Ventilation and Pulmonary Vascular Injury

The Heart of the Matter

Dedicated to Brian Kavanagh

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Adverse Heart–Lung Interactions in Ventilator-induced Lung Injury

Abstract

Rationale: In the original 1974 in vivo study of ventilator-induced lung injury, Webb and Tierney reported that high Vt with a small tidal volume (VT) at a high frequency (f) produced greater lung injury than a low VT at a high f. In the current study, we replicated these findings in rats and investigated whether these results are applicable to other ventilator settings.

Methods and Main Results: We compared the effects of high VT (45/0 cmH2O) and low VT (45/10 cmH2O) on lung injury and pulmonary vascular changes in rats. The rats were divided into two groups: one with high VT and the other with low VT. The results showed that the high VT group had significantly greater lung injury compared to the low VT group. Additionally, the rats in the high VT group showed significant vascular changes as compared to the low VT group.

Conclusion: These findings suggest that high VT may be associated with greater lung injury and vascular changes in ventilator-induced lung injury. Further research is needed to understand the mechanisms behind these findings and to develop strategies to minimize lung injury and vascular changes in ventilator-induced lung injury.
Same lung histology patterns as Webb and Thierney

Perivascular edema
0 to +

Perivascular edema
+++
Ventilation alters cardiac output through 2 main processes

1. Changes in Pleural pressure (Ppl)
   - Alters venous return
2. Changes in Transpulmonary pressure (TP)
   - Alters RV outflow
Which is dominant?
Ventilation alters cardiac output through 2 main processes

1. Changes in Pleural pressure (Ppl)
   - Alters venous return

2. Changes in Transpulmonary pressure (TP)
   - Alters RV outflow
Normal gradient for VR is very small

Therefore, small changes in Pra relative to atmosphere can have large effects on VR and Q

Stressed volume

MSFP

4-8 mmHg

Pra

Q
Change $P_{pl}$ with or without changing $P_{TP}$

Scharf, Caldini, Ingram Am J Physiol. 1997
Change $P_{pl}$ with or without changing $P_{TP}$
Scharf, Caldini, Ingram Am J Physiol. 1997

Cardiac effects

Dominant effect was change in $P_{pl}$

But also some TP effect at TP > 10 mmHg
Ventilation alters cardiac output through 2 main processes

1. Changes in Pleural pressure (Ppl)
   - Alters venous return

2. Changes in Transpulmonary pressure (TP)
   - Alters RV outflow
Pulmonary vascular reservoir and buffer
Does lung inflation increase PVR?

- Whittenberg et al. 1960: Increase in resistance
- Permutt et al. 1962: Vascular waterfall effect

Graphs showing:
- Resistance vs. Change in Palv
- Resistance vs. Change in Palv
Influence of state of inflation of the lung on pulmonary vascular resistance

JAMES L. WHITTENBERGER, MAURICE McDERMOTT,
ERIK BERGLUND and HANS G. BORST
Department of Physiology, Harvard School of Public Health,
Boston, Massachusetts

Whittenberger, James L., Maurice McGregor, Erik
Berglund and Hans G. Borsl Influence of state of inflation of
the lung on pulmonary vascular
8/8-02. 1960.—The in

Rise in PVR with lung inflation
Alveolar Pressure, Pulmonary Venous Pressure, and the Vascular Waterfall

By S. PERMUTT, B. BROMBERGER-BARNEA and H. N. BANE
Lung inflation can load the RV by creating “non-zone III conditions”

Palv then directly impedes RV ejection

\[ P_{alv} < P_{LA} \]

\[ P_{alv} > P_{LA} \]
Permutt et al 1962
Vascular waterfall effect

Diagram: Pulmonary Artery Pressure vs. Cardiac Output with lines showing changes in pulmonary artery pressure (Palv) with different levels of cardiac output. The diagram also shows the relationship between resistance and change in Palv.
Significance of development of non-zone III for the driving pressure

- There is no effect of TP pressure on PVR until a threshold is reached and then there are cyclic loads on the RV.
- The load from Non-zone III condition is distal to the pulmonary exchange vessels and thus increases filtration on each breath.
- The effect depends upon upstream pulmonary resistance, cardiac output and downstream LA pressure PLUS lung compliance and driving pressure.
Development of non-zone III during inspiration.

Ppao is no longer valid – load on RV is Palv

**Post cardiac Sx:** ACV, random changes in TV

Measured change in Peso and change Ppao

-dPpao usually 2-3 mmHg > dPeso (Bellemare et al 2007)
Computer modeling study to resolve the differences

Increase in Ptp alone

A

B
Heart Lung Interaction and Pulmonary Buffering
Magder & Guerard *Resp Physio and Neurobiology* 2012
Sustained changes

Ppl alone

Ptp alone
Cyclic changes

A: Ppl alone

B: MSFP

C: Ptp alone

D: PV

Ppl (mmHg)
0 2 4 6 8 10 12 14 16 18 20
Cardiac Output (ml/min)
0 1000 2000 3000 4000 5000 6000

Ptp (mmHg)
0 10 20 30 40 50
Cardiac Output (ml/min)
0 1000 2000 3000 4000 5000 6000

Pressure (mmHg)
0 4 8 12 16
Ppl (mmHg)
0 4 8 12 16 20

Pressure (mmHg)
0 4 8 12 16
Ptp (mmHg)
0 10 20 30 40 50
Increase in Ppl alone

“Pulmonary Buffering”

Factors:
- Volume in pulmonary vessels
- Cvp and Rvp
- Heart rate
- RR

But not LV

RV SV is almost 0)
Increase in Ptp alone

“No Pulmonary Buffering”

- Volume accumulates in pulmonary vessels
- Large SVV which increase when volume given
- Worse effect on LV

But not RV

But not RV

SV falls
Adverse Heart–Lung Interactions in Ventilator-induced Lung Injury

Bhushan H. Katira\textsuperscript{1,2,3}, Regan E. Giesinger\textsuperscript{1,4}, Doreen Engelberts\textsuperscript{1}, Diana Zabini\textsuperscript{5}, Alik Kornecki\textsuperscript{6}, Gail Otulakowski\textsuperscript{1}, Takeshi Yoshida\textsuperscript{1,2,3}, Wolfgang M. Kuebler\textsuperscript{5,7,8}, Patrick J. McNamara\textsuperscript{1,4}, Kim A. Connelly\textsuperscript{5}, and Brian P. Kavanagh\textsuperscript{1,2,3,8,9}

AJRCCM 2017

<table>
<thead>
<tr>
<th>Paw (cmH\textsubscript{2}O)</th>
<th>Part (mmHg)</th>
<th>RV (mmHg)</th>
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<tr>
<td>45/0 cmH\textsubscript{2}O</td>
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Inspiration  

High Psys on Exp  

Psys is much lower
high peak pressure (and zero positive end-expiratory pressure) causes respiratory swings (obliteration during inspiration) in right ventricular filling and pulmonary perfusion, ultimately resulting in right ventricular failure ….. The lung injury and acute cor-pulmonale is likely due to pulmonary microvascular injury, the mechanism of which is uncertain, but which may be due to cyclic interruption and exaggeration of pulmonary blood flow.
Lower Psyst but steady

No change in LVEDP
Importance of high driving pressure

• What ever the starting value from PEEP, the higher the driving pressure –
  – The greater the inspiratory decrease in venous return
  – The greater potential to create non-zone III conditions
Primary cause of injury – Lung or Heart

• They are mirror images!
• Affected by same variables
• Primary increase in edema is perivascular
• Does high changes in shear stress in pulmonary circulation cause the injury?
• Increase in pulmonary capillary pressure from increase TP?
• Transient decrease in systemic flows and MOD?
Solutions (work for both hypothesis!)

1. Trans-pulmonary pressure
   - Avoid excessive PEEP
     - It can lower Q and PAP
   - Tidal volume
     - Use low T\(_v\) (6 ml/kg)
   - Improve lung compliance
     - Best PEEP!
   - Other possibilities
     - Decrease PVR?
     - Avoid too low Pla?
     - Function of RV?
Does lung inflation increase PVR?

- Whittenberg et al 1960
  - Increase in resistance

- Permutt et al 1962
  - Vascular waterfall effect
Lung inflation does not load the RV unless the positive pressure creates zone II conditions. It then directly impedes RV ejection.

\[ P_{LA} > P_{alv} \]

Expiration

\[ P_{LA} < P_{alv} \]
Cardiac Output is determined by a return function and a cardiac function.
Conclusions:

• Small changes in Ppl can have a large effect on VR and cardiac output
• Development of non-zone III creates critical closing pressure ("waterfall" or "flow-limitation" which loads the RV
• Avoid larger tidal volumes
• Be careful with PEEP
• Improve lung compliance
• Consider cardiac status (RV, LA, PVR)
Fig. 4. — Diagram from Humphrey's article in 1937 which demonstrates that inflation of the lungs may directly compress the cardiac fossa and the inferior vena cava.
Adverse Heart-Lung Interactions in Ventilator-induced Lung Injury

Lung injury --- THE HEART of the MATTER

St. Michael’s Hospital, Toronto, Ontario, Canada; and Department of Pediatrics, London Health Sciences Centre, London, Ontario, Canada

Abstract

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Measurements and Main Results: The original Webb and Tierney results were replicated in terms of lung/body weight ratio (45/0 > 45/10 ≈ 30/0 ∼ 14/0; \( P < 0.05 \)) and histology. In 45/0, pulmonary edema was overt and rapid, with survival less than 30 minutes. In 45/0 (but not 45/10),

Or

Things are not always what they seem
Lowering pH raises Ppa for same Palv

Indicates that acidemia increases Pcrit

Consider implications for permissive hypercapnea

Lopez-Muniz et al 1968
? Rise in pulmonary vascular resistance?

Inspiration (Paw = 20 cmH$_2$O)

But this does not occur because fluids are not compressible
Effect of PEEP on Venous Return

Nanas & Magder Am Rev Respir Dis 1992

- MSFP (mmHg) vs Blood Volume (ml/kg)
- VR (ml/min) vs Blood Volume (ml/kg)
- PEEP levels: 0, 10, 20
- Q is restored
Can the respiratory variation in Pra during triggered breaths be used to predict the response to PEEP?

S. Magder, D Lagonidis, F Erice 2001; JCCM :16
Pulmonary vascular reservoir and buffer
Increase in Ptp alone

R Heart  |  L Heart

“No Pulmonary Buffering”
- Volume accumulates in pulmonary vessels
- Large SVV which increase when volume given

But not RV

LV SV falls

P (mmHg)

Volume (ml)

Time
Striking rise of RV Pressure during Exp
No pressure during insp
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