DONOR ALLIANCE
Organ & Tissue Donation

Maximizing Organ Donation through Donor Management Goals

Mary Laird Warner, MD, FCCP

Medical Director, Intensive Care Unit

Swedish Medical Center

Associate Professor,

Pulmonary and Critical Care Medicine,

National Jewish Health

2013 Western Colorado DONATION SUMMIT

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

Organ	United States	Colorado
Total	130,195	2,454
Kidney	104,773	1,683
Liver	16,530	621
Pancreas	1,185	24
Kidney / Pancreas	2,122	34
Heart	3,616	46
Lung	1,666	46
Heart / Lung	48	0
Intestine	255	0

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

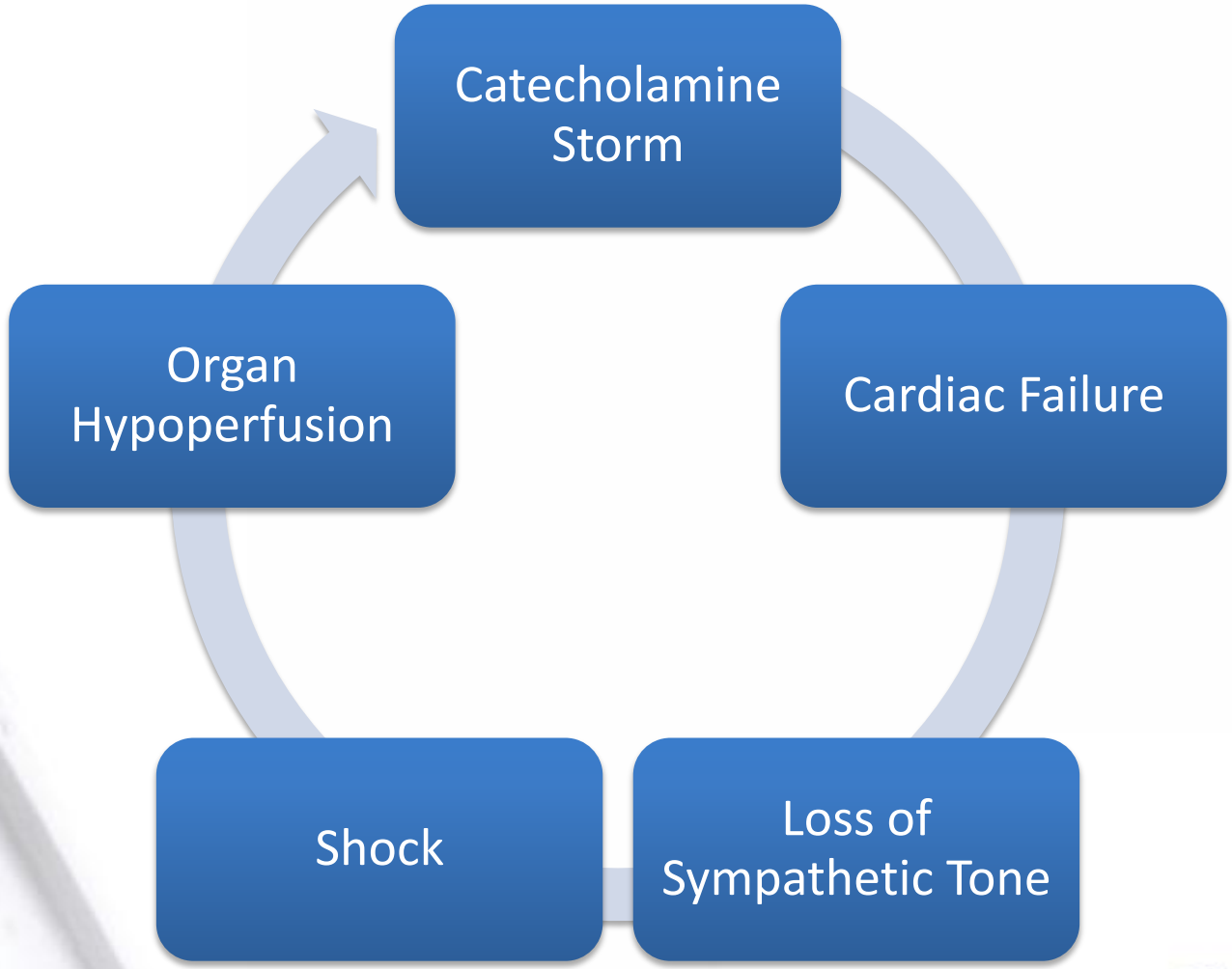
- Donation after Brain Death (BD):
  - Heart
  - Lungs (2)
  - Kidneys (2)
  - Liver
  - Pancreas
  - Small Intestine
- Donation after Cardiac Death (DCD):
  - Lungs (2)
  - Kidneys (2)
  - Liver

Pathophysiology of Brainstem Death

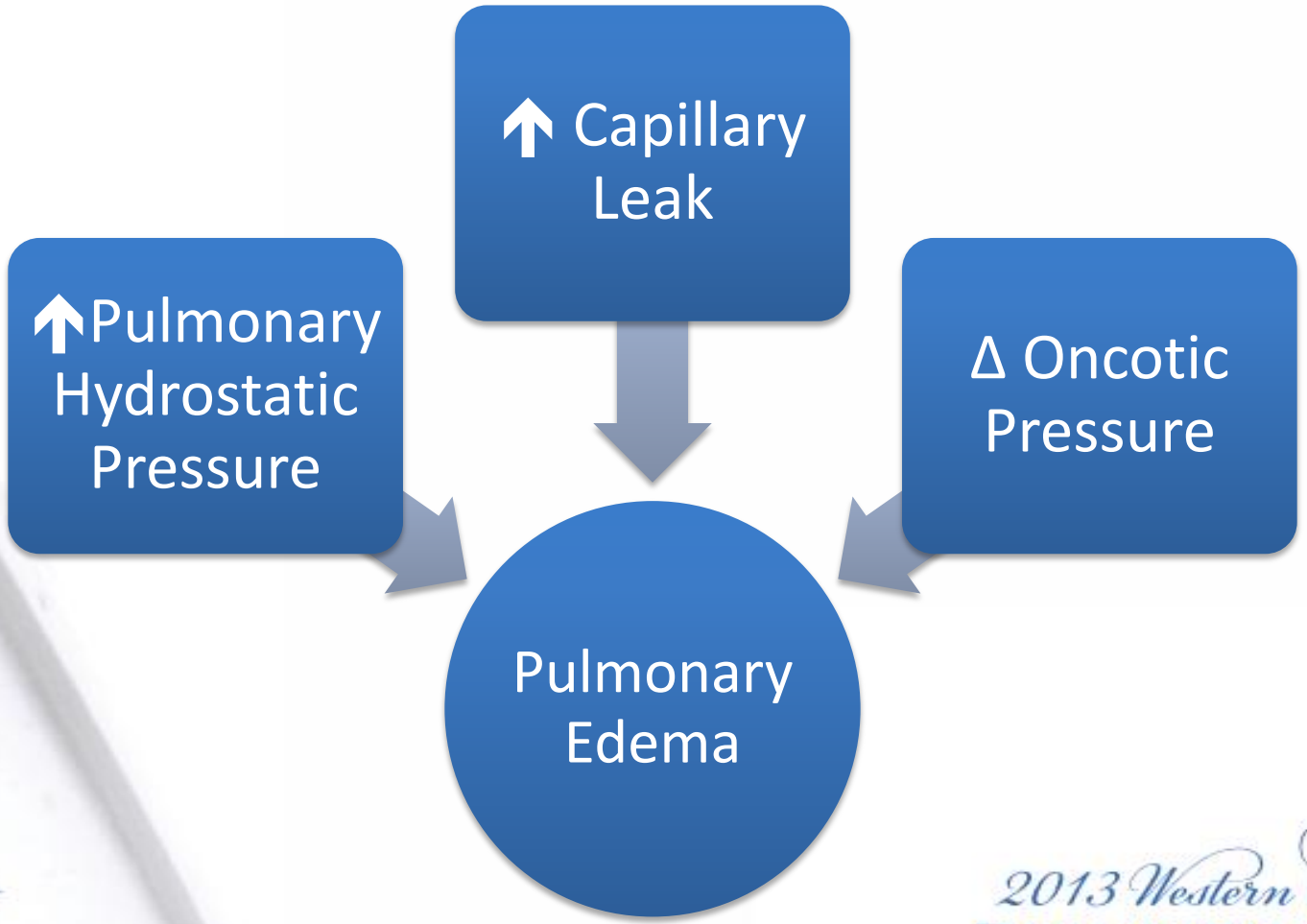
Increased intracranial pressure (ICP) causes

- Cushing's reflex
- Catecholamine surge
- Visceral ischemia
- Pro-inflammatory state
- Disseminated intravascular coagulation
- Multi-organ failure

Pathophysiology of Brain Death: Cardiovascular Changes



Pathophysiology of Brain Death: Pulmonary Changes



Pathophysiology of Brain Death: Endocrine and Metabolic Changes

Anterior Pituitary Failure:

↓ ACTH → Adrenal Insufficiency

↓ TSH → Sick Euthyroid

Posterior Pituitary Failure:

↓ Vasopressin → Diabetes Insipidus

Hypothalamic Failure

Adrenal Insufficiency:

↓ Cortisol

↓ Insulin

Hypothermia

↓ Basal Metabolic Rate

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.

Am J Transplant. 2002 (2): 761-768.
Can J Anaesth. 2006: 53 (8); 820 – 820
Br. J. Anaesth. (2012) 108 (suppl 1): i96-i107

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

Can J Anaesth 1990;37:806-12

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

Am J Transplant 2002 (2): 761-768.

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 (pCO_2 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 (pCO_2 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° 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/cm^5
   - Cardiac Index ≥ 2.5 l/min/M^2
   - Left Ventricular Stroke Work Index > 15
   - dopamine dosage < 10 mcg/kg/min

UNOS Critical Pathway (CP): 1999 pilot study

Table 1: Organs recovered

	Pre-Critical Pathway		Critical Pathway	
Organ	N	Per 100 donors	N	Per 100 donors
Kidney	255	182.1	235	180.8
Liver	119	85.0	116	89.2
Pancreas	33	23.6	53	40.8
Heart	77	55.0	78	60.0
Lung	45	32.1	59	45.4
Intestine	5	3.6	6	4.6
Total	534	381.4	547	420.8

10.3% increase in total organs recovered

Am J Transplant 2002; 2: 761-768

UNOS Critical Pathway (CP): 1999 pilot study

Table 2: Organs transplanted

Organ	Pre-Critical Pathway N	Pre-Critical Pathway Per 100 donors	Critical Pathway N	Critical Pathway Per 100 donors
Kidney	224	160.0	218	167.7
Liver	109	77.9	99	76.2
Pancreas	26	18.6	41	31.5
Heart	64	45.7	71	54.6
Lung	31	22.1	40	30.8
Intestine	0	0.0	0	0.0
Total	454	324.3	469	360.8

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

Transplantation 2003; 75: 482-487.

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

B J 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

J Trauma. 2011 Oct; 71 (4): 990-5

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

PaO_2: FiO_2 > 300

Na 135 - 160 mEq/L

Glu < 150 mg/dL

UOP 0.5 – 3 mL/kg/hr

J Trauma. 2011 Oct; 71 (4): 990-5

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

J Trauma. 2011 Oct; 71 (4): 990-5

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)

J Trauma. 2011 Oct; 71 (4): 990-5

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

Crit Care Med. 2012 Oct; 40 (10): 2773-80

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

PaO_2: FiO_2 > 300

Na 135-155 mEq/L

Glu < 150 mg/dL

UOP 0.5 – 3 mL/kg/hr

Crit Care Med. 2012 Oct; 40 (10): 2773-80

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

Crit Care Med. 2012 Oct; 40 (10): 2773-80

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

Crit Care Med. 2012 Oct ; 40 (10): 2773-80

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

Am Surg. 2010 Jun; 76 (6): 587-94.

UNOS Region 11 Prospective Study: Donor Management Goals

- MAP
- CVP
- pH
- paO_2
- Na
- Glucose
- Single pressor use
- UOP

Am Surg. 2010 Jun; 76 (6): 587-94

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

Am Surg. 2010 Jun; 76 (6): 587-94

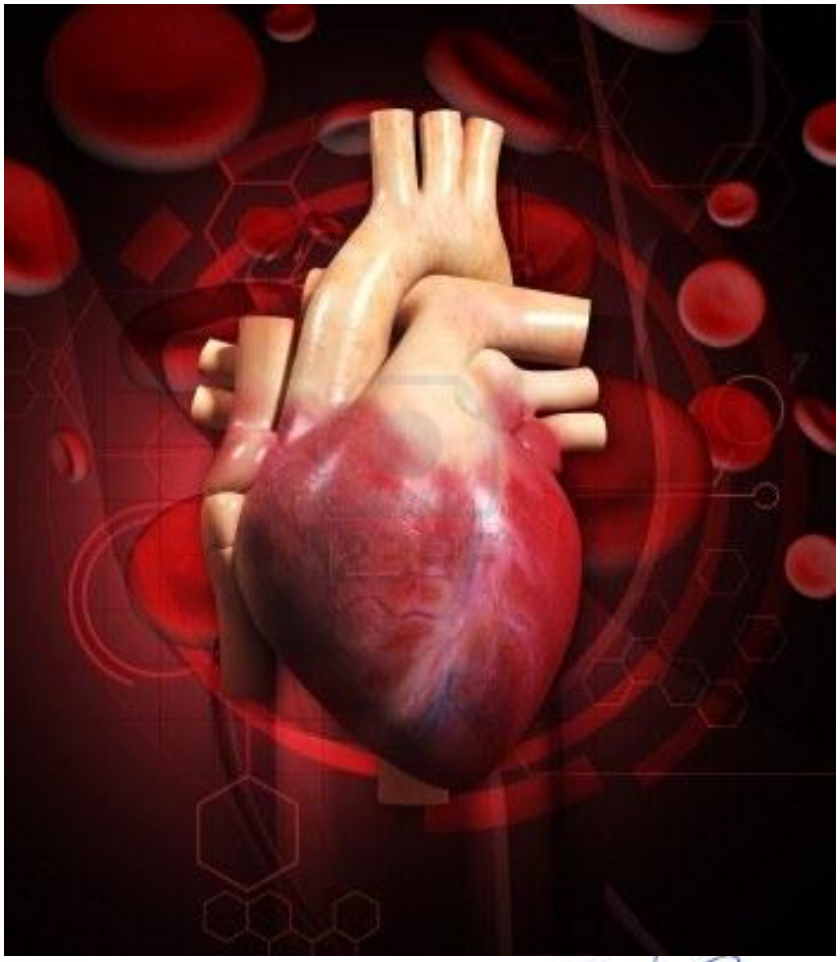
UNOS Region 11 Prospective Study: Results

- 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

Am Surg. 2010 Jun; 76 (6): 587-94

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

Lung Protective Strategy	**Conventional Strategy**
VT 6-8 mL/kg IBW	VT 10-12 mL/kg IBW
PEEP 8-10 cm H_2O	PEEP 3-5 cm H_2O
Recruitment maneuvers after vent disconnects	No recruitment maneuvers
Apnea tests on CPAP	Apnea tests without CPAP

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

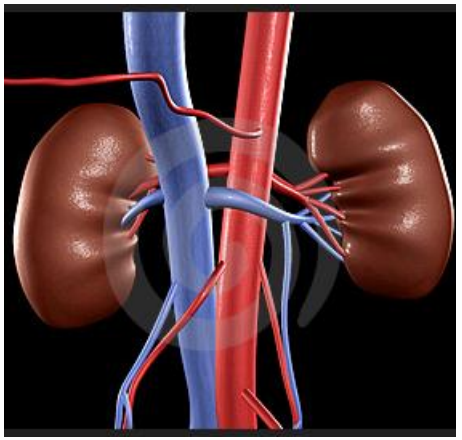
54% vs. 27% ($p = 0.04$)

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

Dialysis P value	DA	Non-DA
Any 0.01	24.7%	35.4%

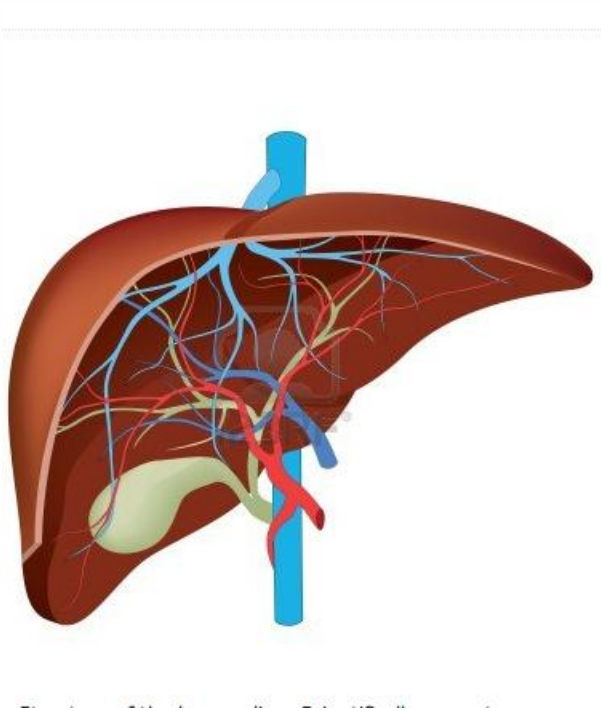
Multiple dialyses associated with graft failure at 3 years. HR 3.61 (2.39-5.45)

JAMA. 2009 Sep 9; 302(10): 1067-75

Organ-specific management: Liver

- Maintain Na < 155

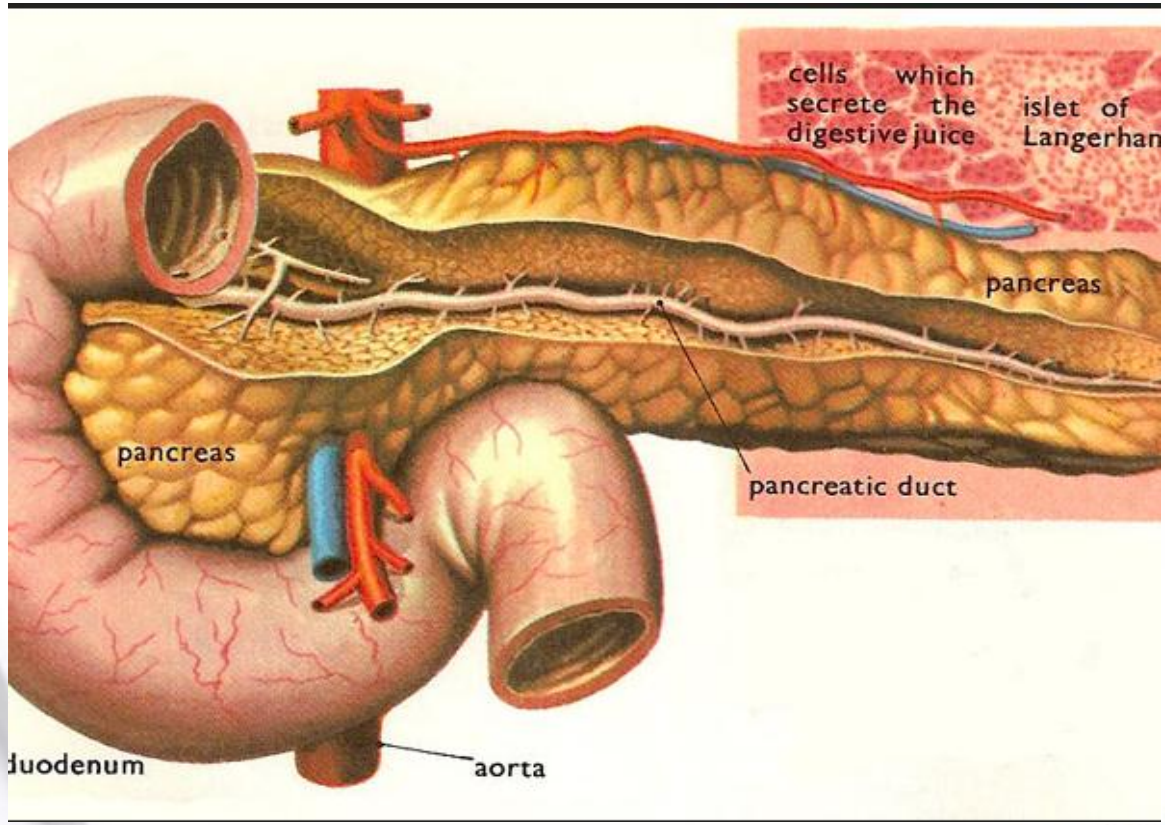
  Na > 155 can cause swelling after liver transplant



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

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Swedish Medical Center: Organ Donation

	2010	2011	2012	2013 January-Sept (Annualized)
Brain Dead Donors	17	11	15	10 (13)
DCD Donors	1	3	5	3 (6)
Total Organs	61	44	58	40 (53)
OTPD	3.39	3.14	2.94	3.07
Timely Referral Rate	91%	96%	98%	100%

Swedish Medical Center: Tissue and Eye Donation

	2010	2011	2012	2013 January – Sept (Annualized)
Tissue	80	53	62	47 (63)
Eye	91	96	95	106 (141)

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 $\geq$ 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

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