 3.4
  - 1991: 4.6
  - 1992: 5.7
  - 1993: 5.4
  - 1994: 7.1
  - 1995: 7.5

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Relative Risk of Second Graft Loss Within Five Years (by Time of Primary Graft Loss)

<table>
<thead>
<tr>
<th>Time of First Graft Loss</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 weeks</td>
<td>0.50</td>
</tr>
<tr>
<td>2 weeks-3 mo</td>
<td>1.00</td>
</tr>
<tr>
<td>4-12 mo</td>
<td>1.50</td>
</tr>
<tr>
<td>13-24 mo</td>
<td>2.00</td>
</tr>
<tr>
<td>25-36 mo</td>
<td>2.50</td>
</tr>
<tr>
<td>37-48 mo</td>
<td>3.00</td>
</tr>
</tbody>
</table>

*P<0.001

- Retain Slide 69 from previous presentation regarding repeat transplant recipients

Combination of donor and recipient factors:
- Delayed Graft Function

- Combination of donor and recipient factors:
  - Delayed Graft Function

- Retain Slides 72, 73, 74
Factors influencing long-term graft survival

- Combination of donor and recipient factors
  - HLA match
  - Cross match
  - Cold ischemia time
  - Acute Rejection
  - Delayed graft function

Kaplan-Meier Plot for Death Censored Graft Survival by Indications of DGF
Deceased Donor Transplants 1990-2000

- No DGF: 94.8%
- DGF: 82.0%

Kaplan-Meier Plot for Overall Graft Survival by Indications of DGF in “Ideal Situations”
Deceased Donor Transplants 1990-2000

- No DGF: 10-year survival = 55.2%
- DGF: 10-year survival = 46.2%

Association of DGF and Pulsatile Perfusion

Adjusted Odds Ratio of DGF

AMERICAN JOURNAL OF TRANSPLANTATION 4: 473-473 1152 Suppl. 8 2004
Donor/Recipient Factors: HLA Match

With evolving clinical practice, including the provision of safer and more potent immunosuppressive therapy, the significance of HLA matching has diminished.
• Donor/Recipient Factors
  – Acute Rejection

• Insert slides 78-82
Donor/Recipient Factors: Acute Rejection

Graft Survival in Patients With and Without Acute Renal Rejection

Acute Rejection Predicts Graft Loss

Graft Survival by % Functional Difference (Cockcroft) from before AR
**Acute Rejection by 24 Months**

<table>
<thead>
<tr>
<th></th>
<th>Belatacept MI</th>
<th>Belatacept LI</th>
<th>CsA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline → Month 12</td>
<td>22%</td>
<td>17%</td>
<td>7%</td>
</tr>
<tr>
<td>Number of cases, Month 12 → Month 24</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Baseline → Month 24</td>
<td>24%</td>
<td>17%</td>
<td>9%</td>
</tr>
</tbody>
</table>

* <3% of patients in each group had recurrent acute rejection episodes

**Benefit - MDRD GFR at Month 24 With or Without Acute Rejection***

<table>
<thead>
<tr>
<th></th>
<th>Belatacept MI</th>
<th>Belatacept LI</th>
<th>CsA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean MDRD GFR (ml/min/1.73 m²)</td>
<td>68 ± 5</td>
<td>69 ± 4</td>
<td>48 ± 4</td>
</tr>
</tbody>
</table>

*GFR with imputation: for patients with death or graft loss, cGFR = 0; for other patients with missing values, LOCF

**Causes of Graft Loss and Death**
Death with a functioning graft: the most common cause of graft loss in kidney transplant recipients beyond the first year after transplantation.

Incidence of Chronic Allograft Nephropathy (CAN) over 10 Years

- 959 biopsies from 120 patients with type 1 diabetes (119 with kidney-pancreas transplants)
- Grade I CAN present in 94% of patients by 1 year
- Grade II or III CAN present in 90% at 10 years


Pathogenesis of CAN

<table>
<thead>
<tr>
<th>Immuneologic Factors</th>
<th>Non-immuneologic Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor HLA matching and previous sensitization</td>
<td>Delayed graft function</td>
</tr>
<tr>
<td>Chronically allograft nephropathy</td>
<td>Cytotoxic T-cell-mediated injury</td>
</tr>
<tr>
<td>Nonadherence of patient</td>
<td>Chronic toxic effects of cyclosporine or tacrolimus</td>
</tr>
<tr>
<td>Suboptimal immunosuppression</td>
<td>BK virus nephropathy</td>
</tr>
</tbody>
</table>

Why has improved early Graft Survival NOT translated into better late Graft Survival?

- Increased immunosuppression may have early benefits but late adverse effects on graft survival
- Late graft failure may occur via mechanisms unrelated to immune injury
- Immunosuppression may be inadequate late post-transplantation because of nonadherence and minimization treatment strategies

BK nephropathy, other late infections, malignancies, CVD
CNI nephrotoxicity, recurrent disease, senescence
Multiple and/or late acute rejection episodes, subclinical rejection

CVD = cardiovascular disease; CNI = calcineurin inhibitor.


Short term Living Donor Morbidity

- Survey UNOS kidney transplant programs for outcomes between 1/1/99-7/1/01
  - 171 (73%) responded
  - These centers did 85% of the living donor transplants during that period
    - 5660 open (52.3%)
    - 2239 hand assisted LN (20.7%) HA-LN
    - 2929 non-hand assisted LN (27%) non-HA LN
- Death
  - 0.02% perioperative
  - 0.01% vegetative state
  - 3 others died unrelated to surgery
    - Murder
    - Suicide
    - Trauma
- Complications
  - Reoperation - 0.4% open, 1.0% HA-LN, 0.9% non-HA LN
  - Pneumothorax - 0.09% open, 0.05% HA LN
  - Bleeding - 0.25% open, 0.63% in LN
  - Rhabdomyolysis - 0.12% in LN
  - DVT/PE - 0.02% open, 0.1%

Long term Risks

- Incremental risks
- Risk for normal donor
- Risk for not normal donors

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The Data Quality Issue: Few/ Small Controlled studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Reference</th>
<th>Living Donors &amp; Matched Patents</th>
<th>Average Follow-up (years)</th>
<th>Hypertension</th>
<th>Proteinuria</th>
<th>Low GFR Filtration Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neproton IS et al.</td>
<td>JASN, 1993</td>
<td>1) 76 living donors 2) 66 siblings</td>
<td>23.7</td>
<td>Use of anti-hypertensives 1) 22% (23-44%) 2) 44% (33-52%) (no difference)</td>
<td>24-hour urine &gt; 150 mg 1) 29% (14-36%) 2) 23% (14-36%) (no difference)</td>
<td>Mean 24-hour urine creatinine clearance 1) 92 mL/min 2) 89 mL/min (no difference)</td>
</tr>
<tr>
<td>Williams et al.</td>
<td>Ann. Int. Med. 2004</td>
<td>1) 26 living donors 2) 12 siblings 3) 5 healthy controls</td>
<td>12.6</td>
<td>Blood pressure &gt; 140/90 mm Hg or hypertension 1) 4% (22-52%) 2) 7% (17-50%) 3) 24% (21-30%) (not significantly different)</td>
<td>Blood pressure &gt; 150 mg 1) 21% (9-47%) 2) not reported 3) not reported</td>
<td>Mean 24-hour urine creatinine clearance 1) 93 mL/min 2) 79 mL/min (significant difference)</td>
</tr>
<tr>
<td>Kiberd and Clase</td>
<td>JASN, 2002</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Incremental risk: Lifetime risk of kidney failure in unselected non-donors

From age of 20 years
- Black woman 7.8%
- Black man 7.3%
- White woman 1.8%
- White man 2.5%

Risk in Normal Donor
- Normal donor defined
  - No hypertension
  - No proteinuria
  - No hematuria
  - No diabetes and at low risk for mature onset diabetes
  - No history of stones/recurrent UTIs
  - No family history of kidney disease

Long-term risk: Normal donor
- Information is available for
  - Survival
  - Kidney Failure
  - Cardiovascular Disease
  - Hypertension
  - Proteinuria
  - Low GFR/GFR Progression
Long-term risk: Normal donor

- Information is available for
  - SURVIVAL
  - Kidney Failure
  - Cardiovascular Disease
  - Hypertension
  - Proteinuria
  - Low GFR/GFR Progression

Kidney Donors Live Longer

WWII and Field Nephrectomy for Trauma

<table>
<thead>
<tr>
<th>Survival</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>24</td>
</tr>
<tr>
<td>0.75</td>
<td>46</td>
</tr>
<tr>
<td>0.50</td>
<td>68</td>
</tr>
<tr>
<td>0.25</td>
<td>84</td>
</tr>
</tbody>
</table>

Nerius-Burgess et al., Kidney International 1993;42:1110-1115

Kidney Donors Live Longer

<table>
<thead>
<tr>
<th>Observed and Expected Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>time (years) since donation</td>
</tr>
</tbody>
</table>

Fehrman-Ekholm, Transplantation 1997;64:976
Living donor survival

Kidney Donors Live Longer

No evidence for increased risk

- Studies with longest follow-up:
  - 62 ex-servicemen
    - uninephrectomy at mean age 25yrs
    - followed 45 years
    - no increase in mortality
  - 111 children
    - uninephrectomy for cancer
    - no increase in mortality
- Studies in live donors:
  - 459 live donors from single center in Sweden over 20 yrs (1964)
  - 430 had complete f/U
  - Actuarial survival 85% vs expected survival 66%
  - “KIDNEY DONORS LIVE LONGER”
Long-term risk: Normal donor

• Information is available for
  ▪ Survival
  ▪ KIDNEY FAILURE
  ▪ Cardiovascular Disease
  ▪ Hypertension
  ▪ Proteinuria
  ▪ Low GFR/GFR Progression

Living Donor Outcomes – ESRD

• 1,112 consecutive living kidney donors who underwent nephrectomy from 1965 until 2005
• 6 donors (that is 0.5% similar to age matched controls) had reached ESRD during the years 2001-2006
  – ESRD developed 36-41 years after start of the living donor program
  – 45-89 years old, median 77 years
  – Time since donation was 14-27 years, median 20 years
  – The diagnoses were nephrosclerosis (4 cases), postrenal failure (1 case), and renal carcinoma (1 case).

Ferhman-Ekholm et al. Transplantation. 2006 Dec 27;82(12):1646-8

Observed vs expected kidney failure in donors

• 23, 936 donors 1967-1992
• Administrative data – expect 18.5 cases of kidney failure
• 11 donor had kidney failure
• ? Due to screening

Bia et al Transplantation 1995

ESRD in American Donors

Cherikh et al AJT 2011

• 54,456 donors 1994-2003
• N= 126 developed ESRD
• 0.134/1000 years at risk
• Compared to ESRD rate in general U.S. population 0.354 per 1000 population
• Average follow up 9.8 years

Table 1: Basic demographics of LDKs with posttransplant ESRD and all LDKs during October 1, 1997–March 31, 2003

<table>
<thead>
<tr>
<th></th>
<th>Posttransplant ESRD</th>
<th>All LDKs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>N= 126</td>
<td>N= 54,456</td>
</tr>
<tr>
<td>Male</td>
<td>70</td>
<td>32,412</td>
</tr>
<tr>
<td>Female</td>
<td>53</td>
<td>22,044</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td>0.354/1000 population</td>
</tr>
<tr>
<td>White</td>
<td>54</td>
<td>18,586</td>
</tr>
<tr>
<td>Black</td>
<td>99</td>
<td>15,023</td>
</tr>
<tr>
<td>Other</td>
<td>13</td>
<td>6,847</td>
</tr>
<tr>
<td>Donor relationship to recipient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological</td>
<td>27</td>
<td>10,744</td>
</tr>
<tr>
<td>Biological, blood related donor</td>
<td>21</td>
<td>8,514</td>
</tr>
<tr>
<td>Biological, blood related donor, 2nd living</td>
<td>64</td>
<td>22,260</td>
</tr>
<tr>
<td>Biological, blood related full sibling</td>
<td>16</td>
<td>9,470</td>
</tr>
<tr>
<td>Other</td>
<td>120</td>
<td>58,458</td>
</tr>
<tr>
<td>Total</td>
<td>126</td>
<td>54,456</td>
</tr>
</tbody>
</table>

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Screening donors does not negate ethnic differences in ESRD

<table>
<thead>
<tr>
<th>Donors</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>(per 100 patient years)</td>
<td>(per 1000 population)</td>
</tr>
<tr>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>0.134 per 1000 pt years</td>
<td>0.354</td>
</tr>
<tr>
<td>Black</td>
<td>Black</td>
</tr>
<tr>
<td>0.423</td>
<td>0.998</td>
</tr>
<tr>
<td>White</td>
<td>White</td>
</tr>
<tr>
<td>0.086</td>
<td>0.273</td>
</tr>
</tbody>
</table>

Donors (per 100 patient years) (Cherikh et al AJT 2011)

Donors

Time to ESRD and Etiology of ESRD Suggests Screening Problems

Long-term risk: Normal donor

- Information is available for
  - Survival
  - Kidney Failure
  - CARDIOVASCULAR DISEASE
  - Hypertension
  - Proteinuria
  - Low GFR/GFR Progression

Risk of death or major cardiovascular event

Risk of cardiovascular disease was unchanged in decade after donation

Hazard ratio: 0.73 (95% CI 0.43, 1.24; p=0.25)
Long-term risk: Normal donor

- Information is available for
  - Survival
  - Kidney Failure
  - Cardiovascular Disease
  - HYPERTENSION
  - Proteinuria
  - Low GFR/GFR Progression

Blood Pressure-Meta-analysis

Controlled studies with average follow-up ≥ 5 years after donation (range, 6 to 13 years).

Blood pressure was 5 mm Hg higher in donors than in control participants (the weighted mean for systolic blood pressure using 4 studies involving 157 donors and 128 control participants was 6 mm Hg [95% CI, 2 to 11 mm Hg].

The weighted mean for diastolic blood pressure using 5 studies involving 196 donors and 161 control participants was 4 mm Hg [CI, 1 to 7 mm Hg]).

There was statistical heterogeneity among the 6 controlled studies that assessed hypertension; an increase in risk was noted in 1 study (relative risk, 1.9 [CI, 1.1 to 3.5]).
Hypertension estimates ranged from 9 to 74% pooled incidence 31% (95% CI 22 – 40%)

Racial Disparities in Medical Diagnoses such as HTN Persist in Living Donors
Lentine et al NEJM 2010; 363:724-32

<table>
<thead>
<tr>
<th>Race</th>
<th>Living Donor</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4.5%</td>
<td>29%</td>
</tr>
<tr>
<td>Female</td>
<td>4.6%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Proteinuria- Meta-analysis

- Urinary protein was higher in donors and became more pronounced with time
- Three studies totaling 59 controls and 129 donors; controls 83 mg/day, donors 147 mg/day, weighted mean difference 66 mg/day, 95% confidence interval (CI) 24–108).

Long-term risk: Normal donor
- Information is available for
  - Survival
  - Kidney Failure
  - Cardiovascular Disease
  - Hypertension
  - PROTEINURIA
  - Low GFR/GFR Progression
Proteinuria estimates ranged from 3 to 39%. Pooled incidence 18% (95% CI 11 – 25%).

Long-term risk: Normal donor

- Information is available for
  - Survival
  - Kidney Failure
  - Cardiovascular Disease
  - Hypertension
  - Proteinuria
  - LOW GFR/GFR PROGRESSION

Kidney Function - GFR

- Literature is variable - No change and even an increase have been reported
- 75% of pre-nephrectomy value
- Rate of decline after nephrectomy consistent with normal aging  
  - No evidence for hyperfiltration injury

An initial decrement in GFR after donation was not accompanied by losses over that anticipated with normal aging (six studies totaling 189 controls and 239 donors; controls 96 ml/min, donors 84 ml/min, weighted mean difference 10 ml/min, 95% CI 6–15; difference not associated with time after donation.)
Serum Creatinine and GFR in kidney donors >20 years after donation

Summary Of Available Data In Normal Donor

- Donors have an above average life expectancy
- Normotensive donors are probably at no higher risk of HTN than the general population
- Around 20-30% of donors develop asymptomatic, non-progressive proteinuria
- Donors have 75% of normal kidney function, which declines normally with age
- The risk of developing kidney failure is less than in the general population

Summary of long-term safety data in normal donors

- No large studies with an appropriate control group with long-term follow up data
- Limited data in racial minority groups
- Ethnic differences persist

Limited data in NOT normal donors

- We need studies demonstrating.....
- Risk of kidney failure in patients with single kidneys and an abnormality such as
  - Hypertension
  - Proteinuria
  - Hematuria
  - Family history of kidney disease
  - Diabetes
  - Low GFR
  - History of stones

- 24 donors ABPM >135/85 and >140/90 in clinic compared to 124 normotensive donors
- Mean f/u 282 days
- BP in hypertensive donors fell with pharmacological and non-pharmacological treatment 142/85 to 132/80 (p<0.01)
- HTN donors had lower post donation GFR 61 vs 68 ml/min

In absence of data we can extrapolate risks from people with 2 kidneys

- Prevalence of abnormalities in general population
- Determine the incidence of kidney failure associated with that abnormality

Example Hypertension

- 50 million adults have BP >140/90
- Incidence of hypertensive ESRD is 20,000 year
- Yearly risk is 1/2500 and 20 year risk is < 1%
- Similar data from MRFIT trial 30 year risk 1/1000

Example Hematuria

- 2% of population have isolated hematuria = 15 million
- GN that would present with isolated hematuria cause 1550 cases of kidney failure/year
- Risk is 1550/15 million = 1/10,000 per year
Proteinuria and risk of ESRD

Okinawa

- Okinawa mass screening project
- 106,177 subjects 20-98 years dipstick proteinuria 1983
- f/u through 2000
- Data from Okinawa dialysis study registry
- Logistic regression to determine odds of developing kidney failure in patients with proteinuria

Not normal donor-Diabetes

- Presence of diabetes is a contraindication to donation
- Little information about the incremental risk of uninephrectomy in diabetic patients
- Family hx of diabetes
  - Lifetime risk of type 2 DM 38%
  - First degree relative with Type 2 DM ..relative risk of 3
  - First degree relative plus BMI > 30 – very high risk
  - Risk factors alone are not sufficiently predictive of an individual's risk of diabetes…positive risk factors are not an absolute contraindication to donation
  - Univ of Minnesota: 19/250 donors developed DM
  - 10 had family hx and family hx increased risk from 6-11%

Prediction of ESRD by Dipstick Proteinuria

Cumulative Incidence of ESRD by baseline results for proteinuria

Diabetes and Single Kidney

N= 184 N=20 N=17

Albuminuria

Type 2 SKD SKN Control

0 20-200 200+
Not Normal Donor-Low GFR

Decline in kidney function with age

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean intra clearance Ml/min/1.73m²</th>
<th>Standard Deviation</th>
<th>Mean ± 2 STDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-29</td>
<td>123</td>
<td>16</td>
<td>90</td>
</tr>
<tr>
<td>30-38</td>
<td>115</td>
<td>11</td>
<td>93</td>
</tr>
<tr>
<td>40-49</td>
<td>121</td>
<td>23</td>
<td>74</td>
</tr>
<tr>
<td>51-59</td>
<td>99</td>
<td>15</td>
<td>70</td>
</tr>
<tr>
<td>61-68</td>
<td>96</td>
<td>26</td>
<td>45</td>
</tr>
<tr>
<td>70-78</td>
<td>89</td>
<td>20</td>
<td>49</td>
</tr>
</tbody>
</table>

How low can you go?

- No consensus on an absolute lower limit
- Donors will lose 25%
- CKD complications (in non-donors) increase with GFR <60

Not Normal Donor and Obesity

Summary- Not Normal Donors

- Limited data
- How many NOT normal individuals have donated???
- Increased pressure to accept these individuals as donors
Pregnancy outcomes after kidney donation appear similar to those reported in the general population, but inferior to pre-donation pregnancy outcomes

<table>
<thead>
<tr>
<th></th>
<th>Pre-donation pregnancies (n=204)</th>
<th>Post-donation pregnancies (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full-term birth</td>
<td>166 (71.6%)</td>
<td>118 (67.1%)</td>
</tr>
<tr>
<td>Preterm</td>
<td>16 (7.4%)</td>
<td>16 (9.2%)</td>
</tr>
<tr>
<td>Fetal loss</td>
<td>43 (21.1%)</td>
<td>43 (24.6%)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (4.7%)</td>
<td>12 (6.4%)</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>33 (70.7%)</td>
<td>36 (57.7%)</td>
</tr>
<tr>
<td>Abortion</td>
<td>8 (18.8%)</td>
<td>5 (11.9%)</td>
</tr>
<tr>
<td>Maternal outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>1 (0.5%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Gestational</td>
<td>1 (0.5%)</td>
<td>63 (3.5%)</td>
</tr>
</tbody>
</table>

Ibrahim HN et al AJT 2009 9(4): 825-34.

Preeclampsia after kidney donation appear similar to that reported in the general population, but inferior to pre-donation pregnancy outcomes

Quality of Life

• Systematic Review
• No change or improved after donation in altruistic donors
• AJT 2006 6(12):2965-77