Lung Volume optimization

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Conflict of interest statement:

Dr Lista has received honoraria for lectures from Chiesi, Draeger and Vyaire Company. None of these Companies had any input into the content of this presentation.
Mechanisms of ventilator-induced lung injury in premature infants

Mohammad Ali Attar and Steven M. Donn

Mechanical ventilation in premature infants may injure the lungs or exacerbate the pre-existing condition that led to the need for mechanical ventilation. Ventilator-induced lung injury (VILI) may be associated with alveolar structural damage, pulmonary oedema, inflammation, and fibrosis. This injury is not uniform and is associated with surfactant dysfunction. Recovery from VILI includes clearance of pulmonary oedema and alveolar structural repair. Mechanisms of VILI include high airway pressure (barotrauma), large gas volumes (volutrauma), alveolar collapse and re-expansion (atelectotrauma), and increased inflammation (biotrauma). Injury to the lung may lead to other organ dysfunction. The premature lung is more susceptible to VILI and lung injury may exacerbate the disturbance of lung development that occurs after birth.

Therapies targeting specific processes in lung injury, and which complement the protective ventilator management strategies to avoid atelectotrauma and lung overdistension are an area of active research.

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### Table 1. Mechanisms of VILI

<table>
<thead>
<tr>
<th>Barotrauma</th>
<th>Volutrauma</th>
<th>Atelectotrauma</th>
<th>Biotrauma</th>
<th>Rheotrauma</th>
</tr>
</thead>
</table>

Partially modified
Editorial

Open up the lung and keep the lung open

B. Lachmann

Department of Anesthesiology, Erasmus University Rotterdam, The Netherlands

Since its introduction into clinical use more than 40 years ago artificial ventilation has proven to be a life-saving method of therapy in intensive care. Yet, it has remained a topic of much discussion and controversy because artificial ventilation involves a disturbance to normal respiratory and cardiovascular function.

It is an established fact that artificial ventilation, especially with large tidal volumes and high peak inspiratory pressures, leads to a decrease in lung compliance and dysfunction of gas exchange. Of even greater importance is the realization that ventilation itself can lead to formation of atelectasis, pulmonary edema, pneumonitis and fibrosis (for review see [1–4]); that is why the adult respiratory distress syndrome (ARDS) may be, in part, a product of our therapy — rather than the progression of the underlying disease.

To date no adequate explanation of the pathophysiologic basis of these changes caused by artificial ventilation has been documented. The main contributing factors which emerge from almost all the above-mentioned references seem to be the ventilatory modes which fail to prevent partial (or complete) end-expiratory lung collapse combined with high peak inspiratory pressures.

In this issue Sjöstrand's group, using an animal model of ARDS induced by surfactant depletion, applied five established ventilator modes, adjusting either volume or pressure at preset frequencies to keep end-expiratory alveolar pressure at about 16 cmH₂O and PaCO₂ constant (±4 kPa). From their study the following three remarkable results emerge:

1. To open up partially collapsed lungs ventilated in their control mode, a peak pressure of 55 cmH₂O (= opening pressure) in combination with an end-expiratory alveolar pressure of about 16 cmH₂O, resulting in a pressure amplitude of approximately 40 cmH₂O, had to be applied for 5–10 min.

2. After opening the lungs (PaO₂ > 50 kPa) they could then be adequately ventilated (PaO₂ and PaCO₂ remained stable) with pressure amplitudes of only 16 to 23 cmH₂O in those ventilator modes which created intrinsic PEEP.

3. In the volume controlled mode, with an external PEEP of 8 cmH₂O, a pressure amplitude of almost twice that required by modes creating internal PEEP was necessary for adequate ventilation and even then the lungs could not be kept completely open (PaO₂ about 40 kPa).

Why is it so important to ventilate lungs with as small as possible pressure amplitude?

More than twenty years ago Mead et al. stated that: "at a transpulmonary pressure of 30 cmH₂O, the pressure tending to expand an atelectatic region surrounded by a fully expanded lung would be approximately 140 cmH₂O" [5]. Such forces may well be the major cause of structural damage (especially to bronchial epithelium, alveolar epithelium and capillary endothelium) and may not only be the basis for formation of hyaline membranes but may also cause the release of mediators from the disrupted parenchyma — triggering the pathophysiologic mechanisms of ARDS [6].

During ventilation of patients with ARDS, who almost always have atelectatic lung regions, pressure differences of 30 cmH₂O or higher are quite common. We have to understand, however, that it is not the 30 cmH₂O pressure difference that damage the lungs but rather the resulting shear forces of more than 140 cmH₂O which are responsible for the barotrauma.

Sjöstrand's group does not present morphologic data, but from other experiments related to different modes of artificial ventilation in ARDS lungs (see referred reviews) it was clearly demonstrated that lungs ventilated with modes which did not prevent end-expiratory alveolar collapse, thus creating shear forces, showed more severe morphologic damage (and lower arterial PaO₂ compared to modes which kept the entire lungs open during the whole respiratory cycle.

It must be concluded that in order to prevent lung damage due to high shear forces between open and closed lung units only ventilation modes which result in the smallest possible pressure amplitude should be used.
Achiving and maintaining lung volume in the preterm infant: from the first breath to the NICU

Gianluca Lista¹ · Andrés Maturana² · Fernando R. Moya³

What is Known:

• Experimental and clinical studies have shown that the transition from fetal to adult type cardiorespiratory circulation needs an adequate lung ventilation. An appropriate management in the delivery room should lead to the achievement of an early FRC, and through the following steps, the neonatologist should aim at maintaining an adequate lung volume.

• Literature underlines the importance of a respiratory tailored management of preterm infants during the whole NICU stay to maintain the benefits of a successful postnatal adaption.

What is New:

• Herewith, we describe the most relevant and recent interventions which can be performed from the delivery room to the NICU stay to guarantee an adequate tradition to postnatal life and an effective cardiorespiratory stability.
STATE-OF-THE-ART

Delivery room interventions to prevent bronchopulmonary dysplasia in extremely preterm infants

EE Foglia¹,², EA Jensen¹,² and H Kirpalani¹,²
Manual Ventilation with a Few Large Breaths at Birth Compromises the Therapeutic Effect of Subsequent Surfactant Replacement in Immature Lambs
Lars J Björklund, Jonas Ingimarsson, Tore Curstedt, Joseph John, Bengt Robertson, Olof Werner and Carsten T
Pediatric Research (1997) 42, 348–355
Initiation of Resuscitation with High Tidal Volumes Causes Cerebral Hemodynamic Disturbance, Brain Inflammation and Injury in Preterm Lambs

Graeme R. Polglase, Suzanne L. Miller, Samantha K. Barton, Ana A. Baburamani, Flora Y. Wong, James D. S. Aridas, Andrew W. Gill, Timothy J. M. Moss, Mary Tolcos, Martin Kluckow, Stuart B. Hooper

1 The Ritchie Centre, Monash Institute of Medical Research, Monash University, Clayton, Victoria, Australia, 2 Department of Obstetrics and Gynecology, Monash University, Clayton, Victoria, Australia, 3 Centre for Neonatal Research and Education, School of Women’s and Infants’ Health, The University of Western Australia, Crawley, Western Australia, Australia, 4 Department of Neonatal Medicine, Royal North Shore Hospital and University of Sydney, Sydney, New South Wales, Australia

Abstract

Aims: Preterm infants can be inadvertently exposed to high tidal volumes (VT) in the delivery room, causing lung inflammation and injury, but little is known about their effects on the brain. The aim of this study was to compare an initial 15 min of high VT resuscitation strategy to a less injurious resuscitation strategy on cerebral haemodynamics, inflammation and injury.

Methods: Preterm lambs at 126 d gestation were surgically instrumented prior to receiving resuscitation with either: 1) High VT targeting 10–12 mL/kg for the first 15 min (n=6) or 2) a protective resuscitation strategy (Prot VT), consisting of prophylactic surfactant, a 20 s sustained inflation and a lower initial VT (7 mL/kg; n=6). Both groups were subsequently ventilated with a VT 7 mL/kg. Blood gases, arterial pressures and carotid blood flows were recorded. Cerebral blood volume and oxygenation were assessed using near infrared spectroscopy. The brain was collected for biochemical and histologic assessment of inflammation, injury, vascular extravasation, hemorrhage and oxidative injury. Unventilated controls (UVC; n=6) were used for comparison.

Results: High VT lambs had worse oxygenation and required greater ventilatory support than Prot VT lambs. High VT resulted in cerebral haemodynamic instability during the initial 15 min, adverse cerebral tissue oxygenation index and cerebral vasoparalysis. While both resuscitation strategies increased lung and brain inflammation and oxidative stress, High VT resuscitation significantly amplified the effect (p = 0.014 and p<0.001). Vascular extravasation was evident in the brains of 60% of High VT lambs, but not in UVC or Prot VT lambs.

Conclusion: High VT resulted in greater cerebral haemodynamic instability, increased brain inflammation, oxidative stress and vascular extravasation than a Prot VT strategy. The initiation of resuscitation targeting Prot VT may reduce the severity of brain injury in preterm neonates.
between the groups (p = 0.271). The number of 4HN 
positive cells, indicators of oxidative injury, was significantly higher in High VT lamb within the periventricular white matter compared to UVC (p<0.001) and showed a strong trend to be greater than Prot VT lamb (p = 0.034). There was no difference observed in the subcortical white matter (p = 0.13; Table 1).

Figure 1. Peak inspiratory pressure (A), tidal volume (B), dynamic compliance (C) and the fraction of inspired oxygen (FiO2; D) in High VT (open circles) and Prot VT (closed circles) lambs. *p<0.05 High VT vs. Prot VT.
doi:10.1371/journal.pone.0039535.g001

Figure 2. The partial pressure of arterial (Pa) carbon dioxide (CO2; A), oxygen (O2; B), oxygenation index (C) and the alveolar-arterial difference in oxygen (A-aO2; D) in High VT (open circles) and Prot VT (closed circles) lambs. *p<0.05 High VT vs. Prot VT
doi:10.1371/journal.pone.0039535.g002

Figure 5. Lung pro-inflammatory mRNA cytokine expression of interleukin (IL)-1β, IL-6 and IL-8 in unventilated controls (open bars), Prot VT (shaded bars) and High VT (black bars) lambs. Values are expressed relative to UVC. Resuscitation, irrespective of the strategy, increased lung inflammation. *p<0.05 vs UVC.
doi:10.1371/journal.pone.0039535.g005

= unventilated
= Prot VT
= high VT

June 2012 | Volume 7 | Issue 6 | e39535
In summary, this study has shown that resuscitation increases brain inflammation and oxidative stress, but an initial high VT resuscitation strategy further exacerbated cerebral hemodynamic instability, brain inflammation and injury. This study highlights the critical role that the initial respiratory support has on the development of brain inflammation and injury, and the requirement for better monitoring of delivered tidal volumes to preterm infants in the delivery room. It also demonstrates that brain injury can be seen within 90 minutes of the onset of an injurious stimulus, and the severity of brain injury can be reduced by protective resuscitation strategies in the delivery room.
Respiratory Function Monitor (RFM)

Figure 2. In panel A, the clinical team is guiding positive pressure ventilation by observing chest rise compared with panel B where a respiratory function monitor is used to guide expired tidal volume ($V_{Te}$) delivery. Initially, no chest rise is observed, the inflation and expiratory flow curves are small, and the measured $V_{Te}$ is $\sim 1$ mL/kg. The clinical team is increasing the peak inflation pressure (PIP) to 42 cm H$_2$O, which results in an increase in $V_{Te}$ to 5 to 8 mL/kg; however, there was still no chest rise visible. The clinical team continued to increase the PIP to 50 cm H$_2$O PIP, which resulted in an increase of $V_{Te}$ to 14 mL/kg and visible chest rise. In comparison, in B, the initial $V_{Te}$ was 3 mL/kg. After an increase in PIP, $V_{Te}$ increased to 10 mL/kg. After the clinical team recognized the large $V_{Te}$, the PIP was reduced to 20 cm H$_2$O, which resulted in a decrease in the delivered $V_{Te}$ to $\sim 5$ mL/kg.
Background: SI and transition

- SI and PEEP allow an early FRC and uniformity of lung areation
  (te Pas A et al., Pediatric Research 2009)

- SI improves the respiratory and cardiovascular transition at birth in preterm lambs
  (Sobotka K et al, Pediatric Research 2011)

- SI improves speed of circulatory rate and lung compliance in near-term asphyxiated lambs
  (Klingenbergr C et al, Arch Dis Child Fetal Neonatal)
Initiation of Resuscitation with High Tidal Volumes Causes Cerebral Hemodynamic Disturbance, Brain Inflammation and Injury in Preterm Lambs

Graeme R. Polglase¹,², Suzanne L. Miller¹,², Samantha K. Barton¹, Ana A. Baburamani¹, Flora Y. Wong¹, James D. S. Aridas¹, Andrew W. Gill³, Timothy J. M. Moss¹,², Mary Tolcos¹, Martin Kluckow⁴,⁵, Stuart B. Hooper¹,²

¹The Ritchie Centre, Monash Institute of Medical Research, Monash University, Clayton, Victoria, Australia, ²Department of Obstetrics and Gynecology, Monash University, Clayton, Victoria, Australia, ³Centre for Neonatal Research and Education, School of Women’s and Infants’ Health, The University of Western Australia, Crawley, Western Australia, Australia, ⁴Department of Neonatal Medicine, Royal North Shore Hospital and University of Sydney, Sydney, New South Wales, Australia

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Results: High VT lambs had worse oxygenation and required greater ventilatory support than Prot VT lambs. High VT resulted in cerebral haemodynamic instability during the initial 15 min, adverse cerebral tissue oxygenation index and cerebral vasoparalysis. While both resuscitation strategies increased lung and brain inflammation and oxidative stress, High VT resuscitation significantly amplified the effect (p = 0.014 and p<0.001). Vascular extravasation was evident in the brains of 60% of High VT lambs, but not in UVC or Prot VT lambs.

Conclusion: High VT resulted in greater cerebral haemodynamic instability, increased brain inflammation, oxidative stress and vascular extravasation than a Prot VT strategy. The initiation of resuscitation targeting Prot VT may reduce the severity of brain injury in preterm neonates.
Sustained Inflation at birth did not protect preterm fetal sheep from lung injury

Noah H. Hillman
Matthew W. Kemp
Peter B. Noble
Suhas G. Kallapur
Alan H. Jobe


Table 2: Proteins released into fetal lung fluid and bronchoalveolar lavage fluids

<table>
<thead>
<tr>
<th>Group</th>
<th>HSP70</th>
<th>HSP60</th>
<th>Total Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FLF 15m</td>
<td>FLF 45m</td>
<td>BALF</td>
</tr>
<tr>
<td>PEEP</td>
<td>5±0.4</td>
<td>33±4</td>
<td>105±5</td>
</tr>
<tr>
<td>SI</td>
<td>36±3*</td>
<td>45±6</td>
<td>105±7</td>
</tr>
<tr>
<td>MV</td>
<td>42±2*</td>
<td>50±3*</td>
<td>150±10†</td>
</tr>
<tr>
<td>MV + SI</td>
<td>48±3†</td>
<td>51±3*</td>
<td>156±8†</td>
</tr>
</tbody>
</table>

Values: Mean±SEM  * p<0.05 vs PEEP  † p<0.05 vs PEEP and SI groups
• «A prolonged SI at birth will recruit a variable FRC without worsening the lung injury from MV

• If a prolonged SI decreases intubation rates or the length of MV in preterm infants, our animal model suggests this is a reasonable intervention»

Hillmann NH, 2013
Part 7: Neonatal Resuscitation
2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Jeffrey M. Perlman, Co-Chair*; Jonathan Wyllie, Co-Chair*; John Kattwinkel; Myra H. Wyckoff; Khalid Aziz; Ruth Guinsburg; Han-Suk Kim; Helen G. Liley; Lindsay Mildenhall; Wendy M. Simon; Edgardo Szyld; Masanori Tamura; Sithembiso Velaphi; on behalf of the Neonatal Resuscitation Chapter Collaborators

(Circulation. 2015;132[suppl 1]:S204-S241.)

Treatment Recommendation

We suggest against the routine use of initial SI (greater than 5 seconds duration) for preterm infants without spontaneous respirations immediately after birth, but an SI may be considered in individual clinical circumstances or research settings (weak recommendation, low-quality evidence).

European Resuscitation Council Guidelines for Resuscitation 2015
Section 7. Resuscitation and support of transition of babies at birth

Jonathan Wyllie a,*, Jos Bruinenberg b, Charles Christoph Roehr d,*, Mario Rüdiger f, Daniele Trevisanuto*, Berndt Urlesberger g
Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes (Review)

Authors’ conclusions

Sustained inflation was not better than intermittent ventilation for reducing mortality in the delivery room and during hospitalisation. The number of events across trials was limited, so differences cannot be excluded. When considering secondary outcomes, such as need for intubation, need for or duration of respiratory support, or bronchopulmonary dysplasia, we found no evidence of relevant benefit for sustained inflation over intermittent ventilation. The duration of mechanical ventilation was shortened in the SLI group. This result should be interpreted cautiously, as it can be influenced by study characteristics other than the intervention. Future RCTs should aim to enrol infants who are at higher risk of morbidity and mortality, should stratify participants by gestational age, and should provide more detailed monitoring of the procedure, including measurements of lung volume and presence of apnoea before or during the SLI.

......SI and its definitive role (efficacy and safety) in the DR: it is still under investigation.
BACKGROUND: optimal technique for lung recruitment at birth?

OBJECTIVE: To compare 3 ventilation strategies at birth, and the timing of surfactant delivery, in an extremely preterm lamb model.

DESIGN/METHODS: 127d GA lambs (n=8/group, mean BW 2.97 kg) ventilated for 70-min with one of three strategies from delivery:

1. Sustained Inflation (SI): 20-sec 35cmH₂O SI (then PPV+Targeted TV (TTV;7mL/kg, PEEP 6cmH₂O, FiO₂ 0.21) and surfactant at 10-min. FiO₂ and TTV adjusted to maintain SpO₂ 88-92% and PaCO₂ 45-55mmHg.

2. SurfSI: Pre-delivery surfactant otherwise as pre SI.

3. Stepwise PEEP recruitment (SPR): PEEP increased by 2cmH₂O every 10 inflations from 4 to 20 cmH₂O (using PPV+TTV then decreased to the PEEP resulting in maximal $C_\text{rs}$ (Mean (SD) PEEP 7.9(1.6)cmH₂O). Surfactant administered at 10-min.

Measurements: Regular BG analysis. SpO₂, PAW, $C_\text{rs}$, total and regional $V_T$ and end-expiratory lung volume (EELV; respiratory inductive plethysmography and EIT-electrical impedance tomography) were recorded for the first 15-min, and with BG analysis. Statistics: ANOVA.
RESULTS: After the recruitment maneuver, SPR and SurfSI resulted in better EELV, Crs and AaDO₂ compared to SI, with EELV being 18 (SD 9) mL/kg after SPR vs 4 (6) mL/kg after SI (p<0.0001). Crs was 0.22 (0.1) mL/cmH₂O greater than SI for both SurfSI and SPR (p<0.05). Surfactant administration generally negated these differences, but by 70-min SPR again resulted in better AaDO₂, Crs and EELV compared to SI. SI group required a higher TTV (p=0.0017; ANOVA) to maintain desired PaCO₂ range. SI resulted in the least uniform distribution of ventilation.

CONCLUSION: An SEP at birth improved gas exchange, lung mechanics, and EEV, without increasing lung injury, compared to the SI strategy used.
Lung mechanics after surfactant

<table>
<thead>
<tr>
<th>MISURA</th>
<th>PRE-SURFATTANTE</th>
<th>POST-SURFATTANTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISTENSIBILITÀ</td>
<td>0.500 ± 0.086</td>
<td>0.538 ± 0.099</td>
</tr>
<tr>
<td>FRC</td>
<td>9.85 ± 2.10</td>
<td>22.16 ± 3.70</td>
</tr>
<tr>
<td>A/a O₂</td>
<td>3.92 ± 0.70</td>
<td>1.63 ± 0.21</td>
</tr>
</tbody>
</table>

/promedio ± SEM

* P < 0.05


AJ Davis, 1998
**STATE-OF-THE-ART**

Delivery room interventions to prevent bronchopulmonary dysplasia in extremely preterm infants

EE Foglia1,2, EA Jensen1,2 and H Kilpeläniemi1,2

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**...surfactant should be given early (< 2 hrs of life) and modality of administration could influence its effect**

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![Image](image-url)
Therefore it may be a role for **Lung recruitment maneuver** before surfactant replacement in all preterm infants at risk for RDS in order to optimize its effect.
Conclusions: the spatial distribution of ventilation (greater ventilation) in the lavaged lung is significantly modified by a R maneuver performed after Surf administration.
Therefore it may be a role for 1) **a first Lung recruitment maneuver** (e.g. SLI procedure, stepwise increment of PEEP) before surfactant replacement in all preterm infants at risk for RDS in order to optimize its effect.

2) **a second Lung recruitment maneuver** (=High lung volume strategy) after surfactant replacement in all preterm infants in mechanical ventilation for RDS to optimize lung volume with minimal VILI.
Comparison of four methods of lung volume recruitment during HFOV. Int Care Med 2009; 35: 1990

4 lung recruitment methods
(N= 10 piglets, RDS, CMV..then HFOV)
All methods were tested in each animal during HFOV

Escalating-step-wise P Step to PIP= 35 cmH2O in 6’

Sustained dynamic inflation To a PIP= 35 cmH2O for 20”

Repeated dynamic Inflation To a PIP= 35 cmH2O for 1” x 6 times

Standard MAP set
Conclusions: escalating recruitment produced the greatest increase in Thoracic Gas Volume-TGV (p =0.042 ANOVA) and resolution of atelectasis (p=0.016), and it is recommended for lung volume recruitment upon initiation of HFOV

Pellicano A et al
Comparison of four methods of lung volume recruitment during HFOV.
Int Care Med 2009; 35: 1990

TGV= thoracic gas volume
How to optimize lung volume...

NICU management

(Mechanical ventilation: *which strategy* ?)
Open lung strategy both in HFOV and CMV using «low tidal volume»

Gentle concession by P. Tagliabue
Lung Recruitment Using Oxygenation during Open Lung High-Frequency Ventilation in Preterm Infants

Anne De Jaegere, Mariëtte B. van Veenendaal, Agnes Michiels, and Anton H. van Kaam


At the start of HFV, set the CDP at 6–8 cmH₂O and the FiO₂, resulting in a SpO₂ between 86–94%

Increase the CDP 1–2 cmH₂O every 2–3 min and stepwise (0.05–0.10) reduce FiO₂ as oxygenation improves. Stop recruitment when oxygenation no longer improves and/or the FiO₂ ≤ 0.25

Decrease the CDP 1–2 cmH₂O every 2–3 min until oxygenation deteriorates

Recruit the lung once more with the known CDPₜ for 2–3 min and set the CDP 2 cmH₂O above CDPₜ

Obtain chest radiograph Administer surfactant

5–10 min following surfactant treatment decrease the CDP 1–2 cmH₂O every 5 min until oxygenation deteriorates

Increase the CDP in steps of 1–2 cmH₂O every 2–3 min until oxygenation is restored

Set the CDP 2 cmH₂O above the postsurfactant CDPₜ

First recruitment maneuver

Presurfactant opening pressure (CDPₒ)

Presurfactant closing pressure (CDPₜ)

Presurfactant optimal pressure (CDPₒpt)

Obtain chest radiograph Administer surfactant

Second recruitment maneuver

Figure 1. Pre- and postsurfactant recruitment procedures. CDP = continuous distending pressure; CDPₜ = closing pressure; CDPₒ = opening pressure; CDPₒpt = optimal pressure; Fₒ₂ = fractional inspired oxygen; HFV = high-frequency ventilation; SpO₂ (Stco₂) = transcutaneous oxygen saturation.
Step recruitment on the basis of \textit{SpO2} in clinical setting

incremental-decremental CDP trial

De Jaegere et al

\textit{Lung recruitment using oxygenation during open lung high-frequency ventilation in preterm infants.}
Step recruitment on the basis of SpO2 in clinical setting decremental CDP trial

**Optimized CDP = the lowest possible CDP to maintain an open lung**

De Jaegere et al
*Lung recruitment using oxygenation during open lung high-frequency ventilation in preterm infants.*

Gentle concession by P. Tagliabue
Mechanical Ventilation of the Neonate: Should We Target Volume or Pressure?

Steven M Dunn MD and Win Boon MD

Introduction
Gas Delivery
Limitations of Volume Ventilation
Volume-Targeted Modalities
Hybrid Modalities Providing Volume-Targeted Ventilation
Volume-Guarantee Ventilation
Pressure-Regulated Volume Control Ventilation
Volume-Assured Pressure Support
Volume-Support Ventilation
Pressure Augmentation

The Evidence
Volume-Controlled Ventilation
Volume-Guarantee Ventilation
Pressure-Regulated Volume Control
Meta-analysis
Why Does It Work?
Summary

For more than 40 years conventional mechanical ventilation has been used for the treatment of neonatal respiratory failure. Until relatively recently, this was accomplished with time-cycled pressure-limited ventilation, using intermittent mandatory ventilation. Earlier attempts at volume-targeted ventilation were largely ineffective because of technological limitations. The advent of microprocessor-based devices gives the clinician an option to choose either target variable to treat neonatal patients. This paper reviews the principles of each and the accumulated evidence. Key words: newborn, respiratory failure, mechanical ventilation, pressure-targeted, volume-targeted. [Respir Care 2006;51(9):1236–1243. © 2009 Daedalus Enterprises]

Introduction

The traditional method of mechanical ventilation to treat neonatal respiratory failure has been time-cycled pressure-limited ventilation. Originally this was accomplished by modification of adult ventilators. Time-cycled pressure-limited ventilation was easy to use and was left to safeguard against barotrauma because the peak inspiratory pressure (PIP) could be limited and the ventilator would not exceed this pressure. Unfortunately, the delivered tidal volume ($V_t$) would fluctuate according to pulmonary compliance; a smaller volume of gas would be delivered at low

Low risk of hypoventilation

Volume-targeted ventilation

Fig. 3. Schematic comparison of pressure-volume loops in pressure-targeted (left) and volume-targeted (right) ventilation. During pressure-targeting a decrease in pulmonary compliance (moving from light loop to dark loop) results in a loss of tidal volume, despite consistency of inspiratory pressure. During volume-targeting, a decrease in compliance (moving from the dark loop to the light loop) results in an automatic increase in pressure to assure constant volume delivery.
### Table 1

Major outcomes assessed in the meta-analysis of 11 randomized clinical trials of volume-targeted vs pressure-limited ventilation [15].

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of studies</th>
<th>No. of subjects</th>
<th>RR (95% CI) or mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>11</td>
<td>767</td>
<td>0.73 (0.51–1.05)</td>
</tr>
<tr>
<td>Any IVH</td>
<td>11</td>
<td>759</td>
<td>0.65 (0.42–0.99)*</td>
</tr>
<tr>
<td>Grade 3–4 IVH</td>
<td>11</td>
<td>707</td>
<td>0.55 (0.39–0.79)*</td>
</tr>
<tr>
<td>BPD at 36 weeks</td>
<td>9</td>
<td>596</td>
<td>0.61 (0.46–0.82)*</td>
</tr>
<tr>
<td>Cystic PVL</td>
<td>7</td>
<td>531</td>
<td>0.33 (0.15–0.72)*</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>8</td>
<td>595</td>
<td>0.46 (0.25–0.86)*</td>
</tr>
<tr>
<td>Failure of assigned mode</td>
<td>4</td>
<td>405</td>
<td>0.64 (0.43–0.94)*</td>
</tr>
<tr>
<td>Any hypocapnia</td>
<td>2</td>
<td>58</td>
<td>0.56 (0.33–0.96)*</td>
</tr>
<tr>
<td>Duration of supplementary O₂ (d)</td>
<td>2</td>
<td>133</td>
<td>−1.68 (−2.5 to −0.88)*</td>
</tr>
</tbody>
</table>

RR, relative risk; CI, confidence interval; IVH, intraventricular hemorrhage; BPD, bronchopulmonary dysplasia; PVL, periventricular leukomalacia.

* *p < 0.05.*
Lung protective ventilation in extremely preterm infants

Peter A Dargaville\textsuperscript{1,2} and David G Tingay\textsuperscript{3,4,5}

**Key Points**

1. The extremely preterm lung is structurally and biochemically immature and vulnerable to injury from positive pressure ventilation. Implementation of lung protective strategies is vital to minimise the harm caused by mechanical ventilators.

2. Where there is severe respiratory distress syndrome and persistent atelectasis, a lung protective approach composed of recruiting the lung with stepwise pressure increments, followed by reduction of pressure in search of an optimal point at which to maintain ventilation. This form of lung protection is more effectively applied with high frequency oscillatory ventilation than on a conventional ventilator.

3. Where there is minimal atelectasis, limiting damage to the vulnerable preterm lung involves avoidance of overdistension. This can be achieved by setting positive end-expiratory pressure at the lowest value that maintains oxygenation and restricting tidal volume using a volume-targeted mode of ventilation.

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**Fig. 1** Stepwise positive end-expiratory pressure (PEEP) manoeuvre during conventional mechanical ventilation (CMV) in a recruitable lung. Pressure-volume tracing during a stepwise PEEP manoeuvre in a mechanically ventilated piglet after repeated saline lavage. PEEP alterations of 5 cm H\textsubscript{2}O with a concomitant change in peak inspiratory pressure were made every 15 s. Y-axis shows lung volume measured by respiratory inductance plethysmography, and scaled to total lung capacity (TLC). Complete tracing is shown in grey, and the final breath at each PEEP level in black, and the tidal breath compliance (mL/cm H\textsubscript{2}O/kg) for each of the final breaths is indicated in italics. Optimal PEEP as determined by compliance is on the deflation limb at around 5 cm H\textsubscript{2}O. Data derived from same experimental series as reference.\textsuperscript{21}

**Fig. 2** Lung recruitment and volume optimisation during high-frequency oscillatory ventilation (HFOV). Diagrammatic representation of the pressure-volume (PV) curve in an atelectatic diseased lung. Dashed grey line shows the PV trajectory firstly during escalation of P\textsubscript{aw} from P\textsubscript{aw} until the lung is maximally recruited (P\textsubscript{rec} and thereafter with stepwise P\textsubscript{aw} decrements until oxygenation deteriorates (closing pressure, P\textsubscript{cl}). Note the hysteresis in PV behaviour with relatively high lung volume maintained on the deflation limb. A broad region of optimal oxygenation is found on the deflation limb (white bar),\textsuperscript{6} and a more narrow region in which lung mechanics are optimised (grey fill). HFOV is likely to be most lung protective if applied in the region of optimal mechanics, usually 2–4 cm H\textsubscript{2}O above P\textsubscript{cl}.\textsuperscript{6}
PEEP – a “cheap” and effective lung protection

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Summary Mechanical ventilation is a complex therapy with several different parameters which can be altered. In preterm and term infants, more attention has been paid to the levels of peak inspiratory pressure than to the positive end-expiratory pressure (PEEP). An awareness that lung protection can be conferred by an appropriate level of PEEP has increasingly stimulated a renewed interest in achieving the “best PEEP” strategy. We review the history of the introduction of PEEP therapy, some of the early demonstrations of its potential for mischief, the evidence on what levels of PEEP are appropriate in infants, some data concerning the lung-protective value of PEEP and finally some recent efforts at defining measures to determine the so-called “best PEEP”. Some of this work has been performed in adults with the acute respiratory distress syndrome. In newborns, we are regrettably forced to conclude that there is, for the immediate present, no easy substitute for sensible clinical observations coupled with a judicious and cautious adjustment of PEEP. We anticipate that a more logical application of PEEP with individualisation of therapy, based on a pressure–volume relationship, will in future enable targeted tests of PEEP as a lung-protection strategy.

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The role of “adequate” PEEP

✓ The percentage fractional area of collapsed alveoli in preterm lambs is significantly higher for 0 PEEP

NaiK AS; Am J Respir Crit Care Med 2001
How to search the optimal PEEP?

Lung recruitment: optimal PEEP to reach lung volume on the deflation limb of P/V curve
SLI manouvre in DR; in mechanically ventilated (AC plus VG: Vt 6ml/kg; Draeger VN 500; initial PEEP = 5 cmH₂O) with persistent high request of FiO₂ and PIP level; surfactant; monitor TcpO₂ / TcpCO₂, SpO₂, BP, HR

- Increments of PEEP (0.2 cmH₂O every 5’) monitoring the falling FiO₂ needs and rising SpO₂ (1)

- When FiO₂ needs fell to 0.3, PEEP is reduced in order to set the lung filling on the safe deflation limb of P/V curve above the critical closing pressure (CCP) (2).

- When oxygenation levels falls and FiO₂ rises, we re-increment PEEP until stable oxygenation is achieved (3).

- In case of initial need of FiO₂< 0.3 we try to reduce PEEP level according to SpO₂ target and FiO₂ request (then we try to reduce Vt)
Table 1  Ventilatory and Gas Analysis Changes During the LRM and in the First 12 Hours of Life

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 10)</th>
<th>Group B (n = 10)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fio₂ at start of LRM (%)</td>
<td>56 ± 24</td>
<td>52 ± 21</td>
<td>0.7</td>
</tr>
<tr>
<td>Lowest Fio₂ (%)</td>
<td>22 ± 2</td>
<td>24 ± 2</td>
<td>0.08</td>
</tr>
<tr>
<td>Time to lowest Fio₂ (min)</td>
<td>94 ± 24</td>
<td>435 ± 221</td>
<td>0.0009</td>
</tr>
<tr>
<td>PEEP at start of LRM (cm H₂O)</td>
<td>5 ± 0.2</td>
<td>5 ± 0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Max PEEP during LRM (cm H₂O)</td>
<td>6.1 ± 0.3</td>
<td>5.3 ± 0.3</td>
<td>0.00</td>
</tr>
<tr>
<td>Final PEEP at the end of LRM (cm H₂O)</td>
<td>5 ± 0.3</td>
<td>5.1 ± 0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>a/Ao₂ ratio at start of LRM</td>
<td>0.25 ± 0.1</td>
<td>0.25 ± 0.1</td>
<td>0.9</td>
</tr>
<tr>
<td>a/Ao₂ ratio final*</td>
<td>0.47 ± 0.1</td>
<td>0.34 ± 0.1</td>
<td>0.03</td>
</tr>
<tr>
<td>Pao₂ at start of LRM (mm Hg)</td>
<td>59 ± 12</td>
<td>64 ± 11</td>
<td>0.3</td>
</tr>
<tr>
<td>Pao₂ final* (mm Hg)</td>
<td>79 ± 20*</td>
<td>66 ± 12</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*In the first 12 h of life.
†p < 0.05 versus at start of LRM.
a/Ao₂, Fio₂, fraction of inspired oxygen; LRM, lung recruitment maneuver; Pao₂; PEEP, positive end-expiratory pressure.
Table 2  Respiratory and Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 10)</th>
<th>Group B (n = 10)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surfactant doses (n)</td>
<td>1.2 ± 0.4</td>
<td>1.8 ± 0.8</td>
<td>0.09</td>
</tr>
<tr>
<td>Extubation failure (n)</td>
<td>1</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Length of respiratory support (d)</td>
<td>24 ± 13</td>
<td>35 ± 17</td>
<td>0.19</td>
</tr>
<tr>
<td>Length of tracheal intubation (d)</td>
<td>8.7 ± 7</td>
<td>18.9 ± 15</td>
<td>0.07</td>
</tr>
<tr>
<td>PDA occurrence (n)</td>
<td>6/10</td>
<td>4/10</td>
<td>0.61</td>
</tr>
<tr>
<td>Maternal chorioamnionitis (n)</td>
<td>4/10</td>
<td>3/10</td>
<td>0.99</td>
</tr>
<tr>
<td>Sepsis (n)</td>
<td>4/10</td>
<td>4/10</td>
<td>NS</td>
</tr>
<tr>
<td>O₂ dependency (d)</td>
<td>29 ± 12</td>
<td>45 ± 17</td>
<td>0.04</td>
</tr>
<tr>
<td>Moderate or severe BPD (n)</td>
<td>0</td>
<td>2 (20%)</td>
<td>0.4</td>
</tr>
<tr>
<td>ROP grade &gt; 2 (n)</td>
<td>3 (30%)</td>
<td>6 (60%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Death (n)</td>
<td>2 (20%)</td>
<td>2 (20%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

BPD, bronchopulmonary dysplasia; NS, not significant; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity.
PEEP TRIAL= 2nd recruitment maneuver

Figure 1 Fraction of inspired oxygen requirements of infants in group A (n = 10) in the course of lung recruitment maneuver (data expressed as mean values). *p < 0.05 versus start level. PEEP, positive end-expiratory pressure; a/AO2

Figure 2 a/AO2 ratio of infants in group A (n = 10) in the course of lung recruitment maneuver (data expressed as mean values). *p < 0.05 versus start level. FiO2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure.

Figure 3 SpO2 and fraction of inspired oxygen (FiO2) changes over time during lung recruitment maneuver in one preterm infant in group A. Positive end-expiratory pressure was observed. No differences were observed in extubation failure, BPD, ROP, and death between the two groups. During the LRM application, no adverse events occurred, circulatory parameters were stable, and the maneuver was well tolerated. All results are presented as mean ± standard deviation or rate and percentage. In Fig. 3, step-by-step changes in SpO2 and FiO2 related to PEEP levels during the LRM application to a male preterm infant of group A are shown. PEEP changes are shown (in white bars) on the abscissa axis as they were progressively applied during maneuver.
“Lung Recruitment for Ventilation: does it work? Is it safe?”

Jobe A. J

Pediatrics 2009; 154: 635-636

• demanding and time consuming assessments are requested

• PAWs used to define the open lung are high

• Risk of air leaks

• Lung stretch may transduce inflammatory signals

• Haemodynamic effect
Cardiorespiratory effects of changes in end expiratory pressure in ventilated newborns

Koert A de Waal, Nick Evans, David A Osborn, Martin Kluckow

| Table 1  Cardiopulmonary response to an increase in positive end expiratory pressure (PEEP) in all 50 infants* |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                | Baseline PEEP 5 cmH2O | Intervention PEEP 8 cmH2O | Return to PEEP 5 cmH2O | p Value |
| Right ventricular output (ml/kg/min) | 234 (103) | 218 (95) | 224 (87) | 0.014 |
| SVC (ml/kg/min)                | 3.7 (1.0) | 3.6 (1.1) | 3.6 (1.0) | 0.040 |
| SVC diameter (mm)              | 92 (36) | 87 (36) | 86 (34) | 0.207 |
| SVC velocity time integral (m/s) | 0.093 (0.032) | 0.097 (0.035) | 0.090 (0.029) | 0.172 |
| Left pulmonary artery velocity (m/s) | 0.33 (0.11) | 0.32 (0.13) | 0.32 (0.12) | 0.669 |
| Duct diameter (mm)             | 2.2 (1.6–3.0) | 2.2 (1.9–28) | 2.1 (1.8–3.1) | 0.628 |
| Ductal shunt (%RL)             | 1.4 (0–25) | 12 (0–27) | 15 (0–28) | 0.760 |
| Middle cerebral artery mean (m/s) | 0.13 (0.09–0.17) | 0.14 (0.10–0.18) | 0.12 (0.09–0.16) | 0.190 |
| Heart rate (beats/min)         | 143 (17) | 141 (20) | 143 (19) | 0.198 |
| Systolic blood pressure (mm Hg) | 47 (9) | 48 (9) | 47 (9) | 0.265 |
| Diastolic blood pressure (mm Hg) | 30 (7) | 30 (6) | 30 (6) | 0.602 |

%RL, percentage of cardiac cycle with right to left shunt; SVC, superior vena cava flow; Vti, velocity time integral.

*Values expressed as mean (SD) or median (IQR) where appropriate.
**Conclusion:** A short-term increase in PEEP does not lead to significant changes in systemic blood flow, although 36% of infants in the present study had clinically important changes in flow (±25%). The intervention can improve dynamic lung function, especially airway resistance. Improvements in compliance tend to be associated with improvements in blood flow.
Alveolar recruitment strategy and PEEP improve oxygenation, dynamic compliance of respiratory system and end-expiratory lung volume in pediatric patients undergoing cardiac surgery for congenital heart disease

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*Department of Anesthesiology, Eemnes Medical Center, Rotterdam | †Department of Cardiothoracic Surgery, Eemnes Medical Center, Rotterdam | ‡Department of Intensive Care, Eemnes Medical Center, Rotterdam, The Netherlands

Summary

Objective: Optimizing alveolar recruitment by alveolar recruitment strategy (ARS) and maintaining lung volume with adequate positive end-expiratory pressure (PEEP) allowing preventing ventilator-induced lung injury (VILI). Knowing that PEEP has its most beneficial effects when dynamic compliance of respiratory system (Crs) is maximized, we hypothesize that the use of 8 cm H2O PEEP with ARS results in an increase in Crs and end-expiratory lung volume (EELV) compared to 8 cm H2O PEEP without ARS and to zero PEEP in pediatric patients undergoing cardiac surgery for congenital heart disease.

Methods: Twenty consecutive children were studied. Three different ventilation strategies were applied to each patient in the following order: 0 cm H2O PEEP, 8 cm H2O PEEP without an ARS, and 8 cm H2O PEEP with a standardized ARS. At the end of each ventilation strategy, Crs, EELV, and arterial blood gases were measured.

Results: EELV, Crs, and \( P_{O_2}/FiO_2 \) ratio changed significantly \( (P < 0.001) \) with the application of 8 cm H2O + ARS. Mean \( P_{CO_2} - PETCO_2 \) difference between 0 PEEP and 8 cm H2O PEEP + ARS was also significant \( (P < 0.05) \).

Conclusion: An alveolar recruitment strategy with relative high PEEP significantly improves Crs, oxygenation, \( P_{O_2}/FiO_2 \), \( P_{CO_2} - PETCO_2 \) difference, and EELV in pediatric patients undergoing cardiac surgery for congenital heart disease.

Keywords: alveolar recruitment; dynamic compliance; pediatric; positive end-expiratory pressure

"Research of optimal PEEP" = not only SpO2 monitoring
HOW EIT WORKS

It is well-known that the bioelectric properties of lung tissue are affected by the air content. Consequently, changes in lung volume due to ventilation result in changes of the thoracic impedance.

To monitor thoracic impedance changes, electrodes have to be placed around the patient’s chest wall, tiny electrical currents are applied to the body through one electrode pair and the resulting voltages are measured simultaneously at other electrode pairs (Fig. 1).

Fig. 1: A first pair of electrodes applies a very small current into the thorax while the remaining 13 electrode pairs measure the resulting voltage signals and their changes.

Fig. 4: Functional EIT image (left) and CT scan from a patient with a pleural effusion after rupture of the diaphragm, resulting in a significantly reduced ventilation of the lower left lung. The red color represents regions with the highest volume changes, the non-ventilated regions are displayed in deep blue.
Fig. 9: PulmoVista 500

Fig. 10: Electrode belt with patient cable connected

Fig. 24: Series of dynamic images representing air filling during inspiration

Fig. 36: Defining optimal PEEP settings based on the assessment of ΔEELI
Measurements of respiratory volumes in mechanically ventilated by utilizing the **opto-electronic plethysmography (OEP)**, a noninvasive method to study the volume and motion of the human trunk through the use of infrared imaging. (OEP system, BTS, Milano, Italy).

Lista G et al. , Respiratory Medicine Case report 2017
Optoelectronic Plethysmography is a new method to evaluate ventilation through an external measurement of the chest wall surface motion.

A number of small reflective markers are placed on the thoraco-abdominal surface by hypoallergenic adhesive tape.

A set of specially designed video cameras analyze the chest wall motion (infrared imaging).

A dedicated software computes the enclosed volume and its variations during breathing.
Case report

Efficacy of lung volume optimization maneuver monitored by optoelectronic plethysmography in the management of congenital diaphragmatic hernia

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a Division of Neonatology, "Buzzi Children's Hospital" - ASST PIF-Sacco, Milan, Italy
b Dipartimento di Elettronica, Informazione e Bioingegneria, Politecnico di Milano, Milan, Italy

Fig. 2. End-expiratory chest wall volume variation (ΔEEcw), pulse oxygen saturation (SpO2), trans-cutaneous partial pressure of carbon dioxide (TcPCO2) and fraction of inspired oxygen (FiO2) during high lung volume strategy after surgery in CMV. Driving pressure is positive end-expiratory pressure (PEEP) and it is reported on the x-axis. The black arrow indicates the starting point and the grey ones clarify the direction of the maneuver.
Lung Volume Optimization in course of MV….and prevention of lung injury

• to know the physiology and to allow fetal-neonatal transition of the lung

• to set a «lung volume optimization strategy» from the DR (e.g.SI + CPAP or stepwise increments of PEEP) to obtain an early FRC

• in CMV: to choice a «targeted-volume ventilation» (first intention) plus the research of the optimal «PEEP»

• appropriate timing for surfactant administration (early!!) and modality (under investigation)

• in HFOV: to choice an «high lung volume strategy» (better as first intention)

• to use clinical monitoring for the lung volume optimization (SpO2/TCpCO2/pO2, BP and HR)

• It is desirable in the future a «bedsite patient control of regional distribution of volume» (by EIT) or a method to evaluate ventilation through an external measurement of the chest wall surface motion (= volume variations of entire chest wall) (by OEP).