Update from the living kidney donor registry

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Outline

• Why a living donor registry?
• Donor demographics
• Donor operative details and complications
• Long-term follow-up
• Conclusions
Age Specific Mortality Rates for Patients Treated with Dialysis or Transplantation Relative to the Australian Population 2009

2009 mortality rates
- Dialysis
- Transplant
- Aust Population

Aust 2009 death and population data from ABS

ANZDATA Report 2010
Living kidney donors

- Transplantation improves quality and duration of life
- Shortage of donors
- Transplants from living donors have better outcomes
- So aim to have living donor if possible
- Lack of data regarding:
  - Donor selection
  - Long-term outcomes of donation
CARI guidelines for kidney donors

• Renal function
  – No recommendations possible based on Level I or II evidence
• Hypertension
  – No recommendations possible based on Level I or II evidence
• Proteinuria
  – No recommendations possible based on Level I or II evidence
• Obesity
  – No recommendations possible based on Level I or II evidence
• DM/Impaired glucose tolerance
  – No recommendations possible based on Level I or II evidence
• Potential child-bearing donors
  – No recommendations possible based on Level I or II evidence
<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Mean Years after Donation, (Range)*</th>
<th>Donors, n</th>
<th>Mean Value SBP (SD), mm Hg</th>
<th>Use of Antihypertensive Medications, %</th>
<th>Controls, n</th>
<th>Mean Value SBP (SD), mm Hg</th>
<th>Use of Antihypertensive Medications, %</th>
<th>Mean Difference in SBP (95% CI), mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Najarian et al., 1992 (50)</td>
<td>8 (1–19)</td>
<td>57</td>
<td>134 (15)</td>
<td>32</td>
<td>50</td>
<td>130 (21)</td>
<td>44</td>
<td>4 (–3.1 to 11.1)</td>
</tr>
<tr>
<td>Undurraga et al., 1998 (53)</td>
<td>11 (1–21)</td>
<td>30</td>
<td>125 (18)</td>
<td>NR</td>
<td>30</td>
<td>118 (13)</td>
<td>NR</td>
<td>7 (–0.9 to 15.2)</td>
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<tr>
<td>Talselth et al., 1986 (54)</td>
<td>11 (10–12)</td>
<td>32</td>
<td>140 (23)</td>
<td>10</td>
<td>32</td>
<td>132 (29)</td>
<td>NR</td>
<td>8 (–4.8 to 20.8)</td>
</tr>
<tr>
<td>Williams et al., 1986 (57)</td>
<td>13 (10–18)</td>
<td>38</td>
<td>136 (25)</td>
<td>†</td>
<td>16</td>
<td>129 (16)</td>
<td>†</td>
<td>7 (–3.7 to 18.5)</td>
</tr>
<tr>
<td>Pooled estimate</td>
<td>157</td>
<td>133 (6)</td>
<td>128</td>
<td>126 (8)</td>
<td></td>
<td></td>
<td></td>
<td>6 (1.6 to 10.5)</td>
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</tbody>
</table>
### 24 h urine protein

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

**Note:** Numbers represent mean and standard deviation.
### Table 1: GFR Donors, post-donation

<table>
<thead>
<tr>
<th>Source</th>
<th>Assessment</th>
<th>Mean (range)</th>
<th>N mean (s.d.)</th>
<th>Controls</th>
<th>GFR mean difference, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>O'Donnell et al.</td>
<td>24 h urine</td>
<td>6 (3–18)</td>
<td>33 100 (22)</td>
<td>33 111 (17)</td>
<td>−12 (−21, −2)</td>
</tr>
<tr>
<td>D'Almeida et al.</td>
<td>24 h urine</td>
<td>7 (1–14)</td>
<td>59 86 (37)</td>
<td>28 98 (37)</td>
<td>−12 (−28, −5)</td>
</tr>
<tr>
<td>Najarian et al.</td>
<td>24 h urine</td>
<td>8 (1–19)</td>
<td>57 82 (15)</td>
<td>50 89 (23)</td>
<td>−7 (−15, 1)</td>
</tr>
<tr>
<td>Undurraga et al.</td>
<td>Cockroft-Gault</td>
<td>11 (1–21)</td>
<td>30 86 (22)</td>
<td>30 97 (27)</td>
<td>−11 (−24, 1)</td>
</tr>
<tr>
<td>Williams et al.</td>
<td>24 h urine</td>
<td>13 (10–18)</td>
<td>38 86 (39)</td>
<td>17 103 (31)</td>
<td>−17 (−37, 2)</td>
</tr>
<tr>
<td>Watnick et al.</td>
<td>Inulin</td>
<td>13 (9–18)</td>
<td>22 66 (14)</td>
<td>31 78 (22)</td>
<td>−12 (−22, −2)</td>
</tr>
<tr>
<td>Pooled estimate</td>
<td></td>
<td>239 84 (11)</td>
<td>189 96 (14)</td>
<td></td>
<td>−10 (−15, −6)</td>
</tr>
</tbody>
</table>

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.
Figure 1. Kaplan-Meier Curves Comparing Cumulative Mortality of Live Kidney Donors and Matched Controls for the Entire Cohort of Live Donors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Model 1 (n = 80,287)</th>
<th>Model 2 (n = 47,695)</th>
<th>Model 3 (n = 22,745)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>1.6 (1.2-2.0)</td>
<td>1.2 (0.8-1.8)</td>
<td>1.0 (0.4-2.3)</td>
</tr>
<tr>
<td>50-59</td>
<td>3.3 (2.6-4.1)</td>
<td>1.8 (1.2-2.8)</td>
<td>0.9 (0.3-2.4)</td>
</tr>
<tr>
<td>≥60</td>
<td>9.4 (7.3-12.1)</td>
<td>5.5 (3.3-9.2)</td>
<td>2.4 (0.8-7.6)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.7 (1.5-2.0)</td>
<td>1.5 (1.1-2.1)</td>
<td>1.3 (0.6-2.6)</td>
</tr>
<tr>
<td>Women</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Black</td>
<td>1.3 (1.0-1.6)</td>
<td>2.0 (1.3-3.0)</td>
<td>1.6 (0.6-4.2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.6 (0.4-0.9)</td>
<td>0.7 (0.4-1.2)</td>
<td>1.0 (0.3-3.2)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;120</td>
<td>NA</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>120-139</td>
<td>NA</td>
<td>1.2 (0.8-1.6)</td>
<td>2.1 (1.0-4.6)</td>
</tr>
<tr>
<td>≥140</td>
<td>NA</td>
<td>1.7 (1.1-2.9)</td>
<td>3.3 (1.1-9.7)</td>
</tr>
<tr>
<td>Smoking (ever)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
<td>5.3 (2.6-10.8)</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
<td>0.9 (0.1-6.6)</td>
</tr>
<tr>
<td>Follow-up, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>6.3 (3.2-9.8)</td>
<td>4.2 (2.1-6.5)</td>
<td>2.1 (1.0-3.1)</td>
</tr>
<tr>
<td>Maximum</td>
<td>15.1</td>
<td>9.3</td>
<td>4.3</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; IQR, interquartile range; NA, not applicable; SBP, systolic blood pressure.

Number of observations (changes because of missing data; see Table 1 for covariate availability). Hazard ratios (95% CIs) were estimated from Cox proportional hazards regression models. Model 1 includes demographics only (age, sex, race/ethnicity); model 2 includes demographics and SBP; and model 3 includes demographics, SBP, smoking, and hypertension.
CARI recommendations for kidney donors

- Renal function
  - GFR ≥80
- Hypertension
  - ≥140/90 relative CI; absolute CI if >2 drugs, end-organ damage or other risk factors
- Proteinuria
  - >300mg/day relative CI
- Obesity
  - BMI >30 relative CI; absolute CI if another risk factor
- DM/Impaired glucose tolerance
  - Absolute CI
- Potential child-bearing donors
  - No recommendation
Living donor registry

• Data since January 2004
• Aims
  – Describe practice patterns of living kidney donation in Aust/NZ
  – Describe relationship between donor factors and recipient outcomes
  – Monitor short- and long-term risks associated with kidney donation
Outline

• Why a living donor registry?
• Donor demographics
• Donor operative details and complications
• Long-term follow-up
• Conclusions
Major overhaul 2010

- **GFR**
  - Measured vs calculated
  - Eg MDRD eGFR ≥60 reported as measured GFR=60
- **Proteinuria**
  - mg/day vs g/day
  - PCR vs ACR vs timed
- **Diabetes**
  - Fasting BGL 6.8 -> 7 -> DM
- **Hypertension**
  - Donors on multiple drugs labelled no HTN
Living donors per year

- 2004: 292
- 2005: 292
- 2006: 322
- 2007: 329
- 2008: 423
- 2009: 393
Distribution of donor age
Distribution of recipient age

Recipient age (years)

Density
Donor age - recipient age

Density

Age difference (years)
Donor demographics

• Age
  – Mean 48.8 years
• Sex
  – Female 1181 (58%)
  – Male 870 (42%)
• Race
  – Caucasoid 88%
  – Asian 7%
  – Other 5% (3.8% Indigenous)
Donor source

• Spouse 459 (22.4%)
• Parent 537 (26.2%)
• Child 95 (4.6%)
• Sibling 468 (22.8%)
• Other related donor 113 (5.5%)
• Unrelated donor 379 (18.5%)
GFR measurement

- Radiolabelled DTPA/EDTA 939 (45.8%)
- Iohexol/Iothalamate 61 (3.0%)
- 24-h creatinine clearance 352 (17.2%)
- Other (mainly eGFR) 312 (15.2%)
- Not reported 387 (18.9%)
Estimated vs measured GFR
Diabetes & IGT

• Reported
  – 5 diabetics

• Based on reported OGTT and report of DM:
  – 18 diabetics
  – 51 IGT
  – 864 normal OGTT
  – 1118 no OGTT
BMI

- Mean 26 kg/m²
- 359 (19%) >30 kg/m²
  - 48 HTN
  - 16 IGT/DM
Hypertension

• 192 reported
• 212 if include definition of ≥140/90
• Number of drugs
  – 0  31
  – 1  136
  – 2  38
  – 3  7
Smoking

- Current: 165 (8%)
- Former: 642 (31%)
- Never: 1191 (58%)
- Unknown: 53 (3%)
Women of childbearing age

- 226 women ≤40
- 642 women ≤50
Outline

• Why a living donor registry?
• Donor demographics
• **Donor operative details and complications**
• Long-term follow-up
• Conclusions
Operative details

• 28 hospitals
  – Between 2 and 301 operations
• 81% Lt kidney
• 20% open, 79% laparoscopic
• 16 >2 arteries, 5 >2 veins
• Days in hospital
  – Median 4, maximum 14
Adverse events – time of surgery

- 118 infections
  - 34 wound
  - 45 lung
  - 23 urine
  - 15 other
- 1 AMI
- 13 bleeds requiring transfusion
- 4 PEs
Adverse events – time of surgery

• 192 other (from constipation, pain to pneumothorax, anaphylaxis, epidural abscess)
• 3 deaths in 2051 operations
  – cf US data 3.1 deaths/10,000 operations
• In total 210 donors with complications (10.5%)
Acute change in GFR

• Discharge vs pre-transplant
  – Creatinine rise
    • Mean 35 μmol/L
  – Ratio of discharge eGFR to pre-transplant eGFR
    • Mean 65%
    • 95% of values 46% to 93%
Outline

• Why a living donor registry?
• Donor demographics
• Donor operative details and complications
• Long-term follow-up
• Conclusions
Long-term follow-up

• Significant loss to follow-up
  – At present 1475 (72%) documented as lost to follow-up
  – Additional 184 donors no post-tx data
Timing of follow-up information

Number of reports

Years post donation
Long-term complications

• 60 documented long-term “renal problems”
  – Various
  – eg low eGFR, low-grade proteinuria, loin pain, bladder symptoms, UTIs

• Assortment of vascular events
  – Too few to be meaningful at this stage
Pregnancies

• 12 pregnancies in 11 donors
  – 8 reported outcomes – 5 live births, all full term
Conclusions

• Many marginal donors accepted
• GFR measurement may be suboptimal
• High surgical complication rate
• Poor long-term follow-up
• Valuable information regarding our practice patterns and short-term risks
• Significant room for improvement in long-term follow-up