Maximizing Organ Donation through Donor Management Goals

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Maximizing Organ Donation

• Discuss the scope of organ donation needs statewide and nationally

• Review pathophysiology of organ dysfunction surrounding brain death

• Discuss intensive care management of the organ donor

• Review studies implementing donor management goals to maximize organs transplanted per donor

• Discuss implementation of donor management goals at Swedish Medical Center Intensive Care Unit
I have no conflicts of interest to disclose.
Levels of Evidence

• Retrospective studies
• Prospective studies with historical controls
• Randomized controlled trials
• Meta-analyses
# The Need: Organ Recipient Wait Lists

Through 9/30/13

<table>
<thead>
<tr>
<th>Organ</th>
<th>United States</th>
<th>Colorado</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>130,195</td>
<td>2,454</td>
</tr>
<tr>
<td>Kidney</td>
<td>104,773</td>
<td>1,683</td>
</tr>
<tr>
<td>Liver</td>
<td>16,530</td>
<td>621</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1,185</td>
<td>24</td>
</tr>
<tr>
<td>Kidney / Pancreas</td>
<td>2,122</td>
<td>34</td>
</tr>
<tr>
<td>Heart</td>
<td>3,616</td>
<td>46</td>
</tr>
<tr>
<td>Lung</td>
<td>1,666</td>
<td>46</td>
</tr>
<tr>
<td>Heart / Lung</td>
<td>48</td>
<td>0</td>
</tr>
<tr>
<td>Intestine</td>
<td>255</td>
<td>0</td>
</tr>
</tbody>
</table>
The Gift of Life

• One organ donor can save up to 8 lives.

• One tissue donor can impact up to 100 lives.

• One eye donor can restore eyesight to two people.
Potential Number of Organ per Donor

• Donation after Brain Death (BD):
  – Heart
  – Lungs (2)
  – Kidneys (2)
  – Liver
  – Pancreas
  – Small Intestine

• Donation after Cardiac Death (DCD):
  – Lungs (2)
  – Kidneys (2)
  – Liver
Pathophysiology of Brainstem Death

Increased intracranial pressure (ICP) causes

- Cushing’s reflex
- Catecholamine surge
- Visceral ischemia
- Pro-inflammatory state
- Disseminated intravascular coagulation
- Multi-organ failure
Pathophysiology of Brain Death: Cardiovascular Changes

- Catecholamine Storm
- Organ Hypoperfusion
- Cardiac Failure
- Shock
- Loss of Sympathetic Tone
Pathophysiology of Brain Death: Pulmonary Changes

↑ Pulmonary Hydrostatic Pressure

↑ Capillary Leak

Δ Oncotic Pressure

Pulmonary Edema
Pathophysiology of Brain Death: Endocrine and Metabolic Changes

Anterior Pituitary Failure:
- ↓ ACTH → Adrenal Insufficiency
- ↓ TSH → Sick Euthyroid

Posterior Pituitary Failure:
- ↓ Vasopressin → Diabetes Insipidus

Adrenal Insufficiency:
- ↓ Cortisol
- ↓ Insulin

Hypothermia
- ↓ Basal Metabolic Rate

Hypothalamic Failure
Care of the brain dead patient

- Progression from brain death to somatic death results in loss of up to 25% of potential donors.
- Intensive monitoring and balanced resuscitation of the donor are needed to maintain organ function and maximize number of organs suitable for transplantation.

Can J Anaesth. 2006: 53 (8); 820 – 820
Goals of Organ Donor Management

• Stabilize patient through catecholamine storm
• Provide balanced resuscitation to donor organs
• Target normal physiology
  – Temperature, hemodynamics, oxygenation, and metabolism
• Avoid positive fluid balance
“Rule of 100”

- Systolic blood pressure > 100 mm Hg
- Urine output > 100 mL/hr
- PaO2 > 100 mm Hg
- Hemoglobin > 100 g/L
Developing Clinical Pathways for Organ Donor Management

- United Network for Organ Sharing (UNOS) Critical Pathway for the Organ Donor – 1999
- Crystal City Consensus Conference – 2001
- Canadian Multidisciplinary Forum on Organ Donor Management – 2002
- “Bundling” Donor Management Goals – 2004 onward
UNOS Critical Pathway (CP): 1999 pilot study

• 5 overlapping phases of patient care from donor referral to organ recovery
  – Phase IV – Donor management

• Study design: 10 OPOs, 88 ICUs, 4-month prospective implementation of CP, compared with 4-month historical control period

• Outcome: Total number of organs recovered and transplanted per 100 donors

Cardio-Thoracic Donor Management

1. **Early echocardiogram for all donors** – Insert pulmonary artery catheter (PAC) to monitor patient management (placement of the PAC is particularly relevant in patients with an EF < 45% or on high dose inotropes.)
   - use aggressive donor resuscitation as outlined below

2. **Electrolytes**
   - Maintain Na < 150 meq/dl
   - Maintain K+ > 4.0
   - Correct acidosis with Na Bicarbonate and mild to moderate hyperventilation (pCO₂ 30–35 mm Hg)

3. **Ventilation** – Maintain tidal volume 10–15 ml/kg
   - keep peak airway pressures < 30 mm Hg
   - maintain a mild respiratory alkalosis (pCO₂ 30–35 mm Hg).

4. **Recommend use of hormonal resuscitation as part of a comprehensive donor management protocol** – Key elements
   - Tri-iodothyronine (T3): 4 mcg bolus; 3 mcg/hr continuous infusion
   - Arginine Vasopressin: 1 unit bolus; 0.5 – 4.0 unit/hour drip (titrate SVR 800–1200 using a PA catheter)
   - Methylprednisolone: 15 mg/kg/bolus (Repeat q 24 h PRN)
   - Insulin: drip at a minimum rate of 1 unit/hour (titrate blood glucose to 120–180 mg/dl)
   - Ventilator: (See above)
   - **Volume Resuscitation**: Use of colloid and avoidance of anemia are important in preventing pulmonary edema
     - albumin if PT and PTT are normal
     - fresh frozen plasma if PT and PTT abnormal (value ≥ 1.5 X control)
     - packed red blood cells to maintain a PCWP of 8–12 mm Hg and Hct > 10.0 mg/dl

5. **When patient is stabilized/optimized** repeat echocardiogram. (An unstable donor has not met 2 or more of the following criteria.)
   - Mean Arterial Pressure ≥ 60
   - CVP ≤ 12 mm Hg
   - PCWP ≤ 12 mm Hg
   - SVR 800–1200 dyne/sec/cm⁵
   - Cardiac Index ≥ 2.5 l/min/M²
   - Left Ventricular Stroke Work Index > 15
   - dopamine dosage < 10 mcg/kg/min
UNOS Critical Pathway (CP): 1999 pilot study

10.3% increase in total organs recovered

**Table 1: Organs recovered**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Pre-Critical Pathway</th>
<th>Critical Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Per 100 donors</td>
</tr>
<tr>
<td>Kidney</td>
<td>255</td>
<td>182.1</td>
</tr>
<tr>
<td>Liver</td>
<td>119</td>
<td>85.0</td>
</tr>
<tr>
<td>Pancreas</td>
<td>33</td>
<td>23.6</td>
</tr>
<tr>
<td>Heart</td>
<td>77</td>
<td>55.0</td>
</tr>
<tr>
<td>Lung</td>
<td>45</td>
<td>32.1</td>
</tr>
<tr>
<td>Intestine</td>
<td>5</td>
<td>3.6</td>
</tr>
<tr>
<td>Total</td>
<td>534</td>
<td>381.4</td>
</tr>
</tbody>
</table>

Am J Transplant 2002; 2: 761-768
UNOS Critical Pathway (CP): 1999 pilot study

**Table 2: Organs transplanted**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Pre-Critical Pathway</th>
<th>Critical Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Per 100 donors</td>
</tr>
<tr>
<td>Kidney</td>
<td>224</td>
<td>160.0</td>
</tr>
<tr>
<td>Liver</td>
<td>109</td>
<td>77.9</td>
</tr>
<tr>
<td>Pancreas</td>
<td>26</td>
<td>18.6</td>
</tr>
<tr>
<td>Heart</td>
<td>64</td>
<td>45.7</td>
</tr>
<tr>
<td>Lung</td>
<td>31</td>
<td>22.1</td>
</tr>
<tr>
<td>Intestine</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>454</td>
<td>324.3</td>
</tr>
</tbody>
</table>

**19.5% increase in hearts transplanted**

**11.3% increase in all organs transplanted**

*Am J Transplant 2002; 2: 761-768*
Hormonal Resuscitation

Combination of hormone supplements provided to replace those lost from failing hypothalamic-pituitary-adrenal axis

• Methylprednisolone
• Arginine Vasopressin
• Triiodothyronine (T3) or L-Thyroxin (T4)
• Insulin
Meta-analysis of thyroid hormone administration to brain dead potential organ donors

• 4 placebo-controlled RCTs
• 209 donors (108 Thyroid hormone rx; 101 placebo)

Results:
  – No significant effect of thyroid hormone on cardiac index
  – No benefit of combination hormonal therapies

Comment:
  – Limited numbers of hemodynamically unstable patients in donor pool may have missed a small treatment effect of thyroid hormone supplementation.

_Crit Care Med._ 2012 May; 40(5): 1635-44
Methylprednisolone

Reduces inflammatory response associated with brain death and hemodynamic instability

• Lung – Improves oxygenation, reduces capillary leak, increases, lung yield
• Decreases inflammation in heart, kidney, liver
• Increases overall organ retrieval
• Most effective when administered early

BJ Anaesthesia 2012; 108 (S1): i96-i107.
Achieving donor management goals before deceased donor procurement is associated with more organs transplanted per donor

• Retrospective study of whether meeting donor management goals (DMG) before procurement increases organs transplanted per donor (OTPD)

• Setting: UNOS Region 5, 5 SW states, 8 OPOs

• Intervention: Meeting 8+/ 10 DMG at time of organ recovery by protocolized patient care

Retrospective DMG Study

MAP 60 – 100 mm Hg

CVP 4 – 10 mm Hg

EF > 50%

Pressor ≤ 1; low dose

Thyroid hormone

ABG pH 7.30 – 7.45

PaO₂: FiO₂ > 300

Na 135 - 160 mEq/L

Glu < 150 mg/dL

UOP 0.5 – 3 mL/kg/hr

Retrospective DMG Study: Results

320 standard criteria donors, 3.6 ± 1.6 OTPD

Donors with 8+/10 DMG
- More OTPD (4.4 vs. 3.3, p<0.001)
- More likely 4+ OPTD (70% vs. 39%, p < 0.001)

Independent predictors of > 4 OTPD
- Donor-dependent criteria: Age, serum Creatinine
- Critical Care: Thyroid hormone administration
- Donor management goals met:
  - 8+/10 goals; specific DMGs

Retrospective DMG Study

Results

Achieving specific DMGs independently predicted ≥ 4 OTPD

- CVP 4 - 10 mm Hg (OR 1.9)
- EF > 50% (OR = 4.0)
- P:F > 300 (OR = 4.6)
- Na 135 – 160 mEq/L (OR = 3.4)

The impact of meeting donor management goals on the number of organs transplanted per donor: UNOS Region 5 DMG study

• Prospective, interventional study of whether meeting donor management goals increases organs transplanted per donor

• Setting: UNOS Region 5, 5 southwestern states, 8 organ procurement organizations, 2008 - 2009

• Time points:
  – Time of consent
  – 12 - 18 hours later
  – Time of organ recovery

Prospective UNOS 5 DMG Study

MAP 60 – 100 mm Hg
CVP 4 – 10 mm Hg
EF > 50%
VP ≤ 1 and low dose
ABG pH 7.30 – 7.45
PaO₂: FiO₂ > 300
Na 135-155 mEq/L
Glu < 150 mg/dL
UOP 0.5 – 3 mL/kg/hr

Prospective UNOS 5 DMG Study: Results

- 380 donors, 3.6 ± 1.7 OTPD

- 7+/ 9 DMG met over time:
  - 15% at time of consent
  - 33% at 12-18 hours
  - 48% at time of recovery

Prospective UNOS 5 DMG Study: Results

Independent predictors of > 4 OTPD

- 7+/9 DMG met at consent, recovery
- Increase in DMG met at 12-18 hr
- Age
- Serum creatinine

Optimization of donor management goals yields increased organ use

• Prospective interventional study of 8 DMGs during pre-recovery phase
• Setting: UNOS Region 11, 5 Southeastern states, 7 OPOs; from 2008 - 2009
• Intervention: Protocolized care to achieve 7+/8 DMGs prior to recovery.
• Analysis: Univariate and multivariate regression analysis correlating DMG with OTPD

UNOS Region 11 Prospective Study: Donor Management Goals

- MAP
- CVP
- pH
- \( \text{paO}_2 \)
- Na
- Glucose
- Single pressor use
- UOP

UNOS Region 11 Prospective Study: Results

- 805 donors, 2685 organs transplanted
  - Includes SCD, ECD, DCD
- All 8 DMGs met 18-66%
- OPTD
  - 2.85 - 2.96 < 8 DMGs met
  - 3.34 - 3.44 all 8 DMGs met
- Lung transplants increased 2.4 fold when all 8 DMGs met

UNOS Region 11 Prospective Study: Results

- DMGs maximizing OTPD
  - Low vasopressor use
  - P:F > 200
  - CVP 4 - 10
- DMG optimizing specific organs
  - Heart: Na, low vasopressor use
  - Lung: CVP, P:F
  - Pancreas: glucose control

Organ-specific management: Heart

- MAP 60-100 mmHg
- CVP 4 - 10 mmHg
- EF > 50 %
- Single vasopressor use & Low Dose
Organ-specific management: Lung

- CVP 4 – 10 mm Hg
- ABG pH 7.3 – 7.45
- P:F ratio > 300
Organ-specific management: Lung

• Lung recruitment maneuvers
• Early Bronchoscopy
• Serial CXR
• Turn, Suction, Mouth care Q 2hours
• CPT Q 4hours
• Vent Settings:
  – VT 10 – 12 mL/kg
  – PEEP 5
  – FiO$_2$ to SaO$_2$ > 90%
Effect of lung protective strategy for organ donors on eligibility and availability of lungs for transplantation

Design: RCT of conventional vs. lung protective ventilator management strategy

Setting: 118 patients (59 in each group)

Outcome:
1° - Eligibility criteria for lung recovery
2° - Lungs actually transplanted

JAMA 2010; 304: 2620 - 27
Effect of lung protective strategy for organ donors on eligibility and availability of lungs for transplantation

<table>
<thead>
<tr>
<th>Lung Protective Strategy</th>
<th>Conventional Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT 6-8 mL/kg IBW</td>
<td>VT 10-12 mL/kg IBW</td>
</tr>
<tr>
<td>PEEP 8-10 cm H₂O</td>
<td>PEEP 3-5 cm H₂O</td>
</tr>
<tr>
<td>Recruitment maneuvers</td>
<td>No recruitment</td>
</tr>
<tr>
<td>after vent disconnects</td>
<td>maneuvers</td>
</tr>
<tr>
<td>Apnea tests on CPAP</td>
<td>Apnea tests without CPAP</td>
</tr>
</tbody>
</table>

JAMA 2010; 304: 2620 - 27
Effect of lung protective strategy for organ donors on eligibility and availability of lungs for transplantation

Results: Lung protective strategy favored

Higher proportion of lungs met eligibility criteria
95% vs. 54% (p < 0.01)

Greater number of lungs transplanted
54% vs. 27% (p = 0.04)

JAMA 2010; 304: 2620 - 27
Organ-specific management: Kidney

- Use single pressor and low dose
- Urine Output 0.5 – 3mL/kg/hr over 4 hours
Effect of donor pretreatment with dopamine on graft function after kidney transplantation

- RCT, open-label, parallel study of 264 brain dead donors of 487 kidneys. 2004-2007. 60 European centers
- Intervention: randomized to low dose dopamine = 4 mcg/kg/min or none
- Outcomes: Need for dialysis in first week post transplant

*JAMA*. 2009 Sep 9; 302(10): 1067-75
Donor pretreatment with dopamine: Results

<table>
<thead>
<tr>
<th>Dialysis P value</th>
<th>DA</th>
</tr>
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<tbody>
<tr>
<td>Any</td>
<td>24.7%</td>
</tr>
<tr>
<td>0.01</td>
<td></td>
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</table>

Multiple dialyses associated with graft failure at 3 years. HR 3.61 (2.39-5.45)

JAMA. 2009 Sep 9; 302(10): 1067-75
Organ-specific management: Liver

• Maintain Na < 155
  Na > 155 can cause swelling after liver transplant
Organ-specific management: Pancreas and Intestine

Tight Glucose control < 150 mg/dL

OGT/NGT Low Intermittent Wall Suction
Role of Intensivist in Donor Management

Increase in organs recovered with close involvement of intensivist in donor care

66/210 → 113/258 potential organs recovered

Am J Transplant 2011; 11: 1-5
# Swedish Medical Center: Organ Donation

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013 January-Sept (Annualized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain Dead Donors</td>
<td>17</td>
<td>11</td>
<td>15</td>
<td>10 (13)</td>
</tr>
<tr>
<td>DCD Donors</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Total Organs</td>
<td>61</td>
<td>44</td>
<td>58</td>
<td>40 (53)</td>
</tr>
<tr>
<td>OTPD</td>
<td>3.39</td>
<td>3.14</td>
<td>2.94</td>
<td>3.07</td>
</tr>
<tr>
<td>Timely Referral Rate</td>
<td>91%</td>
<td>96%</td>
<td>98%</td>
<td>100%</td>
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</table>
# Swedish Medical Center: Tissue and Eye Donation

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013 January – Sept (Annualized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue</td>
<td>80</td>
<td>53</td>
<td>62</td>
<td>47 (63)</td>
</tr>
<tr>
<td>Eye</td>
<td>91</td>
<td>96</td>
<td>95</td>
<td>106 (141)</td>
</tr>
</tbody>
</table>
National Goals for Organ Donation from HHS/HRSA

- Organs transplanted per Donor (OTPD) 3.75
- 10% of donations by DCD
- >97% Timely referral rate
  Within 60 minutes of clinical triggers
National Goals for Organ Donation from HHS/ HRSA

• OTPD 3.75
  SMC = 2.94 for 2012. 3.07 for 2013.

• 10% of donations to be DCD
  SMC = 25% for 2012. 23% for 2013.

• >97% Timely referral rate
  Within 60 minutes of clinical triggers
  SMC = 98% for 2012. 100% for 2013
Organ Viability Research Project at Swedish Medical Center

- **Focus:** Collect data of 9 DMGs from time of brain death declaration to DA management

- **Goal:** Develop protocol for donor management to increase OTPD $> 3.7$

- **Scope:** Prospective chart review, starting June 2013
SMC Donor Management Order Set

• Initiated at time of declaration of brain death
• Directs care of patient until Donor Alliance team arrives in ICU to assume donor care
• Targets 9 Donor Management Goals of UNOS 5 and UNOS 8 studies
• Protocolized fluid resuscitation followed by pressor administration
• Modifies ventilator management to target tidal volume 8-10 mL/kg