How to ventilate a patient without

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Division of Critical Care

Department of Anesthesia
Disclosure
Conflicts of Interest 2001–2011

Research Grants & Payments (cost reimbursements, speaker fees)

- Draeger Medical
- Air Liquide
- Hamilton Medical
- Hospira
- Fresenius Kabi
Definition of ALI

• AECC Criteria
  • acute onset
  • bilateral (neutrophil) infiltrate on CXR
  • oxygenation impairment (P/F ratio < 300 mmHg)
  • not caused by left heart failure

Definition of ALI mild ARDS

- **AECC Criteria**
  - acute onset
  - bilateral (neutrophil) infiltrate on CXR / CT
  - oxygenation impairment (P/F ratio < 300 mmHg)
  - not caused by left heart failure
  - Medical condition predisposing to ARDS

Common Etiology of ALI/
Common Etiology of ALI/

Direct Injury
• pneumonia
• gastric aspiration
• near drowning
• fat/amnion embolism
• pulmonary contusion
• alveolar hemorrhage
• smoke/gas inhalation
• reperfusion injury
### Common Etiology of ALI/

#### Direct Injury
- pneumonia
- gastric aspiration
- near drowning
- fat/amnion embolism
- pulmonary contusion
- alveolar hemorrhage
- smoke/gas inhalation
- reperfusion injury

#### Indirect Injury
- sepsis
- transfusion
- shock
- pancreatitis
- brain injury
- trauma
- cancer
Mister X.
Mister X.

- 74y male with perforated viscus, 4 quadrant peritonitis
Mister X.

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- Colon resection, on-table lavage, primary closure
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- Hemodynamically instability despite aggressive volume resuscitation
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- 74y male with perforated viscus, 4 quadrant peritonitis
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- Hemodynamically instability despite aggressive volume resuscitation
- Intubated, PEEP 5 cmH$_2$O
Mister X.

- 74y male with perforated viscus, 4 quadrant peritonitis
- Colon resection, on-table lavage, primary closure
- Hemodynamically instability despite aggressive volume resuscitation
- Intubated, PEEP 5 cmH$_2$O
- FiO2 50%, PaO2 186 mmHg
How would you ventilate?
How would **you** ventilate?

Does not have ALI
How would you ventilate?

Does not have ALI
Does have SIRS / sepsis / septic shock
How would you ventilate?

Does not have ALI
Does have SIRS / sepsis / septic shock
How would you ventilate?

Does not have ALI
Does have SIRS / sepsis / septic shock

• Tidal volume?
How would you ventilate?

Does not have ALI
Does have SIRS / sepsis / septic shock

• Tidal volume?
• PEEP?
How would you ventilate?

Does not have ALI
Does have SIRS / sepsis / septic shock

• Tidal volume?
• PEEP?
• Controlled vs. assisted ventilation
How would you ventilate?

Does not have ALI
Does have SIRS / sepsis / septic shock

• Tidal volume? Low VT (6 ml/kg IBW)
  “minimum PEEP”
• PEEP?
• Controlled vs. assisted ventilation

Surviving Sepsis Campaign Guidelines
Crit Care Med / Intensive Care Med 2004
Mechanism of biotrauma

Excessive tidal volume
or excessive PEEP
Mechanism of biotrauma

Excessive tidal volume or excessive PEEP

Consequences:

• Overstretching
• Alveolar/capillary damage
• Inflammation => Biotrauma

TNF-α
IL-6
IL-8
Septic ALI caused by

Herrera MT et al. ICM 2003; 29:1345

PEEP modulates local and systemic inflammatory responses in a sepsis-induced lung injury model
Septic ALI caused by

Design:

20 rats each group, Sepsis by coecum ligation & puncture

Herrera MT et al. ICM 2003; 29:1345

PEEP modulates local and systemic inflammatory responses in a sepsis-induced lung injury model
Design:

20 rats each group, Sepsis by coecum ligation & puncture
2 control groups, ventilation for 3h:

shv: sepsis + high tidal volume, zero PEEP

Herrera MT et al. ICM 2003; 29:1345
PEEP modulates local and systemic inflammatory responses in a sepsis-induced lung injury model
TNF-α in Plasma [pg/ml]

Herrera MT et al. ICM 2003; 29:1345
20 ml/kg
6 ml/kg
6 ml/kg + PEEP

TNF-α in Plasma [pg/ml]

Herrera MT et al. ICM 2003; 29:1345
Lung injury scoring

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Intraoperative Ventilator Settings and activation of inflammatory
Intraoperative Ventilator Settings and activation of inflammatory

• Prospective randomized study
Intraoperative Ventilator Settings and activation of inflammatory

- Prospective randomized study
- 39 patients
  - Extra-thoracic surgery

Wrigge et al Anesthesiology, 2000
Intraoperative Ventilator Settings and activation of inflammatory

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- Monitored for pro-inflammatory cytokines

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- I: Tidal volume 15 ml/kg, ZEEP

Wrigge et al. Anesthesiology, 2000
Prospective randomized study

39 patients
  - Extra-thoracic surgery

Monitored for pro-inflammatory cytokines

I: Tidal volume 15 ml/kg, ZEEP
II: Tidal volume 6 ml/kg, ZEEP

Wrigge et al. Anesthesiology, 2000
Intraoperative Ventilator Settings and activation of inflammatory

- Prospective randomized study
- 39 patients
  - Extra-thoracic surgery
- Monitored for pro-inflammatory cytokines

- I: Tidal volume 15 ml/kg, ZEEP
- II: Tidal volume 6 ml/kg, ZEEP
- III: Tidal volume 6 ml/kg, PEEP = 10 cmH2O

Wrigge et al Anesthesiology, 2000
Results: Cytokine after 1h ventilation

A

High $V_T$ / ZEEP

Low $V_T$ / ZEEP

Low $V_T$ / PEEP
Should patients without ALI/
Age, Duration of Mechanical Ventilation, and Outcomes of Patients Who Are Critically Ill
Age, Duration of Mechanical Ventilation, and Outcomes of Patients Who Are Critically Ill

- **Design:** Retrospective chart review of patients admitted to hospital ICU between 2003-2008.

Feng et al. Chest 2009; 136; 759-764
Age, Duration of Mechanical Ventilation, and Outcomes of Patients Who Are Critically Ill

- **Design:** Retrospective chart review of patients admitted to hospital ICU between 2003-2008.
- **Study Population:** 4,238 adult (>18) patients who were admitted to ICU and received invasive mechanical ventilation.
Age, Duration of Mechanical Ventilation, and Outcomes of Patients Who Are Critically Ill

• **Design:** Retrospective chart review of patients admitted to hospital ICU between 2003-2008.

• **Study Population:** 4,238 adult (>18) patients who were admitted to ICU and received invasive mechanical ventilation.

• **Hypothesis:** Age and duration of mechanical ventilation will provide prognostic information as the trial of therapy proceeds.

Feng et al. Chest 2009; 136; 759-764
30% of patients ventilated >24h do not survive!

Feng et al. Chest 2009; 136; 759-764
Intraoperative Ventilator Settings and Acute Lung Injury after Elective Surgery: a Nested Case–
Intraoperative Ventilator Settings and Acute Lung Injury after Elective Surgery: a Nested Case–Prospective, observational study
Intraoperative Ventilator Settings and Acute Lung Injury after Elective Surgery: a Nested Case–Prospective, observational study

- Prospective, observational study
- 4420 patients from 2005-06
  - Elective surgery
  - Post-OP pulmonary complications
  - Developed ALI within PO day 5 (3.4%)
Intraoperative Ventilator Settings and Acute Lung Injury after Elective Surgery: a Nested Case–

- Prospective, observational study
- 4420 patients from 2005-06
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- Each matched with 2 controls for age, gender, ASA, surgery

Gajic et al, Thorax 2009
Intraoperative Ventilator Settings and Acute Lung Injury after Elective Surgery: a Nested Case–

- Prospective, observational study
- 4420 patients from 2005-06
  - Elective surgery
  - Post-OP pulmonary complications
  - Developed ALI within PO day 5 (3.4%)
- Each matched with 2 controls for age, gender, ASA, surgery
- 60-day (1 year) survival
  - ALI: 72%  Non-ALI: 99%  p<0.001

Gajic et al, Thorax 2009
Ventilatory risk factors for

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (N=166) Mean (SD)</th>
<th>Cases (N=83) Mean (SD)</th>
<th>Adjusted Odds Ratio (95%CI)*</th>
<th>P Valu</th>
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<tbody>
<tr>
<td>First Hour</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tidal volume/ Kg PBW</td>
<td>8.7 (1.7)</td>
<td>8.9 (1.6)</td>
<td>1.03 (0.84-1.26)</td>
<td>0.80</td>
</tr>
<tr>
<td>PEEP, cmH$_2$O</td>
<td>1.7 (2.2)</td>
<td>1.4 (2.5)</td>
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<td>Peak airway pressure, cmH$_2$O</td>
<td>19 (4.8)</td>
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<td>Respiratory rate, cycles/min</td>
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<td>FIO$_2$, %</td>
<td>73 (18)</td>
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Gajic et al, Thorax 2009
Impact of intraoperative lung protective interventions in patients undergoing lung

- Observational cohort study (10 y)
- 5 y of LPV protocol 2003-2008 (n=558)
- comparison with historic cohort 1998-2003 (n=533)

Licker et al, Critical Care 2009, 13:R41
Impact of intraoperative lung protective interventions in patients undergoing lung

VT 8 ml/kg PBW
PPLAT < 35 cmH2O
PEEP 4–10 cmH2O
vital capacity maneuvers
(35 cmH2O for 10 sec)
# Protective ventilation for lung surgery

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<th>PLV</th>
<th>P</th>
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<tbody>
<tr>
<td>Atelectasis</td>
<td>8.8</td>
<td>5.0</td>
<td>0.018</td>
</tr>
<tr>
<td>ALI</td>
<td>3.8</td>
<td>0.9</td>
<td>0.032</td>
</tr>
<tr>
<td>ICU Admit</td>
<td>9.4</td>
<td>2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardio Compl.</td>
<td>12.0</td>
<td>11.3</td>
<td>0.723</td>
</tr>
<tr>
<td>Mortality</td>
<td>2.8</td>
<td>2.3</td>
<td>0.753</td>
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Licker et al, Critical Care 2009, 13:R41
Does a Protective Ventilation Strategy Reduce the Risk of Pulmonary Complications After Lung
Does a Protective Ventilation Strategy Reduce the Risk of Pulmonary Complications After Lung

- Prospective trial 122 pts. Elective lobectomy

Yang M et al CHEST 2011;139:530-537
Does a Protective Ventilation Strategy Reduce the Risk of Pulmonary Complications After Lung

- Prospective trial 122 pts. Elective lobectomy
- General anesthesia + TEA

Yang M et al CHEST 2011;139:530-537
Does a Protective Ventilation Strategy Reduce the Risk of Pulmonary Complications After Lung Lobectomy?

- Prospective trial 122 pts. Elective lobectomy
- General anesthesia + TEA
- During one-lung ventilation
  - CV: 10 ml/kg IBW, ZEEP
  - PV: 5 ml/kg PBW, PEEP 5 cmH2O

Yang M et al CHEST 2011;139:530-537
Does a Protective Ventilation Strategy Reduce the Risk of Pulmonary Complications After Lung

- Prospective trial 122 pts. Elective lobectomy
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- No randomization

Yang M et al CHEST 2011;139:530-537
Does a Protective Ventilation Strategy Reduce the Risk of Pulmonary Complications After Lung

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- No randomization
- No blinding

Yang M et al CHEST 2011;139:530-537
Conventional vs. protective

Yang M et al CHEST 2011;139:530-537
Ventilation in ICU
Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation
Ventilator–associated lung injury in patients without acute lung injury at the onset of mechanical ventilation

- Retrospective, single center cohort study
Ventilator–associated lung injury in patients without acute lung injury at the onset of mechanical ventilation

- Retrospective, single center cohort study
- All patients admitted to ICU in 2001 and ventilated >48h (447)
  - No ALI present at onset of ventilation (332)
  - No exclusion criteria (long-term vent, neuromuscul. Disease, no consent)
Ventilator–associated lung injury in patients without acute lung injury at the onset of mechanical ventilation

- Retrospective, single center cohort study
- All patients admitted to ICU in 2001 and ventilated >48h (447)
  - No ALI present at onset of ventilation (332)
  - No exclusion criteria (long-term vent, neuromuscul. Disease, no consent)
- Analysis for ventilation parameters & risk factors

Gajic et al, Crit Care Med, 2004
Results: Influence of tidal

High VT was associated with

- female gender
- short height
- routine post-op
- Lesser severity of disease
- better gas exchange parameters

Gajic et al, Crit Care Med, 2004
High VT was associated with

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Gajic et al, Crit Care Med, 2004
# Results: Risk factors

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<th>N=80</th>
<th>Adjusted OR</th>
<th>P-value</th>
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<tbody>
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<td>High VT, per ml/kg</td>
<td>1.29 (1.12–1.51)</td>
<td>&lt;0.001</td>
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<td>Low pH (&lt; 7.35)</td>
<td>2.0 (1.1–3.79)</td>
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<td>Blood transfusion</td>
<td>2.97 (1.56–5.9)</td>
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<td>Restrictive lung disease</td>
<td>3.6 (1.0–12.6)</td>
<td>0.044</td>
<td></td>
</tr>
</tbody>
</table>

24% of patients developed ALI, mostly within 3 days of admission

Gajic et al, Crit Care Med, 2004
Low $V_T$ vs. Traditional $V_T$

Determann J et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without ALI: a preventive randomized controlled trial. Crit Care 2010; 14:R1
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- Secondary objective:
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Determann J et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without ALI: a preventive randomized controlled trial. Crit Care 2010; 14:R1
All Patients
All Patients

only Patients With ALI
6 vs. 10 ml/kg PBW in Pts.

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Ventilation group and higher PEEP independent predictors of ALI in multivariate model

Weaknesses:
- Stopped after interim analysis (underpowered)
- No difference for primary objectives

Determann J et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without ALI: a preventive randomized controlled trial. Crit Care 2010; 14:R1
LPV prevents development of
Experimental Sepsis in rats

- LPS 15 mg/kg IV, fluid resuscitation
- Ventilation for 5h
  - 8 ml/kg
  - PEEP 5 cmH2O
  - FiO₂ 0.4
- Septic lung injury

PaO$_2$–FiO$_2$ ratio / Lung

PaO$_2$–FiO$_2$ ratio / Lung

Diffuse Alveolar Damage

Controls

Sepsis

Sepsis induced by CASP

10 rats each, lung protective ventilation

P/F

Sepsis induced by CASP
10 rats each, lung protective ventilation

P/F

390.000
365.625
341.250
316.875
292.500

BL 1hr 4hr

CV control
CV sepsis
PS control
PS sepsis

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Effects on microcirculation

Leukocyte adhesion V1

Figure 1a: Leukocyte adhesion [n/30s] in submucosal collecting (V1) venules
* p<0.05 vs. control

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FCD: Musc.long.function.

Figure 2a: Functional capillary density
* p<0.05 vs. control ; # p<0.05 vs. PSV
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Long-term effects of spontaneous breathing during ventilatory support in patients with acute lung injury.

• 30 patients with chest trauma with or at risk for ALI/ARDS
• pressure control (PCV) vs. airway pressure release ventilation (APRV)
• 72h Sedation in PCV
• Outcomes: Oxygenation, hemodynamics, progression to

Putensen et al. AJRCCM 2001; 164:43-9
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Preserved spontaneous breathing in early ARDS: Effects on oxygenation

![Graph showing changes in PaO2/FiO2 over time with APRV and PCV]
Preserved spontaneous breathing in early ARDS: Effects on cardiac output

Putensen et al. AJRCCM 2001; 164:43-9
## APRV vs. PCV: Outcomes

<table>
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<tr>
<th></th>
<th>APRV Group</th>
<th>PCV Group</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>Number of patients, n (%)</td>
<td>15 (100)</td>
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<td>–</td>
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<tr>
<td>Survivors, n (%)</td>
<td>12 (80)</td>
<td>11 (74)</td>
<td>ns</td>
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<td>ARDS, n (%)</td>
<td>3 (20)</td>
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<tr>
<td>1</td>
<td>8 (53)</td>
<td>10 (67)</td>
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<tr>
<td>2</td>
<td>6 (38)</td>
<td>7 (47)</td>
<td>ns</td>
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<tr>
<td>≥ 3</td>
<td>1 (9)</td>
<td>0 (0)</td>
<td>ns</td>
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<tr>
<td>Sepsis, n (%)</td>
<td>9 (75)</td>
<td>10 (30)</td>
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<tr>
<td>Length of ventilatory support, d</td>
<td>15 ± 2</td>
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Conclusion I
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• Short-term lung protective ventilation during surgery may have an influence on outcome
  • PROVHILO study (900 pts)
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- Short-term lung protective ventilation during surgery may have an influence on outcome
  - PROVHILO study (900 pts)
- Low tidal volume ventilation with PEEP on admission to ICU reduces the risk of developing ALI
Conclusion II

• It may be that ALI/ARDS is largely a ‘man-made’ syndrome, developing as a consequence of the aggressive treatment applied to acutely ill patients.

Villar J & Slutsky A. Is ARDS an iatrogenic disease? Crit Care 2010; 14:120
Conclusion II

- It may be that ALI/ARDS is largely a ‘man-made’ syndrome, developing as a consequence of the aggressive treatment applied to acutely ill patients.

- If so, ... ALI/ARDS is no longer a syndrome that must be treated, but is a syndrome that should be prevented.

Villar J & Slutsky A. Is ARDS an iatrogenic disease? Crit Care 2010; 14:120
Thank you!

Department of Anesthesia

Dalhousie University
Inspiring Minds
Faculty of Medicine