Expanding the Donor Pool

ECD/DCD: Evaluation of the Marginal Kidney Donor

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Senior Scientist, Ottawa Hospital Research Institute
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Disclosure Slide

• Grant/Research Support in the past 5 years: Astellas Canada, CIHR, Public Health Agency of Canada, Kidney Foundation of Canada

• Consultant/Speaker Fees: none
Why are we Discussing this Topic?

Not Enough Donors
or
Not Using the Donors we Have?
(or Both)

CORR Data
Definitions

- **SCD** – Standard Criteria Donor
- **ECD** – Expanded Criteria Donor
- **DCD** – Donation after Cardiocirculatory Death
- **NDD** – Neurological Determination of Death ("Brain Death")
- **KDRI** – Kidney Donor Risk Index
- **KDPI** - Kidney Donor Profile Index
Definitions

• **ECD** – Expanded Criteria Donor
  • *Kidneys that have 70% increased risk of graft failure compared to SCD*
    • Age ≥ 60 years
    • Age 50-59 with any 2 of the following criteria
      • Death due to CVA
      • History of hypertension
      • Terminal creatinine ≥ 1.5 mg/dl (133 umol/L)

• **SCD** – Standard Criteria Donor
  • All brain dead deceased donors without any ECD criteria

• **DCD** – Donation after Cardiocirculatory Death

• **NDD** – Neurological Determination of Death (“Brain Death”)
KDRI/KDPI: Kidney Donor Risk Index/Kidney Donor Profile Index

- **KDRI**: Risk score based on 10 donor factors
- Interpreted as the relative risk of post-transplant graft failure from a specific donor compared to a reference donor (median donor, 50th percentile of score)
- Donor with KDRI of **1.28** confers an estimated risk of graft failure that **28%** higher than that of the median donor (typically ranges from **0.5 to 3.5**)
- **KDPI** is mapping of the RR to a cumulative percentage (0-100%)
- Donor with KDPI of **85%** has a RR of graft failure that is **higher** than **85%** of all recovered kidneys in the previous year

[Box with KDRI/KDPI risk factors]

- Age
- Height
- Weight
- Ethnicity
- History of Hypertension
- History of Diabetes
- Cause of Death
- Serum Creatinine
- Hepatitis C Virus (HCV)
- Donation after Circulatory Death
Increasing KDRII Associated with Worse Graft Survival
Why do we need to know how to evaluate marginal kidney donors?

- SCD: 8% discarded
- ECD: 41% discarded
- DCD: 25% discarded
- ECD-DCD: 51% discarded
- Age > 65 years: 60%
- KDPI > 90: 63%

~1500 kidneys/year discarded

No Canadian Data!!

American Journal of Transplantation 2008; 8: 783–792
Discard Rate is Highly Variable for Marginal Donors

Discard rate: 14-60%

Why would one region routinely discard kidneys that others would transplant?

American Journal of Transplantation 2008; 8: 783–792
Evaluation of the Marginal Kidney Donor

• Why are Kidneys Discarded?
  • Anatomic abnormalities
  • Damage during procurement
  • Tumour
  • Poor flush

• Avoidance of Risk
  • Risk of transmissable disease
  • Risk of premature graft failure:
    • We need kidneys to function adequately and long enough
    • We don’t need all kidneys to last forever and that is our problem....
    • We are very conservative and tend to discard kidneys that will most likely function adequately and long enough for certain recipients
Kidney Transplant Survival

Donor type | Tx | 1 year | 2 years | 3 years | 4 years | 5 years |
---|---|---|---|---|---|---|
Living donor | 100.0 | 97.1 | 95.4 | 94.1 | 91.8 | 90.0 |
Deceased donor | 100.0 | 93.4 | 90.7 | 87.7 | 85.2 | 81.8 |

CORR 2014
15% of Dialysis patients will die in the first year of treatment.

Only 45% will be alive after 5 years of treatment.

This prognosis is worse than many cancers.
Many Patients Willing to Accept ‘Marginal’ Kidneys

Adults willing to accept an ECD kidney or KDPI >85%

Survival Benefit of Primary Deceased Donor Transplantation With High-KDPI Kidneys

A. B. Massie¹,², X. Luo¹, E. K. H. Chow¹, J. L. Alejo¹, N. M. Desai¹ and D. L. Segev¹

Relative risk
high-KDPI KT vs waiting for a lower-KDPI kidney

Survival Benefit
Patients >50 years old
Median wait time at centre >33 months

American Journal of Transplantation 2014; 14: 2310–2316
What Information Can We Use to Evaluate a Marginal Kidney Donor

• Type of Donor
  • DCD vs. NDD
  • ECD vs. Non-ECD

• Clinical Parameters
  • Age
  • GFR
  • Hypertension/Diabetes
  • Cause of Death

• Donor Risk Scores

• Biopsy

• Perfusion Parameters: cold, normothermic *(next talk, Dr. Selzner)*

• Biomarkers: urine, blood, perfusate
ECD kidneys have decreased survival compared to non-ECD donors.

DCD vs DBD does NOT matter.
Graft Survival Identical with DCD and DBD Donors

SRTR 2015
Is the Kidney Biopsy Helpful?

USA: 50.4% of all donors have procurement biopsy (74.8% ECD)

No Canadian data but rarely done in Ontario

Eurotransplant Centres rarely use procurement biopsy (<5%)
Pre-Transplant Kidney Biopsy

- Procurement vs. Implantation biopsy
- Frozen section vs. Paraffin embedded
- “On-call” pathologist interpretation vs. Renal pathologist retrospective review
- Wedge vs. Core biopsy
# Donor Biopsy Scoring Systems

<table>
<thead>
<tr>
<th>Name (year published)</th>
<th>Variables scored</th>
<th>Predictive value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Banff scheme-based scores</td>
<td>Variables</td>
<td>Points</td>
<td>(a) AUC: 0.79 [29]</td>
</tr>
<tr>
<td>(a) Remuzzi (1999)</td>
<td>Global glomerulosclerosis (a–c)</td>
<td>0–3</td>
<td>(b) AUC: 0.76 [29]</td>
</tr>
<tr>
<td>(b) CADIX (1994)</td>
<td>Interstitial fibrosis, ci (a–c)</td>
<td>0–3</td>
<td>(c) AUC: 0.74</td>
</tr>
<tr>
<td>(c) Total chronic Banff (2008)</td>
<td>Tubular atrophy, ci (a–c)</td>
<td>0–3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vessel narrowing, cv (a–c)</td>
<td>0–3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mesangial matrix increase, mm (b–c)</td>
<td>0–3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Interstitial inflammation, i (b)</td>
<td>0–3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glomerular double contour, cg (c)</td>
<td>0–3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arteriolar hyalinosis, ah (c)</td>
<td>0–3</td>
<td></td>
</tr>
<tr>
<td>Maryland Aggregate Pathology Index (2008)</td>
<td>Variables</td>
<td>Points</td>
<td>AUC: 0.70–0.74</td>
</tr>
<tr>
<td></td>
<td>Periglomerular fibrosis: present/absent</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arteriolar hyalinosis: present/absent</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Scar: focus of sclerosis and IFTA ≥10 tubules: present/absent</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Global glomerulosclerosis ≥15%</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wall:Human ratio of intertubular arteries ≥0.5</td>
<td>2</td>
<td>5-year graft survival</td>
</tr>
<tr>
<td></td>
<td>Low risk group (score sum: 0–7)</td>
<td></td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>Intermediate risk group (score sum: 8–11)</td>
<td></td>
<td>63%</td>
</tr>
<tr>
<td></td>
<td>High risk group (score sum: 12–15)</td>
<td></td>
<td>53%</td>
</tr>
<tr>
<td>French clinicohistopathological composite score (2008)</td>
<td>Variables</td>
<td>Points</td>
<td>AUC: 0.84</td>
</tr>
<tr>
<td></td>
<td>Global glomerulosclerosis ≥10% (GS)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Donor hypertension and/or donor serum creatinine ≥150 µmol/l (CP)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>eGFR &lt;25 ml/min at 1 year</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GS = 0 and CP = 0</td>
<td></td>
<td>5.2%</td>
</tr>
<tr>
<td></td>
<td>GS = 1 and CP = 0</td>
<td></td>
<td>12.5%</td>
</tr>
<tr>
<td></td>
<td>GS = 0 and CP = 1</td>
<td></td>
<td>13.5%</td>
</tr>
<tr>
<td></td>
<td>GS = 1 and CP = 1</td>
<td></td>
<td>35.1%</td>
</tr>
</tbody>
</table>
Pirani – Remuzzi Score

Glomerular global sclerosis
Based on three sections (the first, middle, and last sections, if available); the number of globally sclerosed expressed as a percentage.
0 none globally sclerosed
1+ <20% global glomerulosclerosis
2+ 20 to 50% global glomerulosclerosis
3+ >50% global glomerulosclerosis

Tubular atrophy
0 absent
1+ <20% of tubuli affected
2+ 20 to 50% of tubuli affected
3+ >50% of tubuli affected

Interstitial fibrosis
0 absent
1+ <20% of renal tissue replaced by fibrous connective tissue
2+ 20 to 50% of renal tissue replaced by fibrous connective tissue
3+ >50% of renal tissue replaced by fibrous connective tissue

Arterial and arteriolar narrowing
For the vascular lesions, if the changes are focal, the most severe lesion present gives the final grade.
0 absent
1+ increased wall thickness but to a degree that is less than the diameter of the lumen
2+ wall thickness that is equal or slightly greater to the diameter of the lumen
3+ wall thickness that far exceeds the diameter of the lumen with extreme luminal narrowing or occlusion.

Figure 1. Representative Light Micrographs of Kidney Sections Illustrating the Histologic Scoring Criteria.
Panel A shows three sections of a kidney from a 65-year-old male donor of a single transplant (global score, 2). Panel B shows three sections of a kidney from a 65-year-old male donor of a dual transplant (global score, 3). Panel C shows three sections of a discarded kidney from a 65-year-old man (global score, >7). In each panel, the left section mainly shows glomerular changes, the middle section tubular interstitial changes, and the right section vascular changes.
OUTCOME OF KIDNEY TRANSPLANTATION FROM HIGH-RISK DONORS IS DETERMINED BY BOTH STRUCTURE AND FUNCTION.

Karpinski, Jolanta; Lajoie, Ginette; Catrann, Daniel; Fenton, Stanley; Zaltzman, Jeffrey; Cardella, Carl; Cole, Edward

<table>
<thead>
<tr>
<th>High-risk donor: kidney used (n=34)</th>
<th>High-risk donor: kidney not used (n=31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>61±7</td>
<td>63±7</td>
</tr>
<tr>
<td>Male</td>
<td>67%</td>
<td>22%</td>
</tr>
<tr>
<td>CrCl (ml/min)</td>
<td>98±30</td>
<td>66±28</td>
</tr>
</tbody>
</table>

Reasons for biopsy

- Age > 60: 53% vs. 73%, NS
- Hypertension: 56% vs. 50%, NS
- Vascular disease: 29% vs. 23%, NS

Biopsy score

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Glomerulosclerosis</th>
<th>Tubular atrophy</th>
<th>Interstitial fibrosis</th>
<th>Vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk donor: kidney used (n=34)</td>
<td>4.3±1.7</td>
<td>0.9</td>
<td>0.7</td>
<td>0.8</td>
<td>2.0</td>
</tr>
<tr>
<td>High-risk donor: kidney not used (n=31)</td>
<td>5.8±1.2</td>
<td>1.25</td>
<td>1.0</td>
<td>0.9</td>
<td>2.6</td>
</tr>
</tbody>
</table>

<sup>a</sup> Abbreviations: NS, not significant.

High Risk Donor
- Age > 60
- DM, Hypertension

Bx: Remuzzi scoring system

*Transplantation 67(8):1162; 1999*
OUTCOME OF KIDNEY TRANSPLANTATION FROM HIGH-RISK DONORS IS DETERMINED BY BOTH STRUCTURE AND FUNCTION.

Karpinski, Jolanta; Lajoie, Ginette; Cattran, Daniel; Fenton, Stanley; Zaltzman, Jeffrey; Cardella, Carl; Cole, Edward

<table>
<thead>
<tr>
<th>Function and vessel score associated with outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CrCl &gt;100</strong></td>
</tr>
<tr>
<td>Low risk (n=19)</td>
</tr>
<tr>
<td>DGF</td>
</tr>
<tr>
<td>Dialysis</td>
</tr>
<tr>
<td>6 mo Cr</td>
</tr>
<tr>
<td>12 mo Cr</td>
</tr>
<tr>
<td>1 yr Cr&gt;200 μmol/L</td>
</tr>
<tr>
<td>Graft loss</td>
</tr>
</tbody>
</table>

Transplantation 67(8):1162; 1999
The Prognostic Utility of Deceased Donor Implantation Biopsy in Determining Function and Graft Survival After Kidney Transplantation

Sandra M. Cockfield, Ronald B. Moore, Gerald Todd, Kim Soley, and Sita Gourishankar

491 donors; 730 recipients
- Implantation biopsy after revascularization in the recipient
- Biopsy scored as per Banff scheme for transplanted kidneys

Independent Predictors of Graft Loss
- Repeat transplant: 2.21 (1.33-3.67)
- Old donor age: 1.72 (1.03-2.88)
- Rejection: 3.23 (1.97-5.28)
- Donor CrCL: not significant
- Arteriolar hyalinosis only biopsy finding associated with graft loss: 1.67 (1.03-2.71)
- GS, IF, TA, fibrous intimal thickening not significant
Biopsy if: age $\geq 65$, CrCl $< 60$, Proteinuria $> 1$ g/d

- Core biopsy taken at time of procurement
- Permanent sections fully stained and read by trained on-call pathologist
- Graded using Pirani-Remuzzi score
- Decision to use donor made solely based on biopsy findings: if biopsy score 0-4 then kidneys transplanted as singles
The Kidney Donor Profile Index (KDPI) of Marginal Donors Allocated by Standardized Pretransplant Donor Biopsy Assessment: Distribution and Association With Graft Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Marginal</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DUAL</td>
<td>SINGLE Sc. &lt; 4</td>
<td>SINGLE Sc. = 4</td>
</tr>
<tr>
<td>ECD donor, %</td>
<td>85.0</td>
<td>78.0</td>
<td>88.5</td>
</tr>
<tr>
<td>KDRI</td>
<td>1.70 (0.31)</td>
<td>1.53 (0.32)</td>
<td>1.57 (0.34)</td>
</tr>
<tr>
<td>KDPI</td>
<td>89.3 (9.9)</td>
<td>82.6 (15.1)</td>
<td>83.9 (15.2)</td>
</tr>
<tr>
<td>KDPI 80–90, %</td>
<td>18.6</td>
<td>25.7</td>
<td>32.8</td>
</tr>
<tr>
<td>KDPI 91–100, %</td>
<td>66.0</td>
<td>41.8</td>
<td>39.3</td>
</tr>
</tbody>
</table>

Lots of High KDPI Kidneys being Transplanted
Excellent Graft Survival Even for High Biopsy-Score Kidneys
Biopsy may Reduce Discard of ‘Marginal’ Kidneys

Discard rate in Current Study

- 15% if KDPI 80-90
- 37% if KDPI 91-100

Discard rate UNOS Registry

- 36% if KDPI 80-90
- 63% if KDPI 91-100
Baseline Donor Chronic Renal Injury Confers the Same Transplant Survival Disadvantage for DCD and DBD Kidneys

ECD kidneys had higher biopsy score regardless of DCD or DBD status

DBD: 44% ECD
DCD: 46% ECD
Baseline Donor Chronic Renal Injury Confers the Same Transplant Survival Disadvantage for DCD and DBD Kidneys

Score ≤ 4: 2.6%
Score >4: 12.5%

Table 4: Multiple variable Cox regression analysis of kidney allograft survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBD</td>
<td>Reference</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>DCD</td>
<td>0.95</td>
<td>0.42–2.17</td>
<td>0.903</td>
</tr>
<tr>
<td>Remuzzi biopsy score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td>Reference</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>&gt;4</td>
<td>3.88</td>
<td>1.78–8.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Graft number</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>Reference</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Second/Third</td>
<td>1.88</td>
<td>0.52–6.75</td>
<td>0.336</td>
</tr>
<tr>
<td>Cold ischaemic time (per hour)</td>
<td>1.01</td>
<td>0.93–1.10</td>
<td>0.823</td>
</tr>
<tr>
<td>Recipient sensitization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-sensitized</td>
<td>Reference</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sensitized¹</td>
<td>1.23</td>
<td>0.49–3.04</td>
<td>0.657</td>
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<tr>
<td>Donor age (per decade)</td>
<td>1.15</td>
<td>0.69–1.90</td>
<td>0.602</td>
</tr>
<tr>
<td>Extended criteria donor (ECD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not ECD</td>
<td>Reference</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>ECD</td>
<td>1.86</td>
<td>0.43–8.01</td>
<td>0.406</td>
</tr>
<tr>
<td>Donor terminal creatinine (per unit increase)</td>
<td>1.00</td>
<td>0.99–1.01</td>
<td>0.510</td>
</tr>
</tbody>
</table>
Is the Kidney Biopsy Helpful?

Maybe not always...
Utility of applying quality assessment tools for kidneys with KDPI ≥80

Doshi M, Reese PP, Hall IE, Schröppel B, Ficek J, Formica RN, Weng FL, Hazs RD, Thiessen-Philbrook H, Parikh C

388 donors with KDPI ≥80

50 donors excluded for whom at least one kidney was discarded due to the following reasons (provided by UNOS): vascular damage, diseased organ, anatomical abnormalities, surgical damage

338 donors with KDPI ≥80 & no kidneys discarded due to the above reasons

676 kidneys

154 (46%) donors had none kidneys discarded
• 308 kidneys harvested
GROUP 1

46 (14%) donors had one kidney discarded
• 96 kidneys harvested
GROUP 2

136 (40%) donors had both kidneys discarded
• 272 kidneys harvested
GROUP 3

Biopsy: 92%
Discarded: 47%

Discarded:
45% mild findings
55% mod-severe findings

Transplantation 2017; June 101(6):1125-1133
Biopsy and Pump Parameters not Helpful

No differences in biopsy findings or pump parameters between transplanted kidney and mate kidney that was discarded.

<table>
<thead>
<tr>
<th></th>
<th>GROUP 2 One discarded (N=96)</th>
<th>Transplanted (N=148)</th>
<th>Discarded (N=148)</th>
<th>P (Transplanted vs discarded)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney Biopsy Taken</td>
<td>88 (92%)</td>
<td>44 (92%)</td>
<td>44 (92%)</td>
<td>≈1</td>
</tr>
<tr>
<td>ATN**</td>
<td>Absent</td>
<td>40 (77%)</td>
<td>20 (77%)</td>
<td>≈1</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>4 (8%)</td>
<td>2 (8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate/Severe</td>
<td>8 (15%)</td>
<td>4 (15%)</td>
<td></td>
</tr>
<tr>
<td>Arteriosclerosis</td>
<td>Absent</td>
<td>36 (42%)</td>
<td>17 (40%)</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>42 (49%)</td>
<td>22 (51%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate/Severe</td>
<td>8 (9%)</td>
<td>4 (9%)</td>
<td></td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Absent</td>
<td>34 (40%)</td>
<td>18 (42%)</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>46 (53%)</td>
<td>22 (51%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate/Severe</td>
<td>6 (7%)</td>
<td>3 (7%)</td>
<td></td>
</tr>
<tr>
<td>Glomerulonephrosis</td>
<td>Indeterminate or less than 10%</td>
<td>63 (72%)</td>
<td>33 (75%)</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td>11%-20%</td>
<td>18 (20%)</td>
<td>8 (18%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>More than 20%</td>
<td>7 (8%)</td>
<td>3 (7%)</td>
<td></td>
</tr>
<tr>
<td>Pumped</td>
<td>46 (48%)</td>
<td>23 (48%)</td>
<td>23 (48%)</td>
<td>NA</td>
</tr>
<tr>
<td>Renal resistance, mmHg/mL/min (hour 1)</td>
<td>0.29 [0.22, 0.41]</td>
<td>0.36 [0.38]</td>
<td>0.36 [0.15]</td>
<td>0.01 [0.41] 0.12</td>
</tr>
<tr>
<td>Pump flow, mL/min (hour 1)</td>
<td>103 [74, 113]</td>
<td>100.62 [33.76]</td>
<td>94.72 [38.20]</td>
<td>7.83 [36.43] 0.25</td>
</tr>
</tbody>
</table>

*Transplantation 2017; June 101(6):1125-1133*
Urine Biomarkers do not seem Helpful

<table>
<thead>
<tr>
<th></th>
<th>ALL ((N_{donor}=338))</th>
<th>GROUP 1 None discarded ((N_{donor}=154))</th>
<th>GROUP 2 One discarded ((N_{donor}=48))</th>
<th>GROUP 3 Both discarded ((N_{donor}=136))</th>
<th>P (GRP 1 vs. GRP 2)</th>
<th>P (GRP 1 vs. GRP 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 1 urine biomarker sampled</td>
<td>335 (99%)</td>
<td>152 (99%)</td>
<td>47 (98%)</td>
<td>136 (100%)</td>
<td>0.695</td>
<td>0.182</td>
</tr>
<tr>
<td>NGAL, ng/mL</td>
<td>60 [17.5, 199.6]</td>
<td>52.1 [17, 164.85]</td>
<td>61.3 [19.1, 123.9]</td>
<td>81.35 [17.45, 239.1]</td>
<td>0.934</td>
<td>0.116</td>
</tr>
<tr>
<td>KIM-1, pg/mL</td>
<td>1411.28 [635.59, 3315.15]</td>
<td>1312.83 [644.57, 3305.89]</td>
<td>1374.13 [591.21, 3110.94]</td>
<td>1499.7 [635.36, 3472.53]</td>
<td>0.825</td>
<td>0.634</td>
</tr>
<tr>
<td>L-FABP, ng/mL</td>
<td>15.4 [5.2, 60]</td>
<td>12.8 [4.4, 56.4]</td>
<td>11.2 [4.8, 35.6]</td>
<td>19.8 [6.4, 71.2]</td>
<td>0.538</td>
<td>0.122</td>
</tr>
</tbody>
</table>

Transplantation 2017; June 101(6):1125-1133
All Outcomes Similar Between Groups

Overall Graft Survival

Death-Censored Graft Survival

aHR for Death-Censored Graft Survival: $1.30 \ (0.72-2.37)$

Transplantation 2017; June 101(6):1125-1133
Kidneys of similar quality are being discarded by some and transplanted by others.

Current tools of biopsy, pump parameters and novel biomarkers do not seem to discriminate between kidneys that will and will not work.

### All Outcomes Similar Between Groups

<table>
<thead>
<tr>
<th></th>
<th>GROUP 1 None discarded (N_kidney=308)</th>
<th>GROUP 2 One kidney discarded (N_kidney=48)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGF</td>
<td>118 (38%)</td>
<td>21 (44%)</td>
<td>0.477</td>
</tr>
<tr>
<td>PNF</td>
<td>11 (4%)</td>
<td>1 (2%)</td>
<td>0.605</td>
</tr>
<tr>
<td>6-month acute rejection</td>
<td>25 (8%)</td>
<td>3 (7%)</td>
<td>0.686</td>
</tr>
<tr>
<td>1-year death censored graft failure</td>
<td>28 (9%)</td>
<td>5 (10%)</td>
<td>0.769</td>
</tr>
<tr>
<td>1-year recipient death</td>
<td>21 (7%)</td>
<td>5 (10%)</td>
<td>0.382</td>
</tr>
<tr>
<td>1-year composite outcome (death or graft failure)</td>
<td>38 (12%)</td>
<td>9 (9%)</td>
<td>0.194</td>
</tr>
<tr>
<td>2-year death-censored graft failure</td>
<td>41 (13%)</td>
<td>6 (13%)</td>
<td>0.877</td>
</tr>
<tr>
<td>2-year recipient death</td>
<td>30 (10%)</td>
<td>6 (13%)</td>
<td>0.560</td>
</tr>
<tr>
<td>2-year composite outcome (death or graft failure)</td>
<td>59 (19%)</td>
<td>10 (21%)</td>
<td>0.786</td>
</tr>
<tr>
<td>1-year eGFR, mL/min/1.73m²</td>
<td>41.5 (18)</td>
<td>41.4 (22)</td>
<td>0.977</td>
</tr>
</tbody>
</table>

*Transplantation 2017; June 101(6):1125-1133*
All ECD donors underwent biopsy

Glomerulosclerosis, interstitial fibrosis, tubular atrophy, intimal thickening, and arteriolar hyalinosis all evaluated using Banff criteria

Scores from each compartment summed up for overall score
  - Mild damage: score ≤ 3
  - Intermediate: score 4-5
  - Advanced: 6-7

Biopsies read real-time by on-call pathologist then retrospectively reviewed by trained renal pathologist
The reproducibility and predictive value on outcome of renal biopsies from expanded criteria donors

M. Antonieta Azancot, Francesc Moreso, Maite Salcedo, Carme Cantarell, Manel Perello, Irina B. Torres, Angeles Montero, Enric Trilla, Joana Sellarés, Joan Morote and Daniel Seron

- Agreement between on-call and renal pathologist
  - Glomerulosclerosis: $k=0.86$ (0.77-0.95)
  - Interstitial fibrosis: $k=0.31$ (0.15-0.46)
  - Tubular atrophy: $k=0.14$ (0.06-0.34)
  - Intimal thickening: $k=0.37$ (0.22-0.51)
  - Arteriolar hyalinosis: $k=0.25$ (0.10-0.39)

Kappa < 0.4 - poor agreement

Kidney International (2014) 85, 1161–1168;
Scoring by On-call Pathologist was Not Associated with 12-Month GFR
Scoring by On-call Pathologist was Not Associated with Composite of Death-Censored Graft Loss or GFR <30

The Role of Procurement Biopsies in Acceptance Decisions for Kidneys Retrieved for Transplant


Procurement Biopsy: 29.8% discarded

No Biopsy: 6.6% discarded
Pre-Implantation Biopsy performed on all donors to establish baseline but not used in decision to accept/decline donor.
Data suggests it might be better to skip the biopsy which will delay decision-making and adds to cold ischemic times.

BMJ 2015; 351:h3557
Summary

• There is a high discard rate with marginal kidneys

• Variability in practice suggests that the evidence we are using to make decisions is not ideal

• Non-ECD DCD kidneys have excellent outcomes and should not be considered marginal kidneys – focus on ECD or high KDPI kidneys

• Pre-transplant biopsy scores, especially when considering chronic vascular damage, are associated with outcomes in most studies

• Recent data examining biopsy, perfusion parameters and novel biomarkers together failed to show any advantage of using these tools in high KDPI kidneys
Summary

• There are well recognized limitations of procurement biopsies including reliability of findings, training of those reading the slides etc.

• Many of the positive studies used retrospective review of implantation biopsy rather than real-time reading of procurement biopsy

• Many European centres have excellent ECD results but rarely use biopsy for decision-making

• Moving Forward – variability in practice and data suggests proper RCT could be conducted to assess risks/benefits of procurement biopsy
RCT – stepped wedge design
Biopsy: will be done in all donors >65 yrs
Powered to detect a 10% increase in organ utilization
The PITHIA trial

Does having access to a biopsy result increase the number and quality of kidneys for transplantation?

UK trial
20 centres
Stepped-wedge
Registry
Power – 10%
4ml/min eGFR
Economic Analysis
Feb 2017
21 months, +12

Month

0
4
8
12
16
20

Randomly selected transplant centre

No Biopsy
Biopsy

fps:pt.com
Expanding the Donor Pool

ECD/DCD: Evaluation of the Marginal Kidney Donor

2017 CST/Astellas Canadian Transplant Fellows Symposium
Halifax World Trade and Convention Centre, Halifax, NS
September 25, 2017

Greg Knoll MD MSc
Head, Division of Nephrology, The Ottawa Hospital and the University of Ottawa
Senior Scientist, Ottawa Hospital Research Institute
Professor of Medicine, University of Ottawa
The PITHIA trial has two relatively novel elements of trial design: firstly, it is a registry-based, randomised clinical trial. Secondly, it is has a ‘stepped-wedge cluster’ design. These elements should help keep the costs of the trial to a minimum, just a fraction of the costs of a typical national, multi-centre trial. In addition, the trial design aims to minimise the time and effort required by busy clinicians and patients.