THORACIC ORGAN DONOR MANAGEMENT

A. Neyrinck, MD
University Hospitals Leuven
Department of Anesthesiology

Arne.neyrinck@uzleuven.be
• outline:
  – pathophysiology of brain death
  – the catecholamine roller coaster
  – hormonal resuscitation
  – biomarkers
  – donor management protocols
  – specific aspects of heart/lung donor management
DONOR ORGAN INJURY

INFLAMMATORY DONOR ORGAN INJURY

OXIDATIVE STRESS

INFLAMMATION

HOMEOOSTASIS

PHYSICAL FORCES

NHBD

Preservation

Reperfusion

Warm ischemia

Brain death
Warm ischemia
PATHOPHYSIOLOGY OF BRAIN DEATH
**BRAIN DEATH**

- ↑ Intracranial pressure
- Venous outflow obstruction
- Brain swelling
- Arterial compression
- Pituitary + hypothalamic disregulation
- Cushing response: bradycardia and hypertension
- Autonomic storm: tachycardia and hypertension
- Sympathetic paralysis: bradycardia and hypotension

BRAIN DEATH → SOMATIC DEATH
BRAIN DEATH

Supratentorial expanding mass

Brain Ischemia

Brain swelling

Intracranial pressure

Venous outflow obstruction

At i l i

Brain Ischemia

Spinal cord ischemia

at least up to mid cervical level

Vagal + sympathetic (pontine)

Vagal + sympathetic (lower medulla)

Vagal + sympathetic

Cushing response: bradycardia and hypertension

Autonomic storm: tachycardia and hypertension

Sympathetic paralysis: bradycardia and hypotension

BRAIN DEATH

SOMATIC DEATH

HR▼ MAP▼ CO▼

HR▼ MAP▼ CO▼

HR▼ MAP▼ CO▼

HR▼ MAP▼ CO▼

HR▼ MAP▼ CO▼

(Cardiovascular collapse)
BRAIN DEATH: neural phase
BRAIN DEATH: *humoral phase*

- hypothalamic/pituitary gland dysfunction
- adrenocortical dysfunction
- hypothyroidism

- diabetes insipidus
- glucose – electrolyte disturbances
- fluid disturbances
- anaerobic metabolism
BRAIN DEATH: inflammatory phase

- HORMONAL AND METABOLIC DERANGEMENT
- CATECHOLAMINE STORM VASOCONSTRICTION
- RELEASE OF NEUROPEPTIDES
- CIRCULATING MEDIATORS ISCHEMIC BRAIN
- INFLAMMATION IN PERIPHERAL ORGANS
- PERIPHERAL ISCHEMIA
- ACTIVATION OF ENDOTHELIUM
BRAIN DEATH: *inflammatory phase*

- **DONOR**
- **Hyperdynamic storm**
  - **Neurogenic hypotension**
  - **Endothelial activation**
    - ICAM
    - VCAM
    - selectins
  - **Inflammatory cell infiltration**
  - **Pro-inflammatory cytokines (IL-6, TNF-@, IL-8)**
  - **Early graft dysfunction**
  - **Late graft dysfunction**

Kidney, Heart, Lung, (Liver)
DIRECT CARDIAC DYSFUNCTION

CNS-injury

Sympathetic discharge

$\alpha$-adrenergic

Myocardial oxygen demand
Coronary vasoconstriction
Subendocardial ischemia
Structural damage

- myocytolysis
- contraction band necrosis (calcium overload)
- edema formation
- cell infiltration
- ATP production

“Primary cardiac injury”

Systemic vascular resistance

“Indirect cardiovascular collapse”

Systemic vascular resistance

Interstitial norepinephrine
LOAD-DEPENDENT CARDIAC DYSFUNCTION

- Loss of vasomotor tone
  - afterload
    - preload
    - Frank Starling
      - Affinity of contractile proteins to Ca2+
        - Intracellular Ca2+ release
        - Stress activated Ca2+ channels
    - Coronary perfusion
      - reduced oxygen supply
    - contractility
PULMONARY INJURY

Brain death

CNS-injury

Sympathetic discharge

Inflammatory activation

↑ Systemic vascular resistance
↓ Lung blood volume
↓ Pulmonary arterial pressure
↑ Pulmonary arteriolar pressure
↑ Pulmonary Capillary Pressure

↑ Left ventricular output
↓ Left atrial pressure
ventricular constriction

Donor lung injury

Pulmonary Capillary Permeability
• optimal time interval for heart donor management is limited to 72 h
### DONOR CAUSE OF DEATH

<table>
<thead>
<tr>
<th>DONOR CAUSE OF DEATH</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anoxia</td>
<td>10 569 (12.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td>36 945 (42.9)</td>
</tr>
<tr>
<td>Head trauma</td>
<td>35 968 (41.8)</td>
</tr>
<tr>
<td>CNS Tumor</td>
<td>755 (0.9)</td>
</tr>
<tr>
<td>other</td>
<td>1852 (2.2)</td>
</tr>
</tbody>
</table>

Unos Registry Analysis  Transpl Proc 2009; 41: 3539
## DONOR CAUSE OF DEATH

Table 5. Significant Multivariate Donor Predictors of Recipient Outcome

<table>
<thead>
<tr>
<th>Organ</th>
<th>Parameter</th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>DCOD stroke*</td>
<td>1.059</td>
<td>1.005–1.117</td>
</tr>
<tr>
<td></td>
<td>Donor CMV</td>
<td>1.07</td>
<td>1.027–1.116</td>
</tr>
<tr>
<td></td>
<td>Donor age</td>
<td>1.009</td>
<td>1.007–1.011</td>
</tr>
<tr>
<td></td>
<td>Recipient age</td>
<td>0.996</td>
<td>0.995–0.998</td>
</tr>
<tr>
<td>Lung</td>
<td>DCOD anoxia*</td>
<td>0.888</td>
<td>0.797–0.99</td>
</tr>
<tr>
<td></td>
<td>Donor CMV</td>
<td>1.126</td>
<td>1.072–1.182</td>
</tr>
<tr>
<td></td>
<td>Donor diabetes</td>
<td>1.287</td>
<td>1.125–1.473</td>
</tr>
<tr>
<td></td>
<td>Donor age</td>
<td>1.002</td>
<td>1.000–1.004</td>
</tr>
<tr>
<td></td>
<td>Recipient age</td>
<td>1.004</td>
<td>1.002–1.006</td>
</tr>
</tbody>
</table>

CMV, cytomegalovirus infection; DCOD, donor cause of death.
*Reference group is DCOD head trauma.
THE CATECHOLAMINE ROLLER COASTER
HISTORICAL FACTS

- norepinehrine
  - decreased survival after heart transplantation

- dobutamine/dopamine < 10 μg/kg/min

- exogenous cathecholamines induce similar cardiac damage compared to the sympathetic storm after brain death

- Beta-receptor down regulation decreases response to inotropes after heart transplantation
RECENT CONTROVERSIES

• “inotropes and alpha-agonists should be minimized”
  – impaired right ventricular function with NA
  – Dobutamine/dopamine < 10 μg/kg/min
  – noradrenaline < 0.6 μg/kg/min

• “liberal use”
  – organ shortage
  – restoration of loading conditions after loss of sympathetic tone
  – adequate coronary perfusion pressures
  – cathecholamines have immunomodulatory effects
ANOTHER POINT OF VIEW

• “catecholamines are not deleterious”
  
  – no distinction between inotropes/vasopressors
  – methodological pitfalls in limited studies
  – catecholamine administration after catecholamine storm not evaluated on myocardial injury
ANOTHER POINT OF VIEW

• “catecholamines are needed”
  – loss of sympathetic tone
  – fluids alone are not sufficient
ANOTHER POINT OF VIEW

• “catecholamines are beneficial”
  – maintenance of coronary perfusion pressure
  – catecholamines have immunomodulatory effects
HORMONAL RESUSCITATION
HORMONE COCKTAIL

- T3-T4
- vasopressin
- methylprednisone
- insulin

increased organ procurement per donor
increased suitable donors
improved outcome in heart transplants
benefit in hemodynamic unstable donors
T3 – T4

- rationale: reduced levels due to reduce TSH levels (hypothalamus/pituitary) and reduced conversion of T4 (euthyroid sick syndrome)
- reversal of anaerobic metabolism
- restoration of cardiac output
- reduction in inotropes and bicarbonate
- increased organ recovery
- preferable T3 (more T4 in clinical practice)
arginine vasopressin

- V1 receptor: blood vessel – vasopressor
- V2 receptor: antidiuretic effect
- V3 receptor: anterior pituitary - adrenocorticotropic hormone
- diabetes insipidus
- reduced inotropic requirements
- reduction of myocardial ATP depletion
- Doses: 0.5 – 15 U/hr (half life of 15 min)
Desmopressin (DDAVP)

• V2 receptor activation
• Diabetes insipidus:
  – Diuresis > 3-5 ml/kg/h
  – Hypernatremia (> 150mM)
  – R/ saline 0.45% and dextrose 5%
• Doses: 2 – 6 µg every 6 to 8 hours
  (duration of action 6 – 20 hours)
methylprednisone/hydrocortisone

- hydrocortisone
  - 10mg/h
  - catecholamine sparing effect

- methylprednisolone
  - adrenal insufficiency and anterior pituitary gland dysfunction
  - catecholamine sparing effect
  - immunomodulatory effect
Insulin

- Hyperglycemia followed by hypoglycemia
- Improves glycogene reserves in heart and liver
- No studies in donor populations
- Tight glycemic control benefits at the ICU
- Doses: Baseline: 1 – 2 U hour
BIOMARKERS
BIOMARKERS IN DONOR HEART

• cTnT en cTnI
  – predictive for early graft failure
  – predictive for rejection
  – correlates with donor heart function

• TNF-α, IL-6, BNP/NT-proBNP, PCT, SMARCAL1
BIOMARKERS IN DONOR LUNG

• IL-8 levels in BAL donor lungs
  – correlation primary graft dysfunction

• IL-6; IL-1B; IL-8; IL-10; IFN; TNF-A
  – donor lung biopsies
  – IL6/IL10 ratio correlates with mortality

• micro-array studies
DONOR MANAGEMENT
PROTOCOLS
IMPLEMENTATION OF DONOR MANAGEMENT PROTOCOLS

- aggressive donor management protocols
  - improve organ recovery
  - early identification of potential donors
  - intensive care unit admission
  - early and aggressive resuscitation
  - specific targets
  - specific donor interventional studies
  - mainly focused on hemodynamic variables and donor heart management
• Adjust volume status: target CVP = 6-10 mmHg
• Correct acidosis: target pH = 7.4 – 7.45
• Correct hypoxemia: target pO₂ > 80 mmHg, sat >95%
• Correct anemia: target HCT > 30%; Hb > 10 g/dl
• Adjust inotropics to keep MAP > 60 mmHg
  (dopamine/dobutamin < 10 µg/kg/min)

- Rule out structural abnormalities

LVEF ≥ 45%
- Proceed with recovery for transplantation

LVEF < 45%
- Hormonal Resuscitation
  • T3: 4 µg bolus + infusion 3 µg/hour
  • Vasopressin: 1 unit bolus + infusion at 0.5 – 4 units/hour
  • Methylprednisolone: 15 mg/kg bolus
  • Insulin: 1 unit/hour minimum

Hemodynamic Management (duration ≥ 24 hours)
- Place PAC
  • Adjust fluids, inotropes and pressors 15 min to
    minimize use of alpha agonists and meet targets:
    • MAP > 60 mmHg
    • PCWP 8-12 mmHg
    • C.I. > 2.4
    • Dopamine or dobutamine < 10 µg/kg/min
    • CVP 4-12 mmHg
    • SVR 800 – 1200 dune/sec/cm-5

Criteria Met
- Proceed with recovery

Criteria Not Met
- Do not recover heart for transplantation

Crystal City Consensus circulation 2001
Early identification of potential organ donor

ICU admission and management by dedicated ICU team

1. Pulmonary artery catheterization to monitor hemodynamic status and perfusion
2. Aggressive fluid resuscitation

MAP < 70

MAP ≥ 70

Vasopressors

Supportive care

MAP < 70

MAP ≥ 70

T4 protocol administration

Supportive care

Early identification and treatment of brain-death-related complications

Diabetes insipidus—Desmopressin; Vasopressin use if pressors required

Neurogenic pulmonary edema—aggressive optimization of pulmonary function; use of high-frequency percussive ventilation as indicated

Coagulopathy—Aggressive correction (FFP, cryoprecipitate, factor VII utilization)

SIADH—Salt replacement with hypertonic saline, fluid restriction when appropriate

GOALS to overcome hemodynamic instability & coagulopathy
MAP ≥ 60 mmHg, CVP ≥ 10 mmHg, LVEF ≥ 45%
urinary output ≥ 1.0 mL/kg/h, core body temperature ≥ 35°C
blood glucose 80-150 mg/dL, Na < 150 mmol/L
Hemoglobin ≤ 10 g/dL, platelet count ≤ 50,000/mm³, INR ≥ 1.5

Baseline Monitoring Devices
- central venous catheterization
- arterial catheterization
- echocardiography (if heart donation is considered)

Hypertension: esmolol, urapidil, nitroprusside,
Hypotension: volume replacement,
if persisting: dopamine/dobutamine
Tachyarrhythmia: lidocaine, amiodarone
Bradyarrhythmia: isoproterenol, epinephrine

Reassessment of Goals
if necessary

Invasive Hemodynamic Monitoring
- pulmonary artery catheterization
- PiCCO™ (Pulsed Contour Continuous Cardiac Output)

1. Vasoactive Drugs
   - epinephrine, norepinephrine, vasopressin (≤ 0.04 U/min)
2. Hydrocortisone (10 mg/h)
3. Hormonal Replacement Therapy:
   - T3 (4 µg bolus, infusion at 3 µg/h)
   - vasopressin (1 U bolus, infusion at 0.5-4 U/h)
   - methylprednisolone (15 mg/kg bolus)
   - insulin (1 U/h)
Initial Management
Optimise volume status: target CVP 4-10mmHg
If HCT < 30%, Hb < 10g/dl use PRBCs
If PT abnormal (value 1.5 x control) use FFP
Otherwise use human albumin solution
Correct hypoxaemia: target PaO₂ > 100mmHg, O₂ sat. >95%
Optimise PEEP
Tidal volume 6-8ml/kg
Mean Arterial Pressure: 65-70mmHg
T3: 4ug bolus

Haemodynamics
MAP > 60mmHg
CVP 4-10mmHg
Urine Output >0.5ml/kg hr or <2.Oml/kg
Fluid balance < 2000ml +/– 250ml/h

Proceed with organ retrieval

Yes

Targets achieved

No

Hormonal Resuscitation
T3: Infusion 3ug/hour
Vasopressin: 1 unit bolus + infusion 0.5 – 4 units/hour
Insulin: Maintain BG 80 – 110 mg/dl

Haemodynamics
MAP > 60mmHg
CVP 4-10mmHg
Urine Output >0.5ml/kg hr or <2.Oml/kg
Fluid balance < 2000ml +/– 250ml/h

Yes

Targets achieved

No

Haemodynamic Management
Place pulmonary artery catheter
Adjust fluids, inotropes and pressors Q15 minutes
Target Criteria:
MAP > 60mmHg
CVP 4 – 10mmHg
PCWP 8 – 12 mmHg
SVR 800 – 1200dynes/cm²

Yes

Targets achieved

No

Consider extracardiac retrieval

Proceed with organ retrieval
ASPECTS OF CARDIAC MANAGEMENT
DONOR RISK FACTORS FOR HEART TRANSPLANTATION

- Risk factors for primary graft failure
  - donor age > 30 y
  - Donor head trauma
  - high donor inotropes
  - ischemic time > 240 min
**SELECTION CRITERIA FOR HEART DONORS**

<table>
<thead>
<tr>
<th>Characteristics of donors where caution is to be applied during selection</th>
</tr>
</thead>
<tbody>
<tr>
<td>older donors (&gt; 55y)</td>
</tr>
<tr>
<td>prolonged ischemic time (&gt; 5h)</td>
</tr>
<tr>
<td>hepatitis C</td>
</tr>
<tr>
<td>chronic alcohol abuse</td>
</tr>
<tr>
<td>cocaine abuse</td>
</tr>
<tr>
<td>atraumatic intracranial bleed</td>
</tr>
<tr>
<td>size (body weight)</td>
</tr>
<tr>
<td><em>undersizing (&lt;30%) in recipients with pulmonary hypertension</em></td>
</tr>
<tr>
<td><em>oversizing (&gt;30%) in recipients with LVADS</em></td>
</tr>
</tbody>
</table>
HEART DONOR ASSESSMENT

• ECG abnormalities
  – ST depression/elevation and inverted T-waves
  – atrial arrhythmias
  – prolonged QT interval (hypokalemia)
  – short QT interval (gunshot)
  – conduction abnormalities
  – Q-waves (without positive enzymes)
HEART DONOR ASSESSMENT

• echocardiography
  – after optimization of load-indices
  – dobutamine stress echocardiography
  – diffuse wall motion abnormalities
  – limited role for repeat echocardiography

• Swan-ganz catheter

• Troponin-I -T
SODIUM LEVELS

- polyuria: diabetes insipidus (<>hyperglycemia)
  - urine output > 4 ml/kg/h
  - serum Na+ > 145 mMol/L
  - serum Osm > 300 mOsm/l
  - urine Osm < 200 mOsm/l
  - desmopressin 2 – 4 μg/q 6h

<table>
<thead>
<tr>
<th>Na+</th>
<th>fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 145</td>
<td>dextrose 5%</td>
</tr>
<tr>
<td>130-145</td>
<td>NaCl 0.3% + glucose 3,3%</td>
</tr>
<tr>
<td>&lt;130</td>
<td>NaCl 0.9%</td>
</tr>
</tbody>
</table>
SODIUM LEVELS

• hypernatremia and intracellular sodium levels contribute to ischemia-reperfusion injury

• historical no clinical adverse effect on outcome in heart transplantation

• donor hypernatremia is an indicator of suboptimal donor management
SODIUM LEVELS

• donor hypo- and hypernatremia are predictors for increased 1-year mortality

Hoefer et al Transplant International 2009; 23:589
ASPECTS OF PULMONARY MANAGEMENT
<table>
<thead>
<tr>
<th>CURRENT DONOR LUNG CRITERIA GUIDELINES</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO compatible</td>
</tr>
<tr>
<td>Age &lt; 55y</td>
</tr>
<tr>
<td>smoking history &lt; 20 y</td>
</tr>
<tr>
<td>clear chest radiograph</td>
</tr>
<tr>
<td>PaO2 &gt; 300 (FiO2 100%) and 5 cmH2O PEEP</td>
</tr>
<tr>
<td>absence of chest trauma</td>
</tr>
<tr>
<td>no evidence of aspiration/sepsis</td>
</tr>
<tr>
<td>no prior cardiothoracic surgery</td>
</tr>
<tr>
<td>no organisms on donor gram stain</td>
</tr>
<tr>
<td>no purulent secretions on bronchoscopy</td>
</tr>
</tbody>
</table>
# DONOR LUNG CRITERIA

<table>
<thead>
<tr>
<th>Non Compliance with Current Standard Criteria</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>age &gt; 55y</td>
<td>7.7%</td>
</tr>
<tr>
<td>PO2</td>
<td>18%</td>
</tr>
<tr>
<td>smoking history</td>
<td>21%</td>
</tr>
<tr>
<td>abnormal chest radiograph</td>
<td>41%</td>
</tr>
<tr>
<td>purulent secretions</td>
<td>12%</td>
</tr>
<tr>
<td>confirmed blood infection</td>
<td>3.1%</td>
</tr>
<tr>
<td>ABO compatibility</td>
<td>0.058% (accidents)</td>
</tr>
</tbody>
</table>
**DONOR LUNG CRITERIA**

<table>
<thead>
<tr>
<th>NEW DONOR CRITERIA WITH NEGATIVE IMPACT ON SURVIVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>african-american</td>
</tr>
<tr>
<td>high recipient/donor BMI ratio</td>
</tr>
<tr>
<td>diabetic</td>
</tr>
<tr>
<td>blood type A</td>
</tr>
<tr>
<td>CMV antibodies</td>
</tr>
<tr>
<td>head trauma as cause of death</td>
</tr>
<tr>
<td>race mismatch</td>
</tr>
<tr>
<td>gender mismatch</td>
</tr>
</tbody>
</table>
PULMONARY MANAGEMENT

- *no clear donor management protocols available*

- **recruitment**
  - prevention of atelectasis
  - improvement of gas exchange
  - increased organ recovery

- **oxygenation** as important target
PULMONARY MANAGEMENT

• SALT protocol (retrospective)
  – recruitment (PEEP 15cmH20 and AwP 25 cmH20) when P/F ratio < 300
  – IPPV 10 ml/kg and PEEP 5 cmH20
  – head elevation and bronchoscopy
PULMONARY MANAGEMENT

• **hemodynamic resuscitation** of donor lungs
  
  – donor catecholamines lead to impaired gas exchange
  
  – CVP 4-10 mmHg
  
  – PCWP 12-14 mmHg
  
  – alpha-adrenergic antagonism during hypertensive crisis
  
  – correction of neurogenic hypotension
PULMONARY MANAGEMENT

- **hormonal resuscitation** of donor lungs
  - methylprednisone (1g) +/- T3 (0.8μg bolus + 0.113 μg/kg/min)
  - methylprednisone decreased EVLWI
  - no effect on oxygenation
PULMONARY MANAGEMENT

• associated risk factors for lung quality
  – aspiration
  – pneumonia
  – contusion
  – ventilator-induced lung injury

• specific exams
  – chest X-ray
  – (CT-scan)
  – bronchoscopy
VENTILATORY STRATEGY

Overdistention (baby lung)
- volutrauma in functional reduced lung volume
- reduction in tidal volume

Atelectrauma (open lung concept)
- Repetitive opening and closure of atelectatic zones
- recruitment and PEEP
## Table 2. Trials of Volume- and Pressure-Limited Ventilation in Acute Lung Injury and Acute Respiratory Distress Syndrome

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>861</td>
<td>53</td>
<td>116</td>
<td>120</td>
<td>52</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>52</td>
<td>35</td>
<td>57</td>
<td>59</td>
<td>49</td>
</tr>
<tr>
<td>Target intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tidal volume, mL/kg</td>
<td>6 vs 12 PBW</td>
<td>≤6 vs 12 ABW</td>
<td>6-10 vs 10-15 DBW</td>
<td>≤8 vs 10-15 IBW</td>
<td>≤8 vs 10-12 PBW</td>
</tr>
<tr>
<td>Plateau pressure, cm H₂O</td>
<td>≤30 vs ≤50</td>
<td>&lt;20 vs unlimited</td>
<td>25-30 vs ≤60</td>
<td>≤30 vs ≤50</td>
<td>≤30 vs ≤45-55</td>
</tr>
<tr>
<td>Actual intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tidal volume, mL/kg</td>
<td>6.2 vs 11.8</td>
<td>384 vs 768</td>
<td>7.1 vs 10.3</td>
<td>7.0 vs 10.7</td>
<td>7.3 vs 10.2</td>
</tr>
<tr>
<td>Plateau pressure, cm H₂O</td>
<td>25 vs 33</td>
<td>30 vs 37</td>
<td>26 vs 32</td>
<td>22 vs 27</td>
<td>25 vs 31</td>
</tr>
<tr>
<td>Outcomes mortality, %</td>
<td>31 vs 40</td>
<td>38 vs 71</td>
<td>47 vs 38</td>
<td>50 vs 47</td>
<td>50 vs 46</td>
</tr>
<tr>
<td>P value</td>
<td>.007</td>
<td>.001</td>
<td>.38</td>
<td>.72</td>
<td>.61</td>
</tr>
</tbody>
</table>

Abbreviations: ABW, actual body weight; DBW, dry body weight; IBW, ideal body weight, calculated as 25 m²; PBW, predicted body weight, calculated as 50 plus 0.91 (height in centimeters minus 152.4) for men or 45.5 plus 0.91 (height in centimeters minus 152.4) for women.

*Represents peak inspiratory pressure rather than plateau pressure.
†Mean values at earliest recorded time point are reported and represent lung-protective vs control ventilation groups.
‡Tidal volume available in milliliters only.
§Mortality at hospital discharge or at 180 days.
||28-Day mortality.
¶60-Day mortality.
## VENTILATORY STRATEGY:
PROTECTIVE VENTILATION ARDS/ALI?
VENTILATORY STRATEGY: PROTECTIVE VENTILATION DONORS

- Ranieri et al JAMA 2010

<table>
<thead>
<tr>
<th>conventional (6h) n = 59</th>
<th>protective (6h) n = 59</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV 10 – 12 cmH2O</td>
<td>TV 6 – 8 cmH2O</td>
</tr>
<tr>
<td>PEEP 3-5 cmH2O</td>
<td>PEEP 8 – 10 cmH2O</td>
</tr>
<tr>
<td>apnea test by disconnection</td>
<td>apnea test by CPAP</td>
</tr>
<tr>
<td>open circuit airway suction</td>
<td>closed circuit airway suction</td>
</tr>
</tbody>
</table>

- Lung protective strategy
  - increased organ recovery
  - reduced serum IL-6
  - no effect on 6-month survival
ALVEOLAR FLUID CLEARANCE

Modulation of activity
- β2-agonist
- Dopamine
- dobutamine

Modulation of expression
- Glucocorticoids
- EGF
- KGF
- β2-agonist

ALVEOLAR FLUID CLEARANCE

24 h Cumulative Dopamine Dose (mg) vs. Alveolar Fluid Clearance (%/h)

Ware L B et al. J Appl Physiol 2002;93:1869-1874

EX VIVO ASSESSMENT OF REJECTED DONOR LUNGS
ALVEOLAR FLUID CLEARANCE

Lung Wet-to-Dry Weight Ratio vs. Alveolar Fluid Clearance (%/h)

Ware L B et al. J Appl Physiol 2002;93:1869-1874

EX VIVO ASSESSMENT OF REJECTED DONOR LUNGS
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EX VIVO ASSESSMENT OF REJECTED DONOR LUNGS
CONCLUSION

- *hemodynamic* and *inflammatory* changes following brain death are responsible for donor organ injury

- donor organ injury has impact on *transplant outcome*

- *aggressive donor management protocols* might improve organ recovery and outcome

- future donor *organ intervention studies*