Kidney Transplant Outcomes
In Elderly Patients

Simin Goral MD
University of Pennsylvania Medical Center
Philadelphia, Pennsylvania
Case Discussion

- 70 year old 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+
- Prostate cancer: diagnosed 8 months ago, Gleason score 7, treated with cryoablation, most recent PSA is less than 0.1
- PRA: weakly positive
ESRD in the US

• More than 106,000 new patients began therapy for ESRD in 2005; the median age 64.6.
• Prevalent dialysis population 341,000
• Fastest growth is among patients age 45-64, but rising more quickly among those age 65 and older
• By 2020: incident population 150,000, prevalent population 800,000, and dialysis population 534,000

USRDS 2007 Annual Data Report
Incident ESRD Patients: Rates Adjusted for Gender and Race

USRDS 2007 Annual Data Report
All Cause Mortality Rates by Age, 2005

- Age 65 or older: mortality rates are 6 times higher than in the general population.
- For elderly patients on dialysis, 5-year survival is less than 30%.
- The factors influencing survival: race, comorbid conditions such as HTN and DM, cardiovascular diseases, PVD, impairment of vision and ambulation.

2007 USRDS Annual Data Report
Kidney Transplantation

- The prevalent transplant population in 2005: 143,693
- The number of patients on the waiting list for deceased donor (DD) kidney transplant: 70,778-competing for approximately 11,000 kidneys

USRDS 2007 Annual Data Report
Waiting List by Age

- At the end of 2006:
  - 59% of all candidates were 50 yo or older
  - 14% were 65 yo or older
  - In 1997: 43% >50 yo and 7% >65 yo
- Increase in the number of older patients on the waiting list

2007 OPTN/SRTR Annual Report
Wait List Patient Counts

USRDS 2007 Annual Data Report
Kidney Transplantation

- The best treatment option for all 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
Unadjusted 1-yr, 3-yr, and 5-yr Patient Survival, by Donor Type: 2000-2005

2007 OPTN/SRTR Annual Report
Unadjusted 1-yr, 3-yr, and 5-yr Graft Survival, by Donor Type: 2000-2005

![Bar chart showing unadjusted graft survival for different donor types at 1-year, 3-year, and 5-year intervals. The chart includes bars for Living Donor, non-ECD, and ECD donors.]

*Death is included as an event.*

2007 OPTN/SRTR Annual Report
Transplantation in the Elderly: Concerns

- Shorter life expectancy-need to have a transplant early after wait-listing
- Shorter life expectancy-shorter graft survival
- Accelerated atherosclerosis leading to more cardiovascular events (myocardial infarction, stroke and peripheral vascular disease) and death
- Frail with multiple comorbid conditions
Transplantation in the Elderly: Concerns

• Longer initial hospitalization
• Safety of chronic immunosuppression-HTN, salt and water retention, hyperlipidemia, infections and malignancy
• Use of ECD kidneys in this population: Is there increased risk of morbidity and mortality with ECD kidneys in the elderly?
Survival Advantage

• 1991-1996: age older than 60 (on dialysis: 38.8%, on the waiting list: 15%, DD kidney tx: 13%)

• Mortality rate for patients on dialysis who were on the waiting list was about half of all patients on dialysis: selection of healthier patients for waiting list

• In pts 60-74 yo, the cumulative survival rate improved after the first year posttransplant, projected increase in the life span of 4 years and a decrease in the long-term risk of death of 61%
  • 60-64 yo: 4.3 years
  • 65-69 yo: 2.8 years
  • 70-74 yo: 1.0 year

Wolfe RA, et al. NEJM 1999
Studies-Review

- 114 patients, age >60 (25 pts>70), 54% received ECD kidneys; **less waiting time**, mean f/u 27 months, **similar PS and GS** compared to younger groups

- 110 patients, age >60, **lower acute rejection rate** in the elderly group compared to younger pts (age 50-59 yo), median f/u 22 months, **more death in the elderly group**-mainly due to infection, cardiovascular disease and malignancy

Moore PS, et al. Surgery 2007 (from Wake Forest University)
Studies-Review

- 301 patients-old group (age >70 yo) vs 513 patients-senior group (age 60-69 yo) vs 512 patients-control group (age 45-54 yo), transplanted 1990-2005, from Norway
- Less preemptive and LRD transplants in both elderly groups, older donors in the “old” group, higher incidence of death with a functioning graft (45%, 31%, 13%-control group)
- No difference in 5-year graft survival when censored for death
- Leading reasons for death: cardiovascular disease and infections

Studies-Review

• SRTR data, observational: 5667 elderly pts (>70 and older at the time of listing) initially wait-listed from 1/1990 to 12/2004
  • 2078 pts (36.7%) received DD kidney tx (688-33%-had ECD kidneys)
  • 360 (6.4%) LRD tx
  • 1849 (32.6%) died without transplant
  • 1380 (24.4%) were alive but on the waiting list (last f/u 12/2005)
• They excluded pts who received a kidney tx before they started dialysis

Relative Risk of Death for 2078 DD Kidney Tx Recipients vs 5667 Wait-Listed Patients

Cumulative Survival Curves (DD Recipients vs Wait-Listed Dialysis Patients)

### TABLE 3. Unadjusted graft survival among deceased donor and living donor kidney transplant recipients at 1, 2, and 3 years

<table>
<thead>
<tr>
<th>Transplant type</th>
<th>Transplant recipients</th>
<th>Graft survival, including death as an event (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Deceased donor</td>
<td>2078</td>
<td>85.2</td>
</tr>
<tr>
<td>Living donor</td>
<td>360</td>
<td>14.8</td>
</tr>
</tbody>
</table>

### TABLE 4. Unadjusted death-censored graft survival among deceased donor and living donor kidney transplant recipients at 1, 2, and 3 years

<table>
<thead>
<tr>
<th>Transplant type</th>
<th>Transplant recipients</th>
<th>Death-censored graft survival (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Deceased donor</td>
<td>2078</td>
<td>85.2</td>
</tr>
<tr>
<td>Living donor</td>
<td>360</td>
<td>14.8</td>
</tr>
</tbody>
</table>

Studies-Review

• Largest study (pts>70 yo), BUT registry data
• The survival benefit of kidney transplantation in ESRD patients older than the age of 70, especially in patients with HTN and DM
• Transplantation was associated with a 41% lower risk of death-recipients with ECD kidneys had 25% lower mortality risk compared to waiting list patients on dialysis

Recipients of aged 55-64 yrs had the greatest survival benefit of 7.3 yrs with a marginal donor kidney (1992-1997)  

Use of ECD Kidneys in the Elderly

- Retrospective cohort study using SRTR, SS Death Master File and CMS data: 1/1995-12/2002
  - Long-term relative mortality risk was 17% lower for ECD recipients
  - Significant ECD survival benefit in patients older than 40 yrs, both sexes, non-Hispanics, all races, unsensitized patients and patients with DM or HTN
  - In OPOs with long median waiting times (>3.7 years), ECD recipients had a 27% lower risk of death
- ECD kidneys SHOULD be offered to candidates >40 yrs in OPOs with long waiting times and only to diabetics in OPOs with shorter waiting times

Merion RM, et al. JAMA 2005
Marginal Kidneys—Shorter Waiting Time

• SRTR database, all adult solitary renal transplant candidates and recipients registered from 1995 and 2004

• Younger patients (age 18-39 yo): longer life expectancy with a living donation or an SCD kidney after 4 years on dialysis compared to an ECD kidney after 2 years on dialysis

• Older patients (>65 yo): life expectancies with an ECD kidney after 2 years on dialysis comparable to an SCD kidney or living donation after 4 years of dialysis

Projected Life Expectancy after ESRD onset by Recipient Age and Treatment Modality

Marginal Kidneys-Shorter Waiting Time

• 47.5% of candidates were on the ECD donor list
• Increased age, black race, elevated PRA, and diagnoses of DM and HTN: increased likelihood of listing for ECD kidney
• As waiting time accumulated, the relative likelihood of a transplant for older candidates diminished

Relative Risk of NOT Receiving a DD Kidney Transplant

Among recipients >60 yo (n=315), patients survival was worse than for younger recipients but no differences in graft or death-censored graft survival.

Recipients >60 yo who received kidneys from donors >60 yo or older had worse outcomes compared to those receiving donor kidneys less than 60 years old.

Listings Willing to Accept an ECD Kidney

USRDS 2007 Annual Data Report
Listings Willing to Accept an ECD Kidney by Age, 2004-2005

USRDS 2007 Annual Data Report
Eurotransplant Senior Programme (ESP)

- Established in 1999, 7 countries
- Eurotransplant: 12,000 patients on dialysis and 4000 DD kidneys available each year
- To reduce the waiting time of elderly patients and to achieve a higher efficiency in the use of kidneys from elderly donors
- Matches are made between DD $\geq$ 65 yo and recipients $\geq$ 65 yo, PRA less than 5%
- Regional allocation based on waiting time and blood group
Eurotransplant Senior Programme (ESP)  

- 1406 patients >65 yo from 7 countries
- Mean donor age 70.2 yo
- Induction with T-cell depleting agents in 20.8% of patients
- Shorter cold ischemia time (mean CIT: 11.9 h vs >17h)
Eurotransplant Senior Programme (ESP)


Graft Survival

Death-censored Graft Survival
Eurotransplant Senior Programme (ESP)

- 73 patients in ESP and 51 patients as controls (>60 years old)-Germany
- Induction therapy with basiliximab (80% vs 29%)
- Immunos: Csa (74%) or TAC (33%) + AZA (33-41%) or MMF (80% vs 61%) + steroids (99%)

*Bentas W, et al. Nephrol Dial Transplant 2008*
Proportion of Transplant Recipients and Donors ≥65 Years Old

**Intraoperative Arterial Vascular Calcifications**

<table>
<thead>
<tr>
<th></th>
<th>ESP n (%) patients</th>
<th>ETKAS n (%) patients</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>18 (25)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (8)</td>
<td>1 (2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Pronounced</td>
<td>2 (3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>26 (36)</td>
<td>6 (12)</td>
<td></td>
</tr>
<tr>
<td><strong>Recipient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>17 (23)</td>
<td>11 (22)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>13 (18)</td>
<td>0</td>
<td>0.017</td>
</tr>
<tr>
<td>Pronounced</td>
<td>4 (6)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>34 (47)</td>
<td>13 (26)</td>
<td></td>
</tr>
</tbody>
</table>

Eurotransplant Senior Programme (ESP)

- Less time on dialysis (42 mo vs 77 mo)
- Higher frequency of arteriosclerosis of both donors and recipients
- Prolonged mean anastomosis time
- More postoperative complications in the ESP group
- Similar GS and PS rates (up to 5 years)
- 13 patients died during follow-up of 39.5±24 mo, all with a functioning graft

*Bentas W, et al. Nephrol Dial Transplant 2008*
Kidney Transplant Outcomes in Elderly Patients: A Single Center Experience

- **Group I**: patients ≥60 yr old at the time of transplant (n= 214)
- **Group II**: patients 40-59 yr old at the time of transplant (n= 436)
- **Group III**: patients ≥60 yr old at the time of listing who remained on the waiting list (n= 250)
- 34 pts >70 yrs of age (18 of them ECD kidney recipients, 16 SCD recipients)
- Immuno: TAC 90% + MPA + steroids

  *Sahin S, et al. ATC 2008 Toronto, abstract# 698*
<table>
<thead>
<tr>
<th></th>
<th>Elderly ECD Recipients</th>
<th>Elderly SCD Recipients</th>
<th>Elderly on the waiting-list</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n:</strong></td>
<td>71</td>
<td>143</td>
<td>250</td>
</tr>
<tr>
<td><strong>%</strong></td>
<td>33%</td>
<td>67%</td>
<td>%</td>
</tr>
<tr>
<td><strong>Age (yrs) (range)</strong></td>
<td>64.4 (60-80)</td>
<td>63.9 (60-78)</td>
<td>65 (60-90)</td>
</tr>
<tr>
<td><strong>Gender (F/M)</strong></td>
<td>22/49</td>
<td>48/95</td>
<td>92/158</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>45</td>
<td>94</td>
<td>130</td>
</tr>
<tr>
<td>African-American</td>
<td>22</td>
<td>34</td>
<td>100</td>
</tr>
<tr>
<td>Asian</td>
<td>4</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>x</td>
<td>x</td>
<td>7</td>
</tr>
<tr>
<td><strong>Etiology of ESRD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes**</td>
<td>24</td>
<td>42</td>
<td>101</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12</td>
<td>19</td>
<td>45</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>13</td>
<td>31</td>
<td>25</td>
</tr>
<tr>
<td>ADPKD</td>
<td>9</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Others</td>
<td>13</td>
<td>36</td>
<td>67</td>
</tr>
</tbody>
</table>

*Sahin, S, et al. ATC 2008 Toronto, abstract# 698*
<table>
<thead>
<tr>
<th></th>
<th>Elderly ECD Recipients</th>
<th>Elderly SCD Recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n: 71</td>
<td>%</td>
</tr>
<tr>
<td>Prior transplantation</td>
<td>1</td>
<td>4.9</td>
</tr>
<tr>
<td>PRA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>60</td>
<td>84.5</td>
</tr>
<tr>
<td>20-80</td>
<td>7</td>
<td>9.8</td>
</tr>
<tr>
<td>&gt;80</td>
<td>4</td>
<td>5.7</td>
</tr>
<tr>
<td>Waiting time (days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>857*</td>
<td>1043.5*</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.4</td>
<td>27.9</td>
</tr>
<tr>
<td>DGF*</td>
<td>16</td>
<td>22.5**</td>
</tr>
<tr>
<td>Cold ischemia time (min)</td>
<td>892</td>
<td>1010</td>
</tr>
<tr>
<td>Donor age**</td>
<td>64.6*</td>
<td>39.3*</td>
</tr>
<tr>
<td>Induction protocol</td>
<td>66</td>
<td>93</td>
</tr>
</tbody>
</table>

*Induction: majority rabbit anti-thymocyte globulin/few pts with basiliximab

**p=0.03, * p<0.001 Less waiting time, more DGF, older donors in the ECD group

Sahin S, et al. ATC 2008 Toronto, abstract# 698
Elderly ECD

Elderly SCD

1 yr: Elderly ECD 65 pts, Elderly SCD 143 pts
3 yrs: Elderly ECD 41 pts, Elderly SCD 104 pts
5 yrs: Elderly ECD 24 pts, Elderly SCD 39 pts
Patient Survival for Elderly SCD, Elderly ECD and non-Elderly Recipients
Graft Survival in Elderly SCD, Elderly ECD, and non-Elderly Recipients
Unadjusted Patient Survival for Elderly SCD Recipients, Elderly ECD Recipients, and Wait-Listed Candidates
Unadjusted Graft Survival for Elderly SCD Recipients and Elderly ECD Recipients
<table>
<thead>
<tr>
<th></th>
<th>1-year PS</th>
<th>3-year PS</th>
<th>1-year GS</th>
<th>3-year GS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elderly ECD</strong></td>
<td>100%</td>
<td>97%</td>
<td>94.1%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>Elderly SCD</strong></td>
<td>99.2%</td>
<td>95%</td>
<td>96.7%</td>
<td>95%</td>
</tr>
<tr>
<td><strong>Young ECD+SCD</strong></td>
<td>99.7%</td>
<td>98.1%</td>
<td>98.8%</td>
<td>94.4%</td>
</tr>
</tbody>
</table>

Waiting List: 1-year PS 89.9%, 3-year PS 55.9%
<table>
<thead>
<tr>
<th>Death</th>
<th>Elderly wait-listed candidates (≥60 yr)</th>
<th>Elderly transplant recipients (≥60 yr)</th>
<th>Younger transplant recipients (40-59 yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total deaths</td>
<td>108 (43.2%)</td>
<td>34 (15.8%)</td>
<td>46 (10.5%)</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>16</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Infection</td>
<td>3</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Malignancy</td>
<td>7</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Liver disease</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Multisystem organ failure</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary emboli</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>Elective surgical procedure 1, bleeding from access 1</td>
<td></td>
<td>GI bleeding 1, trauma 1</td>
</tr>
<tr>
<td>Unknown</td>
<td>67</td>
<td>20</td>
<td>29</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Elderly ECD Recipients (n:71) 12 solid organ tm + 5 skin ca (23.9%)</td>
<td>Elderly SCD Recipients (n:143) 15 solid organ tm + 13 skin ca (19.6%)</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td>--------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Solid organ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>RCC</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>GIS</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td>-</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PTLD</td>
<td>-</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Skin ca</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCC</td>
<td>3</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>SCC</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
Elderly Transplants - Outcomes

- Acute rejection: 9 elderly patients (4%) vs 57 young patients (13%)
- Death:
  - **Group I:** 34 died (12 in the ECD group - 10 death with a functioning graft; 22 in the SCD group - 18 death with a functioning graft)
  - **Group II:** 46 died - 12 ECD, 9 DFG and 34 SCD - 30 DFG
  - **Group III:** 108 in 250 patients (43.2%) died

*Sahin S, et al. ATC 2008 Toronto, abstract# 698*
Conclusion-UPENN Experience

- In our center, patients >60 yo who received a kidney transplant (ECD and SCD) with our standard IS had excellent graft and patient survival rates comparable to 40-59 yo patients transplanted at the same time.
- Our study demonstrated that elderly patients experienced significant survival benefit with kidney transplantation compared to patients remained on the waiting list.
- Use of ECD kidneys in elderly patients did not appear to jeopardize outcomes.
- Our data support the rising trend of accepting older aged tx candidates and suggest that these older pts can tolerate current IS therapy without high rate of serious adverse events.

Sahin S, et al. ATC 2008 Toronto, abstract# 698
Modifiable Factors Predicting Patient Survival in Elderly Recipients

- Multicenter, population-based, retrospective cohort study from Canada, >60 years or older, 1/1985 and 6/2000
- 256 patients (25% received kidneys from older donors- >51 yo)
- Factors associated with PS: **active smoking at transplantation**, high **BMI**, and long time on dialysis before transplantation—all modifiable
  

- Pretransplant h/o **nonskin malignancy** and **peripheral vascular disease**, and **current smoking** history: risk factors for decreased GS and PS
  

- Poor functional capacity predicts a poor outcome
  
  *Yange AF. Et al. Clin Transplant 2006*
Risks of Kidney Transplantation in Elderly Patients

- Risk for infection or chronic graft dysfunction—not decreased
- Higher mortality after transplantation, mostly due to CVD, infections and malignancy
- Increased likelihood of DGF, especially in ECD kidneys—ways to minimize DGF
Benefits of Kidney Transplantation in Elderly Patients

- Best results with LRD transplants
- Survival advantage compared to patients on dialysis—positive in most studies though less than younger patients
- Quality of life benefits, better compliance than younger patients
- Lower immunosuppression requirements and less acute rejection
- Modifiable risk factors to improve results
- Less use of induction therapy with T-lymphocyte depleting agents—choice of induction—controversial—Is it necessary?
Kidney Transplantation in Elderly Patients

- Majority of older patients are not candidates for kidney transplantation
- Patient selection: careful assessment of risk factors to select patients who would benefit the most
- Special considerations during evaluation: strict standard malignancy screening, evaluation of heart disease and PVD, assessment of cognitive abilities and capacity to ambulate
- “Old for old” concept and discussion of ECD kidney transplants in the elderly
Incidence and Prevalence of ESRD per Million Population
Transplant Rates (per Million Population), by Age, 2005