Expanded Criteria Donor: Revisited?

Bryce Kiberd
Overall AIM of ECD Policy

Increase organ utilization
Objectives

- Review the definitions of ECD
- ECD allocation options
- Evidence supporting the use of ECD
Definition of ECD

- Potential Low Function
  - Heart beating (i.e. older donor)
  - Non-heart beating (Deceased Cardiac Donor)

- Potential High Risk to Recipient
  - Infection (HCV, HBV, others)
  - Cancer (primary brain, historic cancer)

- Bought kidneys?
Many ECD Definitions

- United Network Organ Sharing (UNOS)
- Deceased Donor Score
- Donor Histology
- Donor Age
UNOS criteria
Risk of Graft Loss 1.7 times higher than a standard donor kidney

- >60 year old donor
- 50-60 age donor and 2 of the following 3
  - Hypertension
  - Serum Creatinine 132 µmol/L at any time
  - CVA as cause of death

Current discard rate 40% of these donors
Current utilization is 15% of all transplanted kidneys
Definition of Standard Donor

- Donor age 10-39
- Death Non-CVA
- No hypertension
- Terminal creatinine $< 132 \, \mu\text{mol/L}$
ECD vs SD Graft Survival (Ojo JASN 2001)
Cost Savings ECD and SD vs Dialysis (Schnitzler Transplantation 2003)
UNOS Implementation (Oct 2002)

- Identify willing ECD kidney recipients
- Consent potential recipients
- Minimal cold time

Information on Consent

- Expect increase in delayed graft function
- Expected decrease in graft survival
- Expected decrease in waiting time
- Expected increase in survival compared to waiting.
- Benefit of transplant prior to increased morbidity

Sample consent AJT 2003;3 (suppl 4):124-5
UNOS Problems

Many kidneys discarded that should be used
(WTC 2006 pg 140)

<table>
<thead>
<tr>
<th></th>
<th>Graft Loss</th>
<th>Discard Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor with PVD</td>
<td>0.87</td>
<td>3.49</td>
</tr>
<tr>
<td>Urine protein</td>
<td>1.10</td>
<td>2.20</td>
</tr>
<tr>
<td>Donor age 65-69</td>
<td>1.19</td>
<td>6.98</td>
</tr>
<tr>
<td>Cysts</td>
<td>0.58</td>
<td>1.81</td>
</tr>
<tr>
<td>Resistance (pump)</td>
<td>1.16</td>
<td>5.67</td>
</tr>
</tbody>
</table>

- Re-evaluation of criteria (CVA death vs Hypertension/Creatinine)
Some centers have few awaiting ECD
Some centers have almost all on ECD lists
Deceased Donor Criteria
Nyberg et al AJT 2003

- Donor Age: 0-25 points
- Hypertension: 0-5
- Donor CrCl: 0-4
- CVA death: 0-3
- HLA MM: 0-3

Total: 0-39
Nyberg et al.

Graft survival, %

Time after transplantation, y

A (0–9 points)
B (10–19 points)
C (20–29 points)
D (30–39 points)
Donors > age 60 (recipients >50 age or difference <10 years)

16 gauge needle (40-50 glomeruli)

Evaluate vessels, glomeruli, tubules and interstitium

Score 0-3 each component

Total score (0-12)
  • >6 discard
  • 4-6 dual kidney
  • ≤3 single kidneys
## Criteria Comparison

Luis et al. WTC 2006 pg 143  
\( n=95 \)

<table>
<thead>
<tr>
<th>Graft Survival</th>
<th>Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At 1 year</strong></td>
<td></td>
</tr>
</tbody>
</table>

### Histologic
- **0-3**: 87%  
  Creatinine: **1.30 \( \pm \) 0.44**
- **4-6**: 85%  
  Creatinine: **1.45 \( \pm \) 0.56**

### Deceased Donor Score
- **A**: 96%  
  Creatinine: **0.95 \( \pm \) 0.24**
- **B**: 93%  
  Creatinine: **1.55 \( \pm \) 0.44**
- **C**: 73%  
  Creatinine: **1.64 \( \pm \) 0.60**
Criteria Comparison
Rossini et al WTC 2006 pg 236
n=167 transplants

Concordance Score
- Histologic 0.64 ± 0.08
- DDS 0.73 ± 0.08
- Integrated 0.81 ± 0.08

Integrated score = DDS (0-39) + 13*Glom score (0-3)
Cut point 34 (5 year GS 97% vs 67%)
Old for Old (>64 to >64)

- 43% increase in transplantation of the elderly with reduced wait time (WTC 2006 pg 141)

<table>
<thead>
<tr>
<th></th>
<th>Old for Old</th>
<th>Traditional Allocation</th>
</tr>
</thead>
<tbody>
<tr>
<td>R Age</td>
<td>68±3</td>
<td>64±3 years</td>
</tr>
<tr>
<td>D Age</td>
<td>71±4</td>
<td>45±15 years</td>
</tr>
<tr>
<td>CIT</td>
<td>7.8 ±3.4</td>
<td>14.2 ±5.5 h</td>
</tr>
<tr>
<td>HLA MM</td>
<td>4.2 ± 1.2</td>
<td>1.6 ± 1.7</td>
</tr>
<tr>
<td>PSurvival</td>
<td>85%</td>
<td>89%</td>
</tr>
<tr>
<td>GSurvival</td>
<td>84%</td>
<td>87%</td>
</tr>
</tbody>
</table>
UNOS vs Eurotransplant
Cecka et al AJT (ATC 2004)

- 1500 cadaver kidneys discarded in US annually
- 37% of 61-65 y/o donor kidneys discarded in US vs 7% in ET
- 54% of >65 y/o donors kidneys discarded in US vs 8% in ET
- Eurotransplant Senior Program >65 y/o donor kidneys to >65 y/o recipients
What should be our plan?
Avoid “ECD”

Rather ‘Optimized Allocation’
Optimized Matching
Optimized Matching
Remaining Life Years
Remaining Miles to Travel

Vancouver to St John’s

Gander to St John’s
Optimized Matching

Vancouver to St John’s

Gander to St John’s
Our Current Plan
‘Now Under Review’

- Retrieve All kidneys
- Visibly scarred kidneys should be discarded.
- Biopsy some deceased donors kidneys
  - > age 65
  - > age 55 and donor CrCl < 70 ml/min
  - Discard advanced arteriolar sclerosis or interstitial fibrosis (use 16 g needle)
- Allocate to
  - Older (>59) or diabetic
  - Avoid the sensitized
  - Minimize cold ischemic time
  - Avoid large weight or age mismatches
Still Some Angst

Analysis of Outcomes
Mortality Rate On Wait List
Per 100 patient years

Gill et al Kidney Int 2005
Transplant Rates by Time on List
Gill et al AJT 2005;5 (Suppl 11):261

Rate per 100 patient years

Age

20-39
40-59
60-64
64-69
70+

1 yr
2 yr
3 yr
>3 yr
Probability of Transplantation

Cumulative probability
Overestimated since it ignores removal from the list

Time (years)

- 20-39
- 40-59
- 60-69
- >70
The ECD in deceased donor renal transplantation.

JAMA 2005:294:2726

- Cohort of >109,000 ESRD patients 1/95-12/02
- Compared transplanted outcomes from wait list to death for standard and ECD recipients.
- RR for mortality with ECD kidney (vs SD)
  - RR=1 Implies ECD and SD equivalent
  - RR<1 Implies ECD better than SD
  - RR>1 Implies ECD worse than SD
The ECD in deceased donor renal transplantation.

JAMA 2005:294:2726

<table>
<thead>
<tr>
<th></th>
<th>Short Wait (&lt;3.5 yrs)</th>
<th>Long Wait</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 40-59</td>
<td>0.90</td>
<td>0.71 (0.60-0.85)*</td>
</tr>
<tr>
<td>Age 60+</td>
<td>0.92</td>
<td>0.63 (0.50-0.78)*</td>
</tr>
<tr>
<td>DM</td>
<td>0.77 (0.64-0.94)*</td>
<td>0.74 (0.59-0.924)*</td>
</tr>
</tbody>
</table>
The ECD in deceased donor renal transplantation.
JAMA 2005:294:2726

- Net Benefit
  - Long waiting times
    - Diabetes mellitus and >40 years of age
  - Short waiting times
    - Diabetes mellitus
Selected subsets revealed differences in wait times that equated QALYs for ECD and standard donors:

- **Average**: 3.2 years
- **African Am.**: 4.4 years
- **Age under 30**: 4.0 years
- **Age over 60**: 11 months.
Future Allocation Solutions
Optimized Solution
WTC 2006 pg 322

Recipient Score (1-4 grade based on DM, Age, IHD, Dialysis time)

<table>
<thead>
<tr>
<th>Deceased Donor Score</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+3</td>
<td>-8</td>
<td>-13</td>
<td>-15</td>
</tr>
<tr>
<td>2</td>
<td>+20</td>
<td>+10</td>
<td>+4</td>
<td>+0.4</td>
</tr>
<tr>
<td>3</td>
<td>+24</td>
<td>+14</td>
<td>+8</td>
<td>+4.5</td>
</tr>
<tr>
<td>4</td>
<td>+27</td>
<td>+16</td>
<td>+11</td>
<td>+7</td>
</tr>
</tbody>
</table>

Graft Survival minus Patient Survival in %
Maximizing Value
Meier-Kriesche et al AJT 2005;5:1725

For the 1225 patients receiving younger grafts, 1225*1.5 years = 1838 graft years lost (within 10 years)

Average graft survival 7.4 years (out of 10)

Average patient survival for recipients = 5.9 years (out of 10)
# Matching Recipient and Graft Survival

**Baskin-Bey et al Transplantation 2006; 82:10**

## Table 3
Renal years according to age group and Deceased Donor Score

<table>
<thead>
<tr>
<th>Recipient age (years)</th>
<th>Recipient renal years</th>
<th>Donor renal years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>&lt;18</td>
<td>10808</td>
<td>1126</td>
</tr>
<tr>
<td>18–39</td>
<td>36446</td>
<td>6736</td>
</tr>
<tr>
<td>40–49</td>
<td>25647</td>
<td>8290</td>
</tr>
<tr>
<td>50–59</td>
<td>23950</td>
<td>8173(^a)</td>
</tr>
<tr>
<td>60–69</td>
<td>11689</td>
<td>3667(^b)</td>
</tr>
<tr>
<td>≥70</td>
<td>2117</td>
<td>569(^c)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>110656</strong></td>
<td><strong>28561</strong> +</td>
</tr>
</tbody>
</table>

2002 calculation of renal years = number of transplants × survival (recipient or graft). Recipient survival was substituted for the original graft survival data (see Fig. 5); in these marked areas, graft survival superceded recipient survival. Our model attempts to preclude this occurrence.

\(^a\) Corrected graft survival used for calculation: 13.90 years.

\(^b\) Corrected graft survival used for calculation: 9.70 years.

\(^c\) Corrected graft survival used for calculation: 7.20 years.
# Matching Recipient and Graft Survival

Baskin-Bev et al Transplantation 2006: 82:10

## TABLE 4. Optimized expected renal year supply for 2002

<table>
<thead>
<tr>
<th>Recipient age (years)</th>
<th>Deceased Donor Score</th>
<th>N</th>
<th>Median graft survival (years)</th>
<th>Median recipient survival (years)</th>
<th>Optimized renal years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18</td>
<td>A</td>
<td>193</td>
<td>8.8</td>
<td>26.7</td>
<td>1698</td>
</tr>
<tr>
<td>18–39</td>
<td>A</td>
<td>1365</td>
<td>10.9</td>
<td>26.7</td>
<td>14879</td>
</tr>
<tr>
<td>40–49</td>
<td>A</td>
<td>782</td>
<td>15.1</td>
<td>18.9</td>
<td>11808</td>
</tr>
<tr>
<td>40–49</td>
<td>B</td>
<td>575</td>
<td>12.2</td>
<td>18.9</td>
<td>7015</td>
</tr>
<tr>
<td>50–59</td>
<td>B</td>
<td>1502</td>
<td>17.1</td>
<td>13.9</td>
<td>25684</td>
</tr>
<tr>
<td>50–59</td>
<td>C</td>
<td>221</td>
<td>11.4</td>
<td>13.9</td>
<td>2519</td>
</tr>
<tr>
<td>60–69</td>
<td>C</td>
<td>1205</td>
<td>13.0</td>
<td>9.7</td>
<td>11689</td>
</tr>
<tr>
<td>≥70</td>
<td>C</td>
<td>73</td>
<td>18.0</td>
<td>7.2</td>
<td>526</td>
</tr>
<tr>
<td>≥70</td>
<td>D</td>
<td>221</td>
<td>7.2</td>
<td>7.2</td>
<td>1591</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>6137</td>
<td></td>
<td></td>
<td>77409</td>
</tr>
</tbody>
</table>

Calculation summary: 110,656 years of renal function to meet demand in 2002; 67,926 years of renal function supplied by deceased donors in 2002 (real); 77,409 years of renal function supplied by deceased donors in 2002 (optimized data); + 9483 additional years of renal function saved by optimization; 13.96% increased by optimization; 22.19% deficit reduced by optimization.
THE NET LIFETIME SURVIVAL BENEFIT

KP McCullough et al WTC Abstract #217

- UNOS rethinking allocation of Standard Donors
  - More utility based

- For every donor kidney
  - The net gain in life expectancy is calculated
  - Cox model, years 4-10 with a Weibull model, Models included candidate age, albumin, BMI, years of ESRD, peak PRA, previous transplant, primary diagnosis, KI v. KP, and diabetes mellitus.
THE NET LIFETIME SURVIVAL BENEFIT
Competing Ethical Principles

- Utilitarian
- Net Benefit
- Egalitarian
- Equal Opportunity
Other Organs
ECD Liver Organs
Decrease Wait List mortality
WTC 2006 #603

- ECD Definition
  - >14 hours of cold ischemia time
  - AST>150 Na>170 Macrosteatosis >30%
    (Liver Transpl 2005;11:1184)
  - Non-heart beating donors
  - Split liver
  - Hepatitis C or B donor
Liver Allocation

- **Recipient Scoring System**
  - MELD (Model for End Stage Liver Disease)
  - PELD

- **ECD Allocation** (under review WTC Abstracts)
  - Avoid in Combined Kidney/Liver (#609)
  - Avoid MELD <15 (#607)
  - Avoid in high risk MELD >31 (#1000)
  - Avoid intermediate MELD 15-26 (#1001)
Conclusions

- Maximize use of donor organs
- ECD definitions and allocation will change
  - A Canadian approach is under review (Oct 26)
- Optimized Solution (rather than ECD)
  - Keep it simple
  - Size limitations
    - 65+ to 65+ versus \( \geq 60 \) to \( \geq 60 \) or DM)
Having Enough Patients on the Wait List
Examination of the Wait List

- <14% of adult Halifax program dialysis population on wait list
- 16% of Canada and USA
Access to the Transplant Wait List
Am J Transplant. 2006 Sep 4; [Epub ahead of print]

Kiberd B, Boudreault J, Bhan V, Panek R.

- **Aim:**
  - To examine policy that all patients with ESRD are considered for transplantation

- **Hypotheses**
  - That only about 20% are referred
  - That burden of comorbidity impacts on referral status
  - That a proportion of patients would not be referred despite relatively low comorbidity
Access to the Wait List

Am J Transplant. 2006 Sep 4; [Epub ahead of print]

- 113 consecutive ESRD patients from 4/05-4/06
  - 92 hemodialysis, 13 PD, 8 pre-emptive transplant
  - Age $62 \pm 15$ (25-85)
  - Diabetes Mellitus 35%
  - Cancer 20%
  - CHF 34%
  - IHD 35%
  - Stroke 14%
Access to the Wait List
AJT in Press 2006

- Comorbidity Indices
  - Charlson
    - 14 weighted health states
  - ESRD
    - 12 weighted health states
Access to the Wait List
AJT in Press 2006

- 47 (42%) Referred for transplantation
- 48 (43%) Contraindication
  - Canadian Guidelines 2005 CMAJ
  - Cancer-13, CV event -15, Active Disease-20
- 26 (23%) Not referred and No contraindication
Patients with No Contraindication

<table>
<thead>
<tr>
<th></th>
<th>Referred N=39</th>
<th>Not Referred N=26</th>
<th>prob</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>50±12</td>
<td>75±7</td>
<td>0.000</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>12 (31%)</td>
<td>13 (50%)</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>3 (7.7%)</td>
<td>6 (23%)</td>
<td></td>
</tr>
<tr>
<td>IHD</td>
<td>7 (21%)</td>
<td>9 (35%)</td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>6 (12%)</td>
<td>11 (42%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>35±5</td>
<td>32±6</td>
<td>0.049</td>
</tr>
<tr>
<td>Charlson Index</td>
<td>3.3±1.6</td>
<td>5.1±2.1</td>
<td>0.000</td>
</tr>
<tr>
<td>ESRD index</td>
<td>1.4±1.8</td>
<td>3.3±2.5</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Concordance Statistic
Age 0.99 (0.97-1.00)
Charlson 0.76 (0.61-0.89)
ESRD 0.75 (0.62-0.87)

If no contraindications
Almost everyone <65 is referred
Almost no one >70 is referred

ROC Curve for Referral

Age
Charlson
ESRD
Our Findings

- Higher referral rate than expected
- Are acceptable candidates being discriminated against by age?