Graft quality and Steatosis; surgeon’s perspective

Richard Laing on behalf of Thamara Perera  MBBS, MS, FEBS, MD, FRCS
Consultant surgeon Liver Transplantation
Queen Elizabeth Hospital Birmingham and Birmingham Children’s Hospital
United Kingdom
Marginal Grafts – the “Fear”

Optimal liver graft

Ideal graft function post OLT

Marginal liver graft

Initial poor function
Coagulopathy
Cardiovascular instability
Multi-organ dysfunction
Renal failure
Sepsis
Primary Non-function
Retransplantation
Mortality

?
## Historical perspective

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total transplants</td>
<td>1172</td>
<td></td>
</tr>
<tr>
<td>T0 biopsy available</td>
<td>n=211 (36%)</td>
<td>n=374 (64%)</td>
</tr>
<tr>
<td>Donor age</td>
<td>53.1 (16.6–72.1)</td>
<td>54.1 (18.0–73.4)</td>
</tr>
<tr>
<td>BMI</td>
<td>25.7 (16.5–50.8)</td>
<td>25.7 (16.5–50.8)</td>
</tr>
<tr>
<td>Steatosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>36 (17.1%)</td>
<td>53 (14.2%)</td>
</tr>
<tr>
<td>Severe</td>
<td>10 (4.7%)</td>
<td>3 (0.8%)</td>
</tr>
</tbody>
</table>

*Significant perioperative morbidity and mortality
More grafts (n) of moderate severe steatosis has been used in the later era

Trends of usage in steatotic liver grafts over a ten year period. Lordan et al Transplant International 24, 140
Marginal grafts – Current trends

• Transplant data from Declined organs audit
• Dec 2010 – 2015

206 / 909 (23%) adult transplants were performed
With declined offers
- DCD (n=65)
- DBD (n=146)

206 liver grafts were refused by 731 times – average refusal rate 3.5/liver graft

Marginal grafts – Current trends

- Why do centres reject liver graft offers? Surrogate markers of steatosis

**Reasons for liver offer refusal**

**Heterogenous reasons but majority attributed to marginality**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>87</td>
</tr>
<tr>
<td>ANATOMICAL REASON</td>
<td>32</td>
</tr>
<tr>
<td>CENTRE CRITERIA</td>
<td>35</td>
</tr>
<tr>
<td>FATTY</td>
<td>14</td>
</tr>
<tr>
<td>LOGISTIC</td>
<td>51</td>
</tr>
<tr>
<td>NO RESPONSE</td>
<td>7</td>
</tr>
<tr>
<td>NO SUITABLE RECIPIENT</td>
<td>76</td>
</tr>
<tr>
<td>OTHER</td>
<td>33</td>
</tr>
<tr>
<td>PMH POOR FUNCTION</td>
<td>201</td>
</tr>
<tr>
<td>SIZE</td>
<td>85</td>
</tr>
<tr>
<td>VIROLOGY</td>
<td>41</td>
</tr>
<tr>
<td>WT</td>
<td>15</td>
</tr>
<tr>
<td>HLA/ABO</td>
<td>13</td>
</tr>
<tr>
<td>RECIPIENT BETTER</td>
<td>10</td>
</tr>
<tr>
<td>RECIPIENT UNFIT</td>
<td>3</td>
</tr>
<tr>
<td>RECIPIENT REFUSED</td>
<td>5</td>
</tr>
<tr>
<td>RECIPIENT REFUSED</td>
<td>0</td>
</tr>
</tbody>
</table>
Marginal grafts – Current trends

KEY FACTS

• **Subjective** marginality at the time of organ offer is the key to determine acceptance / decline

• There was no concordance of centre opinions
  – Heterogenous reasons but majority attributed to marginality

• Average refusal rate is higher for DCD vs. DBD (4.2 vs. 3.2)

• Organ failure rate attributable to the graft was 8/206 (3.8%)
Marginal Liver – *the Challenge*

“How to select the **best of the lesser grafts** to achieve **nothing less than the best outcomes**………………..”
Marginal Liver – How far do you push?

- Framework of *guidelines*
  - SaBTO
  - Institutional / local guidelines
  - Age criteria

- Experience of the surgeon

- Information gathered from donor surgeon / reliance

- Visual assessment

- (Lack of) Objective assessment
Contributors to marginality - 1

Donor history

“Donor has poor history that is surrogate with highly predictive delayed graft function/graft failure”

- Demographics; Age, BMI
- Previous medical history – T2DM
- Medical history immediate pre-donation
- Significant down time
- Cause of death
Organ function

“Potential organ (Liver) is dysfunctional and likely to fail/temporarily dysfunction; thus recipient may end up with a bad/suboptimal outcome”

– Dysfunction within donor
  • Significantly elevated transaminases
  • Isolated rise in GGT?

– Severe systemic instability impacting liver

– Severe metabolic acidosis

– (Perceived) degree of steatosis
Logistics

“Acceptable donor and graft quality but the logistics would make it more marginal, therefore the outcomes are likely to be negatively influenced”

- Prolonged donor warm ischaemia time
- Organ travel time
- Total cold ischaemia time
- Multiple offers – “already a pristine quality liver accepted”
Contributors to Marginality - 4

**Retrieval surgeon**

- Expertise and experience of retrieval surgeon
- Assessment of steatosis; “over-call”
- Influence the decision making of Transplanting surgeon
- Insight!
- Procurement injury to already marginal graft
- Procurement, packing and dispatch times
Contributors to Marginality - 5

“Transplant surgeon - calculated risk taker”

- Digs deep for more information
- Search for evidence in similar organ donation scenarios
- Weighs the risks and benefits, potential use of the graft based on the need
- Calls for opinion! And (more) friends
- Chooses the recipient wisely
- Informs the potential recipient with evidence and documents
Marginal graft – Example 1

DBD offer
- 55 Female
- Height 166cm, weight 110Kg (BMI 40)
- Admitted with 37min down time, one week in ITU
- ALT on admission 661IU down to 163IU on donation
- CRP 115
- No ACIDOSIS
- On double inotropic support
- Blood group O

Marginal!
- Age + BMI
- Improving LFT’s but 4x normal
- 7 days in ITU, Possible sepsis

Zonal Allocation centre accepts the offer
Marginal graft – Example 1

Retrieval centre – NORS; not the same centre accepting liver

Retrieval Surgeon –

“There is large haematoma in the LLS approximately 10x10cm, anterior to posterior”.

“MODERATELY FATTY”

- Zonal Allocation centre declines the offer
- Cross clamp pending
- All other centres decline the offer
- Fast Track offer to Birmingham
Marginal graft – Example 1

Our approach

– Blood Group O, DBD

– Haematoma likely from CPR, one week old
  • option to leave alone or reduce the LLS if extensive

– Moderate steatosis
  • “probably over-call”!

– Accept the offer, speak to surgeon and get images

– Buy time by delaying cross-clamping
Marginal graft – Example

Contact made - Retrieval surgeons confirms Moderate steatosis

- When asked “would your centre have transplanted this liver disregarding the injury” – declares himself renal transplant surgeon!

Opinion on size - nearly 1.5kg

- Helpful in sending pictures; healthy appearance (certainly not moderate steatosis)
Marginal graft – Example

- Graft was accepted with the plan to reduce the LLS
- Recipient was chosen with graft qualities in mind
- Successful reduction and transplantation – 2 years now with good LFT’s
- Residual liver segment for pathology – Steatosis 20%
Marginal graft – Example

Contributors to marginality

– Donor history
– Graft function
– Logistics
– Retrieval surgeon

Game changer – for Zonal centre

– Unexpected liver injury
– Retrieval surgeon opinion on steatosis

Game changer – for us

– Consideration of technical options
– Non-reliance on retrieval surgeon opinion of degree of steatosis
40y F, BMI - 29, DBD, ICH, at least moderate steatosis, small parenchymal injury segment VI

2.5 kg liver

Time zero biopsy: macrovesicular steatosis (20%);

Strategy – Short CIT and Implant time

Outcome – Reperfusion syndrome
  Delayed closure
  AKI
  In hospital stay 40 days
  Perfectly well now

Post reperfusion biopsy - STEATOHEPATITIS affecting the donor liver, the predominantly periportal location of steatosis remains unusual, this is a pattern that is recognised to occur in paediatric fatty liver disease. There could be either an alcohol or nonalcohol related aetiology (Kleiner S1 B1 I1= 3/8 fibrosis 1a/4);

? WOULD YOU HAVE TRANSPLANTED IF Steatohepatitis was known?
Marginal graft – Example 3

38y DBD, female, mild to moderate steatosis 50-60% Macrosteatosis on T-1
normal anatomy, 2.5 kg liver

Strategy – CIT - 0902hrs, implant time - 24min;

Outcome – Severe delayed function 24-48hours
  AKI
  In hospital stay 16 days
  Perfectly well now

Post reperfusion biopsy (Shown)
  Steatosis – Upper end of Mild (TO MODERATE)
Marginal graft – Example 4

ODT 134543-Rejected liver

66y M DBD

BMI 26
Hypoxic brain injury- OOHCA(Downtime 30 min)
PMH:HTN
heavy drinker(7-9units/day),
smoker
ALT 357, GGT 222, Bi 32

Offered to Named patient in National allocation
64y F, BMI 33 ,NAFLD (BG O+, UKELD 53) + portal HTN;
PVT grade 2;PMH:T2DM
eGFr 53
Marginal graft – Example 4

Steatosis only mild to moderate (10%)

Possible fibrous bridge

Graft appearance unhealthy and despite 10% steatosis overall risk appears far too much – Transplant cancelled
Marginal graft – Example 4

Core biopsy - paraffin

Wedge paraffin ballooned cells

Wedge fibrosis early bridging

Information available later from Paraffin sections
- Steatosis
- Bridging fibrosis

Right decision not to transplant!
Histopathology in Liver Transplant

- Takes away subjective assessment from retrieval and transplant surgeons
- Helps surgeons “make a case for” transplant when the freedom to select the appropriate recipient is present (examples 1-3)
- Low degree of steatosis on biopsy does not “bind” the surgeon to transplant organ (example 4)
- Accurate and timely histopathology (digital) may reduce organ decline by primarily allocated centres