2nd INTERNATIONAL PEDIATRIC NONINVASIVE VENTILATION CONFERENCE

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# Rationale and benefits of NIV in lung diseases

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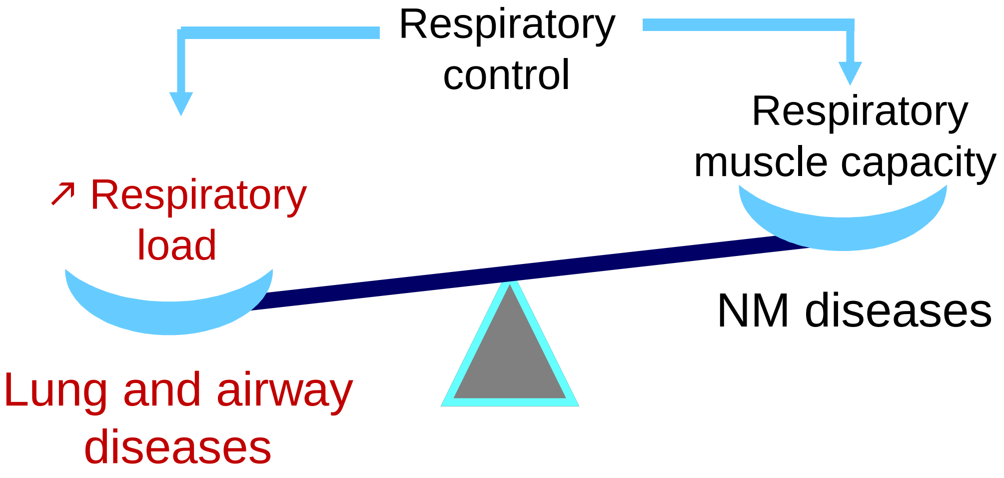
# Rationale and benefits of NIV in lung diseases

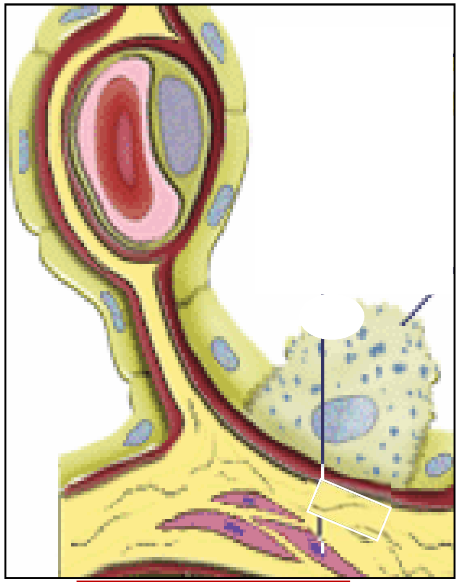
- Introduction
- Cystic fibrosis
- Bronchiolitis obliterans
- Bronchopulmonary dysplasia
- Interstitial lung disease

# Two types of chronic respiratory failure

Abnormalities of the respiratory mechanics

Abnormalities of the alveolar-capillary barrier



**↗ $PaCO_2$**

**↘ $PaO_2$**

# Chronic lung diseases in children

- Obstructive lung diseases
  - Cystic fibrosis
  - BO
  - BPD

Alveolar hypoventilation
=
Hypercapnia & hypoxemia

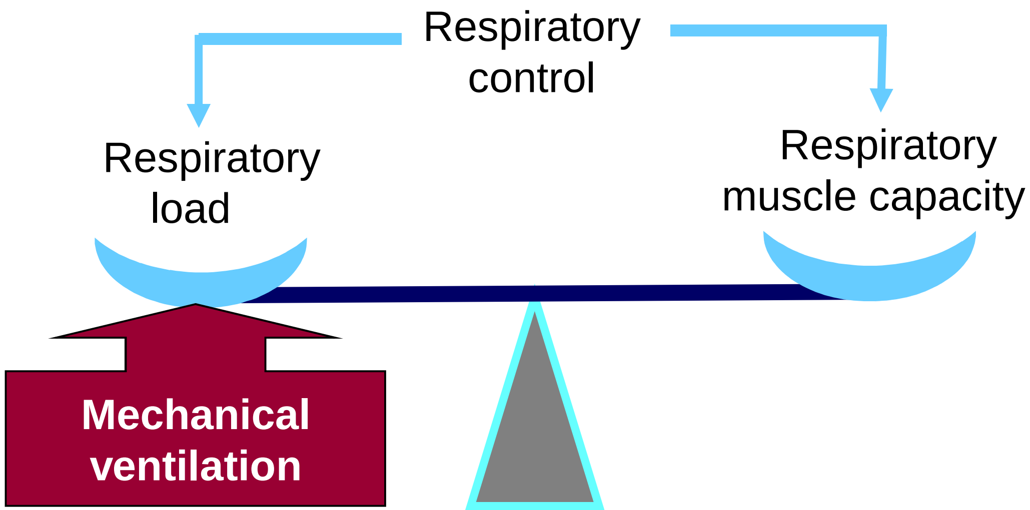
- Interstitial lung disease

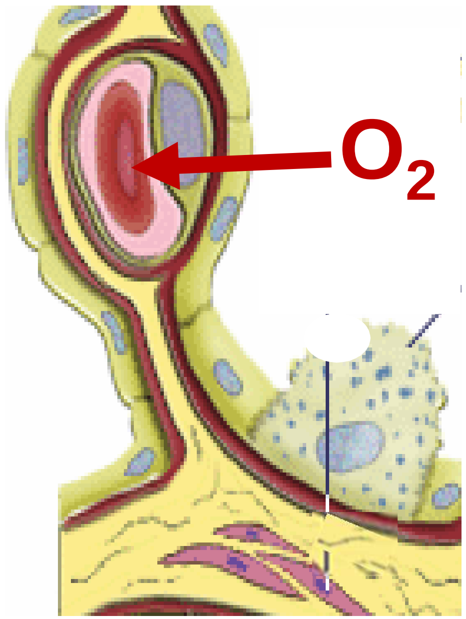
Hypoxemia

# Two types of respiratory treatments

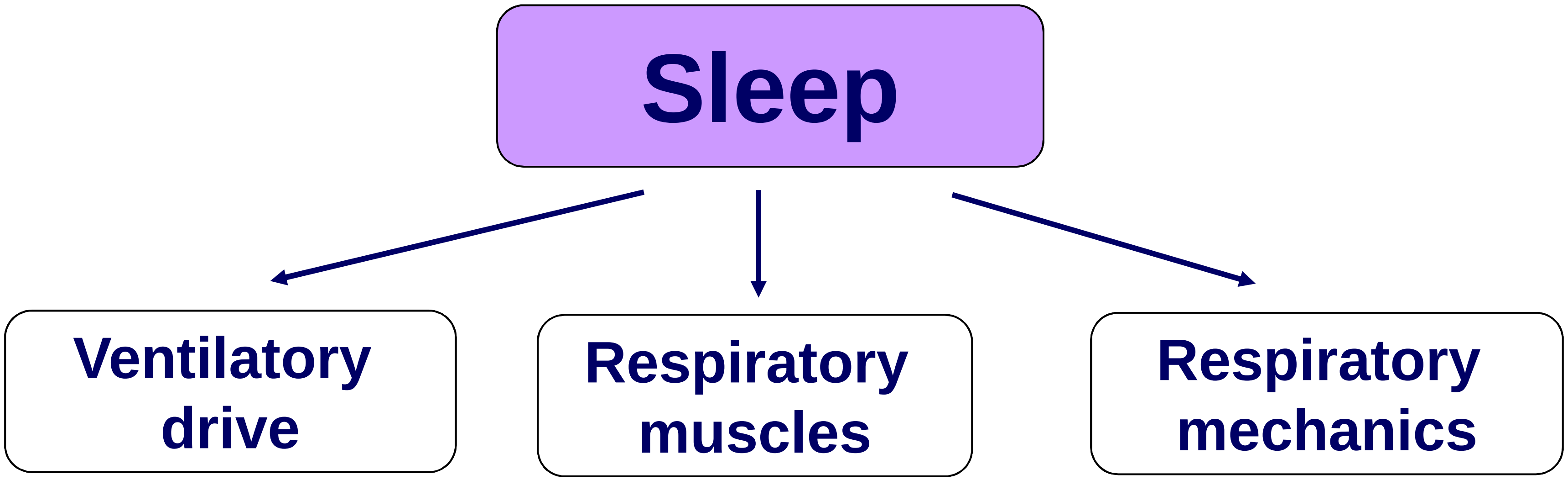
Abnormalities of the respiratory mechanics

Abnormalities of the alveolar-capillary barrier



# Respiratory diseases exaggerate during sleep

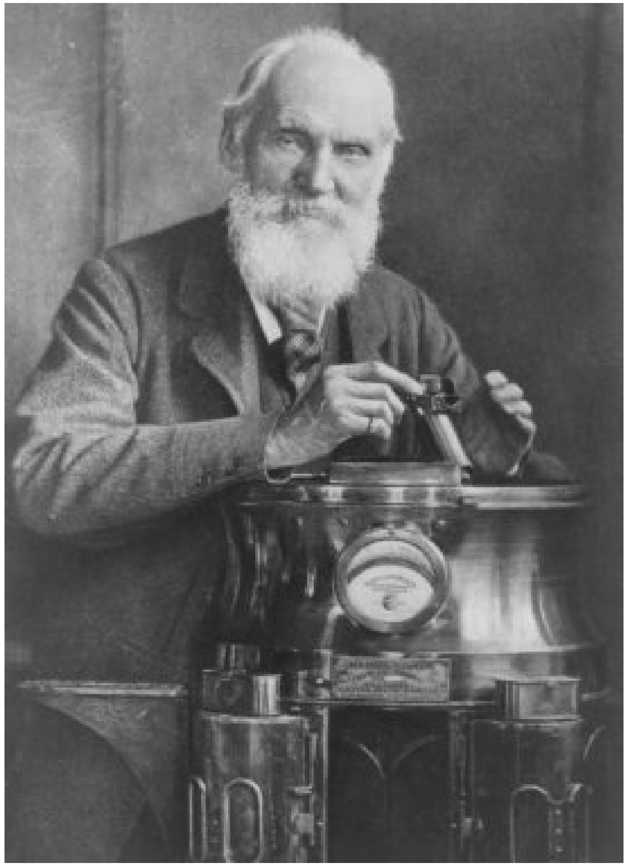



↘ Central drive
↘ Chemoreceptor sensitivity

Preservation of the activity of the diaphragm
↘ Intercostal and upper airway muscles

Ventilation/perfusion mismatch
↗ Airflow resistance
↘ Functional residual capacity

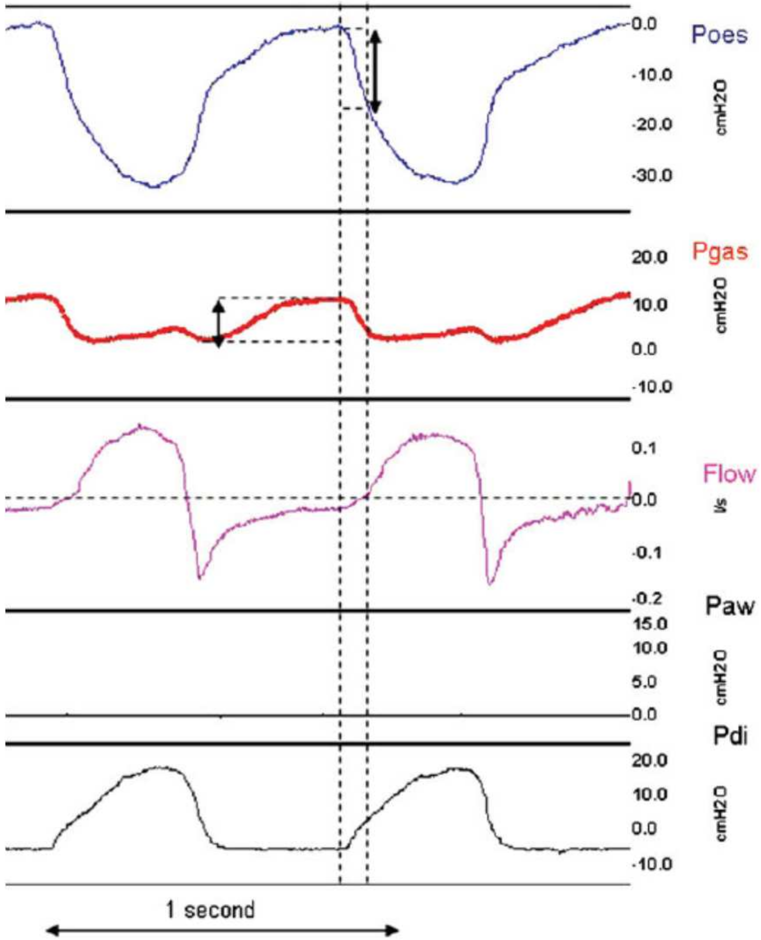
- If you can not measure it, you can not improve it.



William Thomson (1824 - 1907)
or « Lord Kelvin »

physician, founder of the thermodynamics

# Measurement of the work of breathing



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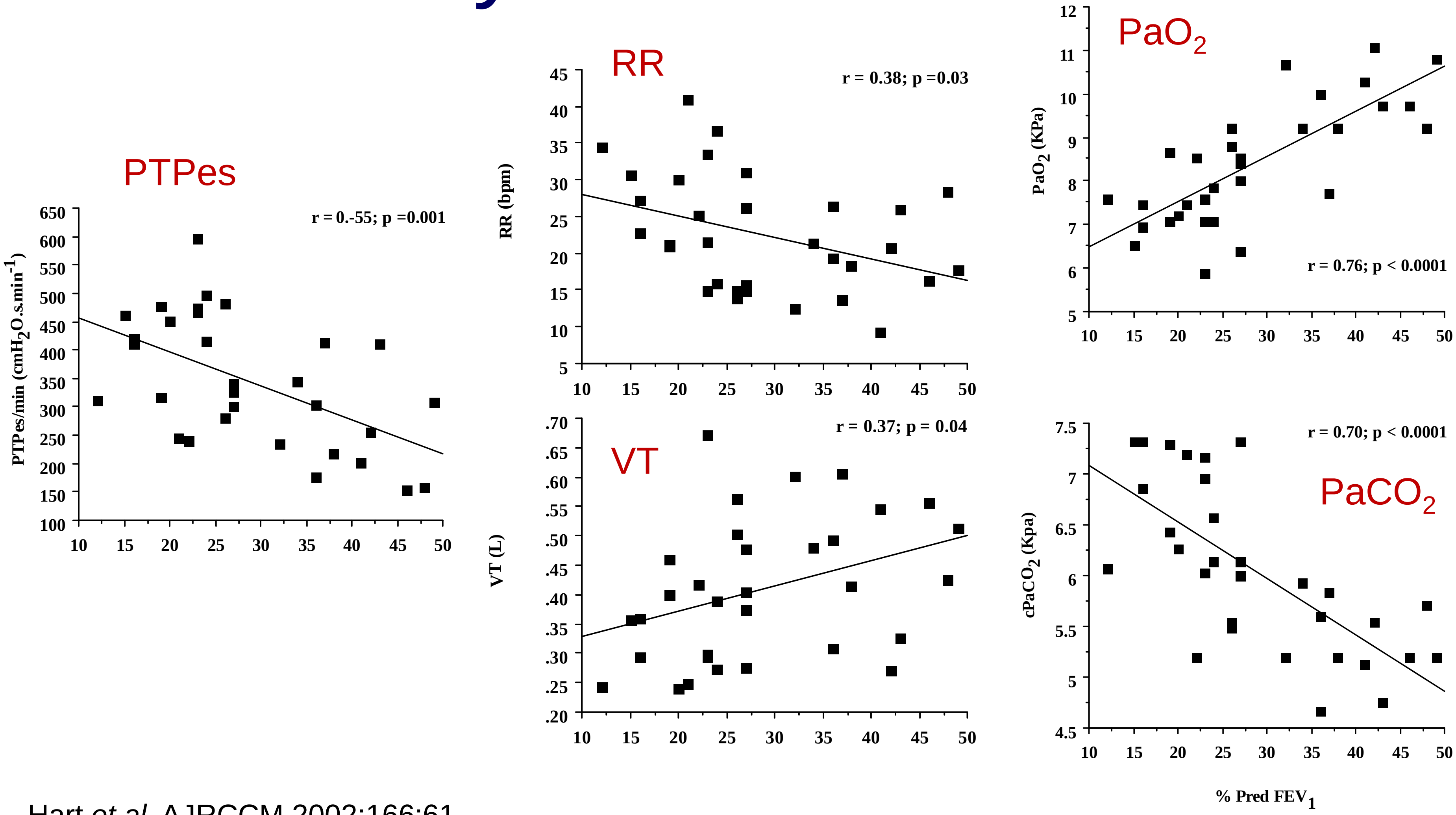
# Respiratory mechanics in cystic fibrosis

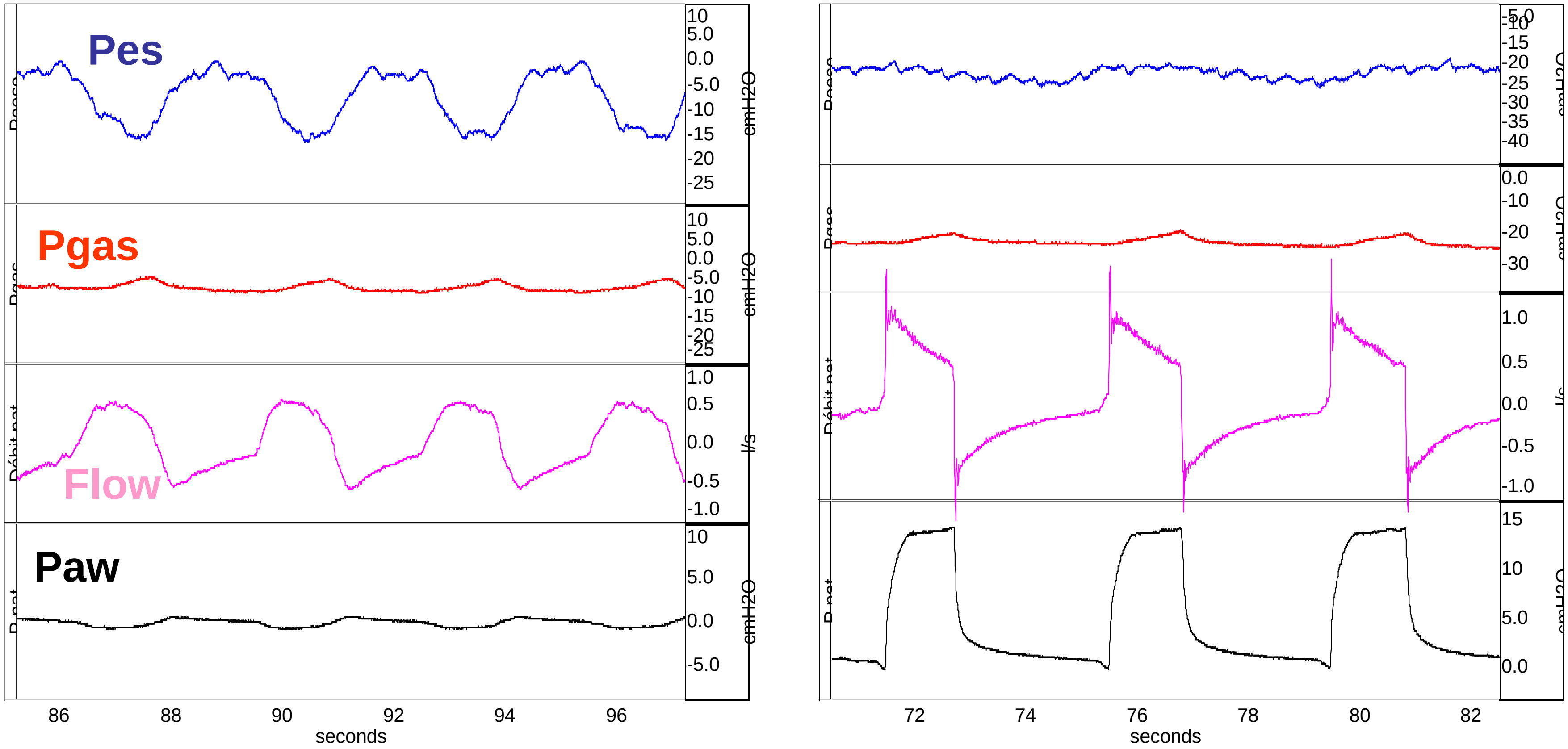



Hart *et al.* AJRCCM 2002;166:61

# Noninvasive ventilation unloads the respiratory muscles in CF

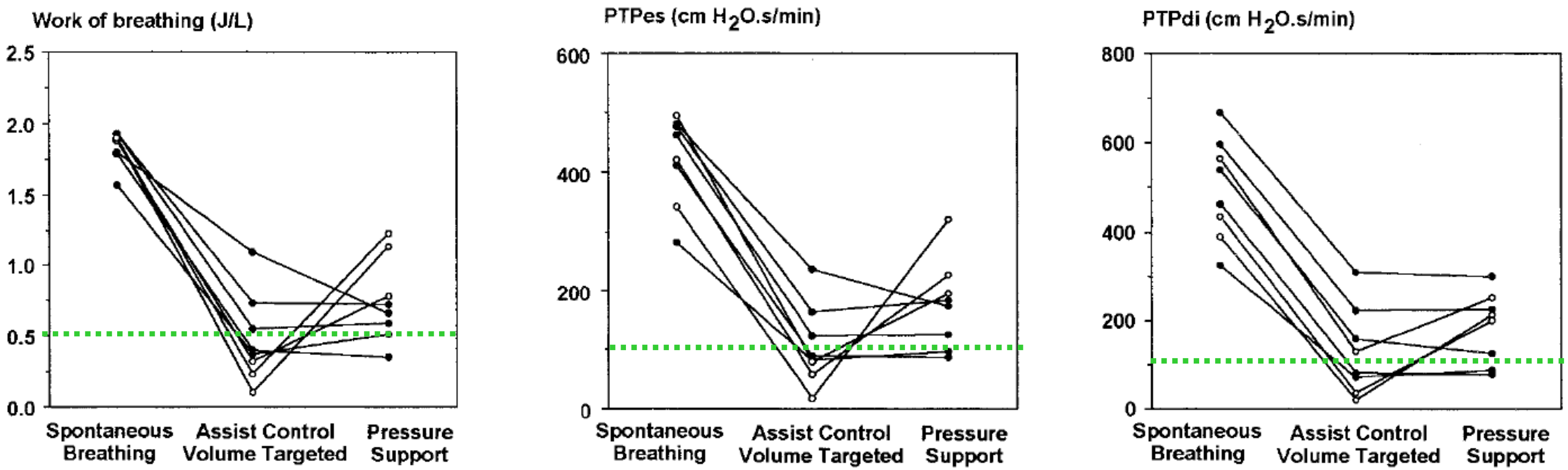
Spontaneous breathing

Pressure support (14 $cmH_2O$)



# NIV decreases the work of breathing in CF

8 children with CF, mean age 13 years, mean FEV1 25%



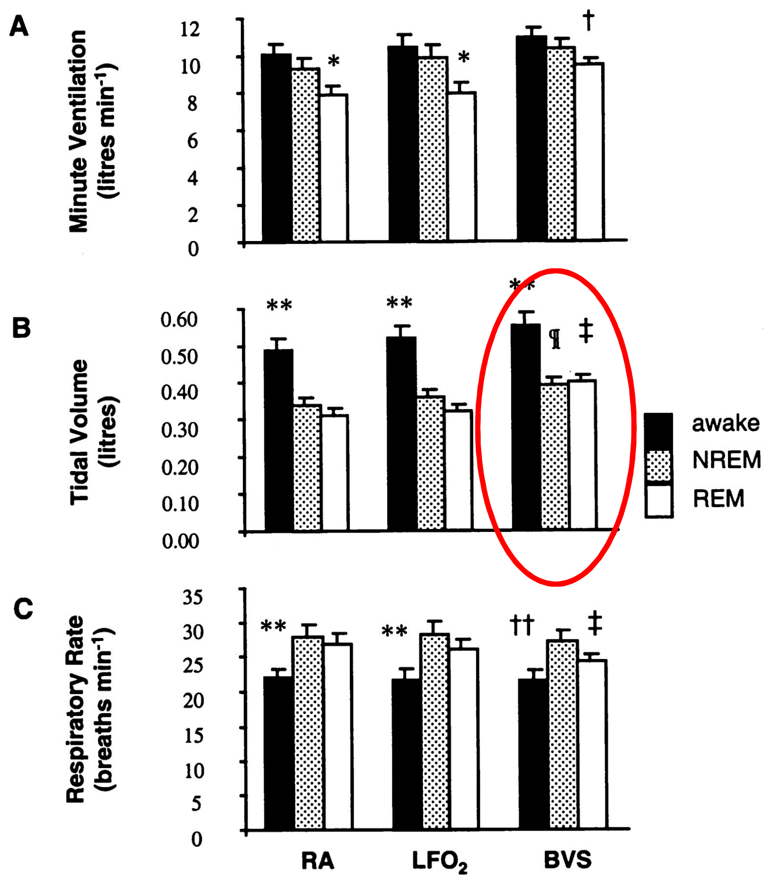

Fauroux *et al.* Crit Care Med 2001;29:2097

# NIV improves gas exchange in CF

| | Spontaneous Breathing | Assist Control/Volume Targeted Ventilation | Pressure Support Ventilation | ANOVA $p$ |
|---|---|---|---|---|
| $\dot{V}_T$, L | 0.41 ± 0.10 | 0.58 ± 0.17[a] | 0.50 ± 0.17[a] | .007 |
| RR, breaths·min$^{-1}$ | 23.3 ± 8.3 | 22.7 ± 8.0 | 21.5 ± 6.5 | NS |
| $\dot{V}_E$, L·min$^{-1}$ | 8.82 ± 1.56 | 12.2 ± 2.6[a] | 11.6 ± 3.0[a] | .02 |
| PEEPI, cm $H_2O$ | 1.8 ± 0.7 | 1.2 ± 0.8 | 1.6 ± 0.5 | NS |
| $\dot{V}_{I}$max, L·s$^{-1}$ | 0.55 ± 0.09 | 0.76 ± 0.20[a,b] | 1.08 ± 0.39[c] | .002 |
| $\dot{V}_T/T_I$, L·s$^{-1}$ | 0.37 ± 0.07 | 0.55 ± 0.12 | 0.50 ± 0.16 | NS |
| $T_I/T_{TOT}$, % | 38.5 ± 4.5 | 36.8 ± 2.5 | 39.9 ± 6.6 | NS |
| $SaO_2$, % | 92.4 ± 2.2 | 95.2 ± 1.9[a] | 94.1 ± 1.7 | .01 |
| $P_{ET}CO_2$, mm Hg | 35.1 ± 4.9 | 32.8 ± 3.6 | 31.2 ± 6.2[a] | .02 |

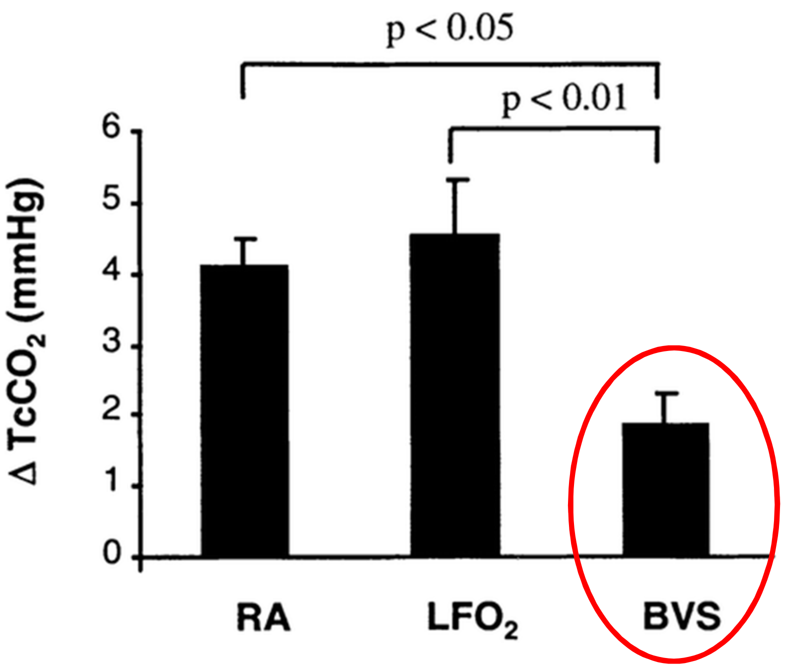
Fauroux *et al.* Crit Care Med 2001;29:2097

# NIV improves (daytime and) nocturnal gas exchange



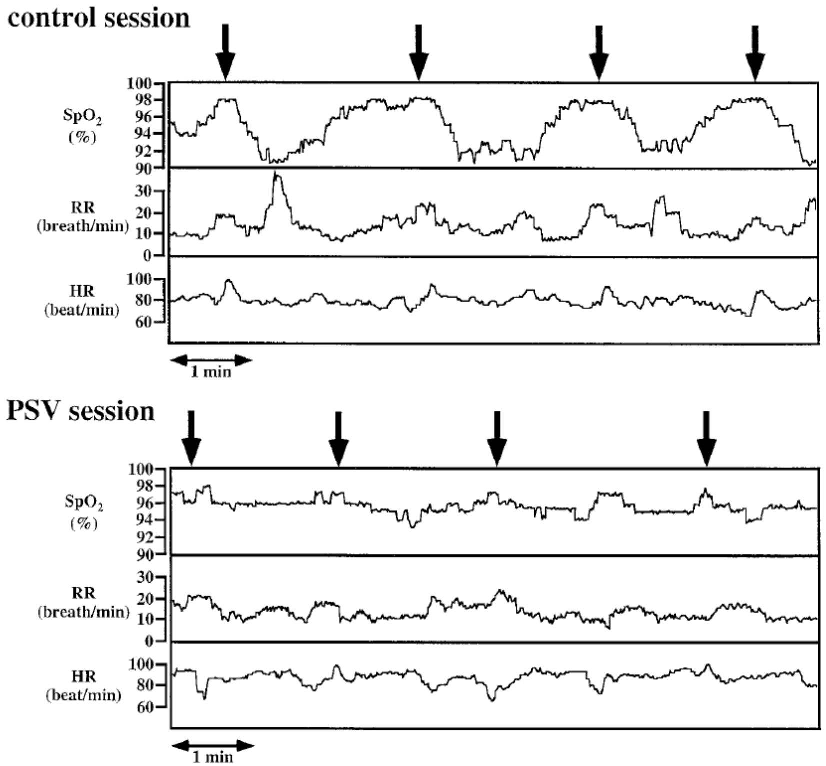

10 adult CF patients

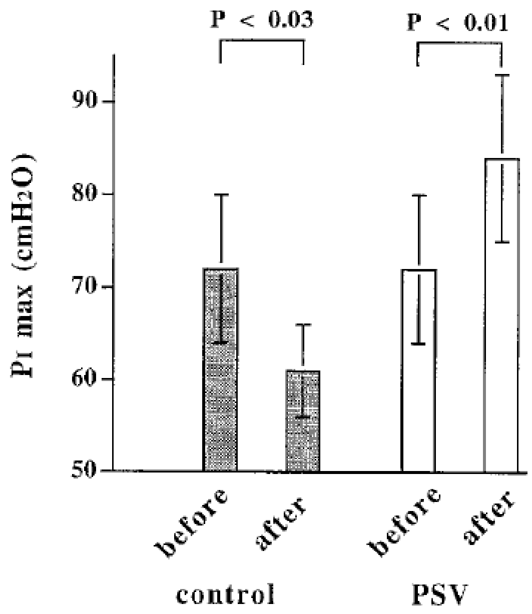
3 nights: air, $O_2$, NIV

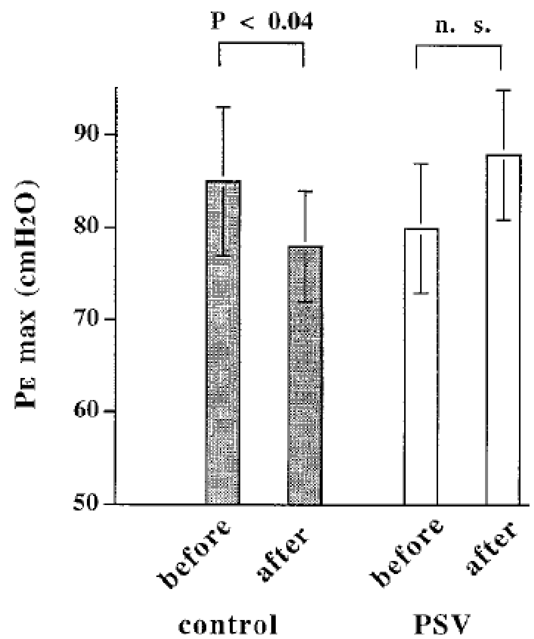



Milross *et al.* AJRCCM 2001;163:129

# NIV prevents oxygen desaturation and respiratory muscle fatigue during chest physiotherapy

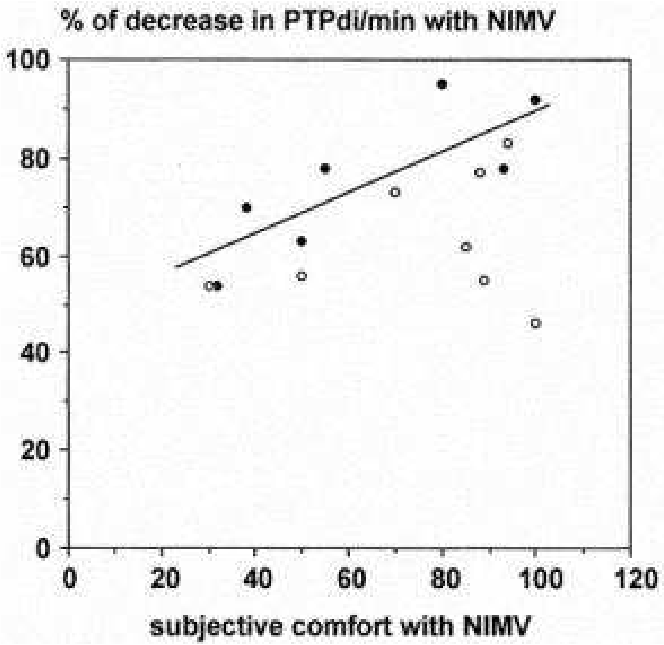


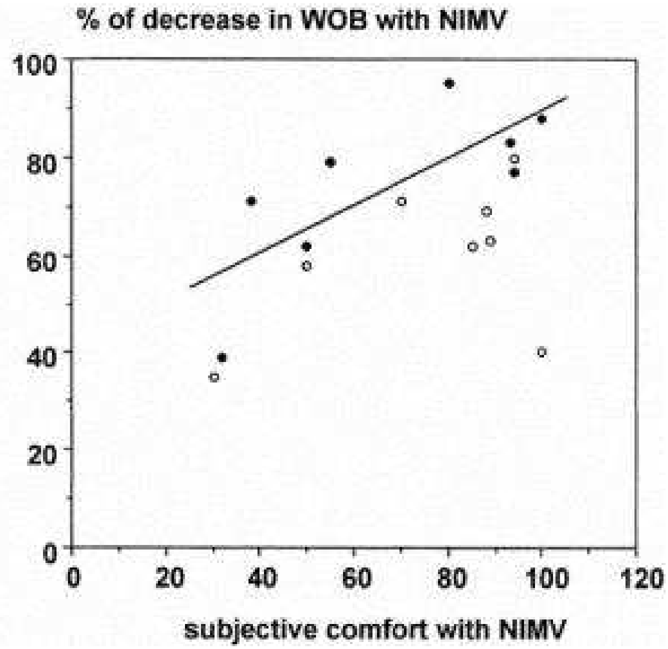



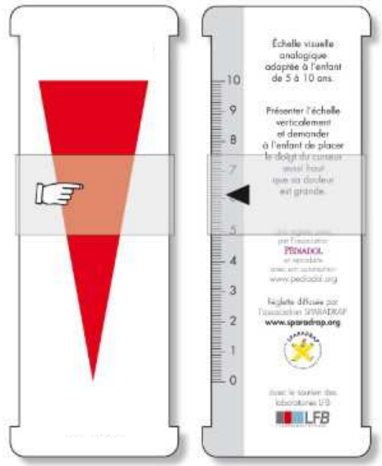




Fauroux *et al.* Pediatrics 1999:103:e32

# NIV is associated with a decrease in dyspnea in CF



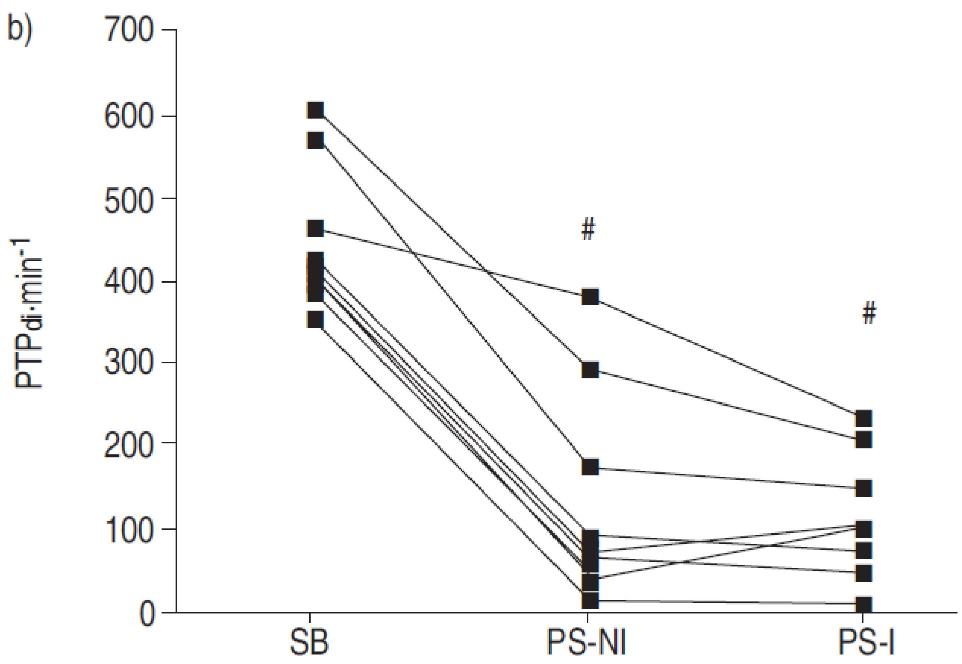





Fauroux *et al.* Crit Care Med 2001;29:2097

# The level of inspiratory pressure should be sufficient




| Patients | Level of PS $cmH_2O$ | |
|---|---|---|
| | PS-NI | PS-I |
| 1 | 14 | 16 |
| 2 | 18 | 18 |
| 3 | 17 | 18 |
| 4# | 16 | 16 |
| 5# | 16 | 16 |
| 6 | 18 | 18 |
| 7 | 12 | 12 |
| 8# | 17 | 15 |
| 9# | 11 | 10 |
| 10# | 16 | 20 |

➔ Mean level 16 $cmH_2O$

Fauroux *et al.* Eur Respir J 2004;24:624

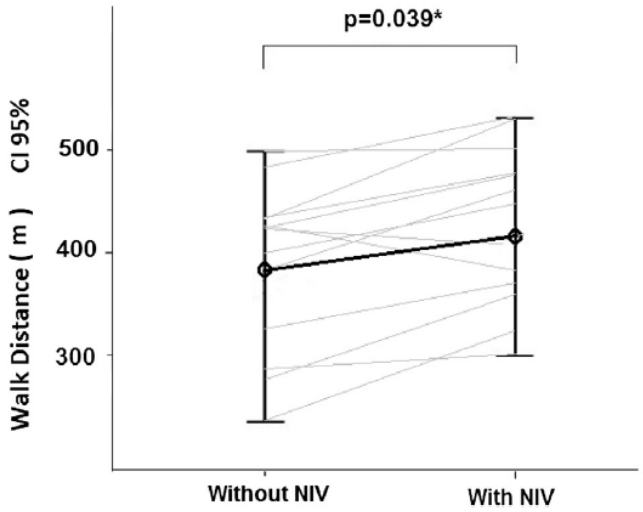
# Expiratory pressure should be low

| | $FEV_1$ (% Pred) | VC (% Pred) | $Pa_{O_2}$ (kPa) | $cPa_{CO_2}$ (kPa) | RR (bpm) | VT (ml) |
|---|---|---|---|---|---|---|
| Mean ± SD | 28.7 ± 10.2 | 42.1 ± 13.4 | 8.4 ± 1.4 | 6.0 ± 0.8 | 22.6 ± 7.8 | 409 ± 120 |
| Range | 12–49 | 16–75 | 5.9–11.1 | 4.7–7.3 | 9.2–40.9 | 241–673 |
| | $Pes_{max}$ (cm $H_2O$) | Mean Pes (cm $H_2O$) | TI/TTOT (%) | PTPes (cm $H_2O \cdot s \cdot min^{-1}$) | PTPes · $cPa_{CO_2}$ (cm $H_2O \cdot s \cdot min^{-1} \cdot kPa \cdot 10^{-2}$) | PTPes · $cPa_{CO_2}$ · RR/VT (cm $H_2O \cdot s \cdot min^{-1} \cdot kPa \cdot bpm \cdot L^{-1} \cdot 10^{-5}$) |
| Mean ± SD | 84.3 ± 23.4 | 14.7 ± 5.1 | 40.2 ± 4.6 | 345 ± 112 | 21.4 ± 8.8 | 14.5 ± 11.2 |
| Range | 43.7–141.1 | 6.0–26.1 | 28.0–47.6 | 152–596 | 7.9–41.5 | 1.8–44.1 |
| | CL dyn (ml · cm $H_2O^{-1}$) | $PEEP_i$ (cm $H_2O$) | RL (cm $H_2O \cdot s^{-1} \cdot L^{-1}$) | $WOB_{tot}$ ($J \cdot min^{-1}$) | $WOB_{el}$ ($J \cdot min^{-1}$) | $WOB_{res}$ ($J \cdot min^{-1}$) |
| Mean ± SD | 42.1 ± 33.0 | 1.1 ± 1.6 | 17.1 ± 9.7 | 12.6 ± 5.0 | 7.6 ± 3.0 | 5.1 ± 2.5 |
| Range | 9–166 | 0–8.2 | 3.1–50.5 | 4.3–21.7 | 2.8–13.8 | 0.8–10.7 |

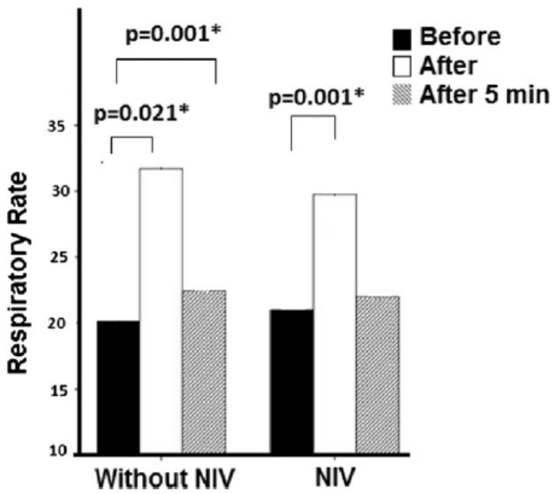
Hart *et al.* AJRCCM 2002;166:61

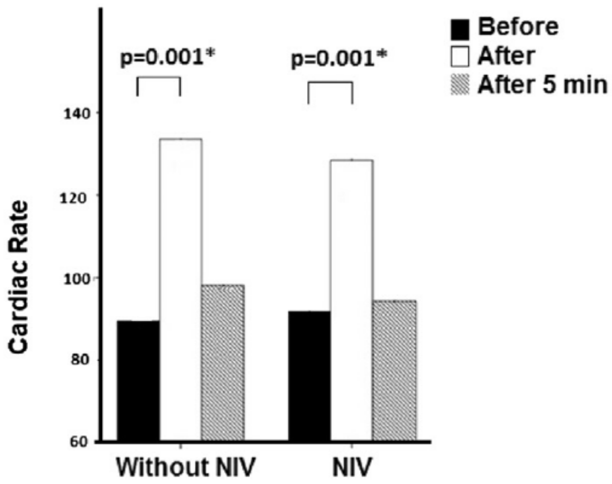
# Effects of noninvasive ventilation on treadmill 6-min walk distance and regional chest wall volumes in cystic fibrosis: Randomized controlled trial

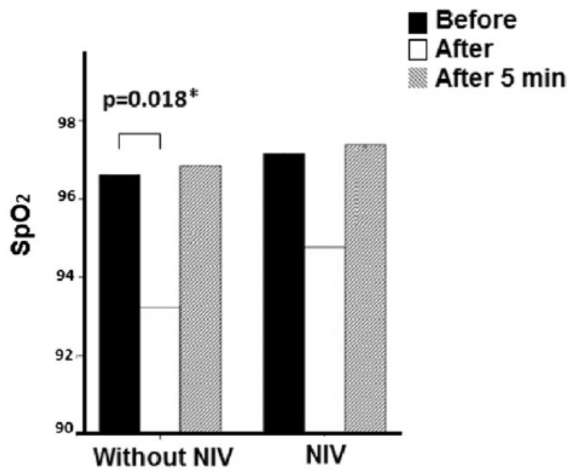
Cibelle Andrade Lima [a],
Armèle de Fátima Dornelas de Andrade [b,*],
Shirley Lima Campos [b], Daniella Cunha Brandão [b],
Guilherme Fregonezi [c], Ianny Pereira Mourato [b],
Andrea Aliverti [d], Murilo Carlos Amorim de Britto [e]




13 children, FEV1 35-79%




Respiratory Medicine (2014) 108, 1460—1468

# Benefits of NIV in cystic fibrosis

## Proven benefits

- Improvement in gas exchange
- Improvement in the tolerance of chest physiotherapy
- Decrease in dyspnea
- Improvement in exercise tolerance
- Stabilisation of the decline in lung function

## Expected benefits

- Increase in survival
- Increase in sleep quality
- Increase in quality of life
- Increase in weigth
- Decrease/correction of PHT
- Improved outcome of lung transplantation

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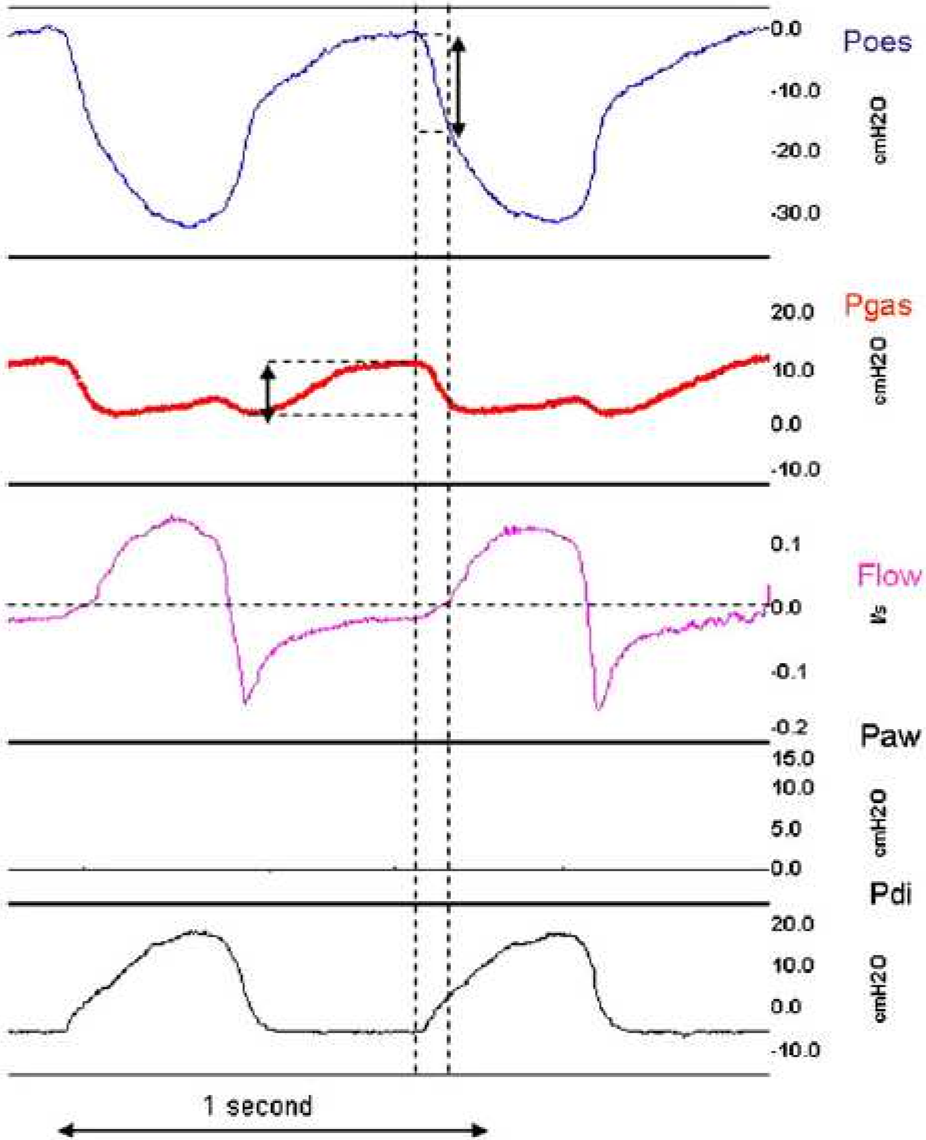
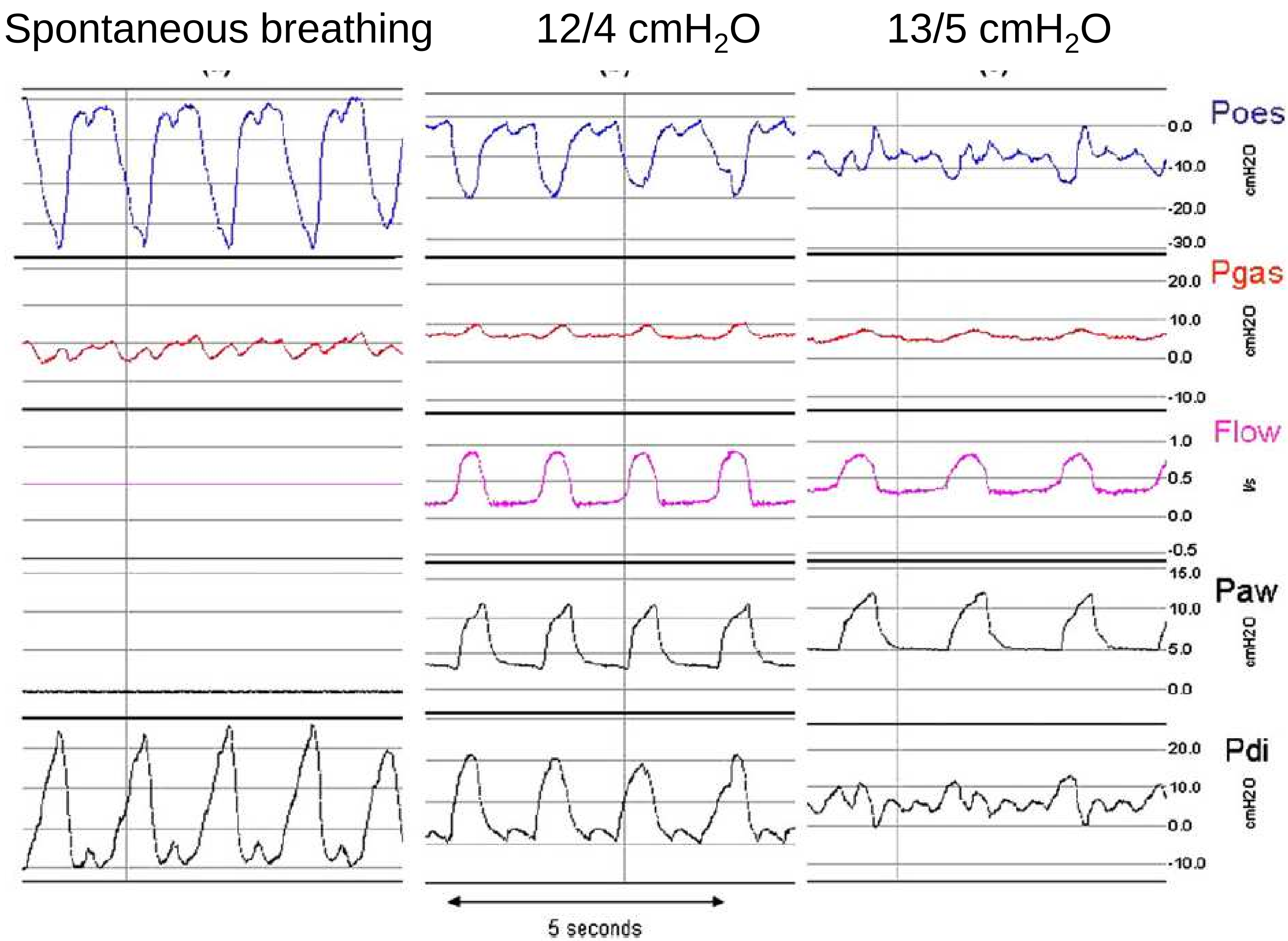
Intensive Care Med
DOI 10.1007/s00134-012-2469-4

Lisa Giovannini-Chami
Sonia Khirani
Guillaume Thouvenin
Adriana Ramirez
Brigitte Fauroux

# Work of breathing to optimize noninvasive ventilation in bronchiolitis obliterans





Spontaneous breathing
12/4 cmH2O
13/5 cmH2O
Poes
Pgas
Flow
Paw
Pdi
cmH2O
l/s
0.0
-10.0
-20.0
-30.0
20.0
10.0
0.0
-10.0
1.0
0.5
0.0
-0.5
15.0
10.0
5.0
0.0
20.0
10.0
0.0
-10.0
5 seconds

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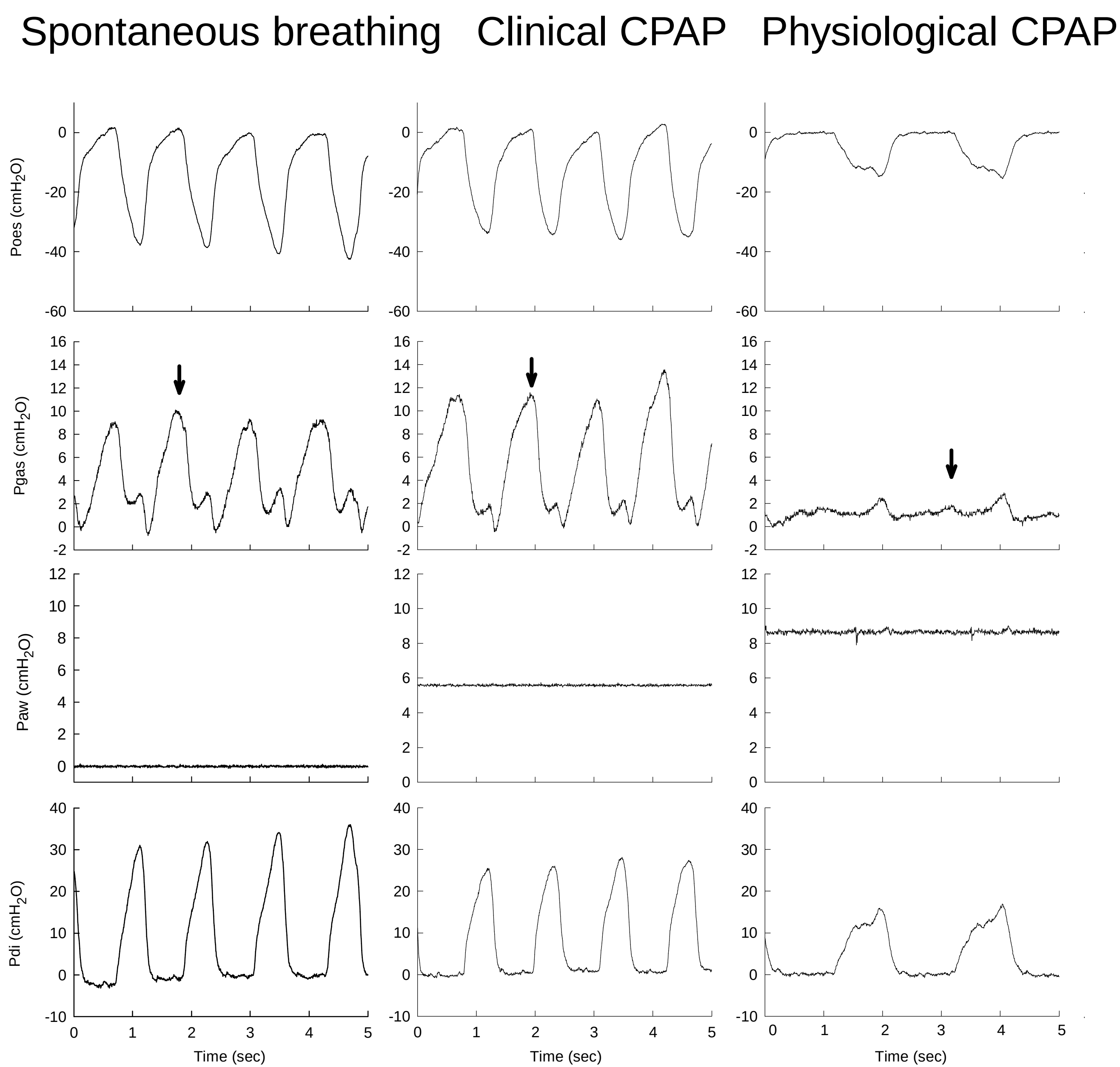


Spontaneous breathing
Clinical CPAP
Physiological CPAP
Poes (cmH2O)
Pgas (cmH2O)
Paw (cmH2O)
Pdi (cmH2O)
Time (sec)
Time (sec)
Time (sec)

Khirani et al. Critical Care 2013, 17:R167
http://ccforum.com/content/17/4/R167

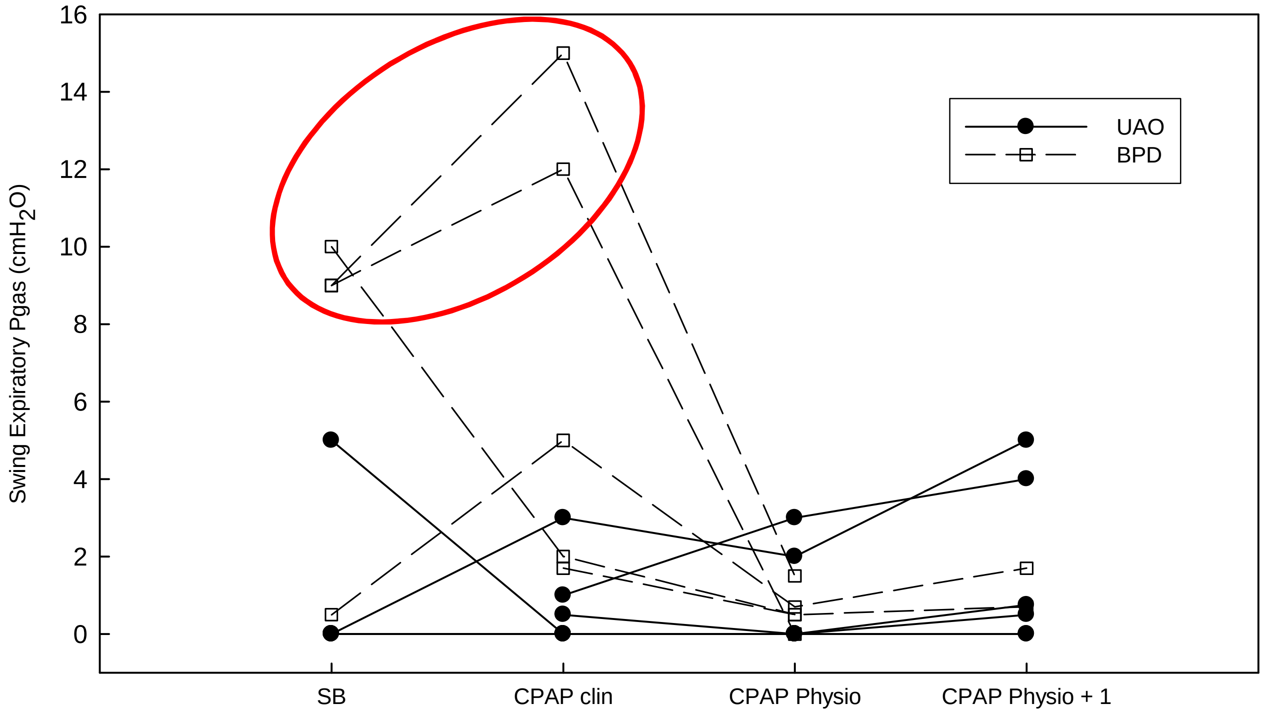
CRITICAL CARE

RESEARCH Open Access

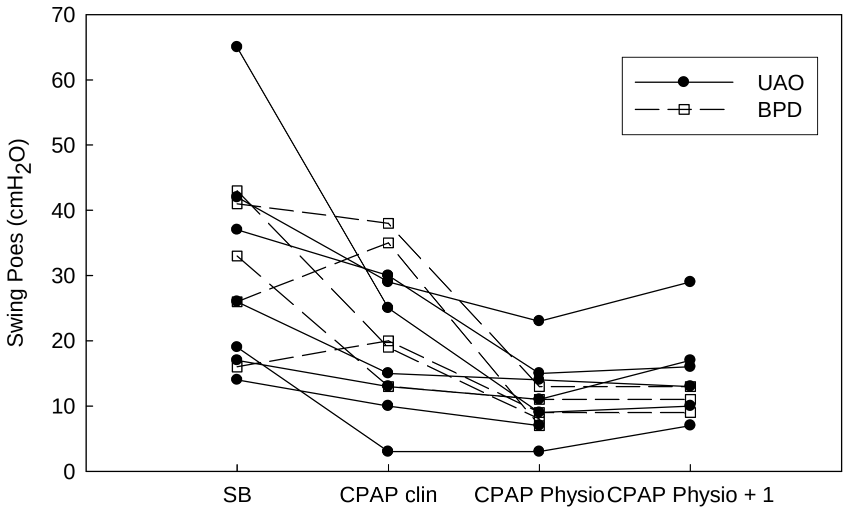
# Continuous positive airway pressure titration in infants with severe upper airway obstruction or bronchopulmonary dysplasia

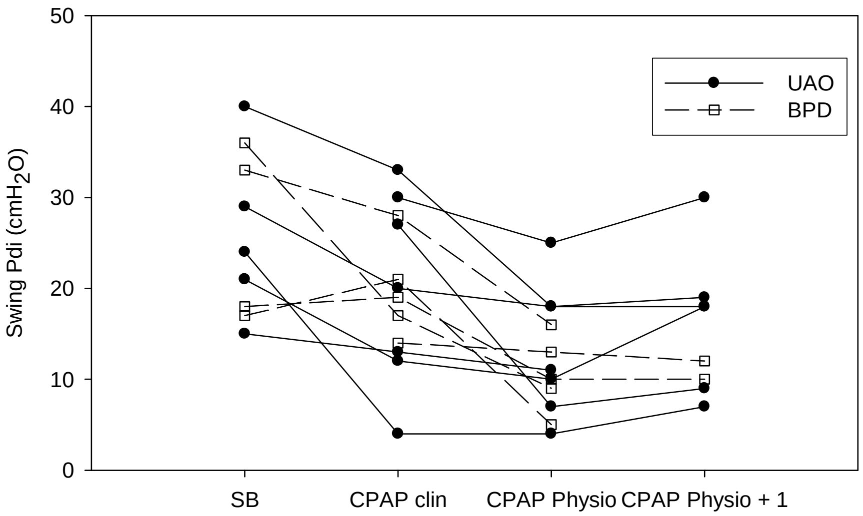
Sonia Khirani[1,2], Adriana Ramirez[2,3], Sabrina Aloui[2], Nicolas Leboulanger[4,5,6], Arnaud Picard[5,7] and Brigitte Fauroux[2,5,6*]

## Expiratory abdominal activity



# Decrease in the respiratory effort with CPAP




Khirani *et al.* Crit Care 2013;17:R167

# Rationale and benefits of NIV in lung diseases

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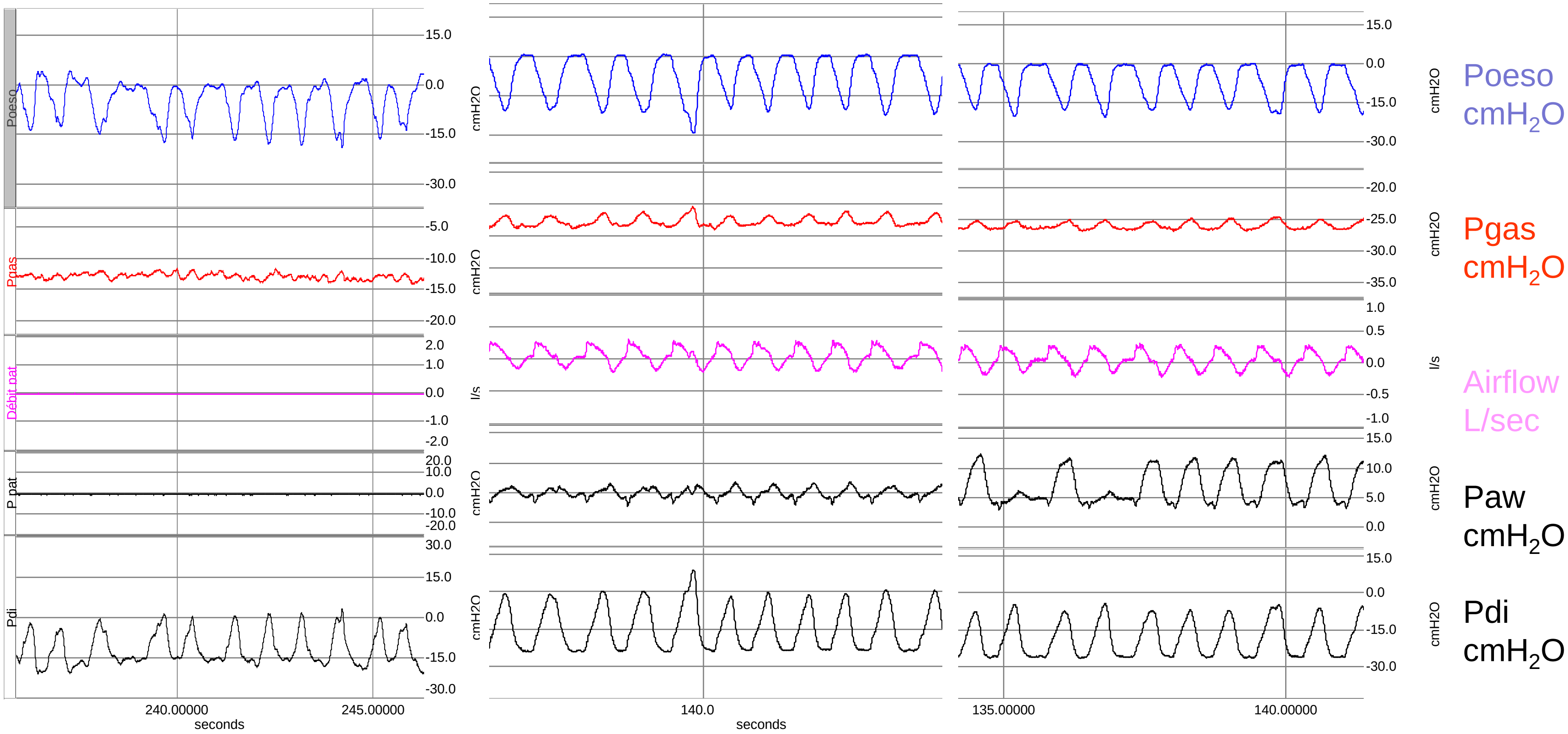
# No benefit of NIV in ILD

## 13 year old girl with « end-stage » ILD




Spontaneous breathing

Nasal CPAP 6 $cmH_2O$

Nasal bilevel PAP 12/6cm $H_2O$

# OSAS in common in adults with interstitial lung disease

**Table 2 Prevalence of obstructive sleep apnoea in interstitial lung disease populations *n* (%)**

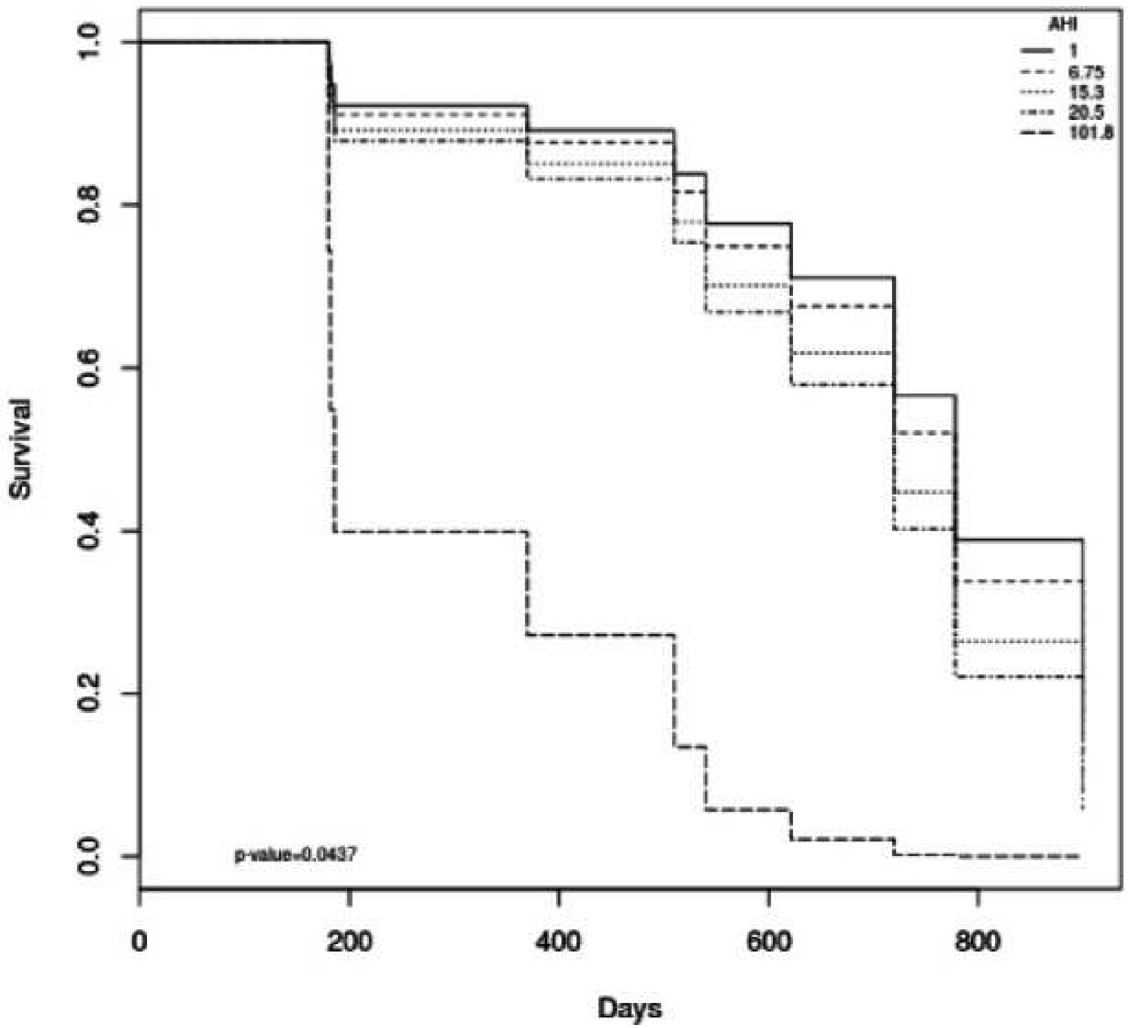
| Ref. | Population | Prevalence of OSA | M/F | Age (mean) | BMI (mean) | Comment |
|---|---|---|---|---|---|---|
| Aydoğdu *et al*[18], 2006 | ILD | 24 (65) | | | | Abstract only |
| Mermigkis *et al*[17], 2007 | IPF | 11 (61) | 12/6 | 68.1 | 33.2 | Retrospective study; subjects with symptoms of SDB |
| Lancaster *et al*[19], 2009 | IPF | 44 (88) | 34/16 | 65.7 | 32.2 | Prospective study of unselected patients; 16 subjects used oxygen during PSG |
| Mermigkis *et al*[20], 2010 | IPF | 20 (59) | 21/13 | 65.0 | 27.3 | Prospective study of subjects with newly diagnosed IPF |
| Kolilekas *et al*[2], 2013 | IPF | 28 (90) | 24/7 | 68.0 | 28.7 | Increased AHI associated with decreased survival, after exclusion of those prescribed CPAP |
| Pihtili *et al*[25], 2013 | ILD | 34 (68) | 14/36 | 53.9 | 25.9 | Prospective study; excluded obese subjects (BMI ≥ 30) |
| | IPF | 14 (82) | | | | |
| | Sarcoidosis | 10 (67) | | | | |
| | Scleroderma | 10 (56) | | | | |

# OSAS is common in ILD

| Variables | No OSA (AHI 0–5 events/h) [n = 6] | Mild OSA (AHI 5.1–15 events/h) [n = 10] | Moderate-to-Severe OSA (AHI > 15 events/h) [n = 34] | p Value* |
|---|---|---|---|---|
| Polysomnography | | | | |
| Latency to sleep, min | 22.5 ± 13.7 | 20.7 ± 25.2 | 21.8 ± 26.3 | 0.99 |
| Sleep efficiency, % | 77.2 ± 12.8 | 75.9 ± 13.7 | 69.8 ± 18.7 | 0.45 |
| Stage 1 sleep, % | 10.4 ± 5.1 | 16.2 ± 7.7 | 22.3 ± 11.2 | 0.02 |
| Stage 2 sleep, % | 70.1 ± 5.1 | 62.9 ± 18.2 | 63.9 ± 11.7 | 0.54 |
| Stage 3/4 sleep, % | 3.2 ± 5 | 1.5 ± 3.1 | 0.2 ± 0.4 | 0.007 |
| Stage REM sleep, % | 16.5 ± 9.6 | 14.2 ± 6.6 | 12.6 ± 7.6 | 0.47 |
| Arousal index | 6.4 ± 5 | 20.2 ± 14.7 | 38.1 ± 20.2 | < 0.001 |
| Periodic Limb Movement index | 22.4 ± 34.8 | 4.0 ± 6.3 | 12.5 ± 20 | 0.22 |
| Respiratory analysis | | | | |
| Total AHI | 1.6 ± 1.6 | 10.7 ± 2.1 | 39.4 ± 25.9 | < 0.001 |
| AHI non-REM | 0.9 ± 1.5 | 8.9 ± 4.1 | 37.5 ± 26.6 | < 0.001 |
| AHI REM | 4.4 ± 5.8 | 23.6 ± 14.1 | 26.1 ± 32.5 | 0.04 |
| Hypopnea index | 1.5 ± 1.5 | 10.0 ± 2.0 | 26.6 ± 19.2 | 0.001 |
| Hypopneas with arousals, % of total | 19.4 ± 21.9 | 52.2 ± 30.2 | 54.8 ± 21.6 | 0.012 |
| Hypopneas | | | | |
| Hypopneas with desaturations, % of total hypopneas | 80.6 ± 21.9 | 47.8 ± 30.2 | 45.2 ± 21.5 | 0.012 |
| Apnea index | 0.1 ± 0.2 | 0.8 ± 1.1 | 7.1 ± 11.4 | 0.09 |
| Minimum saturation, % | 87.3 ± 6.9 | 81.6 ± 6.8 | 78.7 ± 7.3 | 0.03 |
| Saturation at start of NPSG, % | 92.8 ± 6.2 | 94.2 ± 1.9 | 94.9 ± 2.2 | 0.29 |
| Desaturation index | 4.6 ± 5.1 | 9.3 ± 5.3 | 35 ± 19.4 | < 0.001 |

Lancaster *et al.* Chest 2009;136:772

# AHI predicts survival in ILD



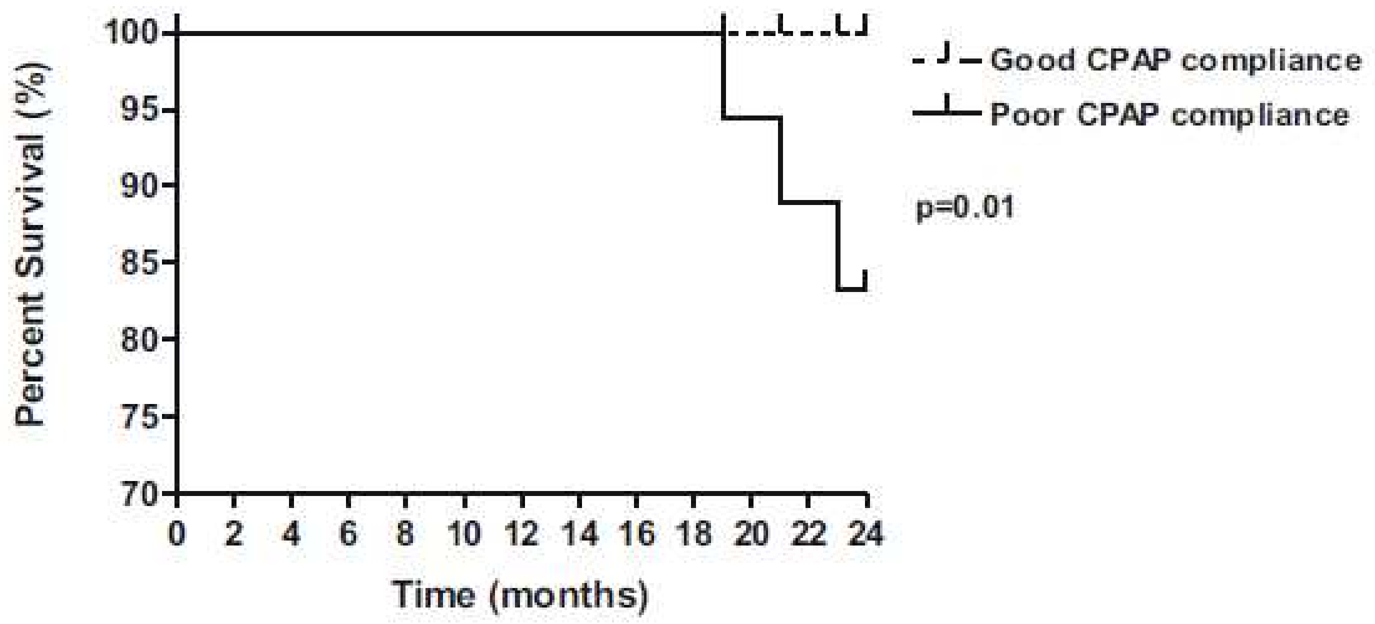

Kolilekas *et al.* J Clin Sleep Med 2013;9:593

Sleep Breath (2015) 19:385–391
DOI 10.1007/s11325-014-1033-6

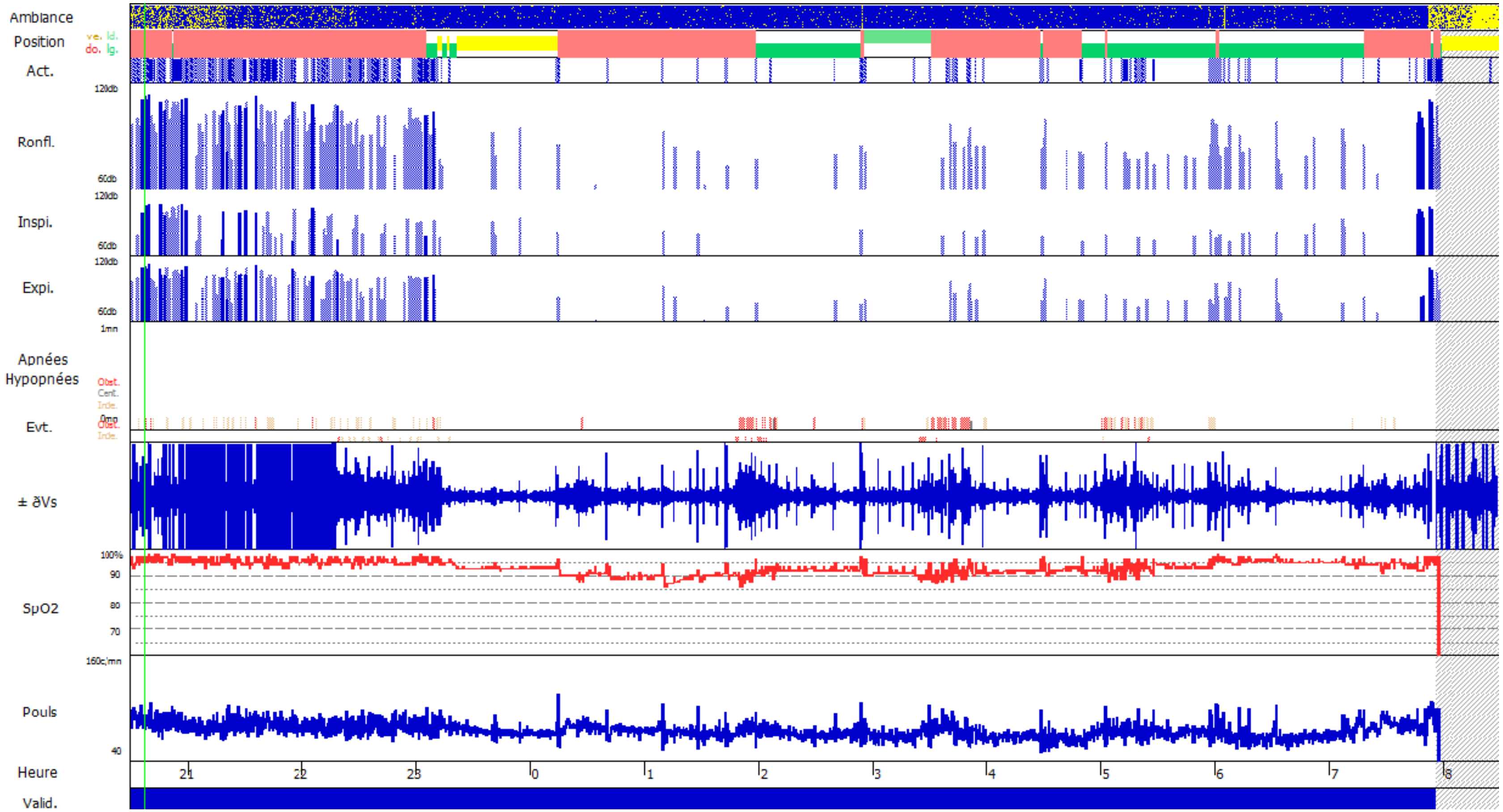
ORIGINAL ARTICLE

# Obstructive sleep apnea should be treated in patients with idiopathic pulmonary fibrosis

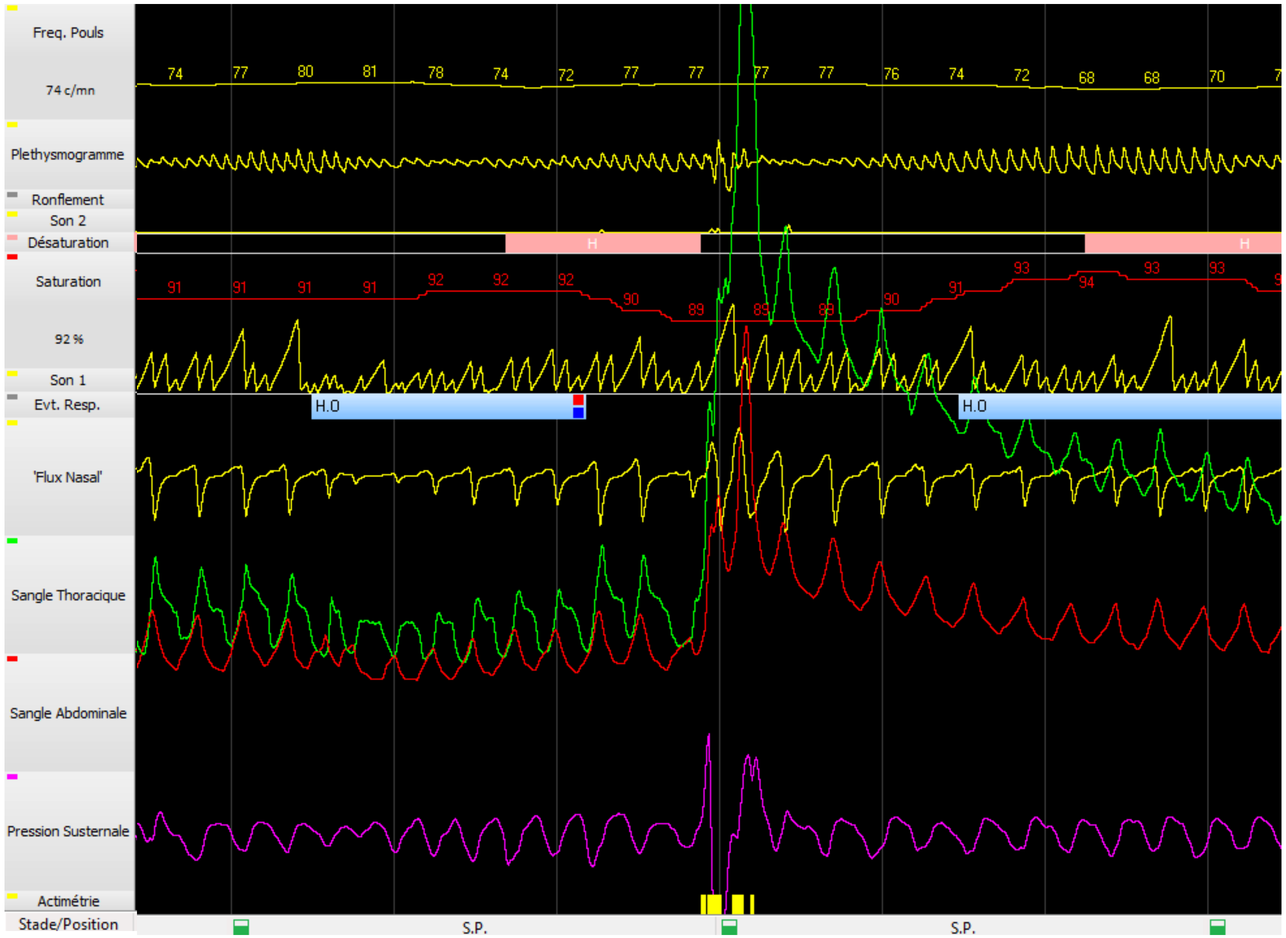
Kaplan Meier survival analysis



# Marie, 10 years, ILD



# 13 year old girl with a mutation of NKX2-1




Polysomnography

Normal sleep quality and structure
No apneas
9 hypopneas/h
70% are obstructive

Mean $SpO_2$ 92%
Minimal $SpO_2$ 86%
Desaturation index 10/h
11% of time with $SpO_2$<90%

Mean $PtcCO_2$ 35 mmHg
Maximal $PtcCO_2$ 40 mmHg

# Conclusion

- Physiological studies show that there is a rationale for NIV in pediatric lung diseases
  - CF, BO, selected BPD, ILD ?
- Necessity of more systematic
  - sleep studies
  - physiological measurements
- Future studies should aim at defining:
  - patients who could benefit most from NIV
  - initiation criteria for NIV
  - clinical benefits from NIV