Management of one lung ventilation during thoracic surgery – Impact on postoperative complications

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Chief, Thoracic Anesthesia
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and MPOG Investigators
Lung Protective Ventilation

• Potential for outcome improvement
• RCTs
  – Bundled ventilator variables \((V_T, PEEP)\)
  – Control groups not reflecting standard practice
  – Large composite primary outcomes
• Incompletely defined
• No clinical standard
LPV Bundles

PEEP cm H\textsubscript{2}O

\(V_T\) ml/kg

4 6 8 10 12

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What we don’t know about LPV

• Exactly what LPV is!
• Ideal
  – $V_T$
  – Combination $V_T$, PEEP
• Whether PEEP 5 cm H$_2$O is sufficient
• Safe limits of airway pressure ($\Delta P$)
• Contribution of practice $\Delta$ to outcome $\Delta$
Overall Aim

• Assess relationship
  – management of 1LV
  • $V_T$, PEEP, $P_{aw}$
  – Postoperative complications
MPOG – STS Integration

Integration obstacles:
Personnel
- Thoracic surgery/CT anesthesia champions
- STS & MPOG site IT champions
Politics
- Data security / privacy
- Collaborative spirit between CT surgery/anesthesia
Regulatory
- MPOG participating site IRB → STS integration language
Outcomes

- **Primary outcome - PPCs**
  - Tracheostomy
  - Empyema requiring treatment
  - Pneumonia
  - Reintubation
  - Initial ventilator support > 48 h
  - ARDS
  - Bronchopleural fistula
  - Pulmonary embolism
  - Air leak > 5 d
  - Atelectasis requiring bronchoscopy
  - Respiratory failure

- **Major morbidity**
  - PPCs – any
  - Unexpected return to OR
  - Dysrhythmia requiring Rx
  - Myocardial infarction
  - Sepsis
  - Renal failure
  - Central neurologic event
  - Unexpected ICU admission
  - Anastomotic leak

- **Composite**
  - Any major morbidity
  - Mortality
Aim 1

• To determine whether adherence to putative LPV regimen predicts improvements in clinical outcomes?
  • LPV = $V_T \leq 5$ ml/kg PBW and PEEP $\geq 5$ cm H$_2$O
  • Non LPV = $V_T > 5$ ml/kg PBW or PEEP $< 5$ cm H$_2$O

• To determine whether the documented increase in adherence to LPV recommendations over the study period is associated with improved clinical outcomes
### Unmatched

<table>
<thead>
<tr>
<th>Demographics</th>
<th>No LPV N=3929</th>
<th>LPV N=621</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63</td>
<td>63</td>
<td>0.203</td>
</tr>
<tr>
<td>Female sex</td>
<td>2084</td>
<td>192</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>27.6</td>
<td>26.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASA Class 3 or higher</td>
<td>74.6%</td>
<td>72%</td>
<td>0.166</td>
</tr>
</tbody>
</table>

- Propensity score matched cohort (12 variables)
- LPV matched 1:1 with controls
<table>
<thead>
<tr>
<th>Ventilation</th>
<th>Non LPV</th>
<th>LPV</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Rate</td>
<td>12</td>
<td>14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIO₂ %</td>
<td>95</td>
<td>95</td>
<td>0.661</td>
</tr>
<tr>
<td>Mean P_{insp}</td>
<td>10</td>
<td>10</td>
<td>0.607</td>
</tr>
<tr>
<td>PIP</td>
<td>22</td>
<td>21.5</td>
<td>0.001</td>
</tr>
<tr>
<td>P_{PLAT}</td>
<td>20.5</td>
<td>20</td>
<td>0.387</td>
</tr>
<tr>
<td>ETCO₂</td>
<td>34.1</td>
<td>38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vₜ (ml/kg) PBW</td>
<td>6.2 (5.6-7.0)</td>
<td>4.5 (4.1-4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PEEP</td>
<td>5 (4.0-5.0)</td>
<td>5 (5.0-5.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>mΔP</td>
<td>16 (13.0-20.0)</td>
<td>14 (11.0-18.0)</td>
<td>0.013</td>
</tr>
</tbody>
</table>
LPV and Outcomes

- Respiratory: P=0.816
- Morbidity: P=0.390
- Morbidity + Mortality: P=0.644
Unmatched

Matched

- LPV Incidence
- PEEP
- Tidal Volume (PBW)
Aim 2

• To assess the interaction between ventilator parameters to determine a “best” combination of $V_T$ and PEEP during 1LV for minimizing postoperative complication rate.
P = 0.718
Aim 3

• To determine whether ventilatory correlates of dynamic alveolar strain – notably $\Delta P (P_{\text{plat}} - \text{PEEP})$ or $m\Delta P$ are predictive of postoperative complications
# Driving Pressure and Complications

$P_{per 1 \text{ cm H}_2\text{O}}$

<table>
<thead>
<tr>
<th>Modified Driving Pressure</th>
<th>Respiratory Complications</th>
<th>Morbidity</th>
<th>Morbidity and Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted Odds (95% CI)</td>
<td>P-value</td>
<td>Adjusted Odds (95% CI)</td>
</tr>
<tr>
<td></td>
<td>1.03 (0.99, 1.08)</td>
<td>0.156</td>
<td>1.05 (1.01, 1.09)</td>
</tr>
<tr>
<td></td>
<td>1.03 (0.99, 1.07)</td>
<td>0.152</td>
<td>1.05 (1.01, 1.09)</td>
</tr>
</tbody>
</table>
P = 0.01
Conclusions

• LPV – as currently defined
  – not ideally protective
• Low $V_T$ not inherently protective
• $\Delta P$ predicts complications
• Large database studies integrating
  – Intraoperative (ventilation)
  – Postoperative (outcome)
  – Role/interaction of $V_T$, PEEP, $P_{aw}$
• 3D surface plot analysis
Acknowledgements

MPOG

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MPOG PI

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- Andrew Chang (UM)
- Brandon Tieu (OHSU)
Thank You

University of Virginia Health System
## Respiratory Complications

<table>
<thead>
<tr>
<th>Event</th>
<th>Total (N = 1220)</th>
<th>No LPV (n = 610)</th>
<th>LPV (n = 610)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARDS</td>
<td>4 (0.3)</td>
<td>2 (0.3)</td>
<td>2 (0.3)</td>
<td>0.999</td>
</tr>
<tr>
<td>Air leak &gt; 5 days</td>
<td>76 (6.2)</td>
<td>46 (7.5)</td>
<td>30 (4.9)</td>
<td>0.041</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>53 (4.3)</td>
<td>21 (3.4)</td>
<td>32 (5.2)</td>
<td>0.131</td>
</tr>
<tr>
<td>Bronchopleural Fistula</td>
<td>2 (0.2)</td>
<td>2 (0.3)</td>
<td>0 (0.0)</td>
<td>N/A</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>42 (3.4)</td>
<td>20 (3.3)</td>
<td>22 (3.6)</td>
<td>0.758</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>28 (2.3)</td>
<td>14 (2.3)</td>
<td>14 (2.3)</td>
<td>0.999</td>
</tr>
<tr>
<td>Other pulmonary event</td>
<td>22 (1.8)</td>
<td>10 (1.6)</td>
<td>12 (2.0)</td>
<td>0.670</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>6 (0.5)</td>
<td>3 (0.5)</td>
<td>3 (0.5)</td>
<td>0.999</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>36 (3.0)</td>
<td>19 (3.1)</td>
<td>17 (2.8)</td>
<td>0.739</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>11 (0.9)</td>
<td>7 (1.1)</td>
<td>4 (0.7)</td>
<td>0.366</td>
</tr>
<tr>
<td>Ventilator support &gt; 48 hours</td>
<td>11 (0.9)</td>
<td>6 (1.0)</td>
<td>5 (0.8)</td>
<td>0.763</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>16%</strong></td>
<td><strong>16%</strong></td>
<td><strong>0.816</strong></td>
<td></td>
</tr>
</tbody>
</table>
## Protective Ventilation Meta Analysis 15 Trials, N=2127

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPC</td>
<td>0.64</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>ARDS</td>
<td>0.45</td>
<td>0.01</td>
</tr>
<tr>
<td>Barotrauma</td>
<td>0.39</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Serpa Neto et al. Anesthesiology 2015; 123: 66-78
Protective Ventilation Meta Analysis 15 Trials, N=2127

<table>
<thead>
<tr>
<th></th>
<th>Median $V_T$ ml/kg</th>
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</thead>
<tbody>
<tr>
<td>Protective</td>
<td>7.3</td>
</tr>
<tr>
<td>Conventional</td>
<td>10.8</td>
</tr>
</tbody>
</table>

32% higher

6.6 X

Serpa Neto et al. Anesthesiology 2015; 123: 66-78
Ventilation Data (MPOG)

Time

Jan 1, 2012  July 1, 2017

1LV

$V_T$ ABW, PBW
PEEP
PIP
$P_{aw}$
$P_{plat}$

RR
Ven mode
$FIO_2$
$ETCO_2$

$\Delta P = P_{PLAT} - PEEP$
$m\Delta P = PIP - PEEP$
STS Thoracic Database

Baseline Patient, Procedural

- Age at surgery
- Female sex
- BMI (kg/m²)
- Zubrod score
- ASA status
- Renal dysfunction
- Current smoker
- Induction chemotherapy or radiation
- Preoperative steroid therapy
- FEV₁ (% predicted)
- Major preoperative morbidity
- Blood product transfusion
- VATS
- Thoracotomy
- Other approach
- Wedge resection
- Bilobectomy/pneumonectomy
- Esophageal procedure
- Lung transplantation
- Pleura/diaphragm/mediastinal/chest wall
- Segmentectomy/lobectomy
- Other thoracic procedure

Outcomes, Complications

- Tracheostomy
- Empyema requiring treatment
- Pneumonia
- Reintubation
- Initial ventilator support > 48 h
- ARDS
- Bronchopleural fistula
- Pulmonary embolus
- Air leak > 5 days
- Atelectasis requiring bronchoscopy
- Respiratory failure
- Unexpected return to operating room
- Atrial arrhythmia requiring treatment
- Ventricular arrhythmia requiring treatment
- Myocardial infarction
- Anastomotic failure requiring treatment
- Sepsis
- Central neurologic event
- Renal failure
- Unexpected ICU admission
- Mortality within 30 days
- Primary outcome
- Secondary outcome
Respiratory Complications
Morbidity
Morbidity and Mortality

Odds Ratios per 1 cm H$_2$O mΔP

Respiratory Complications
Morbidity
Morbidity and Mortality

mDP
PIP

* *
Aim 4

• To determine whether patients known to be at higher risk for receiving high $V_T$/kg PBW – patients with high BMI, short stature, and female gender - are more likely to be subjected to ventilator regimens associated with higher levels of $\Delta P$

• Whether these patients are at higher risk for postoperative complications

• Mixed effects logistic regression modeling
## Results

<table>
<thead>
<tr>
<th></th>
<th>B Coefficient (Std. Err.)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.32 (0.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.01 (0.02)</td>
<td>0.712</td>
</tr>
<tr>
<td>Female Sex</td>
<td>-0.56 (0.35)</td>
<td>0.116</td>
</tr>
</tbody>
</table>
Results

<table>
<thead>
<tr>
<th></th>
<th>Respiratory Complications</th>
<th>Morbidity and Respiratory Complications</th>
<th>Morbidity, Respiratory Complications, and Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted Odds (95% CI)</td>
<td>P-value</td>
<td>Adjusted Odds (95% CI)</td>
</tr>
<tr>
<td>BMI</td>
<td>0.99 (0.95, 1.03)</td>
<td>0.625</td>
<td>1.01 (0.98, 1.05)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.98 (0.95, 1.01)</td>
<td>0.132</td>
<td>0.98 (0.95, 1.00)</td>
</tr>
<tr>
<td>Female Sex</td>
<td>2.35 (1.08, 5.10)</td>
<td>0.031</td>
<td>1.38 (0.72, 2.64)</td>
</tr>
</tbody>
</table>
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Pulmonary Complications

- Lower $V_T$ only
- Higher PEEP only
- Lower $V_T$ and higher PEEP

Odds Ratio

<table>
<thead>
<tr>
<th>0.01</th>
<th>0.1</th>
<th>1</th>
<th>10</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>95% CI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MPOG Perioperative Data

• **Intraoperative Data**
  – Medications, fluids, blood products
  – Physiologic monitoring, ventilator management
  – Procedure/case times

• **Additional Perioperative Data**
  – Lab values – 365 days before/after surgery
  – Anesthesia H&P – some additional concepts
  – Billing/lab-based outcomes data
STS Thoracic Database

• Strengths of STS
  – Outcomes (verified by site data managers)
  – Comorbidities (also verified)
  – Preoperative testing
  – Established national standard, 281 sites
PPCs in Surgical Patients

Open Lung Strategy
ARM
PEEP

ΔP Limitation

Atelectasis

Atelectrauma

Volutrauma
Atelectasis

Overinflation

Tidal recruitment

Overinflation

Guldner et al. Anesthesiology 2015; 123:692-713
Standardizing $V_T$

- Lung volume data not routinely available for surgical patients
- Need measure of functional lung volume
  - Relative to delivered $V_T$
  - Easily measured in surgical patients
- Airway driving pressure
  - Ability of lung parenchyma to accommodate $V_T$
  - $\Delta P$ predicts adverse outcomes
<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Parameter</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br J Anaesth 2015:114;483</td>
<td>ASA 1-3 Excluding COPD</td>
<td>Intratidal compliance</td>
<td>PEEP = 5 insufficient to prevent derecruitment</td>
</tr>
<tr>
<td>Anesth Analg 2008;106:175</td>
<td>ASA 1-2, healthy lungs</td>
<td>Compliance, dead space fraction</td>
<td>Optimal PEEP = 10</td>
</tr>
<tr>
<td>Acta Anaesthesiol Scand 2006; 50: 833</td>
<td>Morbid obesity BMI 49±8</td>
<td>Electrical impedance tomography</td>
<td>Optimal PEEP = 15</td>
</tr>
<tr>
<td>Br. J Anaesth 2017;119:1194</td>
<td>Obesity BMI ≥ 35</td>
<td>Electrical impedance tomography</td>
<td>Individualized mean PEEP = 18.5</td>
</tr>
<tr>
<td>Anesthesiology 2018;128: 531</td>
<td>OLV</td>
<td>Mechanics -P/F, shunt, ΔP</td>
<td>PEEP = 10</td>
</tr>
<tr>
<td>Lancet Resp Med 2018; 6: 193</td>
<td>Elevated risk PPC</td>
<td>Clinical outcomes</td>
<td>PEEP &gt; 10 when individualized</td>
</tr>
</tbody>
</table>
Aim 2 – Morbidity

Response Surface for pred

Predicted Value

init_median_peep

init_median_tv_pbw_re

Standard Error

0.3

0.2

0.1
VILI during OLV

Reexpansion
I/R injury

Atelectasis

Tidal recruitment
Overdistension
Volutrauma

Capillary shear stress

Anesth Analg 2015; 121: 302
What do we know about LPV?

- Supraphysiologic $V_T$ and ZEEP is harmful
- Physiologic $V_T$, moderate PEEP better
- Low $V_T$ not protective per se
Lung Protective 1LV

$V_T \leq 6 \text{ ml/kg PBW}$

PEEP $\geq 5 \text{ cm H}_2\text{O}$

Proportion of Patients Receiving LPV (%)

- Initial Population
- BMI $> 30$
- Height $< 165\text{cm}$
- Female

Year

2009 2010 2011 2012 2013 2014

9.1%

55%

Anesth Analg 2018; 126: 495
Respiratory Complications

16% risk increase per 1 ml/kg PBW

Median PEEP 4.2 cm H$_2$O

Blank et al., Anesthesiology
2016; 124: 1286
Major Morbidity

OR = 1.034
3.4% increased risk/1 cm H₂O ΔP

Log Odds of Secondary Outcome

Driving Pressure (cm H₂O)

Anesthesiology 2016; 124: 1286