Bedside Respiratory Function Monitoring:
Ricadute cliniche
Andrea Dotta
History of Assisted Ventilation

Positive Pressure:

“Respirator Kit” used to revive apparently dead by blowing air into the lungs or rectum in 1770s in London

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History of Assisted Ventilation

Negative pressure:

Spirophore
developed in 1876
with manual
device to create
negative pressure
chamber
History of Assisted Ventilation

Positive pressure:

The Aerophore pulmonaire:- developed by French Obstetrician for short term ventilation of newborns in 1879
MECCANICA RESPIRATORIA
Relazione Volume-Pressione

Compliance $\phi = \frac{\Delta V}{\Delta P}$

Elastanza $(E) = \frac{1}{C}$

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Valutazione della Compliance in condizioni dinamiche

A = Compliance Normale
B = Compliance Ridotta

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Ventilation Strategies aimed to avoid VILI

BAROTRAUMA

VOLUTRAUMA

ATELECTRAUMA

BIOTRAUMA

Increase in number of inflammatory cells and
In the expression of soluble mediators within the lungs

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RESISTENZE DELLE VIE AEREE (Raw)

\[ \text{Raw} = \frac{PA - PB}{V^\circ} \]

\[ R \sim \frac{1}{r^4} \]
Gentle Ventilation?

HFOV or CV?
The role of lung volume measurement in the assessment of disease severity, functional disability, course of disease and response to treatment/ventilation strategies remains to be determined in infants.

Functional residual capacity (FRC) and lung clearance index (LCI) are sensitive parameters for early detection of airway disease in infancy.

- **Body Plethysmography (Gold Standard)** ➔ Includes both air in communication with open airways as well as air trapped within non communicating thoracic compartments.

- **Gas dilution** (O₂, SF₆, He) ➔ Can measure only lung volumes communicating with conducting airways.

- Radiographic imaging methods (Rx-TAC-RMN)
- Opto-electronic plethysmography
MATERIAL AND METHODS

Helium gas dilution technique

- Tests performed during assisted control ventilation before, after surgery and in spontaneous breathing
- At least 3 acceptable maneuvers for each test.
- During measurements we record:
  - Functional residual capacity (FRC)
  - Lung clearance index (LCI)
  - Tidal volume (Tv)

Can only measure lung volumes in communication with conducting airways.
Test is successfully completed when the gas levels decrease to become less than 1/40 for at least 3 successive breaths.

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Mechanical ventilation

Spontaneous breathing
LIMITI DELLA METODICA

• Misura il volume di gas polmonare in comunicazione con le vie aeree e può sottostimare la FRC in caso di air-trapping
• In caso di perdite dal TET la misura non è attendibile
• Durante il test si riduce leggermente la FiO2
• Applicabile solo in ventilazione convenzionale, non ancora in HFOV
• Durata del test circa 30’
• Costo dell’apparecchiatura
APPLICAZIONI CLINICHE NEL NEONATO INTUBATO E VENTILATO

• Ernia Diaframmatica Congenita: confronto pre-post chirurgia e post estubazione; confronto fra HFOV e CV

• Atresia Esofagea: confronto pre-post intervento chirurgico e post estubazione

• Pretermine con MIP: confronto pre-post somministrazione di surfattante

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CDH
Incidenza: 1/2500-4000 births

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Ipoplasia polmonare:

- Ridotta formazione del numero di alveoli e bronchioli
- Abnorme vascolarizzazione polmonare

(ridotto volume e aumento della massa muscolare)
Congenital diaphragmatic hernia

Richard Keijzer, MD, PhD, MSc,
Prem Puri, MS, FRCS, FRCS (Ed), FACS, FAAP (Hon)

First hit: genetic and environmental factors
Second hit: interference with fetal breathing movements

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Changing Perspectives on the Perinatal Management of Isolated Congenital Diaphragmatic Hernia in Europe


<table>
<thead>
<tr>
<th>Pulmonary hypoplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Airway changes:</strong></td>
</tr>
<tr>
<td>• decreased alveoli</td>
</tr>
<tr>
<td>• thickened alveolar walls</td>
</tr>
<tr>
<td>• diminished alveolar air space &amp; gas-exchange surface area</td>
</tr>
<tr>
<td><strong>Vascular changes:</strong></td>
</tr>
<tr>
<td>• reduced number of vessels</td>
</tr>
<tr>
<td>• adventitial thickening</td>
</tr>
<tr>
<td>• medial hyperplasia</td>
</tr>
<tr>
<td>• peripheral extension of muscle layer into smaller intra-acinar arterioles</td>
</tr>
<tr>
<td><strong>Interstitium</strong></td>
</tr>
<tr>
<td>• increased interstitial tissue</td>
</tr>
<tr>
<td>• altered compliance</td>
</tr>
</tbody>
</table>

**Left ventricular hypoplasia** (in a limited number of cases)

- Hypoxia
- Hypercapnia
- Acidosis
- Right to left shunting
- Pulmonary arterial vasoconstriction
- Pulmonary hypertension
- Barotrauma
- Pulmonary interstitial emphysema
- Pneumothorax

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### Table 1-1  Stages of Lung Formation and Major Structural Developments and their Molecular Mediators

<table>
<thead>
<tr>
<th>Developmental stage</th>
<th><strong>GESTATIONAL AGE</strong></th>
<th><strong>Formation/induction of:</strong></th>
<th><strong>Molecular mediators</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryonic</td>
<td>3.5–7</td>
<td>Initial bud outgrowth</td>
<td>SHH, PTC, GLI’s, RA, RARs&lt;br&gt;FGF10, FGF9, FGF7, FGF2&lt;br&gt;LEFTY1, LEFTY2, PITX2, NODAL&lt;br&gt;SPRY2, SPRY4, BMP4, HOXA5&lt;br&gt;TBX4/5, TTF1, FOX’s, CRISP/PLD2</td>
</tr>
<tr>
<td></td>
<td>9.5–14.2</td>
<td>Trachea</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Primary bronchi</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Major airways</td>
<td></td>
</tr>
<tr>
<td>Pseudoglandular</td>
<td>5–17</td>
<td>Preacinic bronchial tree</td>
<td>SHH, PTC, TGFβ, BMP4, RA, RARs&lt;br&gt;FGF7, FGF9, CRISP/PLD2, TBX4/5&lt;br&gt;GATA6, SMADs, TTF1, FOX’s&lt;br&gt;VEGF, FLT1, FLK1</td>
</tr>
<tr>
<td>Canaliculer</td>
<td>16–26</td>
<td>Completion of conducting airways&lt;br&gt;Pulmonary acinus and gas exchange area&lt;br&gt;Increase in capillary bed&lt;br&gt;Start of epithelial differentiation</td>
<td>HIF1α, ARNT, HIF2α&lt;br&gt;GATA6, TTF1, ASCL1, HES1&lt;br&gt;FGF7, FOX’s, MDK&lt;br&gt;ANGPT1, ANGPT2, TIE1, TEK&lt;br&gt;VEGF, FLT1, FLK1</td>
</tr>
<tr>
<td>Saccular</td>
<td>24–38</td>
<td>Saccules</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17.5 d–5 dpn</td>
<td>Alveolar ducts and air sacs&lt;br&gt;Surfactant</td>
<td>FOX’s, MDK&lt;br&gt;ANGPT1, ANGPT2, TIE1, TEK&lt;br&gt;VEGF, FLT1, FLK1</td>
</tr>
<tr>
<td>Alveolar</td>
<td>36–2 ypn</td>
<td>Thinning of alveolar septa&lt;br&gt;Remodeling of pulmonary vasculature&lt;br&gt;Fusion of capillary bilayer</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Birth–3 ypn</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4–14 dpn</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14–21 dpn</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

dpn, days postnatal; ypn, years postnatal.
Risk Factors for Chronic Lung Disease and Mortality in Newborns with Congenital Diaphragmatic Hernia

Total patients in CDH Registry  
\( n = 4,466 \)

Patients born between 2001 and 2006  
\( n = 2,134^* \)

Excluded patients**  
\( n = 56 \)

Included patients  
\( n = 2,078 \)

Patients died at or before day 30  
\( n = 492 \)

No BPD  
\( n = 887 \)

BPD***  
\( n = 624 \)

---

L. van den Hout\(^a\)  I. Reiss\(^a\)  J.F. Felix\(^b\)  W.C.J. Hop\(^c\)  Pamela A. Lally\(^d\)  Kevin P. Lally\(^d\)  D. Tibboel\(^a\)  for the Congenital Diaphragmatic Hernia Study Group

---

*Excludes patients born before 2001 or after 2006.
**Patients with congenital heart defects, incompatible with life, or with other significant congenital anomalies.
***BPD: Bronchopulmonary Dysplasia.
## Table 1. Baseline characteristics for all live-born patients with CDH (n = 2,078) born between 2001 and 2006

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>1,235/2,076</td>
<td>59</td>
</tr>
<tr>
<td>Birth in high-volume center</td>
<td>1,132/2,078</td>
<td>54</td>
</tr>
<tr>
<td>Birth in ECMO center</td>
<td>1,910/2,078</td>
<td>92</td>
</tr>
<tr>
<td>Inborn</td>
<td>837/2,076</td>
<td>40</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>1,021/1,855</td>
<td>55</td>
</tr>
<tr>
<td>Prenatal diagnosis</td>
<td>1,246/2,073</td>
<td>60</td>
</tr>
<tr>
<td>Cardiac abnormality</td>
<td>322/2,077</td>
<td>16</td>
</tr>
<tr>
<td>Chromosomal abnormality</td>
<td>89/2,077</td>
<td>4</td>
</tr>
<tr>
<td>Other abnormality¹</td>
<td>176/2,078</td>
<td>8</td>
</tr>
<tr>
<td>Left-sided defect</td>
<td>1,735/2,060</td>
<td>84</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age at birth, weeks</td>
<td>38</td>
<td>23–42</td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>3.03</td>
<td>0.57–4.90</td>
</tr>
<tr>
<td>Apgar score at 5 min</td>
<td>7</td>
<td>0–10</td>
</tr>
</tbody>
</table>
Table 5. Multivariate logistic regression analysis of BPD and/or death by day 30 (n = 1,686)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age in weeks</td>
<td>0.84</td>
<td>0.81–0.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac abnormality</td>
<td>2.62</td>
<td>1.85–3.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chromosomal abnormality</td>
<td>3.04</td>
<td>1.42–6.51</td>
<td>0.004</td>
</tr>
<tr>
<td>Prenatal diagnosis</td>
<td>3.90</td>
<td>3.00–5.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right-sided defect</td>
<td>2.76</td>
<td>1.96–3.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apgar score at 5 min</td>
<td>0.61</td>
<td>0.57–0.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HFO as initial ventilation mode</td>
<td>2.53</td>
<td>1.95–3.27</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Nonsignificant variables in the multivariate analysis: birth in ECMO center (odds ratio 1.39, 95% confidence interval 0.80–2.44; p = 0.244) and location of birth (odds ratio 1.1, 95% confidence interval 0.83–1.46; p = 0.487). OR = Odds ratio; CI = confidence interval.

Table 6. Multivariate logistic regression analysis for BPD (n = 1,293)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age in weeks</td>
<td>0.87</td>
<td>0.82–0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac abnormality</td>
<td>2.42</td>
<td>1.85–3.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inborn</td>
<td>0.70</td>
<td>0.52–0.95</td>
<td>0.023</td>
</tr>
<tr>
<td>Prenatal diagnosis</td>
<td>4.27</td>
<td>3.05–5.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right-sided defect</td>
<td>2.51</td>
<td>1.73–3.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apgar score at 5 min</td>
<td>0.66</td>
<td>0.61–0.71</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HFO as initial ventilation mode</td>
<td>2.29</td>
<td>1.73–3.04</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Nonsignificant variables in the multivariate analysis: birth in ECMO center (odds ratio 1.81, 95% confidence interval 0.94–3.48; p = 0.074) and having a chromosomal abnormality (odds ratio 1.37, 95% confidence interval 0.57–3.26; p = 0.480). OR = Odds ratio; CI = confidence interval.
Consensus Statement

Neonatology 2010;98:354–364
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Standardized Postnatal Management of Infants with Congenital Diaphragmatic Hernia in Europe: The CDH EURO Consortium Consensus

I. Reiss\textsuperscript{a}  T. Schaible\textsuperscript{b}  L. van den Hout\textsuperscript{a}  I. Capolupo\textsuperscript{c}  K. Allegaert\textsuperscript{d}  A. van Heijst\textsuperscript{e}  M. Gorett Silva\textsuperscript{f}  A. Greenough\textsuperscript{g}  D. Tibboel\textsuperscript{a}

for the CDH EURO consortium

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Standardized Postnatal Management of Infants with Congenital Diaphragmatic Hernia in Europe: The CDH EURO Consortium Consensus

Recommendations

- Adapt treatment to reach a preductal saturation between 85 and 95% and a postductal saturation above 70% (grade of recommendation = D).
- In individual cases, preductal saturation above 80% might be acceptable, as long as organs are well perfused (grade of recommendation = D).
- The target PaCO₂ range should be between 45 and 60 mm Hg (grade of recommendation = D).
- Pressure-controlled ventilation: initial settings are a PIP of 20–25 cm H₂O and a PEEP of 2–5 cm H₂O; ventilator rate of 40–60/min (grade of recommendation = D).
- HFOV: initial setting mean airway pressure 13–17 cm H₂O, frequency 10 Hz, Δp 30–50 cm H₂O depending on chest wall vibration (grade of recommendation = D).
- After stabilization, the FiO₂ should be decreased if preductal saturation is above 95% (grade of recommendation = D).
Standardized Postnatal Management of Infants with Congenital Diaphragmatic Hernia in Europe: The CDH EURO Consortium Consensus

Recommendations

- After delivery, the infant should be intubated immediately without bag and mask ventilation (grade of recommendation = D).
- The goal of treatment in the delivery room is achieving acceptable preductal saturation levels between 80 and 95% (grade of recommendation = D).
- Ventilation in the delivery room may be done by conventional ventilator or ventilation bag with a peak pressure as low as possible, preferably below 25 cm H₂O (grade of recommendation = D).
- An oro-or nasogastric tube with continuous or intermittent suction should be placed (grade of recommendation = D).
- Arterial blood pressure has to be maintained at a normal level for gestational age. In case of hypotension and/or poor perfusion, 10–20 ml/kg NaCl 0.9% should be administered 1–2 times and inotropic agents should be considered (grade of recommendation = D).
- Sedatives and analgesics should be given (grade of recommendation = D).
- No routine use of surfactant in either term or preterm infants with CDH (grade of recommendation = D).
The VICI-trial: high frequency oscillation versus conventional mechanical ventilation in newborns with congenital diaphragmatic hernia: an international multicentre randomized controlled trial

Lieke van den Hout\(^1\), Dick Tibboel\(^1\), Sanne Vijfhuize\(^1\), Harma te Beest\(^1\), Wim Hop\(^2\) and Irwin Reiss\(^1\), for The CDH-EURO Consortium

http://www.biomedcentral.com/1471-2431/11/98
The VICI-trial: high frequency oscillation versus conventional mechanical ventilation in newborns with congenital diaphragmatic hernia: an international multicentre randomized controlled trial

Lieve van den Hout1, Dick Tilboe1, Sanne Vlijhulze1, Harma te Beest1, Wim Hop2 and Irwin Reiss*, for the CDH-EURO Consortium

Inclusion and exclusion criteria

The study population consists of all infants antenatally diagnosed with CDH born at one of the participating centres.

Exclusion criteria are:

- Birth before a gestational age of 34 weeks
- Severe chromosomal anomalies, like trisomy 18 or trisomy 13, which may imply a decision to stop or not to start life-saving medical treatment
- Severe cardiac anomalies, expected to need corrective surgery in the first 60 days of life (such as transposition of the great arteries, truncus arteriosus or double outlet right ventricle)
- Renal anomalies associated with oligohydramnios
- Severe orthopaedic and skeletal deformities, which are likely to influence thoracic, and/or lung development (such as chest wall deformities and spine anomalies)
- Severe anomalies of the central nervous system

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The VICI-trial: high frequency oscillation versus conventional mechanical ventilation in newborns with congenital diaphragmatic hernia: an international multicentre randomized controlled trial

Lieve van den Hour¹, Dick Tibboel¹, Sanne Vlijhulse¹, Harma te Beest¹, Wim Hop² and Irwin Reiss³*, for The CDH-EURO Consortium

Table 1 definition of BPD according to Jobe and Bancelari

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>&lt; 32 weeks</th>
<th>&gt; 32 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time point assessment</td>
<td>36 wks PMA* or DC** to home, whichever comes first</td>
<td>&gt; 28 days but &lt; 56 days of life or discharge to home, whichever comes first</td>
</tr>
<tr>
<td>Mild BPD</td>
<td>On room air at 36 wks PMA or at DC, whichever comes first</td>
<td>On room air at day 56 postnatal age or DC, whichever comes first</td>
</tr>
<tr>
<td>Moderate BPD</td>
<td>&lt; 30% O₂ at 36 wks PMA or DC, whichever comes first</td>
<td>&lt; 30% O₂ at 56 d of life or DC whichever comes first</td>
</tr>
<tr>
<td>Severe BPD</td>
<td>≥ 30% O₂ and/or pos. pressure at 36 wks PMA or DC, whichever comes first</td>
<td>≥ 30% O₂ and/or pos. pressure at 56 d of life or DC whichever comes first</td>
</tr>
</tbody>
</table>

Treatment with oxygen > 21% for at least 28 days PLUS

Figure 1 Overview study procedures.

Antenatal counselling
Birth and randomisation
Day 1 Lab samples
Echo Cor
X-ray
Day 3 Lab samples
Day 7 Lab samples
Day 14 Lab samples
Day 28 Lab samples
Echo cor
X-ray
Lung function 6 months
Lung function 12 months
Standardized Postnatal Management of Infants with Congenital Diaphragmatic Hernia in Europe: The CDH EURO Consortium Consensus

I. Reiss a T. Schaible b L. van den Hout a I. Capolupo c K. Allegaert d A. van Heijst e M. Gorett Silva f A. Greenough g D. Tibboel a for the CDH EURO consortium

- Intubation at birth, measurements of HR, pre-post SaO2, adequate preductal SaO2 (80-95%), PIP ≤ 25. FiO2 started at 1 and adjusted for preSaO2.
- Positioning of NGT/OGT with continuous or intermittent suctioning
- Vascular access with venous and arterial lines (preductal artery)
- Maintain Blood Pressure at normal levels for gestational age. If there is hypotension and/or hypoperfusion use 10-20 ml/kg of saline; if no improvement inotropic and vasopressor agents should be considered
- Sedation and analgesia should be started once the venous line is ready

Neonatology 2010;98:354–364

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- Ventilatory strategies aimed to get preductal SaO2 between 85-95%, postductal above 70%; PaCO2 45-60, pH above 7.2.
- Conventional Ventilation: initial setting PIP 20-25, PEEP 2-5, vent rate 40-60
- HFOV: initial setting MAP 13-17, Freq 10 Hz, ΔP 30-50, I:E=0.33
- Pulmonary hypertension: perform echo within the first 24 hrs of life; iNO should be considered if R-L shunt and OI >20 and/or pre-post SaO2 gradient >10%
- ECMO: inability to maintain preductal saturations >85% or postductal saturations >70%; increased PaCO2 and resp acidosis with pH<7.15; PIP > 28 or MAP > 17; metab acidosis, resistant systemic hypotension; OI ≥ 40

Neonatology 2010;98:354–364

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OPBG AND VICI TRIAL
CASISTICS

Da Aprile 2009 a Novembre 2013:

- 87 casi di CDH trattati
- 54 casi arruolati nel VICI trial
- 29/54 randomizzati in HFOV
- Sopravvivenza totale: 73.5%
- Sopravvivenza VICI: 70.4%
- Sopravvivenza non-VICI: 78.7%

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Cerebral and renal oxygenation during surgery

Early Lung Function Assessment during MV

Differences between HFOV and CV

Long term follow up of Lung function

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EFFECTS OF DIFFERENT VENTILATION MODALITIES ON NEAR INFRARED SPECTROSCOPY IN OPERATED CDH INFANTS


Dr. Claudia Columbo
claudia.columbo@gmail.com

Department of Medical and Surgical Neonatology, Neonatal Intensive Care Unit
Bambino Gesù Children’s Hospital – IRCCS – Rome - Italy
Aim of the study

To evaluate on CDH newborns already enrolled in the VICI TRIAL:
• cerebral and renal NIRS variation during surgery and in the following 24 hours.
• the effects of different ventilation strategies on tissue oxygenation
Near-infrared spectroscopy (NIRS) is a non invasive technique for indirect continuous monitoring of tissue oxygenation (rSO2).

In this study NIRS was carried out using INVOS 5100 - Somanetics, Troy, MI, USA.
Materials and Methods

All CDH admitted

2009 - 2012

All CDH infants
79

Survived
57 (72%)

Died
22 (28%)

NIRS study

2011 - 2012

Alive CDH infants
24

VICI trial
14

NO VICI trial
10

Lost 1

Enrolled
13

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Materials and Methods II

• NIRS evaluation of renal and cerebral \(O_2\) saturation \((rSO_2C, \ rSO_2R)\) from 6h before surgery up to normalization. 20% decrease in \(rSO_2\) compared to the baseline was considered significant.

• Evaluation of:
  \(SaO_2\), Hb, EGA, Urine output, HR, BP
# Results I

<table>
<thead>
<tr>
<th></th>
<th>TOTAL 13</th>
<th>HFOV 7</th>
<th>ACV 6</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GA (wks)</strong></td>
<td>38 (35-40)</td>
<td>38 (36-40)</td>
<td>38 (35-39)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>BW (grams)</strong></td>
<td>3055 (2660-3620)</td>
<td>3055 (2900-3620)</td>
<td>3115 (2660-3480)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>LHR O/E</strong></td>
<td>55 (35-77)</td>
<td>56 (35-77)</td>
<td>55 (43-56)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Time of surgery (hr)</strong></td>
<td>72 (48-216)</td>
<td>120 (72-216)</td>
<td>60 (48-72)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Deaths (post surgery)</strong></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>ns</td>
</tr>
</tbody>
</table>

*Data are expressed as median and range.*
## Results II

<table>
<thead>
<tr>
<th></th>
<th>Before surgery rSO2C</th>
<th>During surgery rSO2C</th>
<th>p</th>
<th>Before surgery rSO2R</th>
<th>During surgery rSO2R</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CEREBRAL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HFOV</td>
<td>81 (70-89)</td>
<td>61 (52-74)</td>
<td>&lt;0.05</td>
<td>78 (71-94)</td>
<td>62 (52-88)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ACV</td>
<td>82 (76-91)</td>
<td>65 (67-93)</td>
<td>&lt;0.05</td>
<td>79 (72-86)</td>
<td>71 (57-72)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><strong>RENAL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as median and range. Mann-Whitney Test and one-way ANOVA were used as appropriate.

* P<0.05 was considered significant
Patient ventilated using ACV
Comparison between HFOV and CV (F. Landolfo)

AIM OF THE STUDY

- To assess applicability of the Helium gas dilution technique during mechanical ventilation in newborns with congenital diaphragmatic hernia

- To evaluate changes in breathing patterns, lung volume and ventilation inhomogeneity (VI) before and after surgical correction

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CDH INFANTS (n = 20)

<table>
<thead>
<tr>
<th></th>
<th>A/C</th>
<th>HFOV</th>
<th>TOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects (n)</td>
<td>14</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>BW (grams)</td>
<td>3075 (2400 – 3780)</td>
<td>2813 (1850 – 4270)</td>
<td>3000 (1850 - 4270)</td>
</tr>
<tr>
<td>GA (wks)*</td>
<td>38 (35 - 41)</td>
<td>37 (36 - 39)</td>
<td>38.5 (35 - 41)</td>
</tr>
<tr>
<td>VICI (n)</td>
<td>6</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>M/F (n)</td>
<td>6/8</td>
<td>1/5</td>
<td>7/13</td>
</tr>
</tbody>
</table>

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## PRELIMINARY DATA

<table>
<thead>
<tr>
<th></th>
<th>Before Surgery (T₀) (n=19)</th>
<th>After surgery (T₁) (n=20)</th>
<th>Spontaneous breathing (T₂) (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CV (n=13)</td>
<td>HFOV (n=6)</td>
<td>CV (n=14)</td>
</tr>
<tr>
<td>Vt (ml/kg)</td>
<td>7.3 (5.0-8.5)</td>
<td>5.2 (4.7-7.5)</td>
<td>5.9 (3.3-7.5)</td>
</tr>
<tr>
<td></td>
<td>6.2 (5.1-7.6)</td>
<td>5.7 (3.9-6.7)</td>
<td>6.6 (5.0-8.7)</td>
</tr>
<tr>
<td></td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>CV (n=14)</td>
<td>HFOV (n=6)</td>
<td></td>
</tr>
<tr>
<td>FRC-Vd (ml/kg)</td>
<td>13.1 (9.3-18.5)</td>
<td>8.6 (2.9-14.8)</td>
<td>21.6 (13.9-28.0)</td>
</tr>
<tr>
<td></td>
<td>16.5 (9.7-25.8)</td>
<td>12.4 (5.0-17.5)</td>
<td>18.1 (15.1-25.9)</td>
</tr>
<tr>
<td></td>
<td>CV&lt;0.05</td>
<td>HFOV&lt;0.05</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>6.6 (5.1-7.5)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>ns</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LCI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.7 (6.3-9.3)</td>
<td>8.7 (7.5-11.7)</td>
<td>6.6 (5.1-7.5)</td>
</tr>
<tr>
<td></td>
<td>7.5 (6.5-8.6)</td>
<td>8.4 (6.5-11.9)</td>
<td>6.1 (5.7-7.5)</td>
</tr>
<tr>
<td></td>
<td>ns</td>
<td>ns</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Data are expressed as median and range
Wilcoxon sign rank test

$FRC – Vd = FRC minus dead space divided by kilograms

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CONCLUSIONS

• This preliminary study suggests that helium gas dilution technique is applicable and reliable not only in spontaneously breathing but also in critical ventilated preterm and term infants.

• This technique is useful to evaluate the efficacy of a surgical procedure or the changes in ventilatory strategies.

• The assessment of FRC and LCI during mechanical ventilation could be the future target to set ventilatory parameters with the aim of optimizing alveolar recruitment and reducing baro and volutrauma.

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FRC and pleural effusion in CDH
Case report
(Francesca Landolfo)
PATIENT o CASE REPORT

Raffaela:

- GA = 39 wks, BW = 3000 g;
- prenatal diagnosis left mild CDH (O/E LHR=47,7);
- VICI trial;
- type B defect;
- liver down;
- no patch positioning.
RESULTS

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Bambino Gesù Children’s Hospital, IRCCS, Rome, Italy
FRC and esophageal atresia
(Francesca Landolfo, Claudia Columbo)

Department of Medical and Surgical Neonatology
Bambino Gesù Children’s Hospital, IRCCS, Rome, Italy
Main clinical and surgical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>Type</th>
<th>GA</th>
<th>BW</th>
<th>Cardiac anomalies</th>
<th>Major anomalies</th>
<th>Referral</th>
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<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>C</td>
<td>37</td>
<td>2170</td>
<td>Pulmonary sling + PDA + DIA</td>
<td>esophageal brocus</td>
<td>Si</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>A</td>
<td>29</td>
<td>1170</td>
<td>DIV + DIA + PDA</td>
<td>-</td>
<td>Si</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>C</td>
<td>36</td>
<td>2160</td>
<td>-</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>C</td>
<td>37</td>
<td>2300</td>
<td>-</td>
<td>Single left Kidney + Single umbelical artery + VACTERL</td>
<td>Si</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>C</td>
<td>35</td>
<td>2830</td>
<td>-</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>C</td>
<td>32</td>
<td>1720</td>
<td>Tetralogy of Taitot + Right Aortic Arch</td>
<td>Duodenal atresia</td>
<td>Si</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>C</td>
<td>37</td>
<td>2760</td>
<td>DIA</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>C</td>
<td>40</td>
<td>2480</td>
<td>DIA + PDA</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>C</td>
<td>36</td>
<td>1920</td>
<td>-</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>C</td>
<td>36</td>
<td>1515</td>
<td>-</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>C</td>
<td>37</td>
<td>2150</td>
<td>Double outlet right ventricle, pulmonary infundibular stenosis</td>
<td>Single umbelical artery + right bronchus hypoplasia + skeletal anomalies</td>
<td>Si</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>C</td>
<td>35</td>
<td>2450</td>
<td>DIA</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>A</td>
<td>38</td>
<td>2270</td>
<td>DIV + patent ductal arteriosus</td>
<td>Single umbelical artery</td>
<td>Si</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>C</td>
<td>39</td>
<td>3480</td>
<td>DIA</td>
<td>Laringo-tracheal cleft + left bronchial isomerism</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>C</td>
<td>35</td>
<td>2420</td>
<td>DIV + infundibular stenosis + Aortic stenosis</td>
<td>-</td>
<td>Si</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>C</td>
<td>39</td>
<td>2820</td>
<td>PDA</td>
<td>Single umbelical artery</td>
<td>Si</td>
</tr>
<tr>
<td>Median</td>
<td></td>
<td></td>
<td>37</td>
<td>2435</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td>29-40</td>
<td>1170-3480</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

16 EA newborns (14 type C, 2 type A) were enrolled
- 13 completed the study safely
- Three were excluded because of technical problems

- median gestational age (GA) was 37 weeks (range 29–40)
- median birth-weight 2435 grams (range 1170 - 3480).

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Main results

<table>
<thead>
<tr>
<th></th>
<th>Before Surgery $(T_0)$ (n=13)</th>
<th>After surgery $(T_1)$ (n=12)</th>
<th>Spontaneous breathing $(T_2)$ (n=9)</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vt (ml/Kg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>7,4</td>
<td>7,5</td>
<td>6,3</td>
<td>0,703</td>
</tr>
<tr>
<td>Range</td>
<td>5,3 – 9,1</td>
<td>6,3 – 13,8</td>
<td>5,3 – 13,9</td>
<td>0,320</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0,616</td>
</tr>
<tr>
<td><strong>FRC (ml/Kg)</strong></td>
<td>24,1</td>
<td>17,3</td>
<td>23,0</td>
<td>0,082</td>
</tr>
<tr>
<td></td>
<td>11,1 – 31,8</td>
<td>12,2 – 24,9</td>
<td>17,6 – 31,9</td>
<td>0,065</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0,920</td>
</tr>
<tr>
<td><strong>LCI</strong></td>
<td>7,0</td>
<td>7,0</td>
<td>5,9</td>
<td>0,277</td>
</tr>
<tr>
<td></td>
<td>4,7 – 7,8</td>
<td>6,5 – 8,3</td>
<td>4,7 – 6,9</td>
<td>0,009</td>
</tr>
</tbody>
</table>

FRC-Vd: FRC minus dead space divided by kilograms; LCI: lung clearance index; Vt: tidal volume; * significant when $p<0.05$

![Changing in FRC](image1)

![Changing in LCI](image2)
Results

- We observed a slight reduction of the FRC after surgery ($T_1$) in comparison with $T_0$ and $T_2$. This early decrement in post-operative FRC could be explained either by iatrogenic partial collapse of the lung due to a surgical extrapleural mediastinal approach to the esophagus or by the frequent right superior lobe atelectasis probably due to the obliged still supine position.

- In some of our patients the measurement of FRC in the post-operative time was also useful to suspect the presence of atelectasias and to suggest the execution of a chest X-ray.

- After extubation in spontaneous breathing FRC returned to baseline values possibly because of the alveolar “re-recruitment”.

- A significant improvement after surgery was observed concerning LCI. This could be explained by the surgical correction of the TEF and the consequent reduction of the VI due to either microinhalation or turbulence of the airway flow.
The observed changes are related to intrinsic surgical need, as partial lung collapse, or ventilator management during surgical procedure but our preliminary data do not indicate any significant postoperative sequelae.

Helium gas dilution technique allowed us to better understand physiological adaptation after esophageal surgery in newborn patients and it is potentially useful to guide ventilatory strategy, reducing the need of chest x-ray when ventilatory inhomogeneity was discovered.
CONCLUSIONS

• The Helium gas dilution technique is a sensitive, safe, quick and easy technique to measure lung volume at patient’s bedside.
• FRC and LCI can potentially serve as valid and sensitive indicators to monitor lung function.
• Their evaluation could be useful both to assess the need and timing for invasive procedures and to determine the effects of surgical repair concurrently with chest X-ray and ultrasonography also in newborns in assisted control ventilation.
FRC and surfactant in premature infants

Department of Medical and Surgical Neonatology
Bambino Gesù Children’s Hospital, IRCCS, Rome, Italy
Background

Premature infants because of their immaturity frequently experience respiratory failure. Surfactant prophylaxis is known to be effective in improving the immediate need for respiratory support and the clinical outcome of these newborns; either treatment strategy reduces the incidence of pneumothorax and improves survival rates.
## Results and conclusion

<table>
<thead>
<tr>
<th></th>
<th>Before surfactant ($T_0$)</th>
<th>After surfactant ($T_1$)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vt (ml/kg)</td>
<td>5.57</td>
<td>5.80</td>
<td>ns</td>
</tr>
<tr>
<td>FRC/kg-Vd (ml/kg)</td>
<td>5.19</td>
<td>19.39</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LCI</td>
<td>12.40</td>
<td>7.33</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Helium Gas Dilution Technique could be useful as a supplementary method to measure the degree of respiratory impairment and to evaluate the need and response to surfactant supplementation.
Take home messages

1. Il reclutamento alveolare ottimale si può valutare attraverso la misurazione diretta della FRC
2. Il LCI è un indicatore della omogeneità della distribuzione della ventilazione utile nel monitorare l’effetto di trattamenti medici o chirurgici
3. L’applicazione di questa metodica è ancora limitata a studi pilota, ma può rappresentare la base per un futuro di ventilazione assistita a target di FRC, ossia il volume polmonare che DEVE essere ottimizzato per gli scambi gassosi e per prevenire il VILI
4. Alcuni anni fa questa metodica era applicata solo nel bambino collaborante in respiro spontaneo, ora si è passati al neonato in ventilazione meccanica
History of Assisted Ventilation

Positive Pressure:

“Respirator Kit” used to revive apparently dead by blowing air into the lungs or rectum in 1770s in London
L’innovazione è un modo nuovo di fare le cose capace di produrre un cambiamento positivo e rende la vita migliore……

Ciò che distingue un leader da un seguace è la capacità di innovare ......

Steve Jobs