When is ‘marginal’ is too ‘marginal’

*taking risks*

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Liver Unit, Freeman Hospital
Newcastle upon Tyne, NHS Trust
A universal problem.

Number of deceased donors and transplants in the UK, 1 April 1998 - 31 March 2008, and patients on the active transplant lists at 31 March

- Donors
- Transplants
- Transplant list

Year
- 1998-1999: 738, 2360
- 1999-2000: 777, 2428
- 2000-2001: 773, 2311
- 2001-2002: 749, 2247
- 2002-2003: 777, 2388
- 2003-2004: 770, 2396
- 2004-2005: 751, 2241
- 2005-2006: 764, 2196
- 2006-2007: 793, 2385
- 2007-2008: 803, 2381

Number
- 1998-1999: 5345
- 1999-2000: 5554
- 2000-2001: 5532
- 2001-2002: 5604
- 2002-2003: 5685
- 2003-2004: 5673
- 2004-2005: 6142
- 2005-2006: 6698
- 2006-2007: 7219
- 2007-2008: 7655
Where have all the ‘ideal’ donors gone?

• Organs previously considered unsuitable are now used regularly

• These are termed ‘marginal’ organs

• The donors are termed "marginal" donors.
  – "expanded" or "extended criteria" donors.
Expanded Criteria Donor (ECD)

• A donor that is not considered to be ‘ideal’ or ‘standard’.

• Characteristics may include advanced donor age, prior infection with hepatitis B or hepatitis C, hypertension or diabetes mellitus, abnormal donor organ function, and DCD status of a deceased donor.

• The preferred term ‘expanded’ rather than ‘marginal’ -
  – an expansion of the donor pool
‘an accepted precise definition of what constitutes an ECD remains elusive.’

– Conceptually, the graft from such a donor is at increased risk of early failure (PNF or DGF) or predisposes to inferior graft or patient survival outcomes.
Five-year graft and patient survival was 53% and 74% for MDK recipients compared with 67% (P, 0.001) and 80% (P, 0.001) for IDK recipients.
The ‘ideal’ donor

- Age < 40
- Trauma as the cause of death
- No cardiovascular or CVD history
- Brain death (DBD)
- Heamo-dynamically stable
- No steatosis, no other liver lesion
- No transmissible disease
- Normal organ function
Standard Criteria Donor (SCD)

- All donors that are younger than 50 yrs
- Kidney
  - Donors younger than 60 and have fewer than two of the three conditions used to determine ECD status:
    - died of stroke,
    - history of hypertension,
    - serum creatinine $>1.5$.
- Liver
  - Donors younger than 60
    - $<30\%$ Steatosis
    - LFT’s $< than twice normal
    - BMI $< 30$
ECD - Kidney

• The ECD is defined as any deceased donor ≥ 60 years of age

• Any deceased donor 50 to 59 years of age with at least 2 of the following risk factors:
  – history of hypertension,
  – SCr level > 1.5 mg/dL,
  – cerebrovascular accident as the cause of death
Age of deceased donors – UK (>20% 60+; 50% 50+)

![Chart showing the percentage of donors by age group from 2000 to 2009. The chart indicates that the percentage of donors aged 60+ fluctuates over the years, with a peak of 20% in 2005. The 50-59 age group consistently makes up a significant portion of the donations, ranging from 50% in 2009 to 70% in 2001. The 18-49 age group also shows variability, with percentages ranging from 50% in 2009 to 60% in 2002. The 0-17 age group remains relatively small, varying from 3% in 2009 to 8% in 2002.)
Cause of death of deceased donors – UK
(>60% ICH; <10% Trauma)
Donor 1

- Male donor:
  - 18yrs old
  - Attempted suicide by hanging
  - Was found by friends and cut down
    - ‘hanging-time’ unknown
      - ??? WIT ???
  - Resuscitated by paramedics
  - No past medical history
  - All his organs offered as a DBD

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>175</td>
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<tr>
<td>Amylase</td>
<td>300</td>
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<tr>
<td>Glucose</td>
<td>12</td>
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<tr>
<td>Bilirubin</td>
<td>18</td>
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<tr>
<td>ALT</td>
<td>302</td>
</tr>
<tr>
<td>Po2</td>
<td>12</td>
</tr>
<tr>
<td>ICU stay</td>
<td>72hrs</td>
</tr>
<tr>
<td>U Output</td>
<td>4L</td>
</tr>
</tbody>
</table>
Donor 1

• How would you view this donor?

  – Standard criteria
  – ‘marginal’
    • Low risk
    • High risk
Donor 1

• Male donor:
  – 18yrs old
  – Attempted suicide by hanging
  – Was found by friends and cut down
    • ‘hanging-time’ unknown
      – ??? WIT
  – Resuscitated by paramedics
  – No past medical history
  – All his organs offered as a DBD

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
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<td>Amylase</td>
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<tr>
<td>Glucose</td>
<td>4</td>
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<td>Bilirubin</td>
<td>18</td>
</tr>
<tr>
<td>ALT</td>
<td>702</td>
</tr>
<tr>
<td>Po2</td>
<td>12</td>
</tr>
<tr>
<td>ICU stay</td>
<td>5days</td>
</tr>
<tr>
<td>U Output</td>
<td>400mls</td>
</tr>
</tbody>
</table>
Donor 2

- Female donor:
  - 63 yrs old
  - SAH
  - BMI - 32
- History of
  - Hypertension and MODM
  - Smoker for 20 yrs
  - ‘liked a drink’
  - Previous breast cancer – stage I – 10yrs before
    » Given the ‘all clear’
- DBD
  - Offer of liver and kidneys

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
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<td>121</td>
</tr>
<tr>
<td>Amylase</td>
<td>40</td>
</tr>
<tr>
<td>Glucose</td>
<td>14</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>18</td>
</tr>
<tr>
<td>ALT</td>
<td>47</td>
</tr>
<tr>
<td>GGT</td>
<td>118</td>
</tr>
<tr>
<td>ICU stay</td>
<td>3 days</td>
</tr>
<tr>
<td>U Output</td>
<td>1400 mls</td>
</tr>
<tr>
<td>Po2</td>
<td>10</td>
</tr>
</tbody>
</table>
Donor 2

• How would you view this donor?

  – Standard criteria
  – ‘marginal’
    • Low risk
    • High risk
**Donor 2**

- Female donor:
  - 63 yrs old
  - SAH
  - BMI - 32
  - History of
    - Hypertension and MODM
    - Smoker for 20 yrs
    - ‘liked a drink’
    - Previous breast cancer – stage I – 10yrs before
      » Given the ‘all clear’
  - DCD
    - Offer of liver and kidneys

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<td>47</td>
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<tr>
<td>GGT</td>
<td>118</td>
</tr>
<tr>
<td>ICU stay</td>
<td>3 days</td>
</tr>
<tr>
<td>U Output</td>
<td>1400 mls</td>
</tr>
<tr>
<td>Po2</td>
<td>10</td>
</tr>
</tbody>
</table>
Donor 3

- Male donor
  - 66 yrs old
  - 50 units of alcohol per week for last 10 yrs
  - Head injury
  - ITU for 7 days
  - Brain dead

- DBD
  - Offering Liver and Kidneys
    - Fatty liver at retrieval

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<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>101</td>
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<tr>
<td>Amylase</td>
<td>140</td>
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<tr>
<td>Glucose</td>
<td>8</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>48</td>
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<tr>
<td>ALT</td>
<td>57</td>
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<tr>
<td>GGT</td>
<td>318</td>
</tr>
<tr>
<td>PT</td>
<td>17</td>
</tr>
<tr>
<td>U Output</td>
<td>3400mls</td>
</tr>
</tbody>
</table>
Donor 3

• How would you view this donor?

  – Standard criteria
  – ‘marginal’
    • Low risk
    • High risk
How do you decide?
Need to see ‘both sides of the coin’
Who is waiting?
Weigh the risks and benefits for a particular individual patient
Calculated risk

• A ‘marginal’ donor is as ‘marginal’ as you want to make it
• The benefits of its use must be assessed
  – Individual patient
    • Need
  – Recipients waiting
    • Utility
  – Community/Society
    • Transplant benefit
Donor 3
(fatty liver)

• **Recipient (a)**
  – 37 yrs old housewife
  – Sero-negative hepatitis in ALF
  – Awaiting ‘super-urgent’ LT
    • ITU for 48hrs
    • Requiring escalating doses of inotropic support
    • CVVH
    • ↑ FiO2
• **Recipient (b)**
  – 57 yr old HCV cirrhotic
  – Gross portal hypertension
    • TIPPS
  – MELD – 16(UKELD – 52)
  – At home
  – Wife says: ‘…..best his been in 6 months…..’
Donor 3

- **Recipient (c)**
  - 40 yr old ALD
    - Abstinent for 2 yrs
  - 5 cm HCC
    - Previously 6.2 cm
    - Down-sized with TACE and RFA
    - Meeting the ‘new criteria’
  - Been waiting 100 days
    - First offer of a liver
Is it worth it.......
Calculated Risk
TAKING RISK

There's a fine line between taking a calculated risk and doing something dumb.
Donor 2

- Female donor:
  - 63 yrs old
  - SAH
  - BMI - 32
  - History of
    - Hypertension and MODM
    - Smoker for 20 yrs
    - ‘liked a drink’
    - Previous breast cancer – stage I – 10yrs before
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    - Offer of liver and kidneys

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<tr>
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<td>1400 mls</td>
</tr>
<tr>
<td>Po2</td>
<td>10</td>
</tr>
</tbody>
</table>
Donor 2 – take a informed risk

old recipient waiting > 5yrs

I don’t care what day it is. Four hours is four hours.
What is risk?

Risk is the chance that any activity or action could happen and harm you. Almost everything we do has an associated risk. Living is a risky business. **People will generally take risks if they feel that there is an advantage or benefit. We need to look at risks and benefits together. Normally the benefits of an action should outweigh the risks.** There is no such thing as a zero risk. How you view risk depends to a large extent on your own circumstances and ‘comfort zone’.
How recipients view the risk depends on one or more of the following:

- the chance of the event occurring (frequency)
  - PNF
- the chance of a condition being detected (detection rate)
  - Infection (HIV) or cancer
- the benefits of the transplant
- how much harm may be caused:
  - if it is life-threatening
  - if it is short-term (temporary) or long-term (permanent)
- how much they feel in control of the decision
- how much they trust the surgeon/physician discussing the risk with them
- whether they feel they understand the situation sufficiently.

Some of these factors will be more important to than others.
• Taking the right decision requires a clear understanding of all the available facts. And often, we obscure the facts with technical language and/or statistics

   — Guy Heynen
Risk can be given as numbers or words, or both.

<table>
<thead>
<tr>
<th>Verbal description*</th>
<th>Risk</th>
<th>Risk description*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>1/1 to 1/10</td>
<td>A person in family</td>
</tr>
<tr>
<td>Common</td>
<td>1/10 to 1/100</td>
<td>A person in street</td>
</tr>
<tr>
<td>Uncommon</td>
<td>1/100 to 1/1000</td>
<td>A person in village</td>
</tr>
<tr>
<td>Rare</td>
<td>1/1000 to 1/10000</td>
<td>A person in small town</td>
</tr>
<tr>
<td>Very rare</td>
<td>Less than 1/100000</td>
<td>A person in large town</td>
</tr>
</tbody>
</table>

* EU-assigned frequency
* Unit in which one adverse event would be expected

This table below shows how risk should be described in healthcare:
• Renal transplant recipients ≥ 60 years of age have almost 3 times the mortality risk of younger patients:
  • 3.9% vs 1.6%, respectively, at 90 days post-KT
  • 9.2% vs 3.5%, respectively, at 1 year post-KT
  – Due largely to their co-mobidity

• **ECD kidney further increases this risk**
  – (Kauffman, 2007)
  – (Foley, 2005)
Is transplantation of ECD kidneys for everyone?

• SRTR retrospective database analysis compared outcomes of standard-criteria donor (SCD) kidney transplants with ECD kidney transplants

• **Overall, perioperative mortality was greater in ECD kidney recipients.**
  – (Merion, 2005)
  – Similar outcomes have been documented by other investigators
    – (Rugginenti, 2006; Remuzzi, 2006; Collini, 2006),

Prompts the question: Are there groups for which ECD kidney transplantation is indicated on the basis of proven benefit?
A Comparison of ECD and SCD Patient and Graft Survival Rates

<table>
<thead>
<tr>
<th>Survival Time</th>
<th>Patient Survival (%)</th>
<th></th>
<th>Graft Survival (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ECD</td>
<td>SCD</td>
<td>ECD</td>
<td>SCD</td>
</tr>
<tr>
<td>3 months</td>
<td>96.0</td>
<td>97.5</td>
<td>90.4</td>
<td>94.0</td>
</tr>
<tr>
<td>1 year</td>
<td>90.6</td>
<td>94.5</td>
<td>81.7</td>
<td>89.3</td>
</tr>
<tr>
<td>3 years</td>
<td>78.5</td>
<td>89.9</td>
<td>65.1</td>
<td>80.4</td>
</tr>
<tr>
<td>5 years</td>
<td>69.9</td>
<td>81.2</td>
<td>48.6</td>
<td>65.2</td>
</tr>
</tbody>
</table>

The half-lives of deceased-donor kidneys

• ECD or SCD are shorter than the half-life of a living-donor kidney.

• The estimated half-life of an ECD and SCD kidney
  • 4 to 6 years compared with 8 to 12 years
Waiting time makes a difference (Merion, 2005)

• Mortality rate after ECD KT vs non-ECD kidney recipients and those still receiving dialysis.

• They found that the relative risk of long-term mortality was 17% less in ECD kidney recipients, especially non-Hispanics, and in those < 40 years of age, un-sensitized, and with diabetes or hypertension.

• In centres with long waiting times, the benefits were even greater: 27% of ECD kidney recipients had a lower mortality risk.

• In centres with short waiting times, only patients with diabetes benefited from ECD kidney transplantation
ECD K and biopsy

• Outcomes of ECD KT are improved when a pre-implantation biopsy of the donor kidney is evaluated using the scoring system
  • (Karpinski, 1999).

• Using this system, donor renal pathology is scored from 0 to 3 (none to severe disease) in 4 areas:
  • glomerulosclerosis, interstitial fibrosis, tubular atrophy, and vascular disease
**Biopsy – ‘vessel score’**

<table>
<thead>
<tr>
<th>Arterial sclerosis (or intimal fibrous thickening - fibroplasia)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = absent</td>
</tr>
<tr>
<td>1 = increased wall thickness but to a degree that is less than the diameter of the lumen</td>
</tr>
<tr>
<td>2 = wall thickness that is equal or slightly greater than the diameter of the lumen</td>
</tr>
<tr>
<td>3 = wall thickness that far exceeds the diameter of the lumen, with extreme luminal narrowing or occlusion</td>
</tr>
</tbody>
</table>

Karpinski, Transplantation., 1999
‘vessel score’ most predictive

• A donor vessel score of 3/3;
  – associated with a 100% incidence of DGF and a mean 1-year SCr level of 275 ± 106 mcmol/L

• A donor vessel score 1-2/3
  – Associated with 43% incidence of DGF and a mean 1 year SCr level of 192 ± 54 mcmol/L ($P < 0.05$)
ECD may benefit old recipients

- A patient > 64 years of age who is on the waiting list for 5 years is estimated to have a 50% risk of dying before a kidney becomes available
  - (Danovitch, 2005).
- A patients 60 to 69 years of age at the time of transplantation with a deceased-donor kidney, the likelihood of dying with a functioning graft was more than twice that for patients 40 to 49 years of age
  - (Baskin-Bey, 2006).

ECD transplantation offers this patient the best chance of survival and potentially prevents waste of life years from a young organ.
Age and wait time
Markov model to determine the best timing for an individual patient to accept an offer of an ECD K

• For the average patient, the break-even point at which the benefits of accepting an ECD kidney began to exceed those of waiting for an SCD kidney was 3.2 years, and it was concluded that such a patient should wait for an SCD kidney.

• For patients > 60 years of age, however, the break-even point was 11 months (factors such as dialysis access failure or diabetes, could shorten this time even further), and for these patients acceptance of an ECD kidney might provide the best outcomes

   – (Schnitzler, 2003)
ECD K and diabetics

• Life expectancies of patients with ESRD secondary to diabetes is lower compared with other adults with ESRD.

• A ECD kidney in a patient with diabetes provides a survival benefit - transplanted sooner
  • (Schold, 2006)
Marginal kidneys are more sensitive to insults during the pre-, peri- and post-operative course of transplantation resulting in progressive decline in renal function and finally contributing to graft failure.
When DDS score was greater than 20, the 6-year graft survival was <70% compared with more than 80% when the DDS score was below 20.
• In the SRTR analysis, 40% of kidneys defined as ECD with >1.7 relative risk of graft failure were discarded
• Only 8% of standard kidneys were discarded the same year
• The reason for the high rate of kidney discard is often attributed to poor organ function and quality;
  — 47% of ECD kidneys were discarded because of biopsy findings

Merion, 2003
Retrospective follow-up of transplantation of kidneys from ‘marginal’ donors

D Dahmane1, V Audard1,6, C Hissse2,5,6, F Pessione2, B Benatarit1, B Barrou3, E Rondeau4, S Cohen2, P Lang1 and P Grimbert1

1Service de Néphrologie et Transplantation, Hôpital Henri-Mondor and Faculté de Médecine, Université Paris XII, Créteil, France; 2Département Médical et Scientifique, Agence de la Biomédecine, Saint Denis, France; 4Hôpital de la Pitié-Salpêtrière, Paris, France; 4Hôpital Tenon, Paris, France and 5Service de Néphrologie, CHV de Ponte d’Ilet, Guadeloupe, France

Table 1 | Main causes of graft refusals in the study group

<table>
<thead>
<tr>
<th>Main cause of refusals</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired donor hemodynamics</td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>28%</td>
</tr>
<tr>
<td>Anuria</td>
<td>16%</td>
</tr>
<tr>
<td>Severe hypotension (collapses)</td>
<td>8%</td>
</tr>
<tr>
<td>Abnormal serum creatinine</td>
<td>4%</td>
</tr>
<tr>
<td>CR &lt; 120 µmol/l</td>
<td>21%</td>
</tr>
<tr>
<td>CR &gt; 200 µmol/l</td>
<td>5%</td>
</tr>
<tr>
<td>CR &gt; 400 µmol/l</td>
<td>13.5%</td>
</tr>
<tr>
<td>CR &gt; 400 µmol/l</td>
<td>2.5%</td>
</tr>
<tr>
<td>Advanced donor age (years)</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>9%</td>
</tr>
<tr>
<td>≥70</td>
<td>6%</td>
</tr>
<tr>
<td>Donor atheroma</td>
<td>14%</td>
</tr>
<tr>
<td>Anatomic abnormalities</td>
<td>7%</td>
</tr>
<tr>
<td>Donor history of hypertension</td>
<td>6%</td>
</tr>
<tr>
<td>Prolonged ischemia (≥32 h)</td>
<td>5%</td>
</tr>
<tr>
<td>Abnormal macroscopic characteristics</td>
<td>4%</td>
</tr>
</tbody>
</table>

*Initial pre-harvesting serum creatinine.*
Dahmane et al, 2006

Table 3 | Causes of graft failure in the study and the control group

<table>
<thead>
<tr>
<th>Causes of graft failure</th>
<th>Study group (n=39)</th>
<th>Control group (n=29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNFK</td>
<td>13</td>
<td>3</td>
<td>0.01</td>
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<tr>
<td>Chronic rejection</td>
<td>16</td>
<td>13</td>
<td>NS</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>6</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Surgical complications</td>
<td>2</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Miscellaneous complications</td>
<td>2</td>
<td>6</td>
<td>NS</td>
</tr>
</tbody>
</table>

PNFK = primary non-functioning kidneys.

Figure 2 | Influence of the ‘acute’ and ‘chronic’ cause of graft refusal on the 5-year graft survival. The ‘acute’ and ‘chronic’ parameters did not influence significantly graft survival up to 5 years post-transplant (P = 0.19). Kaplan-Meier survival curves between 0 and 5 years post-transplant are shown for patients who received organs refused on the basis of ‘acute’ criteria (dashed lines) or ‘chronic’ criteria (solid lines).

Figure 1 | Recipients of study and control kidney transplants have similar graft and patient survival up to 5 years post-transplant.
Increased Kidney Transplantation Utilizing Expanded Criteria Deceased Organ Donors with Results Comparable to Standard Criteria Donor Transplant

Robert J. Stratta, MD, Michael S. Rohr, MD, PhD, Aimee K. Sundberg, PharmD, Greg Armstrong, RN, CPTC, Gloria Hairston, BS, Erica Hartmann, MD, Alan C. Farney, MD, PhD, Julie Roskopf, PharmD, Samy S. Iskandar, MBCh, PhD, and Patricia L. Adams, MD

FIGURE 2. Mean serum creatinine levels at selected time points in ECD versus SCD kidney recipients.
Table 1: Criteria for a seronegative Centers for Disease Control high behavioral risk adult organ donor

(1) Men who have had sex with another man in the preceding 5 years
(2) Persons who report nonmedical intravenous, intramuscular or subcutaneous injection of drugs in the preceding 5 years
(3) Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates
(4) Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years
(5) Persons who have had sex in the preceding 12 months with any person described in items 1–4 above or with a person known or suspected to have HIV infection
(6) Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin or mucous membrane
(7) Inmates of correctional systems
Figure 1: Unadjusted allograft failure or death after kidney transplantation, by donor type. Secondary cohort of kidney transplant recipients from 7/1/2004 to 7/1/2006.
• ‘This week we learned that four Chicago organ transplant recipients got HIV and hepatitis C from a donor who was considered at high risk of carrying the diseases. These cases are very rare—it's been two decades since the HIV virus was transmitted to an organ recipient. But it turns out that donations by those considered high risk are far more common than most Americans might think. About 9 percent of all organs come from people who have reported the kind of behaviour (injecting recreational drugs, spending time in jail or men having sex with other men) that puts them at higher risk for HIV and other diseases.....’
• Mortality risks in two groups of cadaveric renal transplant recipients relative to wait-listed dialysis patients
“The Ideal liver Donor Organ”

*does it still exist??*
‘THE IDEAL DONOR’

Current criteria to be considered for splitting

- Donor age ≤ 40 years
- Donor weight ≥ 50 Kgs (NOT OBESE)
- ITU stay < 5 days (120hrs)
- No deranged LFT’s – ALT/AST/Bilirubin < twice normal
- Haemodynamically stable
  - No prolonged hypotension(<80mmHg for > 1 hour)
  - No high dose inotropes: 
    Adrenaline/Noradrenaline>10µgm/kg/min; Dopamine>15 µgm/kg/min
  - No sepsis
- Satisfactory macroscopic appearance
  - No fat
What constitutes a marginal donor remains controversial.

‘different transplant units have developed their own arbitrary policies that differentiate whether a liver is used or discarded on the basis of broadly accepted guidelines.’
Marginal Donors

- The use of livers from “marginal donors” has been shown in several studies to lead to an increased risk of **primary graft dysfunction**
What is a marginal “liver”

- older than 60 years,
- ITU stay with ventilatory support for more than 4 days
- a cold ischemia time more than 14 hr
- high inotrope drug use,
- prolonged hypotensive episodes for more than 1 hr and less than 60 mm Hg,
- a peak serum sodium more than 160 mEq/L,
- high levels of bilirubin, ALT or AST
- Steatosis (macrovesicular or microvesicular)
  - quantified in four categories:
    - no steatosis,
    - mild (<30%),
    - moderate (30-60%), and
    - severe (> 60%).
MARGINAL GRAFTS - QUALITY

- Fat infiltration associated with
  - Obesity
  - High alcohol intake
  - Diabetes
  - Starvation
- Healthy vs unhealthy fatty liver
- Mild (<30%), moderate (30-60%) or severe (>60%)
- Microvesicular vs. macrovesicular
TYPES OF MARGINAL GRAFTS

- Quantity (liver mass)
- Quality (marginal)
- Or both together

‘Functional liver mass’
### Table 1. Potential Risk Factors Associated With Liver Graft Dysfunction

<table>
<thead>
<tr>
<th>Donor</th>
<th>Perioperative</th>
<th>Recipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Warm ischemia</td>
<td>Age</td>
</tr>
<tr>
<td>Gender</td>
<td>Technical complications</td>
<td>Medical status</td>
</tr>
<tr>
<td>Race</td>
<td>Blood product use</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td>Retransplantation</td>
</tr>
<tr>
<td>Cause of brain death</td>
<td></td>
<td>Use of vasopressors</td>
</tr>
<tr>
<td>Intensive care unit length of stay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of vasopressors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold preservation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High serum sodium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steatosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial liver grafts</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Predictors of Graft dysfunction: Univariate analysis of donor factors

<table>
<thead>
<tr>
<th>Factors</th>
<th>Dysfunction&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>49.63±11.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Liver biopsy (macrosteatosis) &lt;30%</td>
<td>43 (11.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26.55±3.55</td>
<td>0.001</td>
</tr>
<tr>
<td>Inotrope use, yes</td>
<td>43 (14.2)</td>
<td>0.904</td>
</tr>
<tr>
<td>CMV positive</td>
<td>29 (13.7)</td>
<td>0.680</td>
</tr>
<tr>
<td>Type of graft, whole</td>
<td>56 (14.7)</td>
<td>0.706</td>
</tr>
<tr>
<td>Hypotension &gt;1 hr, yes</td>
<td>25 (15.3)</td>
<td>0.620</td>
</tr>
<tr>
<td>Urea &gt;7.1</td>
<td>15 (19.0)</td>
<td>0.190</td>
</tr>
<tr>
<td>Bilirubin &gt;17.1</td>
<td>17 (19.1)</td>
<td>0.147</td>
</tr>
<tr>
<td>ICU days (ventilation)</td>
<td>2.11±1.63</td>
<td>0.413</td>
</tr>
<tr>
<td>Creatinine</td>
<td>107.07±38.58</td>
<td>0.235</td>
</tr>
<tr>
<td>Na</td>
<td>147.96±8.42</td>
<td>0.260</td>
</tr>
<tr>
<td>AST</td>
<td>49.18±43.21</td>
<td>0.533</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>81.58±50.37</td>
<td>0.442</td>
</tr>
<tr>
<td>Albumin</td>
<td>28.70±7.60</td>
<td>0.705</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values are given as No. (%) or median±SD.

<sup>b</sup> P value was calculated using an independent t test and χ² test for continuous and categorical parameters, respectively.

CMV, Cytomegalovirus; ICU, intensive care unit; Na, sodium; AST, aspartate aminotransferase.
BMI of deceased donors – UK (>20% BMI ≥ 30)
The mean age of cadaveric donors: \textit{gradually increased over the ten years from 38.8 in 1994 to 44 in 2003/4.}
Donor Age – ‘willingness’ to LT

- Age < 50 - ideal
- Age > 50 without other risk factors
- Age > 60
  - Post LT cholestasis
  - Steotosis

Figure 1. Relationship of donor age to the number of patients receiving organs. Donor age greater than 50 years has been steadily increasing over the last decade, whereas the number of donors ages 18 to 34 has remained constant. (Data from the UNOS 2001 annual report.)\(^1\)
Rate of dysfunction in marginal and non marginal donors (based on donor score). Outcome in marginal group further analyzed on the basis of cold ischemia time (>12 hr or <12 hr). CIT, Cold ischemia time.
Three-month graft survival comparing nonmarginal donors plus marginal donors with a cold ischemia time of less than 12 hr with marginal donors with a cold ischemia time of greater than 12 hr. CIT, Cold ischemia time.

Graft Survival

Transplantation, Volume 77(3).February 15, 2004.411-416
• Grafts with more than 14 hours of cold ischemia have been associated with a two-fold increase in preservation damage resulting in prolonged postoperative course, biliary stricture, and decreased graft survival.
The injury starts at the retrieval
**PRESEVATION INJURY**

*Figure 1* Storage/reperfusion injury to liver. During cold storage, hepatocytes (H) swell and form cell surface protrusions called blebs. Some rounding of sinusoidal endothelial cells (E) and Kupffer cells (K) also occurs. Its cells (fat-storing or stellate cells, I) change little in structure. After reperfusion, endothelial cells lose viability and stain with supravital dyes like trypan blue. Kupffer cells swell, ruffle, and degranulate, indicating activation. Activated Kupffer cells can release a number of inflammatory mediators, including prostaglandin E2 (PGE2), tumor necrosis factor-α (TNFα), nitric oxide (NO), superoxide radical (O2·−), interleukin-1 (IL-1), and proteases. Hepatocyte structure recovers after reperfusion with resorption of blebs and recovery of volume regulation. Its cells remain relatively unperturbed.

*Figure 2* Scanning electron micrograph of a failing rat liver graft. A rat liver was stored for 18 h in UW solution and transplanted with rearterialization. Under these conditions, graft failure from storage/reperfusion injury occurred in virtually 100% of animals. Two hours postoperatively, the graft was fixed and prepared for scanning electron microscopy. Note that the sinusoidal lining (s) is denuded and that Kupffer cells (k) are rounded and ruffled. Hepatocytes (h) are normal in appearance even though the graft is failing. Margined leukocytes (*) are also present in the sinusoids.
IRI – exacerbated for ‘old + fatty’ livers

Figure 2. Mechanism of ischemia reperfusion injury. A hepatic sinusoid lined by endothelial cells. On the outer surface, hepatocytes line the sinusoid interspersed with Ito cells. The first step in the IR cascade is the liberation of endothelin-1 (ET-1), which activates Ito cells and results in constriction of the hepatic sinusoids. In addition, the Kupffer cells are activated and result in the release of reactive oxygen intermediates (ROI). The combination of these factors results in reduced blood flow through the liver. The second step involves up-regulation of the adhesion molecules (i.e., selectins, integrins, and immune globulins). The activation of adhesion molecules and liberation of chemokines from Kupffer cells stimulates avid rolling and sticking of neutrophils to endothelial cells to the hepatic sinusoid. In addition, platelet aggregation and sinusoidal endothelial cell (SEC) apoptosis result in tissue injury. This mechanism of IR injury is exacerbated in the steatotic liver.
• “MARGINAL” DONOR + “MARGINAL RECIPIENT” = “MARGINAL” OUTCOME
Marginal Recipient

- High MELD(>35)
- HRS
- Obese(BMI>30)
- HCV
- ‘In Hospital recipients’

- marginal grafts for good-risk patients as opposed to placement in high-risk recipients
Initial poor function (IPF) and primary non-function (PNF)

- The incidence:
  - PNF - 6% and IPF - 15%.

- CAUSE - multiple relative risk factors.
  - Donor relative risk factors are:
    - Moderate Steatosis, Cold ischemic time over 12 hr, Donor age > 50 yr,
  - Recipient relative risk factors are:
    - Re-transplantation, High medical risk (UNOS class 4), Renal failure.
  - The most important peri-operative risk factor:
    - Extended warm ischemic time.

  - Rates of PNF and IPF might be reduced by avoidance of combinations of risk factors.

Hepatology 1994; 20 (4 pt 1): 829
Cox regression - identified **seven donor characteristics that independently predicted significantly increased risk of graft failure.**

- Donor age over 40 years (and particularly over 60 years), donation after cardiac death (DCD), and split/partial grafts were strongly associated with graft failure,
- African-American race, less height, CVAr and 'other' causes of brain death were more modestly but still significantly associated with graft failure.
Submaximal Cardiopulmonary Exercise (CPX) testing predicts early postoperative survival following liver transplantation

Prentis J, Manas DM, Roberts DRD, Anderson HA, Snowden CP

Anaesthetic and Hepatobiliary Departments
Freeman Hospital,
Newcastle Upon Tyne, U.K.
DRI and AT

Overall
P=0.06

{Image of box plot with labels:
- Died
- Survived (AT<9.6)
- Survived (AT>9.6)

Key values:
- P=0.04
- 46
Steatosis

- Moderate to severe steatosis is reported to be the most important factor determining post-transplant graft function, with great risk for liver preservation injury, PNF and EAD.
Efficacy and safety of moderately steatotic donor liver in transplantation

Feng Gao, Xiao Xu, Qi Ling, Jian Wu, Lin Zhou, Hai-Yang Xie,
Hui-Ping Wang and Shu-Sen Zheng

Hangzhou, China

BACKGROUND: The discrepancy between available livers and requests for transplantation has forced many centers to use marginal donors in order to expand the donor pool. Many previous studies have demonstrated controversial results of the application of steatotic liver grafts. The aim of the present study was to summarize our experience and evaluate the value of steatotic liver grafts.

KEY WORDS: liver steatosis; liver transplantation; survival; liver function

Introduction
Table 2. Prognosis of recipients (%)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n=24)</th>
<th>Group 2 (n=24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAD</td>
<td>20.8</td>
<td>16.7</td>
<td>NS</td>
</tr>
<tr>
<td>AKI</td>
<td>33.3</td>
<td>29.2</td>
<td>NS</td>
</tr>
<tr>
<td>Patient survival rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>100</td>
<td>95.8</td>
<td>NS</td>
</tr>
<tr>
<td>6 months</td>
<td>87.5</td>
<td>95.8</td>
<td>NS</td>
</tr>
<tr>
<td>1 year</td>
<td>83.3</td>
<td>91.7</td>
<td>NS</td>
</tr>
</tbody>
</table>

Group 1 patients received liver grafts with moderate steatosis (30%-60%); group 2 patients received liver grafts with steatosis less than 30%. EAD: early allograft dysfunction; AKI: acute kidney injury.

Fig. 2. Comparison of patient cumulative survival between groups 1 and 2 (Log-rank, P>0.05). Group 1 patients received liver grafts with moderate steatosis; Group 2 patients received liver grafts with no or mild steatosis.
Controlling multiple factors

- CIT (>14hrs)
- Infection
- Blood Loss
- Preventing renal failure
- Prolonged ITU stay

- [Angele et al](#) - steatotic livers can be transplanted safely with good results for long-term organ survival if all other contraindications are absent
Liver grafts with moderate steatosis and prolonged CIT simultaneously can result in very poor outcomes.

- **Briceno et al** - CIT of more than 14 hours as marginal.

- **Tekin et al** - considered that marginal livers have a high risk of developing early allograft dysfunction with increased CIT > 12 hours.

- **Guo et al** - CIT < 9 hours appeared to positively influence the outcome using steatotic liver donors (30-60%)
• Many centres empirically use local guidelines.

• Livers with moderate steatosis (<60%) should no longer be discarded, but used cautiously, particularly in the presence of other risk factors.
Overall, it was deemed that 61 donors (47.7%) might potentially have been suitable liver donors.
A liver is not a kidney is not a lung
The more you look . . . the more you recognise peoples differing views. . . .

- DCD Livers
DCD Donors

- Clearest form of ‘expanded criteria’ donor
Deceased donors – increase in DCDD

<table>
<thead>
<tr>
<th>Year</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2001</td>
<td>736</td>
</tr>
<tr>
<td>2001-2002</td>
<td>703</td>
</tr>
<tr>
<td>2002-2003</td>
<td>716</td>
</tr>
<tr>
<td>2003-2004</td>
<td>697</td>
</tr>
<tr>
<td>2004-2005</td>
<td>664</td>
</tr>
<tr>
<td>2005-2006</td>
<td>637</td>
</tr>
<tr>
<td>2006-2007</td>
<td>634</td>
</tr>
<tr>
<td>2007-2008</td>
<td>609</td>
</tr>
<tr>
<td>2008-2009</td>
<td>611</td>
</tr>
<tr>
<td>2009-2010</td>
<td>623</td>
</tr>
</tbody>
</table>

DBD

Year
Kidney transplants - UK

Year | DBD | DCD | Living donors
--- | --- | --- | ---
2000 | 1314 | 47 | 348
2001 | 1329 | 58 | 358
2002 | 1265 | 85 | 372
2003 | 1185 | 112 | 451
2004 | 1295 | 147 | 463
2005 | 1111 | 201 | 543
2006 | 1144 | 252 | 671
2007 | 1101 | 313 | 804
2008 | 1107 | 455 | 924
2009 | 1106 | 510 | 982
Need to accept . . .

• DCD results in
  – fewer organs donated per donor
  – more primary non function of the liver and more ischaemic biliary complications
  – more delayed graft function of the kidney
  – and inferior pancreas outcomes compared to DBD (Data on file, Pancreas Advisory Group, NHSBT).
Can guidelines help?

• More than 50% of donated U.S. organs are rejected -- not by transplant recipients, but by their physicians . . .

  – Remuzzi et al, NEJM, 2000
LONG-TERM RENAL FUNCTION IN KIDNEYS FROM NON-HEART-BEATING DONORS: A SINGLE-CENTER EXPERIENCE

Muhammed A. Gok, Pamela E. Buckley, Brian K. Shenton, Shlokaree Balupuri, Mohammed A. F. El-Sheikh, Helen Robertson, Naem Soomro, Bryon C. Jaques, Derek M. Manias, and David Talbot

- Parameters we monitor
  - Flow
  - GST
What makes a difference

• Warm ischemia
  – impairs organ function
  – Patients who die more than 60 min after forgoing life sustaining treatment (LST) are regularly deemed unsuitable for DCD.

**Time points in donation following cardiac death**

The withdrawal period (sometimes called the agonal period)

The asystolic warm period (also known as the primary warm ischaemic time)
• When does functional warm ischaemia begin
  – To date the most practical definition of warm ischaemia:
    • the time from which the systolic blood pressure falls below 50mg Hg and / or oxygen saturation falls below 70% to the start of cold perfusion in the donor.
      – Attempts to estimate the full extent of the ischaemic insult to the potential graft.
      – Implies that BP and oxygen saturation monitoring should be utilised in donors at least until these parameters have been reached.
Ideal DCD profile - liver

Age <50 years
Weight <100kg
Intensive care stay <5 days
Warm ischaemic time <20 minutes
Cold ischaemia time <8 hours
No steatosis (<10%)
• Ideal donors should be utilised without exception

— Heaton 2010
Marginal DCD grafts - liver

Age >50 years
Weight >100kg
Intensive care stay >5 days
Warm ischaemic time >20 minutes (up to 30 minutes)
Cold ischaemia time >8 hours (up to 12 hours)
Steatosis >15%
Marginal DCD livers

• These grafts should be used selectively by units.
• Auditing use and non-use would provide qualitative data regarding unit performance, and all the identification of further subgroups of DCDs that could potentially be utilised.

– Heaton, 2010
Table 2  Incidence of Primary Nonfunction with Donation-after-Cardiac-Death Donors

<table>
<thead>
<tr>
<th>Author/Reference</th>
<th>Date</th>
<th>n</th>
<th>PNF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muiesan\textsuperscript{147}</td>
<td>2005</td>
<td>31</td>
<td>6.45</td>
</tr>
<tr>
<td>Foley\textsuperscript{46}</td>
<td>2005</td>
<td>36</td>
<td>5.56</td>
</tr>
<tr>
<td>Manzarbeitia\textsuperscript{148}</td>
<td>2004</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>Abt\textsuperscript{47}</td>
<td>2004</td>
<td>144</td>
<td>11.8</td>
</tr>
<tr>
<td>Otero\textsuperscript{149}</td>
<td>2003</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>Fukumori\textsuperscript{150}</td>
<td>2003</td>
<td>25</td>
<td>NR</td>
</tr>
<tr>
<td>D’Alessandro\textsuperscript{151}</td>
<td>2000</td>
<td>19</td>
<td>10.5</td>
</tr>
<tr>
<td>Reich\textsuperscript{152}</td>
<td>2000</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Casavilla\textsuperscript{153}</td>
<td>1995</td>
<td>12</td>
<td>17</td>
</tr>
</tbody>
</table>

PNF, primary nonfunction.
1 year transplant survival after deceased donor first adult elective liver only transplant in the UK, 1 Jan 2004 to-date

<table>
<thead>
<tr>
<th>Donor type</th>
<th>N</th>
<th>% transplant survival</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deceased HB</td>
<td>2079</td>
<td>86</td>
<td>84-87</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Deceased NHB</strong></td>
<td><strong>226</strong></td>
<td><strong>79</strong></td>
<td><strong>72-84</strong></td>
<td></td>
</tr>
</tbody>
</table>
Exchange of DCD kidney transplants between centres

Year of donation

Number of transplants

- Export
- Local

- 2005: 176
- 2006: 214
- 2007: 270
- 2008: 383
- 2009: 404
- 2005: 19
- 2006: 24
- 2007: 25
- 2008: 51
- 2009: 87
How far should we push for potential donation?

• Donors with any brain tumour
• Donors with recent history of malignancy
• Donors with high risk social activity
  – Sexual practices
  – Drug use
• Donors with Polycystic disease
• Donors following previous transplantation
• Donors of Kidneys following POD
Health

Fatal cancer passed on by organ transplant

The liver recipient died five months after transplant surgery. Serious doubts have been raised about transplanting organs from cancer sufferers after a recipient contracted the disease following a liver donation.

But doctors are reluctant to change current policies because organs are in such short supply.

The 29-year-old recipient died from widespread cancer five months after the operation involving a donor who had undergone surgery to remove a brain tumour.

Experts were able to match the cancer in the transplant patient to the donor’s disease.

In Britain and other European Union countries, as well as the United States, people with a history of malignant cancer are not normally accepted as organ donors. Brain tumours are exception.
How Safe Is It to Transplant Organs from Deceased Donors with Primary Intracranial Malignancy? An Analysis of UK Registry Data

- Identify all organ donors between 1985 and 2001 inclusive with a primary intracranial malignancy - to identify the occurrence of post-transplant malignancy in the recipients of the organs transplanted.
- Of 11,799 organ donors
  - 179 were identified as having had a primary intracranial malignancy, including 33 with high-grade malignancy (24 grade IV gliomas and 9 medulloblastomas).
- A total of 448 recipients of 495 organs from 177 of these donors were identified.
- **No transmission of donor intracranial malignancy occurred.**

**Conclusion**
- Organs from patients dying from primary intracranial malignancy, including those with high-grade tumours, should be considered for transplantation and the small risk of tumour transmission should be balanced against the likely mortality for potential recipients who remain on the transplant waiting list.

Watson CJE et al, 2010
Wigan transplant patient given lungs of 30-year smoker

The father of a woman who died after a double lung transplant said she would have been "horrified" to discover the organs were from a smoker of 30 years.

Cystic fibrosis sufferer Lynsey Scott, of Wigan, died months after surgery at Wythenshawe Hospital last year.

Allan Scott said she was not told that the donor smoked and is calling for patients to be given more information.

The University Hospital of South Manchester (UHSM) NHS Trust said it had followed national guidelines.

Ms Scott, 28, who was born with cystic fibrosis, underwent the surgery in February 2000 to prolong her life after her condition deteroriated.

She died a few months later in July. Tests later concluded the primary cause of death was pneumonia.

"It was after applying for the medical notes on the transplant that Ms Scott's family discovered the donor was a smoker, although there is no suggestion this contributed to her death."

"I can honestly say she would have been horrified to have known those lungs were from a smoker and quite definitely she would have refused that operation," her father told the BBC.

"The issue is that the use of these organs should be told to the patients themselves by the clinicians."

Allan Scott
Father
Polycystic Kidneys....?

• Criteria for accepting such donors:
  – donor less than 50 years of age,
  – kidney size <15 cm in bipolar length
  – Normal creatinine at the time of retrieval,
  – Pre-transplant renal biopsy is performed and results are discussed with pathologist, nephrologist and surgeon prior to considering transplantation
  – cold ischemia time is preferably <12 hours and not >24 hours.

• PCK can be accepted for transplantation in recipients, who may have a **life expectancy of 10 years or less and who are fully informed regarding consent to receiving a polycystic graft**
Polycystic Kidneys...?

- In the literature, there are around 12 successful cases of polycystic kidneys being used for transplantation. Many of these reports have follow-up ranging from 1 to 15 years.

- Available data suggests that the expected graft survival of a normal or moderately enlarged polycystic kidney with normal function may be about 10 years.

Olsburgh et al, 2009
Liver Transplantation Using Uncontrolled Non-Heart-Beating Donors Under Normothermic Extracorporeal Membrane Oxygenation

Santos Jiménez-Galanes Marchán, Juan Carlos Meneu-Diaz, Almudena Moreno Elola-Olaso, Baltasar Pérez-Saborido, Fundora-Suarez Yiliam, Alberto Gimeno Calvo, Manuel Abradeo Usera, Mercedes Catalán González, Juan Carlos Montejo González, and Enrique Moreno González

Digestive Surgery and Abdominal Organ Transplantation Department, 12 de Octubre University Hospital, Madrid, Spain
Dual kidney transplantation

• Reducing the number of discarded kidneys and increasing the nephron mass
• Similar results to SKT especially with acceptable pre-transplant biopsies
• More PNF
• Maybe the way forward for category II DCDD

  • Remuzzi G, 1999; Tan JC, 2004; Alfrey EJ, 2004; Bunnapradist S, 2003
Consent...

• Timing – when is the best time to get consent
  – At listing
  – At the call-up
  – On the day of transplantation

• Separate list?
UNOS policy

• Requires patients to decide in advance whether they'll accept organs from ECD

• After the Chicago incident, UNOS added a requirement that recipients be informed if organs come from certain high-risk donors, including those considered at risk for HIV
• Allowing a patient to cherry-pick his organs by telling him everything about a potential donor creates the potential for discrimination, inefficiency and inequity in how organs are allocated,”. 
Doctors to warn patients of transplant risks

As many as a quarter of all organs are rated as 'marginal'

By Brian Brindy, Whitehall Editor

Surgeons will be forced to tell transplant patients more about the condition of organs that could save their lives, after a catalogue of complaints about the quality of "higher-risk" organs used in many hospitals. Ministers plan to give potential organ recipients the right to ask for full details of their donors before consenting to go ahead with what could be life-saving transplants.

The review of rules governing the use of "marginal" organs comes amid growing concern about the quality of many hearts, lungs, livers and kidneys harvested from outside a "shrinking pool" of healthy donors. The use of marginal organs, which could be from older people, drug addicts or heavy smokers, has grown in recent years, as transplant centres have struggled to treat more patients without a corresponding increase in the number of healthy young donors available.

In 1998, 13 per cent of all donor organs were rated as marginal, but a decade later the figure had doubled to over one in four of almost 3,500 transplants carried out in the UK.
Disclosing organ transplant risks: Now or later?

Patients should weigh overall options, not individual risks, ethicists argue

By JoNel Aleccia
Health writer

Patients awaiting organ transplants should decide in advance whether they’re willing to take substandard kidneys, livers and other organs, including those at risk for infectious diseases such as HIV or hepatitis C.

That’s the conclusion of University of Pennsylvania scientists and ethicists who want to overhaul a piecemeal system they say fails to adequately inform some patients of potential problems while allowing others to “cherry-pick” donors, accepting or rejecting specific organs based on certain risk factors at the time of transplant.
Organ transplants' hidden risk

By Gerry Northam

File on 4

John Richardson and his wife, Karen, hoped a heart transplant would give him a new life.

But the 37-year-old chef never regained consciousness after receiving his new heart and died five days later on 3 August 2008.

Mrs Richardson’s grief was compounded when an inquest revealed a catalogue of risk factors that had impaired the heart her husband received, and the coroner recorded a verdict of death by medical misadventure.

"I know that he would have got better if he had had a good donor heart," she told BBC File on 4.

She discovered the donor had committed suicide, was a smoker with several body tattoos - creating a risk of hepatitis - and a cocaine user.

Crucially she learned it had taken 15 minutes to restart the donor’s heart after he had been found hanged.

Mrs Richardson said her husband had never been told about the heart.
Summary:
‘rejecting these organs could delay transplant’

• Because patients might be offered marginal organs, they need to understand what accepting them might mean.

• Even with strict screening, there’s still a remote chance that some organs could be infected or otherwise damaged.

• Patients need to know that rejecting substandard organs could reduce the available pool, delaying transplantation and possibly resulting in death before a standard organ becomes available.

• “Most liver patients, they’re not going to pass over anything that might help,” “Liver and hearts, boy, if they pass, they’re not going to get another chance.”

• UNOS - continue to support notifying transplant candidates about both general and individual risks.

• "With any specific transplant opportunity, the level of risk may be acceptable for some candidates but unacceptable for others," they said.
Attention should be made to minimising the CIT of ECD kidneys.

DCD donor kidneys and dual transplants should be allocated locally.

? value of allocating ECD kidneys to older recipients (Old for Old)

Education regarding the risks and benefits of the procedure should be a prerequisite of entry onto the transplant waiting list.

Recipients of ECD or dual kidneys must give specific informed consent

Kidneys from paediatric donors < 15 kg and/or < 5 years should be considered for en-bloc transplantation.

Back table biopsy should be encouraged for allocation
  – preferably involves a needle biopsy (not wedge biopsy) through the upper pole cortex.
When your life depends on a transplant

• What are you willing to compromise?

  – Would you accept a less-than-perfect replacement organ?
  – Would you or your family pressure your brother or sister or child to donate a kidney or part of a liver?
  – Would you buy an organ from a person who is desperately poor?
• "Taking risks sometimes opens up new frontiers and sometimes opens a Pandora's box”

• "The motivation to take risks is that there aren't enough donors to go around and people are dying."

• "To point fingers at those who are aggressive about how they practice transplantation is difficult to do without knowing the nature of the recipient"