Older Living Kidney Donors and Recipients

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Clinical Scenario

- **HPI:** 60 y/o healthy AAM with h/o CKD5 on HD x 2 yrs 2/2 HTN, was evaluated in transplant clinic for potential renal transplant.

- Patient was concerned about how he would be able to tolerate renal transplantation and immunosuppressant medications.

- Patient has a potential donor in his daughter, but is very reluctant about the idea and ask whether he should accept the donation or wait on the list for a deceased kidney.
Objectives

- How does grafts from older donor compare to younger donors?
- How does age of transplant recipients effect transplant outcomes?
- How does outcomes from grafts of living donor defer from deceased donors.
- How should recipient’s age affect immunosuppressant regiments and allocations?
The combination of donor and recipient age is critical in determining host imunoresponsiveness and renal transplant outcome.

Tullius SG, Tran H, Guleria I, Malek SK, Tilney NL, Milford E.
The Combination of Donor and Recipient Age is Critical in Determining Host Immunoresponsiveness

- To evaluate the interaction of donor and recipient age on transplant outcome and immune response.

- They tested the relevance and consequences of recipient and donor age on immuno-responsiveness and transplant outcome in a uni- and multilateral cohort analysis.


- Data were assessed and compared by decades of increasing donor and recipient age with and without censoring transplant loss for death with a functioning graft.

Tullius SG et al, Annals of Surgery, 2010
Patient Survival By Age Cohort

- Patients’ 5 year and 10 year survival decrease with every decade of increasing age.
- P < 0.001 versus previous cohort.

Tullius SG et al, Annals of Surgery, 2010
The need for dialysis within 1st wk increase with age.

Reflects the correlation of organ quality and the risk for delayed graft function.

P < 0.001

Tullius SG et al, Annals of Surgery, 2010
A, Graft survival decreased with increasing recipient age.

Graft survival in the age group 18-29 yrs was slightly reduced and may reflect an age specific pattern of underlying disease and compliance.
Death Censored Graft Survival by Recipient Age Cohort.

- When censoring for death with a functioning graft, transplant survival improves with every decade of recipient age.

- *P 0.001 versus previous cohort

Tullius SG et al, Annals of Surgery, 2010
Acute rejection during the first post-transplantation year increased with each decade of increasing donor age. *$P$ 0.01 versus prior age cohort.

Tullius SG et al, Annals of Surgery, 2010
Acute Rejection and Recipient Age

Acute rejections during the first post-transplant year declined steadily with every decade of increasing recipient age. *P 0.001 versus prior age cohort.

Tullius SG et al, Annals of Surgery, 2010
Graft Loss by Donor and Recipient Age; Censored for DWFG.

- Multivariate relative risk of death censored graft loss was calculated for all combinations of donor and recipient age cohorts (reference group recipients 50–59 and donors 18–29).
- Effect of donor age on relative risk of graft loss is particularly evident in the younger recipient age cohorts, and decreases with increased recipient age.
Conclusions

- Transplant survival was lowest in elderly recipients.

- However, when the analysis was censored for patient’s death with a functioning kidney transplant, survival improved incrementally with each decade of increasing recipient age.

- Older recipients had received less well-matched organs of poorer quality. The frequency of acute rejection decreased dramatically with increasing age, emphasizing the effect of age on the vigor of the recipient’s immune responses.

- In contrast, increasing donor age was associated with more frequent acute rejection rates.

Tullius SG et al, Annals of Surgery, 2010
Conclusions (Con’t)

- The effects of donor and recipient age in combination demonstrated that grafts of older donors fared significantly better in older recipients.

- Our results show that increasing recipient age is associated with an improved transplant survival, lower rates of rejection, and superior outcome of older donor organs.

- Physiological and/or immunologic aspects of organ and recipient age seem to determine, at least in part, the success of renal transplantation.

Tullius SG et al, Annals of Surgery, 2010
Potent Early Immune Response After Kidney Transplantation

100 renal allograft recipients were prospectively evaluated from 2004 to 2005.

Patients >65 years of the ESP receiving kidneys from donors > 65 years were compared with recipients <65 years receiving kidneys from donors younger than 65 years.

Their data demonstrate an initially pronounced immune response in elderly recipients receiving grafts from elderly donors.

This observation supports the concept of a donor and recipient age-adapted immunosuppression.

Pratschke et al, Transplantion, 2009
Clinical Data 6mo after Transplantation

<table>
<thead>
<tr>
<th></th>
<th>Old (n=26)</th>
<th>Young (n=74)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient survival (6 mo)</td>
<td>26 (100%)</td>
<td>73 (98.7%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Graft survival (6 mo)</td>
<td>23 (88.5%)</td>
<td>68 (93.2%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean serum creatinine (6 mo, mg/dL, mean±SD)</td>
<td>1.59±0.50</td>
<td>1.62±0.56</td>
<td>n.s.</td>
</tr>
<tr>
<td>Rejection rate (6 mo)</td>
<td>13 (50.0%)</td>
<td>32 (43.2%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Primary nonfunction</td>
<td>2 (8.3%)</td>
<td>1 (1.4%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>DGF</td>
<td>7 (26.9%)</td>
<td>21 (28.4%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

DGF, delayed graft function, n.s., not significant.
Before transplantation

Numbers of activated cytotoxic cells were elevated with increasing age before and 7 days after transplantation.

Pratschke et al, Transplantion, 2009
Before transplantation, 7 days and 6 months thereafter recipients older than 65 years demonstrated significantly elevated numbers of memory T-cells while counts for naive T-cells were significantly reduced.

Pratschke et al, Transplantion, 2009
6 months post transplantation

Increase memory T cells (CD45RO: 67.33.3 vs. 57.12.4%, \( P (0.0156) \)) and significantly reduced numbers of naive T cells (CD45RA: 20.92.3 vs. 30.51.9%; \( P (0.001) \)), while counts for activated suppressor cells (CD8HLA DR) were comparable with those in younger recipients.
Older Donor Grafts more Immunogenic

- T-cell alloreactivity was more pronounced in older recipients at all time points.

- Only patients with comparable immunosuppression protocols are included

- Older donor grafts per se elicit a stronger immune response in the early period after transplantation because of an increased immunogenicity and reduced resistance to unspecific damages
The new proposal for kidney allocation calls for the assignment of 20% of available organs that are characterized as “high quality” to recipients with a high estimated rate of survival after transplantation.

The remaining 80% of available organs would then be distributed to patients who are within 15 years of the donor’s age (i.e., older or younger).
Accepting kidneys from older living donors: impact on transplant recipient outcomes.


Accepting Kidneys from Older Living Donors

- This retrospective cohort study observed kidney allograft recipients from Ontario, Canada between January 2000 and March 2008.

- Donors to these recipients were older living (≥60 years), younger living, or standard criteria deceased (SCD).

- Recipients received 73 older living, 1187 younger living and 1400 SCD kidneys.

- Recipients of older living kidneys were older than recipients of younger living kidneys.

Young et al, Am J Transplant, 2011
Outcomes

- Baseline glomerular filtration rate (eGFR) of older kidneys was 13 mL/min lower than younger kidneys. Median follow-up time was 4 years.

- The primary outcome of total graft loss was not significantly different between older and younger living kidney recipients [adjusted hazard ratio, HR (95%CI): 1.56 (0.98–2.49)].

- There was no significant difference in total graft loss comparing older living to SCD kidney recipients [HR: 1.29 (0.80–2.08)].

- In light of an observed trend towards potential differences beyond 4 years, uncertainty remains, and extended follow-up of this and other cohorts is warranted.
Table 2: Characteristics of kidney donors at the time of transplantation

<table>
<thead>
<tr>
<th></th>
<th>Living kidney donors</th>
<th>Deceased kidney donors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Older kidney (≥60 years) N = 73</td>
<td>Younger kidney (&lt;60 years) N = 1187</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>63 (3)</td>
<td>42 (10)</td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>62 (60–64)</td>
<td>42 (34–50)</td>
</tr>
<tr>
<td>60–69 years</td>
<td>70 (96)</td>
<td>42 (50)</td>
</tr>
<tr>
<td>≥70 years</td>
<td>≤5 (≤7)&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Gender [Female, n (%)]</td>
<td>36 (49)</td>
<td>731 (62)</td>
</tr>
<tr>
<td>Relationship to their Recipient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent</td>
<td>24 (33)</td>
<td>103 (9)</td>
</tr>
<tr>
<td>Child</td>
<td>≤5 (≤7)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>186 (16)</td>
</tr>
<tr>
<td>Sibling</td>
<td>13 (18)</td>
<td>404 (34)</td>
</tr>
<tr>
<td>Spouse</td>
<td>18 (25)</td>
<td>232 (20)</td>
</tr>
<tr>
<td>Other related</td>
<td>≤5 (≤7)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>84 (7)</td>
</tr>
<tr>
<td>Unrelated</td>
<td>11 (15)</td>
<td>178 (15)</td>
</tr>
<tr>
<td>Serum Creatinine (μmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>77 (14)</td>
<td>75 (14)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>77 (67–86)</td>
<td>73 (65–85)</td>
</tr>
<tr>
<td>CKD-EPI eGFR (mL/min per 1.73 m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>83 (10)</td>
<td>96 (15)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>84 (74–91)</td>
<td>96 (85–106)</td>
</tr>
<tr>
<td>MDRD eGFR (mL/min per 1.73 m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>84 (12)</td>
<td>92 (17)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>83 (74–92)</td>
<td>90 (80–101)</td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>43 (60)</td>
<td>587 (50)</td>
</tr>
</tbody>
</table>

Young et al, Am J Transplant, 2011
The primary outcome of total graft loss was not significantly different between older and younger living kidney recipients [adjusted hazard ratio, HR (95% CI): 1.56 (0.98–2.49)].

This hazard ratio was not proportional and increased with time. Associations were not modified by recipient age or donor eGFR.
Table 4: Association of older living versus SCD deceased with transplant outcome

<table>
<thead>
<tr>
<th>Recipient outcome</th>
<th>SCD deceased (&lt;60 years)</th>
<th>Older living (≥60 years)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total graft loss (n)</td>
<td>355</td>
<td>17</td>
<td>–</td>
</tr>
<tr>
<td>Rates (Events per 100 person-years)</td>
<td>6.1</td>
<td>6.3</td>
<td>0.91</td>
</tr>
<tr>
<td>Unadjusted HR (95% CI)</td>
<td>1.0 (ref)</td>
<td>1.03 (0.64–1.64)</td>
<td>0.30</td>
</tr>
<tr>
<td>Multivariable adjusted HR (95% CI)</td>
<td>1.0 (ref)</td>
<td>1.29 (0.80–2.08)</td>
<td>0.07</td>
</tr>
<tr>
<td>Death (alone), n</td>
<td>201</td>
<td>11</td>
<td>–</td>
</tr>
<tr>
<td>Rates (Events per 100 person-years)</td>
<td>3.1</td>
<td>3.8</td>
<td>0.44</td>
</tr>
<tr>
<td>Unadjusted HR (95% CI)</td>
<td>1.0 (ref)</td>
<td>1.27 (0.69–2.32)</td>
<td>0.44</td>
</tr>
<tr>
<td>Multivariable adjusted HR (95% CI)</td>
<td>1.0 (ref)</td>
<td>1.83 (0.96–3.48)</td>
<td>0.45</td>
</tr>
<tr>
<td>Death-censored graft loss (n)</td>
<td>173</td>
<td>6</td>
<td>–</td>
</tr>
<tr>
<td>Rates (Events per 100 person-years)</td>
<td>3.0</td>
<td>2.2</td>
<td>–</td>
</tr>
<tr>
<td>Unadjusted HR (95% CI)</td>
<td>1.0 (ref)</td>
<td>0.71 (0.32–1.56)</td>
<td>0.39</td>
</tr>
<tr>
<td>Multivariable adjusted HR (95% CI)</td>
<td>1.0 (ref)</td>
<td>0.74 (0.34–1.62)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Notes: All multivariable models adjusted for: Recipient age, dialysis duration and year of transplant. Additional adjustment on the basis of operational confounding criteria depends on outcomes: Total graft loss, Recipient race, Charlson score and peak PRA; Death, Peak PRA; Peak PRA, Death-censored graft loss.

Young et al, Am J Transplant, 2011
Comparison of Graft Survival

Comparison of Patient Survival

Take Home Points

- Increasing recipient age is associated with an improved transplant survival, lower rates of rejection, and superior outcome of older donor organs.

- Physiological and/or immunologic aspects of organ and recipient age seem to determine, at least in part, the success of renal transplantation.

- Data demonstrate an initially pronounced immune response in elderly recipients receiving grafts from elderly donors. This observation supports the concept of a donor and recipient age-adapted immunosuppression.

- With superior graft and patient survival in recipients of transplants from OLDs compared with SCDs and ECDs, OLDs may be an important option for elderly transplantation candidates and should be considered for older patients with a willing and suitable older donor.
The combination of donor and recipient age is critical in determining host immunoresponsiveness and renal transplant outcome.

- Tullius SG, Tran H, Guleria I, Malek SK, Tilney NL, Milford E.

Accepting kidneys from older living donors: impact on transplant recipient outcomes.


Potent early immune response after kidney transplantation in patients of the European senior transplant program.

- Transplantation. 2009 Apr 15;87(7):992-1000.

Outcomes of kidney transplantation from older living donors to older recipients.

- Gill J, Bunnapradist S, Danovitch GM, Gjertson D, Gill JS, Cecka M.