Nursing the proned patient is not so HARDS

ARDS, mechanical ventilation and the prone position

Castro Arias, NP, MN, CNCC(c)

Objectives
- Review ARDS
- History
- Definition
- Pathophysiology
- Lung Protective Ventilation
- Foundational trials
- ARDSnet
- Proning
  - Benefits
  - Mechanisms
- Newer tidbits

History Lesson
- First described in 1821 by Renée Laennac in Treatise on Diseases of the Chest
- Fatal idiopathic pulmonary edema
- 1967 the term “respiratory distress syndrome” was coined by Ashbaugh, Bigelow, Petty & Levine
  - “severe respiratory distress, refractory to oxygen, loss of lung compliance, diffuse alveolar infiltration”
**More History**

- American-European Consensus Conference met in 1994
  - Develop a standardized definition
  - Facilitate research in epidemiology, pathophysiology, and treatment to combat the high mortality

- ARDSNet met in 2012 and arrived at the Berlin Definition
  - Clarified and addressed deficits identified in the previous definitions

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**The Berlin Definition of Acute Respiratory Distress Syndrome**

<table>
<thead>
<tr>
<th>Acute Definitions</th>
<th>ARDS Definition</th>
<th>ARDS Lactulose</th>
<th>Associated with ARDS Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acuteness</td>
<td>Acute onset</td>
<td>No definition of acute onset</td>
<td>Acute illness within 7 days of presentation</td>
</tr>
<tr>
<td>Oxygen Stratification</td>
<td>Removed the term Acute Lung Injury</td>
<td>Mild ARDS vs Moderate ARDS vs Severe ARDS</td>
<td></td>
</tr>
<tr>
<td>Chest Imaging</td>
<td>Bilateral opacities not explained by effusions, lobar consolidation, or nodules</td>
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<td></td>
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<tr>
<td>Etiology of Edema</td>
<td>Must be differentiated from hydrostatic or cardiogenic edema; though they may be superimposed on the ARDS picture, PAOP/PAWP no longer required to diagnose</td>
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</tr>
<tr>
<td>Risk Factors</td>
<td>Identified risks which were previously not stated</td>
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<td></td>
</tr>
</tbody>
</table>

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**The Berlin Definition**

- **Acuteness**
  - An event known to cause ARDS within 7 days of presentation

- **Oxygen Stratification**
  - Removed the term Acute Lung Injury
  - Mild ARDS vs Moderate ARDS vs Severe ARDS

- **Chest Imaging**
  - Bilateral opacities not explained by effusions, lobar consolidation, or nodules

- **Etiology of Edema**
  - Must be differentiated from hydrostatic or cardiogenic edema; though they may be superimposed on the ARDS picture, PAOP/PAWP no longer required to diagnose

- **Risk Factors**
  - Identified risks which were previously not stated
Mortality and Morbidity

- Despite our increased knowledge about ARDS, still has huge mortality.
- Criteria of the Berlin Definition are better able to predict mortality of ARDS patients than AECC.

Table 1: Morbidity and Mortality in the Clinical Evaluation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mortality</th>
<th>Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARDS</td>
<td>26-58%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mortality Summary

- More recent estimation of mortality and morbidity range from 26-58% (Siegel, 2016).
- Surviving through ARDS does not correlate with convalescence.

Morbidity

- Huge long term implications post recovery of ARDS.
Morbidity

- After 5 years patients experience significant sequelae related to ARDS
- Significant costs

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>At 1 Year</th>
<th>At 2 Years</th>
<th>At 3 Years</th>
<th>At 4 Years</th>
<th>At 5 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean costs after initial hospitalization ($ Canadian)</td>
<td>$1,141</td>
<td>$1,052</td>
<td>$1,030</td>
<td>$1,172</td>
<td>$1,215</td>
</tr>
<tr>
<td>Medication costs</td>
<td>$1,175</td>
<td>$1,072</td>
<td>$1,037</td>
<td>$1,156</td>
<td>$1,231</td>
</tr>
<tr>
<td>Hospitalization costs</td>
<td>$2,966</td>
<td>$2,856</td>
<td>$2,815</td>
<td>$3,031</td>
<td>$3,087</td>
</tr>
<tr>
<td>Outpatient costs</td>
<td>$8,963</td>
<td>$8,306</td>
<td>$8,158</td>
<td>$8,653</td>
<td>$7,701</td>
</tr>
<tr>
<td>Total</td>
<td>$12,128</td>
<td>$11,257</td>
<td>$11,041</td>
<td>$12,027</td>
<td>$11,196</td>
</tr>
</tbody>
</table>

Herridge et al., 2011. Functional disability 5 years after acute respiratory distress syndrome

Morbidity

- High levels of psychosocial, social and physical dysfunction even after 5 years
- PTSD related syndromes post ARDS
  - May be amenable to ICU interventions such as diaries
- Caregiver burden is posed as a significant issue
- Prolonged physical deconditioning related ICU-acquired weakness

Take Home Messages

- Despite being around for forever, we still are bad at treating it
- Consensus definition has helped characterize the disease, with the goal of helping research and treatment
- Huge costs: physically, psychosocially, financially
ARDS Pathophysiology

Pathophysiology

● The hallmark characteristics of ARDS:
  ● Inciting event triggers a cyclical pattern of inflammation-response-inflammation
  ● Increased capillary permeability due to colossal inflammatory cascade

Stages of ARDS

● Three distinct phases with an anticipated trajectory and features
  ● Exudative
  ● Fibroproliferative
  ● Resolution
● There may be overlap between stages
Exudative Phase
- Early stage - generally up to 72 hours, up to 6 days
- Characterized by release of pro-inflammatory cytokines
  - TNF-α, IL-1, IL-6
- Neutrophils are drawn and further propagate the immune response, further release enzymes
- All of these reactions, contribute to a leaky alveolar-capillary network
- Lymphatic system attempts to compensate, however, is rapidly overwhelmed

Fibroproliferative
- May occur concurrently with exudative phase; lasts for approximately 2 weeks after insult
- Type II alveolar cells proliferate in large numbers as fibroblasts and myofibroblasts aggregate
- Lay down new matrix, and edema slowly starts to resolve
- This stage is when lungs scar down and become fibrotic:
  - Increased vascular resistance, leading to right sided heart strain
  - Stiff, non-compliant make it more difficult to ventilate

Resolution
- Resolution varies with regard to final recovery, dependent on degree of initial injury
- Fibroproliferative phase may progress to fibrotic phase that culminates in long term V/Q mismatch and ventilatory dependence
- Respiratory function may recover as pneumocytes differentiate (remember-type 2 and type II cells), or may result in continued permanent scarring
- Despite lung recovery, there is often a profound bio-psychosocial ramifications to ARDS
Intrinsic versus Extrinsic ARDS

<table>
<thead>
<tr>
<th>Primary pulmonary injury</th>
<th>Extra-pulmonary sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Aspiration</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Inhalation injury</td>
<td>Trauma</td>
</tr>
<tr>
<td>Pulmonary contusion</td>
<td>DIC</td>
</tr>
<tr>
<td>VILI</td>
<td>Burns</td>
</tr>
<tr>
<td></td>
<td>Bypass</td>
</tr>
<tr>
<td></td>
<td>TRALI</td>
</tr>
</tbody>
</table>

Lung Protective Ventilation

Breathe easy, you’ll soon be able to vent all about how long this talk is.

The Birth of ‘Lung Protective Ventilation’

The ARMA trial (2000)

- Large multi-center trial in which patients with ALI/ARDS were randomized to low tidal volume (6 ml/kg) and \( P_{PLAT} < 30 \text{ cmH}_2\text{O} \) to traditional volumes (12 ml/kg) and \( P_{PLAT} < 50 \text{ cmH}_2\text{O} \)
- Halted trial early
- Findings corroborated by other studies
No HARMa, no foul!

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low PEEP</th>
<th>High PEEP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death before discharge (%)</td>
<td>21.8</td>
<td>28.8</td>
<td>0.0129</td>
</tr>
<tr>
<td>Hospital-free days</td>
<td>40.7</td>
<td>50.0</td>
<td>0.4286</td>
</tr>
<tr>
<td>No of ventilator-free days</td>
<td>6315</td>
<td>18111</td>
<td>0.0001</td>
</tr>
<tr>
<td>No of days without evidence of infections</td>
<td>29</td>
<td>12311</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*The Acute Respiratory Distress Syndrome Network, 2000

 Decreases in 28 day mortality  
 More ventilator free days  
 Less end organ dysfunction

What's the Big Deal PEEP-ple?

The ALVEOLI trial (2004)

- Tried to determine what is the ideal PEEP for patients with ARDS
- Divided into low-PEEP (8.3 ± 3.2 cm) and high-PEEP (13.2 ± 3.5 cm)
- All patients were ventilated with low VTs
- The results?

ALVEOLI was a BUST!

No significance was seen in any of the major outcomes!
Better oxygenation was observed, but not of significance

So then, why do we ventilate ARDS patients with high PEEP?
Clinical Pearls from ARDSNet

- Patient selection is key!
- Renewable lung volumes = benefit from PEEP
- Potential benefits of using less oxygen
- Less oxidative stress, decreased adsorption of lactate
- Learned of the dangers of elevated plateau pressures
- Try to keep them below 30 to avoid barotrauma
- Step-wise approach to PEEP and O₂ titration
- The Ventilator Protocol Tool (see next)

The Ventilator Protocol Tool

**PART I: VENTILATOR SETUP AND ADJUSTMENT**

1. Select any ventilator mode
2. Calculate predicted body weight (PBW)
   - Male: T = 45.5 + 2.3 [height (inches) - 60]
   - Female: T = 50 + 2.3 [height (inches) - 60]
3. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
4. Reduce V tidal volume if possible.
5. Increase RR until pH > 7.30 or PaCO₂ < 25 mmHg (with PS).

**PART II: WEANING**

1. If pH < 7.15:
   - Try to keep them below 30 to avoid barotrauma
2. If pH > 7.45:
   - Alkalosis Management: (pH > 7.45)
   - pH GOAL: 7.30-7.45

**Males**

- May give NaHCO₃
- If pH remains < 7.15, V tidal volume must be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).

**Females**

- The Ventilator Protocol Tool

- The Ventilator Protocol Tool

**UNASSISTED BREATHING**

1. Place on T-piece, T-tube breathing, or CPAP less than or equal to 5 cm H₂O.
2. T-tube breathing, OR
3. Extubated with face mask, nasal prong oxygen, or PS is not allowed.
4. CPAP less than or equal to 5 cm H₂O, room air, OR
5. CPAP less than or equal to 5 cm H₂O and PS is not allowed.

**SPONTANEOUS BREATHING TRIAL (SBT):**

1. Extubated with face mask, nasal prong oxygen, or CPAP less than or equal to 5 cm H₂O.
2. T-tube breathing, OR
3. CPAP less than or equal to 5 cm H₂O and PS is not allowed.
4. CPAP less than or equal to 5 cm H₂O and PS is not allowed.
5. No neuromuscular blocking agents or blockade.

- Conduct a SPONTANEOUS BREATHING TRIAL daily when:
  - Patient has acceptable spontaneous breathing efforts. (May be increased in 1 ml/kg steps until pH > 7.15)
  - No respiratory distress (distress = 2 or more)
  - pH 7.30 ≤ ≤ 7.45 (Maximum set RR = 35).

**PLATEAU PRESSURE GOAL:**

- Higher PEEP/lower FiO₂
- Higher PEEP/lower FiO₂
- Higher PEEP/lower FiO₂
- Higher PEEP/lower FiO₂

**OXYGENATION GOAL:**

- PaO₂ ≥ 80 mmHg without vasopressor support.

**Mechanical Ventilation Protocol Summary**

- NIH NHLBI ARDS Clinical Network: Acute onset of ARDS, defined as ARDS occurring within 14 days of an acute illness or injury or within 14 days of previous hospital admission.

**NIH NHLBI ARDS Network (http://www.ardsnet.org/tools.shtml)**

- NIH NHLBI ARDS Network (http://www.ardsnet.org/tools.shtml)
VILI or VALI

- Ventilator induced lung injury versus ventilator associated lung injury
  - Induced - injury cause by mechanical ventilation
  - Associated - injury from mechanical ventilation or disease state
- Many types:
  - Barotrauma - from too much pressure
  - Volutrauma - from too much volume
  - Atelectrauma - injury from repeated opening
  - Biotrauma - injury causing release of cytokines, further exacerbating injury

VILI and the Prone Patient

- Tends to occur in dependent areas; remember that dependent areas are less compliant
- Prone position homogenizes driving pressure
- Prone position recruits more lung volume
- Prone position with ARDSNet ventilation (high PEEP, low tidal volume)
- Prone position allows less oxygen usage

What is the Prone Position

- Simply put, the prone position involves placing a patient facedown.
- Not so simple to execute in reality
- Many studies demonstrated this previously, but not all demonstrated an improvement of mortality
- Previously may have been used as salvage maneuver, therefore, did not demonstrate a benefit
The PROSEVA Trial

Demonstrated improvements in oxygenation, and improvements in 28-day & 90-day mortality

Guérin et al., 2013. Prone positioning in severe acute respiratory distress syndrome.

Prone Positioning

What are the benefits?

- Added a protocolized approach of which to emulate which allowed for wide range implementation
- Euoxia is dependent on both improved ventilation and respiration
- Improves shunt away from the dorsal (dependent) regions of the lungs
- Improved aeration of a larger volume of lung parenchyma

Proning Benefits - Continued

- Decreased in shunt, as the right ventricle is able to pump blood into a higher surface area of aerated tissue
- Utilization of endogenous nitric oxide
- Improved fluid clearance
  - decreased compression of lymphatic vessels
  - recruitment maneuvers may stimulate fluid clearance
Timing is Everything

- Early rather than later cited as having the largest benefit
  - Helps with secretion clearance (postural drainage)
  - Reduction of edema
  - Prevents VILI
  - Reduces oxidative stress

- How long is optimal?
  - Unclear, but more research is being done
  - PROSEVA had a mean of 17 hours, durations up to 55hrs have been studied in some centers

APRV with ARDS

- “APRV is a mode of mechanical ventilation that has generated enough controversy to fuel a war”
  - Mireles-Cabodevila, Dugar, & Chatburn, 2018
- Putative benefits reducing atelectrauma, reducing biotrauma
- Enhanced recruitment
Airway Pressure Release Ventilation

- Set a high pressure and low pressure (P_HIGH and P_LOW, respectively) and time spent at the P_HIGH and a time spent at the P_LOW (T_HIGH and T_LOW, respectively)

EXTRA! EXTRA!
Read All About It!

Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in acute respiratory distress syndrome

First trial comparing conventional ventilation to APRV

APRV in ARDS

Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in ARDS

*From PulmCrit, at https://emcrit.org/pulmcrit/aprv/*
Everyone’s a Critic
• Populations problems
• High Failure to extubate
• RRT Protocol
• More study is needed

ECMO in ARDS
• CESAR Trial in 2009
  • ECMO is effective at improving outcomes at 60 days in patient with ARDS
  • Thought to give the lungs an opportunity to rest with ventilation to minimalize VILI

EOLIA Trial (2018)

Does early ECMO make a difference at improving outcomes/mortality?
ECMO in ARDS

- At 60 days:
  - 46% survival in ECMO group
  - 36% in the ventilated group
  - But 11% difference NOT significant
- ECMO had more bleeding requiring transfusion and severe thrombocytopenia

Combes et al., 2018

What else do we know?

- Conservative fluid volume is helpful
  - Fluid and Catheter Treatment Trial (FACTT)
- NMBAs are probably beneficial
- Inhaled pulmonary vasodilators
  - Improved oxygenation, no change in mortality
- Steroids? Early versus late. High-dose versus low-dose?

In Summary

- ARDS is bad
- Progress is being made with treatment
- Prone early, prone long, just prone
- New things are always coming
References


