Maximizing the Possibility: Organ Donation

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Objectives

• Overview of donation process
• Define decoupling and its importance
• Overview of donor management process
  – Emphasis on RT-related aspects of care
Declarations

• None
OVERVIEW OF DONATION PROCESS
A brief history

- Early 1900s-European doctors attempted transplant from various animals, including monkeys, pigs and goats.
- 1954: the first successful living-related kidney transplant led by Dr. Joseph Murray and Dr. David Hume at Brigham Hospital in Boston
- 1960: British immunologist Peter Medawar received the Nobel Prize for his discovery of acquired immune tolerance. Anti-rejection drugs follow
- 1962-1967: First successful kidney...lung...pancreas/kidney...liver, all in the US
- 1967: First successful heart transplant led by Barnard at Groote Schuur Hospital in Cape Town, South Africa.
- 1968: First successful heart transplant in the United States led by Shumway at Stanford University Hospital, CA
History

• 1984: National Organ Transplant Act (NOTA)
  – establishes nationwide computer registry operated by the United Network for Organ Sharing (UNOS);
  – authorizes financial support for Organ Procurement Organizations (OPOs);
  – prohibits buying or selling of organs in the United States

• 1989: First successful small intestine transplant (a near-total small bowel from a deceased donor) into a child, led by Goulet in Paris, France.
Organ donation in the US

• To maintain listings of potential organ recipients, the Department of Health and Human Services (HHS) contracts the United Network of Organ Sharing (UNOS)

• Local organ procurement organizations (OPOs): non-profits authorized by the Health Care Financing Administration (now CMMS) and UNOS to manage the procurement of organs in their region.
CMS requirement

- CMS requires every accredited hospital to have a written protocol outlining agreement with an OPO.
- 58 OPOs nationwide.
- Midwest Transplant Network covers KS and western 2/3 of MO.
Midwest transplant network
It’s the law

- KS Statute 77-205: Determination of death (1971)
  - “An individual who has sustained either
    - (1) irreversible cessation of circulatory and respiratory functions
    - or
    - (2) irreversible cessation of all functions of the entire brain, including the brain stem, **is dead.**”

- “A determination of death must be made in accordance with **accepted medical standards**”
The Process... in 1 slide!!

OPOs responsible for organizing and overseeing the following:

- Identification of donors
- Evaluation of potential donors
- Confirmation of diagnosis of brain death or care withdrawal decision by family
- Arranging consent from family
- **Clinical management of organ donor**
- Obtaining permission for visiting transplant surgeons to remove organs at the location of the donor
- Preservation and packaging of organs for transplant
UNOS data
WHAT ROLE DOES APPROPRIATE SUPPORT OF THOSE WITH POTENTIALLY CATASTROPHIC BRAIN INJURIES PLAY IN SUCCESSFUL ORGAN PROCUREMENT?
Case 1

• 17 y/o male diagnosed with Type I diabetes 6 mo prior jumped from moving car to impress his girlfriend. Struck back of head on pavement.

• Rendered unconscious immediately. Transported to ED via EMS C-collar, backboard, non-rebreather mask.

• On arrival to ED unresponsive, grunting respirations, hypertensive and bradycardic.

• Intubated, taken for CT...
Non-Contrast head CT at admit
Non-contrast head CT 30 hours from admit
CHIEF COMPLAINT: Traumatic brain injury with contusions.

HISTORY: A 17-year-old male who jumped out of a car while moving, striking his head.

The patient has continued to deteriorate. The patient is requiring less sedation and is responding less...

Earlier in the day he was decerebrate in the arms, the sedation has been cut in half and when I examined him now he has minimally reactive pupils that are disconjugate and no response to sensory or motor stimuli.

CT done today shows evolutionary changes in the contusion. He has a large left middle cerebral arterial infarction involving most of the left temporal lobe portion of the frontal lobe. There is no shift, however, tentorial herniation is a little more prominent than it was before and he has a new finding of a foramen magnum herniation with the tonsils well down into the foramen magnum with medullary compression.

The loss of gray white distinction is more prominent.

The ventricles are still open. The suprasellar cistern is open, but all of the other cisterns and sulci are closed.

DIAGNOSTIC ASSESSMENT: Significant progression of traumatic brain injury with findings essentially incompatible with life.

I had my morning conversation with the patient's mother, I told her that things had worsened, educate about the foramen magnum and the tentorial area and that I thought it was more likely than not, that we would lose him at this point. She wanted immediately to know what was going to be involved, I said we contact radiology to get isotope set up for an isotope flow study.

We will continue to taper the sedation and if I am correct, as we taper the sedation, he will not become alert.

She verbalized spontaneously that she wanted to donate whatever could be donated, she wanted to be able to have an open casket, so obviously she has been thinking about this.
A QUICK WORD: 
“DECOUPLING”

What is it?

Why does it matter??
Decoupling

• Simple concept: Keep separate the discussion of brain death from the discussion of organ donation

• Garrison et al 1991, study of potential donors with no known objection to donation:
  – In uncoupled discussion, 11/62 donated
  – Employing decoupling, 53/82

• Rodrique et al 2006
  – Donation was more likely when next-of-kin approached about donation by an OPO coordinator
    – (OR= 3.74, CI = 2.2, 6.4)

• LEAVE DONATION DISCUSSION TO THE PROFESSIONALS
Brain Death

• Commonly d/t catastrophic brain injury (CBI)

• Clinical Exam: Absence of brainstem reflexes
  – Pupillary
  – Facial Motor/Sensation (Corneal)
  – Pharyngeal (Gag)
  – Tracheal (Cough)
  – Oculocephalic (doll’s eye)
  – Vestibulo-ocular (Cold Caloric)
Brain death
Apnea testing

• Prerequisites
  – Core temperature ≥ 36°C or 97°F
  – Systolic blood pressure ≥ 90 mm Hg
  – Euvolemia or positive fluid balance in the previous 6 hours
    • i.e. hemodynamically stable

• Before starting apnea test
  – Draw Preliminary ABG (adjust vent to bring pCO2 into the 40’s)
  – Pre-oxygenate for 10 minutes with 100% oxygen
Apnea test

• Connect a pulse oximeter and disconnect the ventilator
• Deliver 100% O₂, 6 l/min, into the trachea

  *Option: put the pt on blow-by*

• Look closely for respiratory movements
  – Abdominal or chest excursions that produce adequate tidal volumes
• Measure arterial PO₂, PCO₂, and pH after approximately 8-10 minutes and reconnect the ventilator

• *Clinician at bedside*

• If hemodynamic instability ensues, discontinue test
Apnea test

• Positive Test: Supports Brain Death
  – respiratory movements are absent
  – arterial PCO₂ is ≥ 60 mm Hg (*option: 20 mm Hg increase in PCO₂ over a baseline normal PCO₂*)

• Negative Test: Does Not Support the Clinical Diagnosis of Brain Death
  – respiratory movements are observed
  – Pt placed back on vent

• Consider other ancillary testing: angiography, EEG, SSEP, TCDs
Pathophysiology of Brain Death

Widespread physiologic changes that cross multiple organ system and can lead to hemodynamic compromise.
Catastrophic Brain Injury

- Endocrine Abnormalities
- Electrolyte Disorders
- Pulmonary Injury
- Neurologic Manifestations
- Coagulopathy
- Hypothermia
The Progression of Brain Death

Cerebral Ischemia:
- Body tries to preserve cerebral blood flow
- Cushing’s Triad: Hypertension, bradycardia and abnormal breathing

Brain Stem Ischemia:
- "Autonomic Storm" - 800 to 1200 times increase in catecholamine levels in blood
- Increased heart rate, mean arterial pressure, cardiac oxygen demands

Spinal Ischemia:
- May occur minutes to hours after storm
- Loss of sympathetic overdrive
- Vasodilation, decreased blood pressure and heart rate
- GREATEST RISK TO ORGAN DONORS
Hormonal and Electrolyte Disorders

• Decrease in Anti-Diuretic Hormone (ADH), T₃, Cortisol and Insulin
  • ADH leads to Diabetes Insipidus = massive fluid loss through urination
  • T₃ Cardiac cells switch to anaerobic metabolism

All of this causes electrolyte disorders:

- Hypernatremia
- Hyper/hypokalemia
- Hypocalcemia
- Hypo/hyperglycemia
Hypothermia

- Loss of function of the hypothalamus leads to poikilothermia (inability to regulate, thus becoming temperature of environment)

Causes:
- Cardiac dysfunction
- Reduced tissue oxygenation
- Impaired renal function, and...
Coagulopathy

• As a result of release of thromboplastin and plasminogen from necrotic brain tissue

• And a result of hypothermia

• ...And Plasmadilution
Pulmonary Injury

- Aspiration...VAP...ARDS
- VILI
- Neurogenic pulmonary edema
Figure 1. Simplified comparison of the complexities of the intensive care unit (ICU) physician's options and those of the airline pilot. *PEEP*, positive end-expiratory pressure.
Michael Moncure, MD:

“THESE ARE THE SICKEST OF THE SICK”

Q: What role does appropriate support of those with catastrophic brain injuries play in successful organ procurement?
CV management

- MAP 60-100 mmHg
- CVP 4-10 mmHg (?)
  - SVV
- EF > 50 %
- Single vasopressor use & Low Dose
Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge.

Osman et al. Crit Care Med 2007;35(1)
Lung Tx Overview

- Lung recruitment maneuvers
  - Carefully...
- Early Bronchoscopy
- Serial CXR
- Turn, Suction, Mouth care q 2hours

- CPT Q 4hours
- Vent Settings:
  - VT 10 – 12 mL/kg
  - PEEP 5
  - FiO2 to SaO2 > 90%
- PRONATE
Lung protective ventilation

The New England Journal of Medicine

VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

ABSTRACT

Background Traditional approaches to mechanical ventilation use tidal volumes of 10 to 15 ml per kilogram of body weight and may cause stretch-induced lung injury in patients with acute lung injury and the acute respiratory distress syndrome. We therefore conducted a trial to determine whether ventilation with lower tidal volumes would improve the clinical outcomes in these patients.

THE mortality rate from acute lung injury and the acute respiratory distress syndrome is approximately 40 to 50 percent. Although substantial progress has been made in elucidating the mechanisms of acute lung injury, there has been little progress in developing effective treatments.

Traditional approaches to mechanical ventilation
Lung protective ventilation

- Traditional ventilation of ARDS → stretch-induced lung injury
- Comparing 12cc/kg vs 6cc/kg PBW
- Ppl 50 cm H20 or less vs Ppl 30 or less

- Low TV reduced mortality (31% vs 39.8%, p=0.007)
  - Why? Less heart, renal, coagulation failure
Effect of a Lung Protective Strategy for Organ Donors on Eligibility and Availability of Lungs for Transplantation
A Randomized Controlled Trial

• RCT of conventional N= 59 (10-12cc/kg IBW) vs. N=59 lung protective (6cc/kg) ventilator management strategy

• 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)
Protocol:

- Alveolar recruitment
  - PC ventilation at an IP of 25 cm H₂O and
  - PEEP of 15 cm H₂O for 2 h.
- Switched to VC with a TV of 10 ml/kg and a PEEP of 5 cm H₂O (22, 23).
  - Successful if P:F improved to greater than 300 and CXR had substantial improvement after 30 min of conventional ventilation (final PaO₂/FiO₂)
- Clinically assessed donor fluid balance, minimized use of crystalloids, and diuretics to maintain a neutral or negative fluid balance after initial resuscitation.
- HOB 30 degrees
- inflated ET balloon to 25 cm H₂O.
- Bronchoscopy
San Antonio Lung Transplant (SALT) protocol

14.5% increase (11.5%-25.5%) in lung procurement rate.

- This increase was WITHOUT compromising pulmonary function, LOS or survival of recipients.
- Increase to 25% procurement rate, if applied nationally, would double lung transplantation procedures.

Lung Tx Overview

- Lung recruitment maneuvers
  - Carefully...
- Early Bronchoscopy
- Serial CXR
- Turn, Suction, Mouth care q 2 hours

- CPT Q 4 hours
- Vent Settings:
  - VT 10 – 12 mL/kg
  - PEEP 5
  - FiO2 to SaO2 > 90%

- PRONATE
Pronating donors?
PROSEVA

- 474 patients randomized 26 French ICUs (and one in Spain) with severe ARDS (PaO₂:FiO₂ ratio of <150 mm Hg, PEEP >5, FiO₂ > 0.60, Berlin definition) to:
  - standard care, vs
  - "proned" 16 hrs/day daily for up to 28 days (or longer at discretion of provider).

- mortality at 28 days
  - 16% prone, (38 deaths in 237 patients) vs.
  - 33% in the supine group (75 of 229 patients), p< 0.001.

- 17% ARR; benefit only slightly smaller at 90 days

Reduced mortality (risk ratio 0.74). **NNT = 11**

Benefits in addition to standard low tidal volume ventilation, which all patients received.

Mortality lower with long durations of prone positioning (>16 hours/day), but not with durations <16 hours/day.

Mortality reduced among patients with severe hypoxemia, but not in mild or moderate hypoxemia.

Notably, prone positioning did not reduce mortality in the authors' pooled analysis of 5 other trials that did not require LT V V.

This + enrollment of patients with less-severe ARDS may explain dilution of effect size.
Pronating donors...?

• Several lines of evidence: prone positioning could prevent ventilator-induced lung injury (e.g. collapsing/reopening cycle, proning markedly reduces overinflated lung areas while promoting alveolar recruitment)

• In several previous trials, observed benefits ≠ better patient outcomes, since no significant improvement was observed in patient survival with prone positioning.

• But RCTs show oxygenation significantly better when patients are in the prone position than when they are in the supine position.
Pronating donors?!
Yes...PRONATION

NOT FOR THE FAINT OF HEART
• CBI pt
• P:F pre-tx: 84

• Q2H CPT, albuterol MDI, LRM. Proned for 8, 14, and 9 hour periods.

• P:F post 462; lungs procured
20-pack year smoker

Trauma; CBI; proned

P:F pre-tx: 107

P:F post: 380

Lungs procured
40-pack year smoker

Baseline CXR
Right Basilar atelectasis

Baseline CXR
CXR nine hours later.
Complete resolution of RLL

P:F pre-tx: 212

P:F post: 377

Proned for 8 hours
Lungs procured.
Benefit of a single recruitment maneuver after an apnea test for the diagnosis of brain death

Marie Paries¹, Nicolas Boccheciampe¹, Mathieu Raux¹,², Bruno Riou³,⁴, Olivier Langeron¹,⁴ and Armelle Nicolas-Robin¹,⁴*

Figure 2 Variation of arterial oxygen tension/fractional inspired oxygen (PaO₂/FiO₂) ratio. (a) From the end of the apnea test before reconnection (T2) to 2 hours after reconnection (T3). (b) From before the apnea test (T1) to 2 hours after reconnection (T3). Values are medians with 25th and 75th percentiles (boxes) and 95th and 5th percentiles (whiskers). RM, recruitment maneuver.

- Marked decrease in P:F as a result of apnea restored by RM.
% potential lung donors with \( \frac{\text{PaO}_2}{\text{FiO}_2} > 300 \text{ mmHg} \) (%)

control    RM

\[ p < 0.05 \]
Meet donor management goals!

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Goal</th>
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<tbody>
<tr>
<td>Mean arterial pressure</td>
<td>60–100 mm Hg</td>
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<tr>
<td>Central venous pressure</td>
<td>4–10 mm Hg</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>&gt;50%</td>
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<tr>
<td>Vasopressors</td>
<td>≤1 and low dose(^a)</td>
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<tr>
<td>Arterial blood gas pH</td>
<td>7.3–7.45</td>
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<tr>
<td>(\text{Pao}_2;\text{Fio}_2)</td>
<td>&gt;300</td>
</tr>
<tr>
<td>Serum sodium</td>
<td>135–155 mEq/L</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>&lt;150 mg/dL</td>
</tr>
<tr>
<td>Urine output</td>
<td>0.5–3 mL/kg/hr over 4 hrs</td>
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</table>
Optimization of Donor Management Goals Yields Increased Organ Use


From the *Department of Surgery, University of Louisville, Louisville, Kentucky; †Kentucky Organ Donor Affiliates, Louisville, Kentucky; and ‡LifeShare of The Carolinas, Charlotte, North Carolina

Multiple strategies have been used in an effort to increase the pool of organs for transplantation. Standardizing donor management has produced promising results. Donor management goals (DMGs) are now being used as end points of intensive care unit care during the prerecovery phase but no prospective results have been reported. Data from the United Network for Organ Sharing Region II were collected for successful achievement of eight common donor management goals (mean airway pressure [MAP], central venous pressure [CVP], pH, PaO₂, sodium, glucose, single pressor use, and urine output) before organ recovery. Two time periods were studied with different panels of DMGs. The analysis identified the success rate of transplantation. Goals were stratified by their statistical correlation with the number of organs transplanted per donor (OTPD) in an effort to identify the most important parameter(s). Eight hundred five organ donors were studied with 2,685 organs transplanted. DMGs were assessed through two phases of the study. Achieving DMGs rose from 18 to 66 per cent associated with significant improvement in OTPD (range, 2.96 to 3.45). The success of transplantation was primarily associated with limitations in vasopressor use and PaO₂. Tight glucose control did affect the rate of pancreatic transplants. Thoracic organs were the most sensitive to DMGs with a 10- to 15-fold increase in lung transplantation when PaO₂ rose above 100 mmHg. MAP, CVP, pH, sodium, and urine output had little effect on transplantation. Standardization of end points of donor management was associated with increased rates of transplantation. Surprisingly, not all standard goals are necessary for optimal organ use. The most significant parameters were the low use of vasopressor agents and oxygenation. Donor management strategies should strive to optimize these goals.
Clinical Investigations

The impact of meeting donor management goals on the number of organs transplanted per donor: Results from the United Network for Organ Sharing Region 5 prospective donor management goals study*

Conclusions: Meeting donor management goals prior to consent and prior to organ recovery were both associated with achieving ≥4 organs transplanted per donor. However, only 15% of donors have donor management goals met at the time of consent. The donor hospital management of patients with catastrophic brain injuries, before the intent to donate organs is known, affects outcomes and should remain a priority in the intensive care unit. (Crit Care Med 2012; 40:2773–2780)
PRESERVING THE OPTION FOR DONATION

• Adequate resuscitation and care

• Brain death testing should be delayed until hemodynamically stable and warm!

• Translates into assuring GOOD PATIENT CARE

  – CBIGs can help
Catastrophic Brain Injury Guidelines

Consider obtaining a critical care consult if not already involved in patient care

**Maintain SBP > 100 (MAP > 60)**
1. Consider invasive hemodynamic monitoring
2. Adequate hydration: Ensure adequate hydration to maintain euolemia
3. Vasopressor support: If hypotensive post adequate rehydration, utilize Neosynephrine as the first pressor of choice up to 2 mcg/kg/min followed by Dopamine if needed

**Maintain Urine Output > 0.5 ml/kg/hr < 400 ml/hr** (consider DI if > 400 ml/hr x 2 hours)
1. Treat Diabetes Insipidus with Vasopressin drip 1-2.5 u/hr, if UO still > 400 ml/hr, give DDAVP 0.5 mcg 1IVP every 2-3 hours
2. If UO falls below 0.5 ml/kg/hr, assess fluid status - may need rehydration or BP support

**Maintain PO2 > 100 & pH 7.35-7.45**
1. Adequate ventilation: 5.0-8.0 PEEP
   - aggressive respiratory hygiene if not contraindicated by patient’s condition (suction and turn every 2 hours)
   - respiratory treatments to prevent bronchospasm

**Other orders to consider:**
1. Monitor and treat electrolytes maintaining the following:
   - Sodium: 134 – 145 mmol/L
   - Potassium: 3.5 – 5.0 mmol/L
   - Magnesium: 1.8 – 2.4 mg/dL
   - Phosphorus: 2.0 – 4.5 mg/dL
   - Ionized Calcium: 1.12 – 1.3 mmol/L
2. Monitor glucose and treat with insulin drip if needed (keep 80-200) rather than SQ
3. Monitor and treat Hgb/Hct/coagulation factors (especially if GSW or other penetrating head injury)
   - Maintain Hgb > 8.0 g/dL and Hct > 24%
   - If PT > 18.0 give 2u FFP
   - If Fibrinogen < 70 give 2u FFP, if < 70 give cryoprecipitate
   - If platelets < 50 give 6pk of platelets
   - *remember to recheck labs after treatment
4. Maintain temp 36-37.5 Celsius with Bair hugger/warming-cooling blanket
Case 1

• Pt a registered donor in the Organ donor registry
• Did *not* become an organ donor.
• Discharged from Rehab and went home with his mother...
• A success of the organ donation process.
11/16 @ 2254: Diffuse bilateral pulmonary opacities left greater than right, pulmonary edema versus atelectasis.
Over the next 35 hours...

- 11/16 @ 2305: 7.24/33.1/192/-13/14.3 99% on 100% FiO2
- 11/17 @ 0107: 7.30/31.8/227/-11/15.8 100% on 100% FiO2
- 11/17 @ 0510: 7.42/30/97/-4.6/18.9 97% on 50% FiO2
- 11/17 @ 1139: 7.38/33.9/123/-5/20 99% on 50% FiO2
- 11/17 @ 1449: 7.42/35.5/447/-1/23 100% on 100% FiO2
- 11/17 @ 1715: 2nd bronch – small amount light yellow secretions in right upper lobe, easily cleared, no re-pooling
- 11/17 @ 2301: 7.52/30.0/431/1/24.3 100% on 100% FiO2
- 11/18 @ 1049: 7.48/38.2/529/5/28.3 100% on 100% FiO2
Lessons Learned: Being Persistent Pays Off
Never say “Never”!!!
Conclusion

• Complex clinical process

• Enlist the professionals

• Have a plan:
  – CBIGs
Conclusions and Relevance  Our analysis demonstrated that more than 2 million life-years were saved to date by solid-organ transplants during a 25-year study period. Transplants should be supported and organ donation encouraged.

Importance  The field of transplantation has made tremendous progress since the first successful kidney transplant in 1954.
Lily received a liver transplant as an infant. Three years post-transplant she had grown to an active 4 year old. And was married on the 24th anniversary of her transplant.
Working together. Saving lives.

UNOS unites the transplant community to save lives through organ transplantation. More >

Transplant Trends

<table>
<thead>
<tr>
<th>Description</th>
<th>Number</th>
</tr>
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<tbody>
<tr>
<td>Waiting list candidates as of today 9:22am</td>
<td>123,364</td>
</tr>
<tr>
<td>Active waiting list candidates as of today 9:22am</td>
<td>78,179</td>
</tr>
<tr>
<td>Transplants January - December 2014</td>
<td>32,109</td>
</tr>
<tr>
<td>Donors January - December 2014</td>
<td>15,670</td>
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Kentucky woman donates kidney to stranger, falls in love

When Ashley McIntyre offered to donate her kidney to a stranger, she had no idea she’d end up spending the rest of her life with him.