Liver Preservation: Current Status and Future Directions

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Professor of Surgery
Weil Cornell Medical College
Director, Sherrie and Alan Conover Center for Liver Disease and Transplantation

Houston Methodist Hospital
Machine Perfusion

- Introduction and definitions
- Normothermic regional perfusion
- Normothermic machine
- Hypothermic machine perfusion
Conventional Preservation and DBD Liver Allografts

Intubated

Cold ischemia

recipient WI

Isolate the liver
Cannulate Aorta
Flush
Ice
X Clamp

procurement

Conventional cold storage

Reperfusion at OLT

2\textsuperscript{nd} warm ischemia

Shapey M and Muiesan, Liver Transplantation 2013
Cold Static Preservation

- Easy to perform
- Low costs
- Effective for “good grafts”

- Ongoing organ damage
- No graft assessment
- No graft repair
- Poorly tolerated by marginal grafts
Factors Affecting Graft Survival

- Donor Age
- Fat content 30%
- Cold Ischemia time CIT
- Warm ischemia time WIT
- Visualization
- Method of procurement DBD vs DCD
DCD Allografts Suffer More Injury than DBD Livers After Conventional Preservation

Extubate

- donor warm ischemia
- no touch rapid procurement
- CA

1st warm ischemia

Conventional cold storage

2nd warm ischemia

Reperfusion at OLT

Shapey M and Muiesan, Liver Transplantation 2013
# Categories of Non-Heart-Beating Donors

## Donors After Cardiac Death

**Maastricht Classification - Netherlands**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Brought in dead</td>
<td>Irreversible on the street</td>
</tr>
<tr>
<td>II</td>
<td>Unsuccessful resuscitation</td>
<td>Resuscitation in ambulance</td>
</tr>
<tr>
<td>III</td>
<td>Awaiting cardiac arrest</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Cardiac arrest after brain-stem death</td>
<td>Insufficient evidence for brain death</td>
</tr>
<tr>
<td>V</td>
<td>Unexpected Cardiac arrest in a hospital inpatient</td>
<td></td>
</tr>
</tbody>
</table>

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*Kootstra G, Daemen JH, Oomen AP, Transplantation Proceedings 1995*

*Sánchez-Fructuoso A I et al, J Am Soc of Nephrol 2000*
Worldwide DCD Donors (PMP)

International Registry for Organ Donation and Transplantation (IRODaT), 2013
Increased DCD Utilization

Netherlands

United Kingdom

USA

Spain

DeOliveira ML, Ann Surg 2012

Fondevila C et al, AJT 2016

SRTR, 2012 Annual Data Report
Meta Analysis of Ischemic Cholangiopathy after cDCD Liver Transplantation

• 489 DCD and 4455 DBD
• 2.4 times increased odds of biliary complications
• 10.8 times odds for ischemic cholangiopathy
• 1.6 times and 2.1 times higher odds for recipient mortality and graft failure

Machine Perfusion

• Repairing putative organ injuries and increase utilization of DCD livers

• Offers the opportunity to test organ quality and test organ function
Immediately after death, efforts were made not only to cool but to perfuse the liver in situ by means of an extracorporeal pump oxygenator into which a heat exchanger had been incorporated.

———

HOMOTRANSPLANTATION OF THE LIVER

Thomas E. Starzl, Thomas L. Marchioro, K. A. Porter, and Lawrence Brettschneider
Department of Surgery, University of Colorado School of Medicine, Denver, Colo., and St. Mary's Hospital and Medical School, London, England

Immediately after death, efforts were made not only to cool but to perfuse the liver in situ by means of an extracorporeal pump oxygenator into which a heat exchanger had been incorporated.
Machine Perfusion

Normothermic
- Perfusion with blood at normothermic conditions
- Minimize cold storage

Hypothermic

In Situ regional perfusion
Ex Situ during or after organ transfer
Strategies to Improve DCD Quality

**In Situ Dynamic Preservation by ARP**

- Abdominal regional perfusion applies extracorporeal membrane oxygenation to deliver oxygen
- Hypothermic RP (HRP) reduces metabolic requirements
- Normothermic RP (NRP) physiologically restores cellular function

*Fondevila C et al, AJT 2012
Jochmans I, AJT 2016*
Advantages of Abdominal Regional Perfusion

- Experimental results show improved transplantation outcomes compared to cold storage
- Normothermic oxygen delivery to tissues allows for regeneration of ATP, NAD and prevents accumulation of toxic metabolites
- Improves the concentration of antioxidants
- Converts a “rapid recovery” rush into a controlled procurement that allows donor liver evaluation
Machine Perfusion

- Hypothermic oxygenated perfusion (HOPE)
- Dual hypothermic oxygenated perfusion (D-HOPE)

Performed after cold storage prior to implantation
Renal Transplantation from Non-Heart Beating Donors: A Promising Alternative to Enlarge the Donor Pool

ANA I. SANCHEZ-FRUCTUOSO,* DOLORES PRATS,* JAIME TORRENTE,* M. JESÚS PEREZ-CONTÍN,‡ CRISTINA FERNA´NDEZ,† JOAQUÍN ALVAREZ,§ and ALBERTO BARRIENTOS*
Departments of *Nephrology, †Preventive Medicine, and ‡Surgery, and §Transplant Coordination, Hospital Clínico San Carlos, Madrid, Spain.

In 1989, kidneys procured from NHBD, donors were maintained - from cardiac arrest to procurement - on cardiopulmonary bypass: extracorporeal circulation, external oxygenator and intense hypothermia

95 of 144 kidneys were transplanted: PNF 6%, 94% successful, DGF 61%
Machine Perfusion

• Introduction and definitions

• Normothermic regional perfusion in uncontrolled DCD

• Normothermic machine

• Hypothermic machine perfusion
Liver Transplantation from Maastricht Category 2 - uNHBD

La Coruna and Madrid – Spain 2003

1. Cardiac arrest (CA)
2. CPR time followed
3. 5 min after declaration of death, Cardiopulmonary Support (CPS): combined mechanical chest and abdominal compression, PaO$_2$ 100, MAP 100, pH > 7.10
4. WIT: CA to CPS

1. Cardiac arrest (CA)
2. CPR time followed
3. 5 min after declaration of death, Cardiopulmonary Bypass (CPB)/ECMO is started
4. WIT: CA to ECMO

Otero et al, Transplantation 2003
Liver Transplantation from Maastricht Category 2 – uNHBD

La Coruna and Madrid - Spain

- Cardiopulmonary support (CPS) n=6

- Cardiopulmonary bypass (CPB, ECMO)
  - Hypothermic perfusion (HR) at 15-20 °C n=7
  - Normothermic perfusion (NRP) at 37 °C n=7

Otero et al, Transplantation 2003
Liver Transplantation from Maastricht Category 2 – uNHBD

La Coruna and Madrid - Spain

<table>
<thead>
<tr>
<th></th>
<th>CPS n=6</th>
<th>CPB/ECMO n=14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt survival</td>
<td>100 %</td>
<td>71 %</td>
</tr>
<tr>
<td>Graft survival</td>
<td>83 %</td>
<td>43 %</td>
</tr>
<tr>
<td>PNF</td>
<td>1 (16%)</td>
<td>4 (28%)</td>
</tr>
</tbody>
</table>

- CPS, if efficient, is better than CPB and should not exceed 130 min
- CPB/ECMO can provide an additional 150 min
- No livers failed if CPB <150 min
- No difference between hypothermic and normothermic perfusion

*Otero et al, Transplantation 2003*
Biliary Complications in Maastricht
Category 2 - uNHBD

<table>
<thead>
<tr>
<th></th>
<th>P value</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHBD</td>
<td>0.002</td>
<td>47.1</td>
</tr>
<tr>
<td>HAT</td>
<td>&lt;0.001</td>
<td>98.7</td>
</tr>
</tbody>
</table>

Suarez F et al, Transplantation 2003
Liver Transplant Using Donors After Unexpected Cardiac Death: Novel Preservation Protocol and Acceptance Criteria
C Fondevila et al, AJT 2007; 1849-1855

NECMO - NRP

- 10 of 40 uDCD livers were transplanted
- Only 1 of 10 with biliary anastomotic stricture and 1 HAT

Fondevila C et al, AJT 2007
## Single Center Experience for Abdominal Regional Perfusion using NECMO in uDCD

<table>
<thead>
<tr>
<th>Group period</th>
<th>Pump flow L/min</th>
<th>Perfusion time (min)</th>
<th>N</th>
<th>PNF %</th>
<th>Ischemic biliary lesion %</th>
<th>1-yr graft survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barcelona 2015 (^1)</td>
<td>1.7</td>
<td>195 (184-230)</td>
<td>43</td>
<td>9</td>
<td>12</td>
<td>74</td>
</tr>
<tr>
<td>Madrid 2009 (^2)</td>
<td>3.3±0.6</td>
<td>174 ± 46</td>
<td>20</td>
<td>10</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>Paris 2015 (^3)</td>
<td>2-3</td>
<td>240 (209-319)</td>
<td>13</td>
<td>23</td>
<td>7</td>
<td>69</td>
</tr>
</tbody>
</table>

\(^1\) Fondevila C et al, AJT 2012  
\(^2\) Jimenez-Galanes, Liver Transplantation 2009  
\(^3\) Savier E, Liver Transplantation 2015
Parameters for Donor Utilization in Maastricht Category 2 - uDCD

- **Time limits:** <15 min cardiac arrest without CPR
  <150 min advanced cardiorespiratory support
  < 4 hr NECMO
- **Pump parameters:** 1.7 l/min, temp 35.5 - 37.7 °C
- **Most common contraindications to donate:**
  - age > 65
  - poor venous return
  - Elevated enzymes > 3x normal
  - Macro appearance of allograft
  - History of alcohol or liver disease
  - Judicial refusal

*Fondevila C et al, AJT 2012*
Logistical Analysis of Activation of uDCD Donation Protocol

- 400 protocol activations
  - 110 excluded during CRS
- 290 canulations
  - 145 excluded during NECMO
- 145 organ donors
  - 111 excluded at organ recovery
- 34 OLT

- Transplant 9%
- Donor contraindication 18%
- Suboptimal evolution 32%
- Refusal of consent 17%
- Other 1%
- Technical or logistical failure 23%

Fondevila C et al, AJT 2012
Patient and Graft Survival of uDCD Recipients

Fondevila C et al, AJT 2012
## Perioperative Care of uDCD Recipients

<table>
<thead>
<tr>
<th></th>
<th>uDCD (n = 40)</th>
<th>DBD (n = 80)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAD (%)</td>
<td>20 (50)</td>
<td>16 (20)</td>
<td>0.001</td>
</tr>
<tr>
<td>PNF (%)</td>
<td>2 (5)</td>
<td>1 (1)</td>
<td>0.215</td>
</tr>
<tr>
<td>Surgical reintervention (%)</td>
<td>21 (53)</td>
<td>11 (14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal replacement therapy (%)</td>
<td>6 (15)</td>
<td>2 (3)</td>
<td>0.010</td>
</tr>
<tr>
<td>Mechanical ventilation (h)</td>
<td>58 (7–120)</td>
<td>7 (5–24)</td>
<td>0.001</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>7 (4–11)</td>
<td>5 (3–6)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>22 (16–42)</td>
<td>16 (13–21)</td>
<td>0.003</td>
</tr>
<tr>
<td>Retransplantation (%)</td>
<td>6 (15)</td>
<td>1 (1)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*Fondevila C et al, AJT 2016*
Utilization of uDCD – Lessons Learned

• Potential donors can be increased by thousands

• Despite logistical challenges, uDCD maybe only option in some countries where DBD donors are not utilized

• Application of Ex Vivo RP have resulted in good patient survival but reduced graft survival rates

• Although some European countries and only New York City have adopted protocols for uDCD, most donor increases have come from cDCD

Magliocca JF, AJT 2016
Hessheimer AJ et al, AJT 2016
Machine Perfusion

• Introduction and definitions

• Normothermic regional perfusion in controlled DCD

• Normothermic machine

• Hypothermic machine perfusion
The University of Michigan Experience

Agonal period 5-30 min
VA ECMO at 37°C in ICU
45 ml/kg/min
Elective Surgery

Rojas-Pena, Clin Transl Res 2014
## ECMO Utilization in Recovery in cDCD: Comparison to Cold Storage

<table>
<thead>
<tr>
<th></th>
<th>Rapid Recovery Cold Storage</th>
<th>E-DCD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organs donated</strong></td>
<td>Kidneys/occasional livers</td>
<td>All except heart</td>
</tr>
<tr>
<td><strong>Goal</strong></td>
<td>Deep cooling/ decrease metabolism</td>
<td>Restore warm circulation and oxygenation/normal metabolism</td>
</tr>
<tr>
<td><strong>Time to procurement</strong></td>
<td>Urgent</td>
<td>Elective</td>
</tr>
<tr>
<td><strong>Cold Storage</strong></td>
<td>Routine followed by pump perfusion</td>
<td>Pump perfusion not necessary</td>
</tr>
<tr>
<td><strong>Organ Assessment</strong></td>
<td>During pump perfusion</td>
<td>At recovery and pump perfusion</td>
</tr>
<tr>
<td><strong>Post Tx Function</strong></td>
<td>40-60% DGF</td>
<td>8-30% DGF</td>
</tr>
</tbody>
</table>

*Rojas-Pena, Clin Transl Res 2014*
Logistical Analysis of Activation of cDCD Donation Protocol

37 donors, 38.7 (9-65) yrs, 79.5 (30-143.6) Kg

<table>
<thead>
<tr>
<th></th>
<th>Kidneys</th>
<th>Livers</th>
<th>Pancreas</th>
<th>ORPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered</td>
<td>73</td>
<td>21</td>
<td>2</td>
<td>2.59</td>
</tr>
<tr>
<td>Transplanted</td>
<td>48</td>
<td>13</td>
<td>1</td>
<td>1.68</td>
</tr>
</tbody>
</table>
## Change of Arterial Blood Gases with ECMO

<table>
<thead>
<tr>
<th>Variable</th>
<th>At Initiation</th>
<th>At Termination</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.09 ± 0.02</td>
<td>7.28 ± 0.02</td>
</tr>
<tr>
<td>SVO₂</td>
<td>45.5 ± 3.6</td>
<td>67.0 ± 3.2</td>
</tr>
<tr>
<td>PaO₂</td>
<td>304.8 ± 39.2</td>
<td>373.3 ± 41.3</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>55.5 ± 8.4</td>
<td>34.5 ± 2.4</td>
</tr>
<tr>
<td>SaO₂ %</td>
<td>84.4 ± 3.5</td>
<td>90.4 ± 34</td>
</tr>
<tr>
<td>K⁺</td>
<td>6.1 ± 0.8</td>
<td>4.9 ± 0.5</td>
</tr>
</tbody>
</table>

Rojas-Pena, Clin Transl Res 2014
### Single Center Experience for Abdominal Regional Perfusion using NECMO in cDCD

<table>
<thead>
<tr>
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<th>Ischemic biliary lesion %</th>
<th>1-yr graft survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michigan 2014 (^1,^2)</td>
<td>3.5</td>
<td>86 ± 5</td>
<td>13</td>
<td>0</td>
<td>7</td>
<td>86</td>
</tr>
<tr>
<td>UK 2009 (^2)</td>
<td>1.7 - 4</td>
<td>120 (34-156)</td>
<td>11</td>
<td>9</td>
<td>0</td>
<td>NR</td>
</tr>
</tbody>
</table>

\(^1\) Rojas-Pena, Clin Transl Res 2014  
\(^2\) Magliocca et al, J Trauma 2005  
\(^3\) Oniscu GC, AJT 2014
Can ECMO be improved?
Machine Perfusion

- Introduction and definitions
- Normothermic regional perfusion
- Normothermic machine
- Hypothermic machine perfusion
Machine Perfusion Devices
A randomized trial of normothermic preservation in liver transplantation

David Nasralla1*, Constantin C. Coussios2*, Hynek Mergental3, M. Zeeshan Akhtar1,4, Andrew J. Butler5,20, Carlo D. L. Ceresa1, Virginia Chiocchia6,7, Susan J. Dutton8, Juan Carlos García–Valdecasas9, Nigel Heaton10, Charles Imber11, Wayel Jassem10, Ina Jochmans12,13, John Karani10,14, Simon R. Knight1,15, Peri Kocabayoglu16, Massimo Malago11, Darius Mirza3, Peter J. Morris1,15, Arvind Pallan17, Andreas Paul16, Mihai Pavel9, M. Thamara P. R. Perera3, Jacques Pirene12,13, Reena Ravikumar1, Leslie Russell18, Sara Upponi10, Chris J. E. Watson5,20, Annemarie Weissenbacher1, Rutger J. Ploeg1, Peter J. Friend1* for the Consortium for Organ Preservation in Europe

Liver transplantation is a highly successful treatment, but is severely limited by the shortage in donor organs. However, many potential donor organs cannot be used; this is because sub-optimal livers do not tolerate conventional cold storage and there is no reliable way to assess organ viability preoperatively. Normothermic machine perfusion maintains the liver in a physiological state, avoids cooling and allows recovery and functional testing. Here we show that, in a randomized trial with 220 liver transplantations, compared to conventional static cold storage, normothermic preservation is associated with a 50% lower level of graft injury, measured by hepatocellular enzyme release, despite a 50% lower rate of organ discard and a 54% longer mean preservation time. There was no significant difference in bile duct complications, graft survival or survival of the patient. If translated to clinical practice, these results would have a major impact on liver transplant outcomes and waiting list mortality.
Randomized Controlled trial
NEsLP vs Cold Storage

NEsLP (n=121/ DCD=34) vs SCS (n=101/DCD=21)
• Portable perfusion, Metra device
• Acceptable for transplantation

Nasralla, Nature 2018; 557(7703):50-56
## Randomized Control Trial NEsLP vs SCS (Outcomes)

<table>
<thead>
<tr>
<th></th>
<th>NMP ((n = 121))</th>
<th>SCS ((n = 101))</th>
<th>Effect (95% CI)</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peak AST</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT⁵</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted</td>
<td>488.1 (408.9–582.8)</td>
<td>964.9 (794.5–1,172.0)</td>
<td>0.5 (0.4–0.7)</td>
<td>0.0000</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>484.5 (406.4–577.6)</td>
<td>973.7 (795.2–1,192.3)</td>
<td>0.5 (0.4–0.5)</td>
<td>0.0000</td>
</tr>
<tr>
<td><strong>Test for interaction by donor type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subgroup analysis by donor type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBD</td>
<td>526.2 (427.3–647.9)</td>
<td>880.2 (708.5–1,093.5)</td>
<td>40.2% (19.3–55.7%)</td>
<td>0.0009</td>
</tr>
<tr>
<td>DCD</td>
<td>389.7 (278.0–546.4)</td>
<td>1,458.1 (944.7–2,250.5)</td>
<td>73.3% (53.7–84.6%)</td>
<td>0.0000</td>
</tr>
<tr>
<td>PP analysis</td>
<td>498.6 (414.8–599.4)</td>
<td>982.9 (810.4–1,192.2)</td>
<td>0.5 (0.4–0.7)</td>
<td>0.0000</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discard rates⁹</td>
<td>16 (11.7%)</td>
<td>32 (24.1%)</td>
<td>−12.4% (−21.4 to −3.3%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Primary non-function⁹</td>
<td>1 (0.8%)</td>
<td>0 (0.0%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Post-reperfusion syndrome</td>
<td>15 (12.4%)</td>
<td>32 (33.0%)</td>
<td>−20.6% (−31.6 to −9.6%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Post-reperfusion lactate⁹</td>
<td>3.6 (2.6–4.2)</td>
<td>4.1 (3.2–5.0)</td>
<td>0.263 (0.126–0.550)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Early allograft dysfunction</td>
<td>12 (10.1%)</td>
<td>29 (29.9%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Randomized Control Trial NEsLP vs SCS (Outcomes)

Perfusate lactate levels during NMP

Subgroup analysis

Nasralla, Nature 2018; 557(7703):50-56
Graft Survival

Nasralla, Nature 2018; 557(7703):50-56
• All usable livers

• How does normothermic MP perform with extended criteria livers
Transplantation of Rejected Liver Grafts After NEsLP

- 6 rejected livers (4 DCD/ 2 HBD)
- DCD organs rejected due to prolonged WIT
- HBD organs rejected due to high LFTs

Outcomes:
- Median Hospital stay was 10 days
- The mean for ALT peak was 1386 IU/L
- No EAD
- No Ischemic cholangiopathy at 7 months (median) after transplant

Machine Perfusion

- Introduction and definitions
- Normothermic regional perfusion
- Normothermic machine
- Hypothermic machine perfusion
First Comparison of Hypothermic Oxygenated PErfusion Versus Static Cold Storage of Human Donation After Cardiac Death Liver Transplants

An International-matched Case Analysis

Philipp Dutkowski, MD, * Wojciech G. Polak, MD, PhD, † Paolo Mutiesan, MD, ‡ Andrea Schlegel, MD,* Cornelia J. Verhoeven, † Irene Scalera, MD, ‡ Michelle L. DeOliveira, MD, * Philipp Kron, MD, * and Pierre-Alain Clavien, MD, PhD, FACS (Hon)*
First comparison of HOPE-PV (n=25) vs SCS (n=50) in DCD livers

- Decrease in peak ALT (HOPE-PV: 1239 U/L vs SCS: 2065 U/L; \( P = 0.02 \))
- Less intrahepatic cholangiopathy (HOPE-PV: 0% vs SCS: 22%; \( P = 0.015 \))
- Decrease in EAD (HOPE-PV: 20% vs SCS: 44%; \( P = 0.046 \))
- Improved 1 year graft survival (HOPE-PV: 90% vs SCS: 69%; \( P = 0.035 \))

HOPE in Human DCD Allograft

Hypothermic oxygenated machine perfusion (HOPE-D)

- DCD livers [HOPE-D: 10 livers vs SCS: 20 livers]

- Less stroma necrosis ($p=0.002$) and injury of the deep peribiliary glands (PBG) ($p=0.02$) in HOPE-D compared to the baseline in the SCS group

Superior Preservation of DCD Livers With Normothermic Perfusion

Experimental groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>NECMO + NMP (n=6)</td>
<td>100%</td>
</tr>
<tr>
<td>NECMO + CS (n=6)</td>
<td>83%</td>
</tr>
<tr>
<td>CS (n=6)</td>
<td>0</td>
</tr>
</tbody>
</table>

NECMO + NMP resulted in superior survival, reduced pro-inflammatory responses, histological injury and endothelial activation.

Fondevila et al et al, Ann Surg 2011
Protective Strategies in the Lab

Ischemic Preconditioning; Pentoxifylline; histidine; glycine; Cyclosporine, FK506, FTY, epoprostenol; caspase-inhibitors; prostaglandins; CGS21680; anisomycine; soluble TNF receptors; tauroursodeoxycholate; dipyridamole; doxorubicine; ozone; NO; CO; superoxide dismutase; cobra venom factor; adenosine; alanine; picroliv; geranyl-geranyl-acetone; vitamine E; arginine; salviainolic acid A; L-carnitine; cobalt protoporphyrin; diethylmaleate; p38 mitogen-activated protein kinase inhibitor; phentolamine; ascorbic acid 2-glucoside; sodium nitroprusside; calcium; taxol; dichloroacetate; anti-ICAM-1 mAb; hydrophilic bile salts; linomide; magnolol; nicaraven . . . .
Protective Strategies in the Clinic

None
Search Continues for Optimal Preservation Technique

- Allows prolonged organ storage
- No preservation injury
- Assessment of organ function during preservation
- Permit organ repair and graft improvement
Acknowledgment

Dr Nazia Selzer
Toronto General Hospital
Conclusions

• Machine perfusion is in the early phase of development

• Perfusion technologies provide a great potential to influence allograft function

• It is not clear which type of perfusion would salvage extended criteria and DCD allografts

• Ongoing randomized controlled trials may clear the path for clinical utilization
Cell migration, chimerism, and graft acceptance

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Pittsburgh Transplant Institute and the Departments of Surgery (T. E. Starzl, MD, N. Murase, MD, S. Ildstad, MD, C. Ricordi, MD), Pathology (A. J. Demetris, MD), and Pediatrics (M. Trucco, MD), University of Pittsburgh Health Science Center, Pittsburgh, Pennsylvania 15213, USA.
A liver allograft from a donor whose oxygen delivery was maintained by extracorporeal membrane oxygenation (ECMO) for 29 days before suffering an anoxic brain injury from ECMO dysfunction. Liver transplantation was successfully performed in a patient with fulminant hepatic failure.
DCD Activity in Spain According to Maastricht Categories

Fondevila C et al, AJT 2016
DCD Liver Utilization in the U.S

SRTR, 2012 Annual Data Report
Extracorporeal perfusion for obtaining postmortem homografts

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