

Place de la VNI dans la prise en charge de l'asthme aigu grave!!!

Encore loin de la réalité!

Mabrouk Bahloul

**Service de Réanimation médicale CHU Habib
Bourguiba**

Sfax-Tunisie

Détresse respiratoire aigue...

Indication de la VNI...



organisée conjointement par
la SFAR, la SPLF et la SRLF

Ventilation Non Invasive
au cours de l'insuffisance respiratoire aiguë
(nouveau-né exclu)

Avec la participation de la SFMU,
du SAMU de France,
du GFRUP
et de l'ADARPEF

Le 12 octobre 2006
Paris, Institut Montsouris
42, boulevard Jourdan
75014 Paris

3^e Conférence de Consensus commun

ESUME



Détresse respiratoire aigue...

Indication de la VNI...

Niveaux de recommandation pour les indications de la VNI dans l'IRA



Intérêt certain...Il faut faire (G1+)

Décompensation aigue de BPCO

OAP cardiogénique



**Intérêt non établi de façon certaine
Il faut probablement faire (G2+)**

IRA hypoxémique de l'immunodéprimé

Décompensation d'IRC restrictives

Mucoviscidose

Traumatisme thoracique fermé

.....



**Aucun avantage démontré
Il ne faut probablement pas faire**

SDRA

Pneumopathie hypoxémiante

....



Situations sans cotation possible

Asthme aigu grave

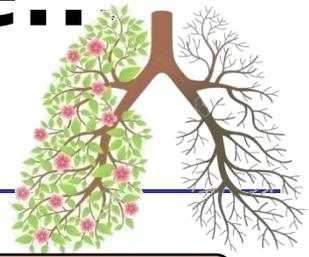
Syndrome obésité hypoventilation

...

O₂

Insuffisance respiratoire..

Conséquences...

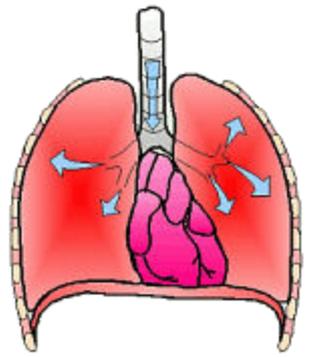


Insuffisance respiratoire

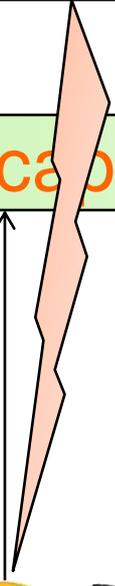
Ventilation assistée

Hypercapnie

W musculaire ↗ ↗

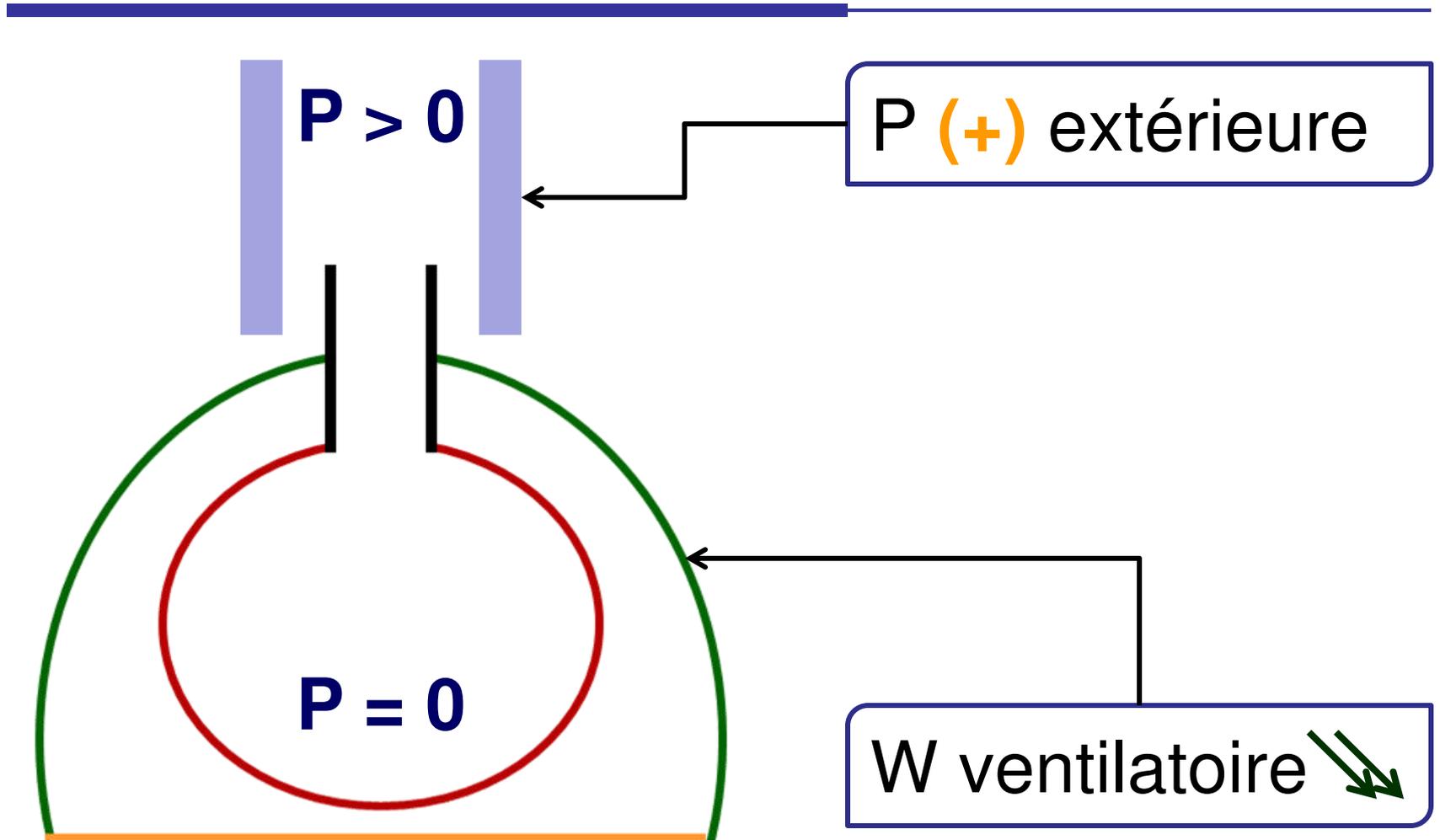


Fatigue musculaire

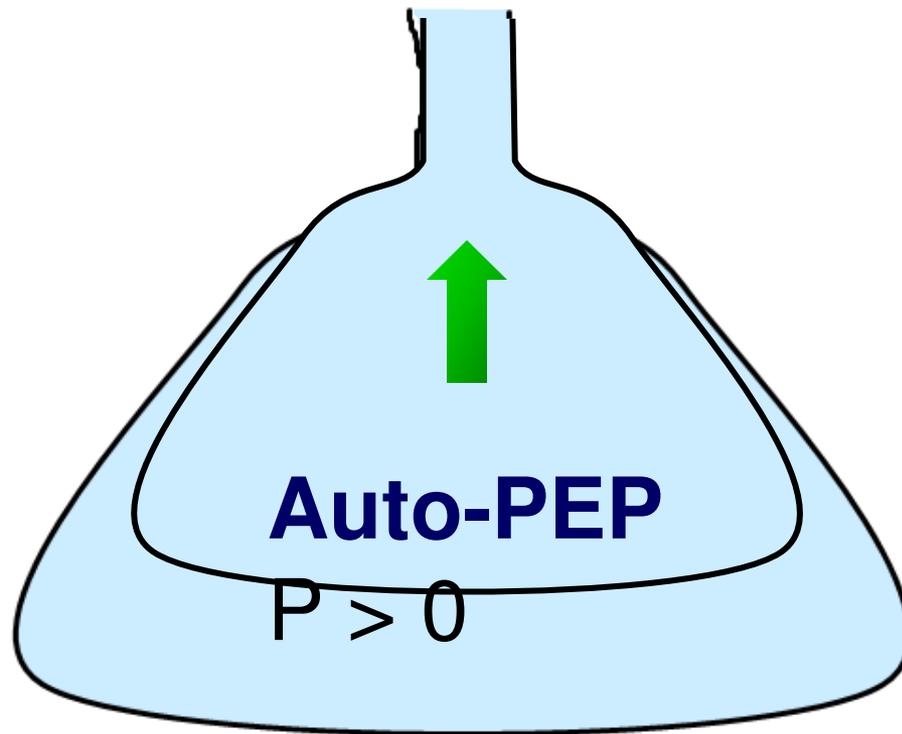


Ventilation assistée...

A pression positive...

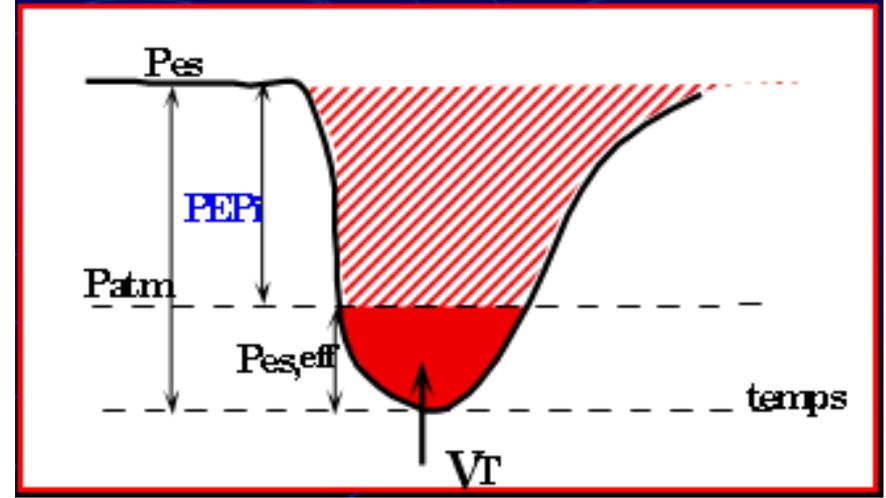
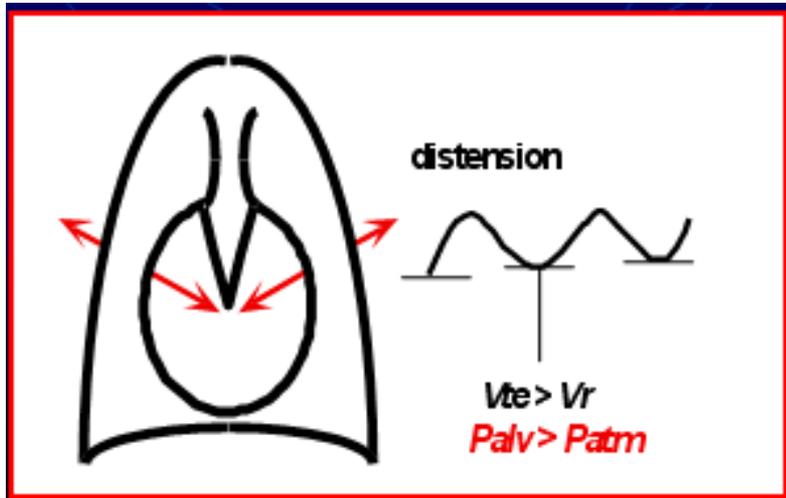
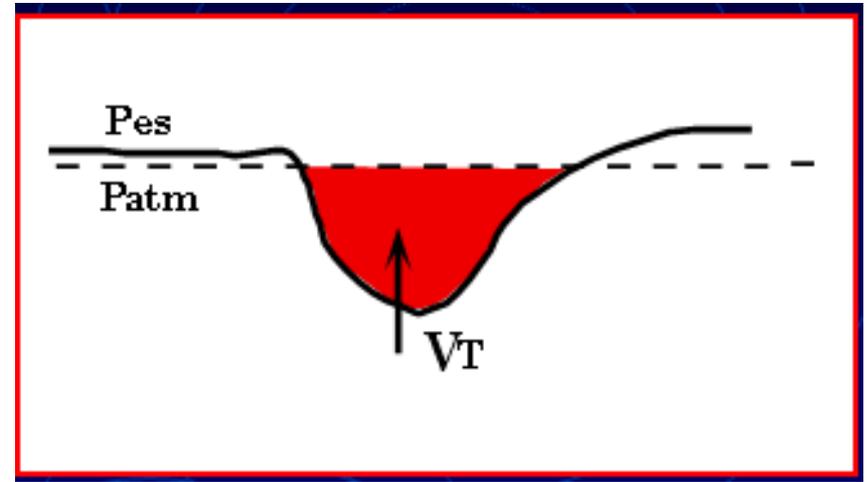
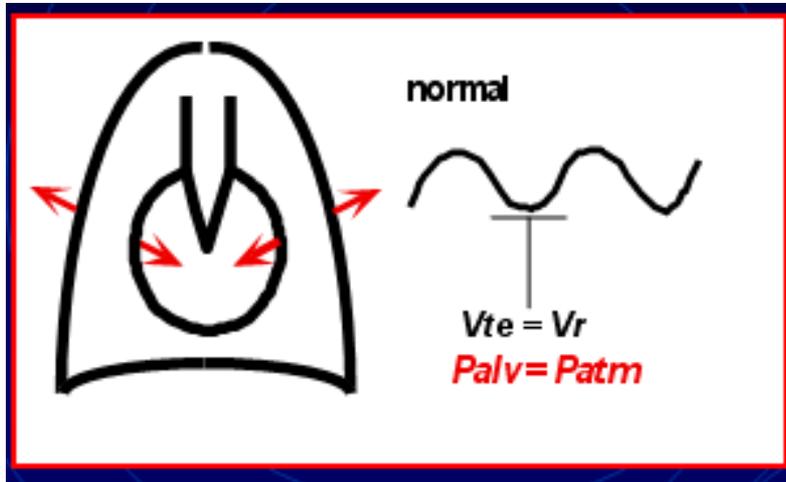


Pathologies respiratoires obstructives...



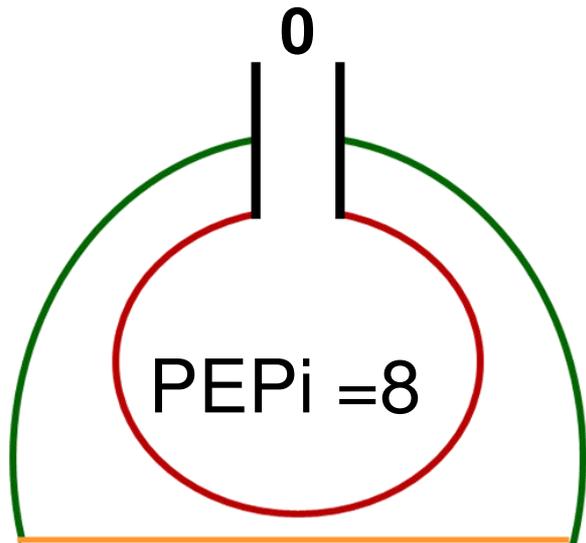
Piégeage expiratoire

DISTENSION : SEUIL INSPIRATOIRE



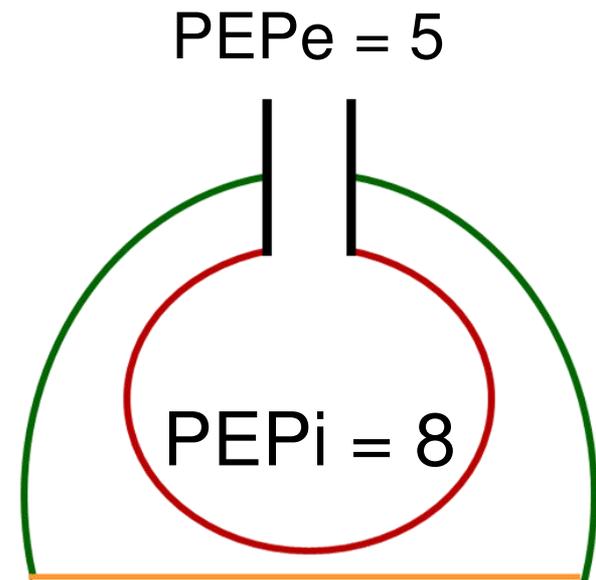
PEPe...&...expiration...BPCO

Effort = - 8



BPCO

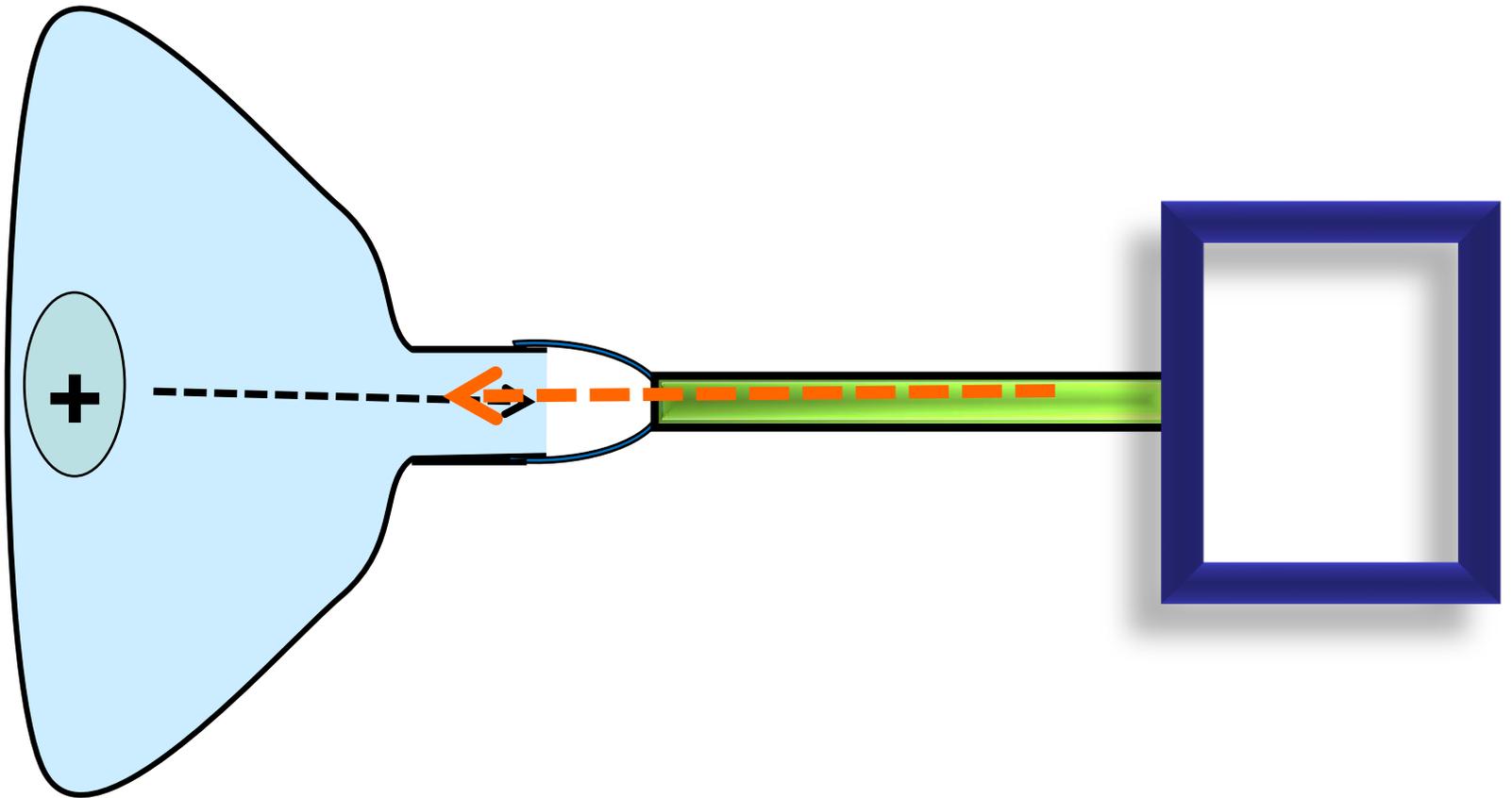
Effort = - 3



BPCO + PEPe

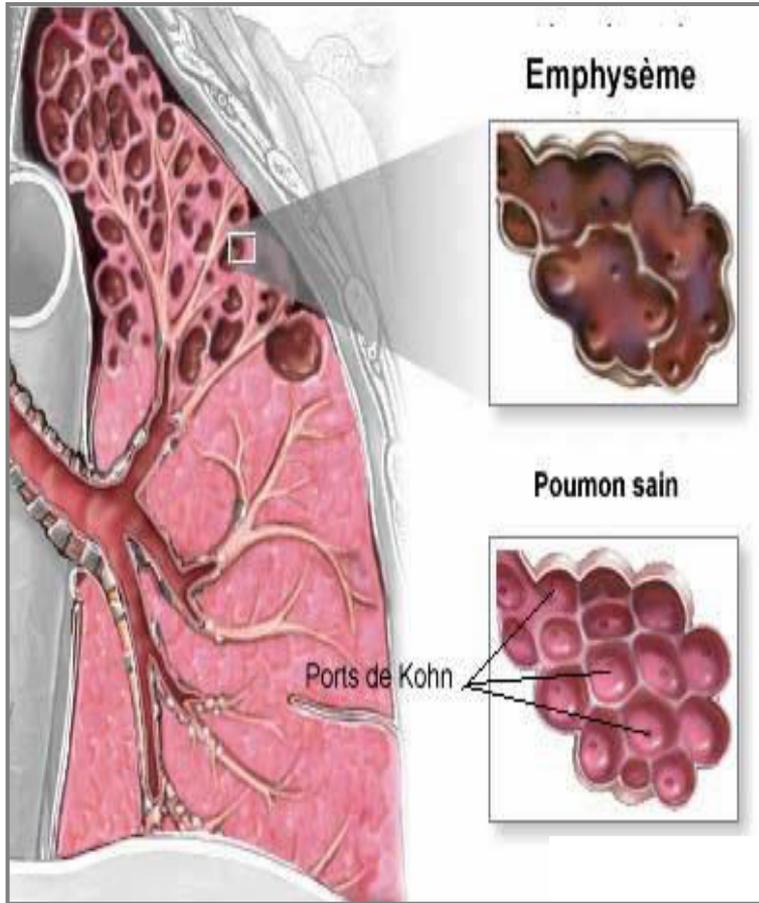
PEPe facilite le déclenchement inspiratoire

BIPAP et BPCO

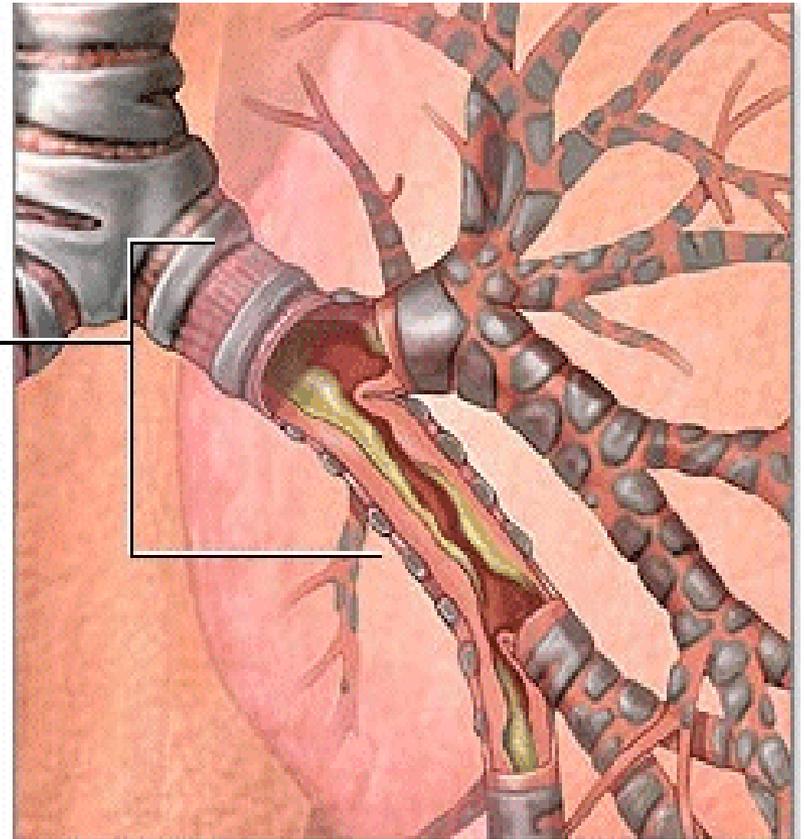


ASTHME / BPCO

BPCO



Asthme:



PEPe...&...expiration...AAG

Effort = - 3

PEPe = 5

PEPi = 8

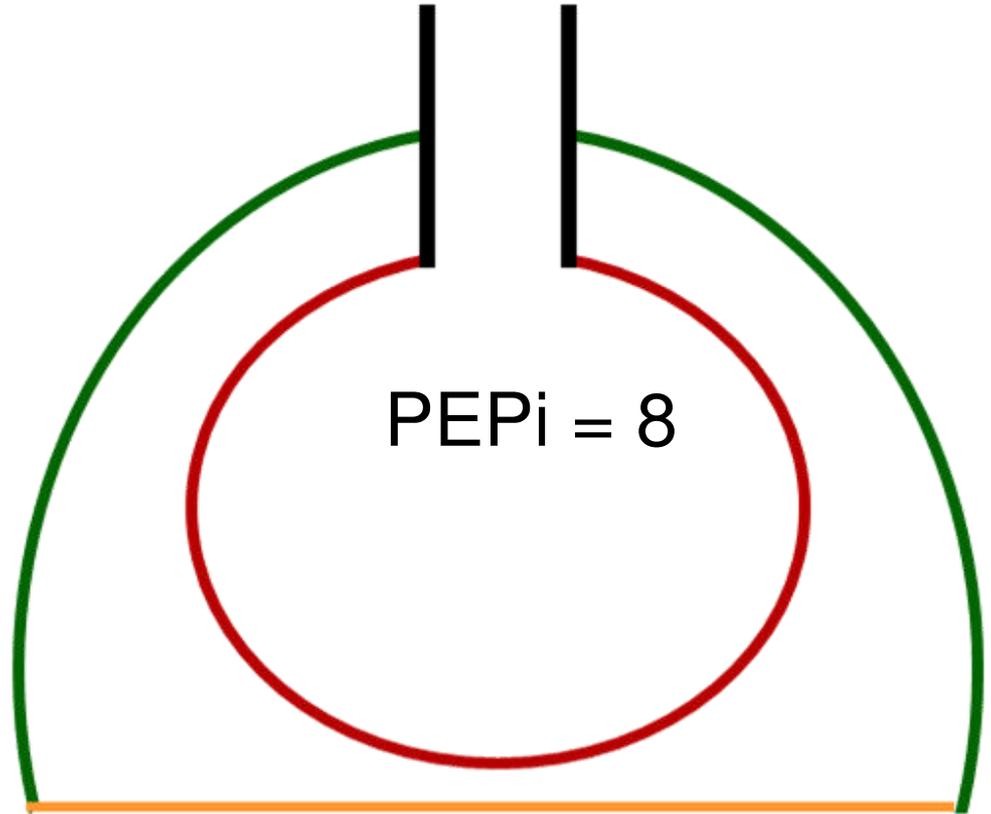
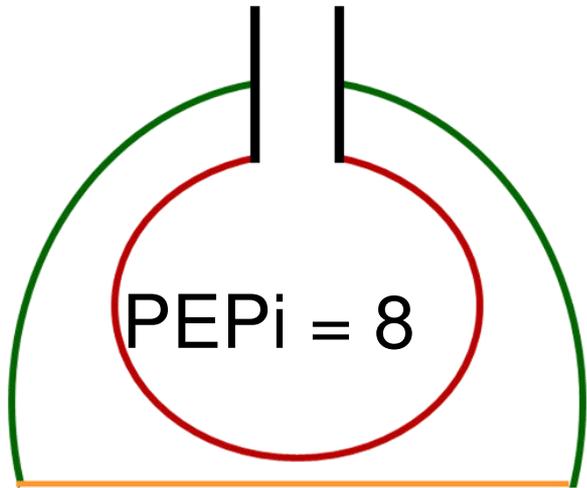
BPCO + PEPe

Effort +++

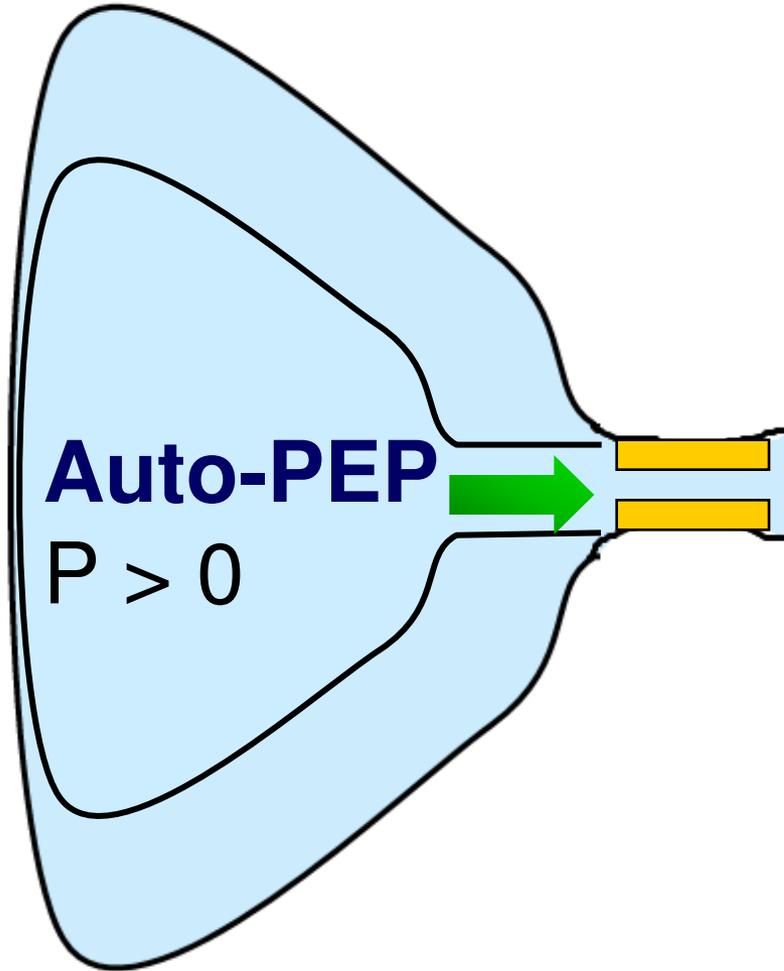
PEPe = 5

PEPi = 8

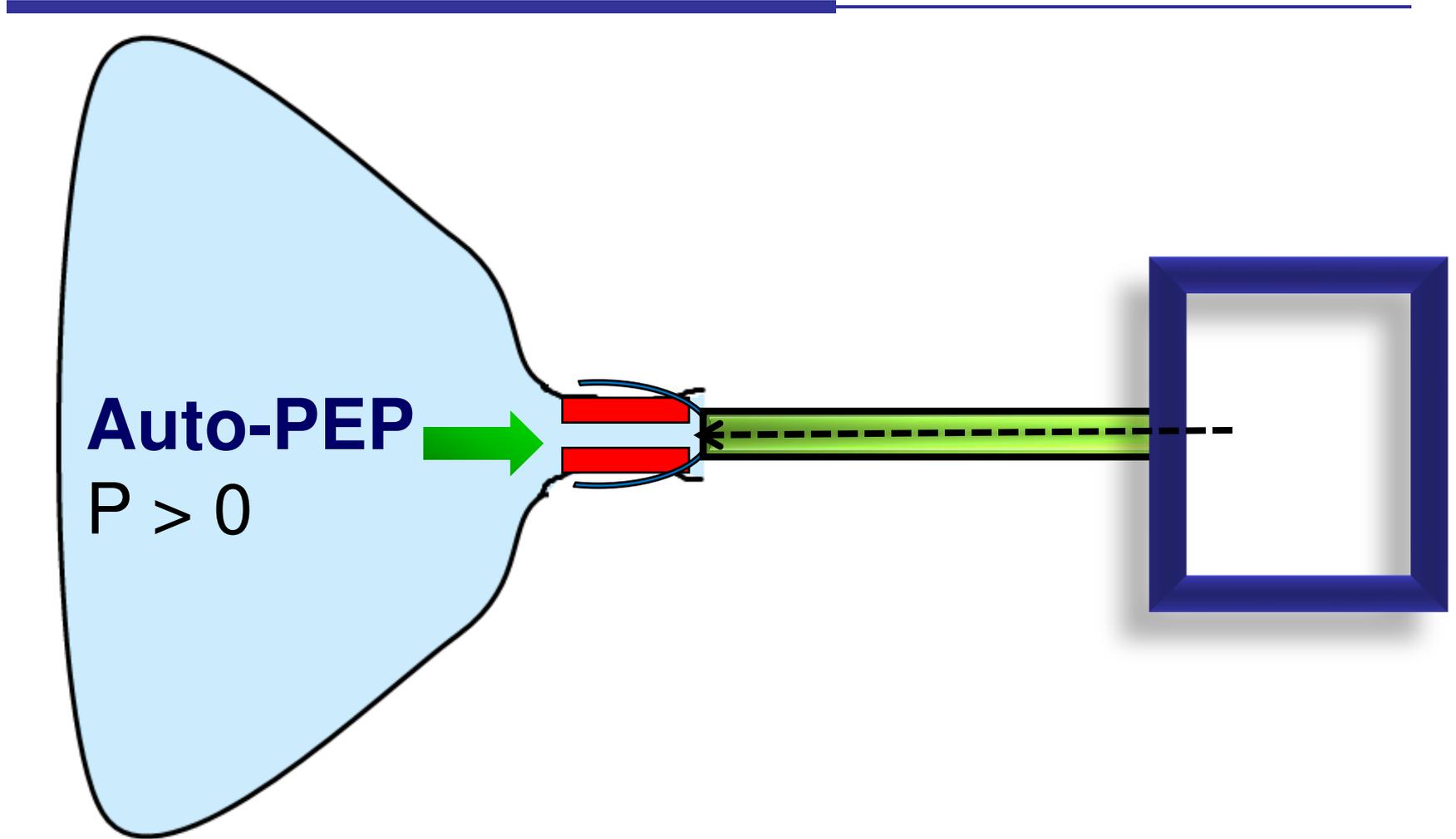
AAG + PEPe



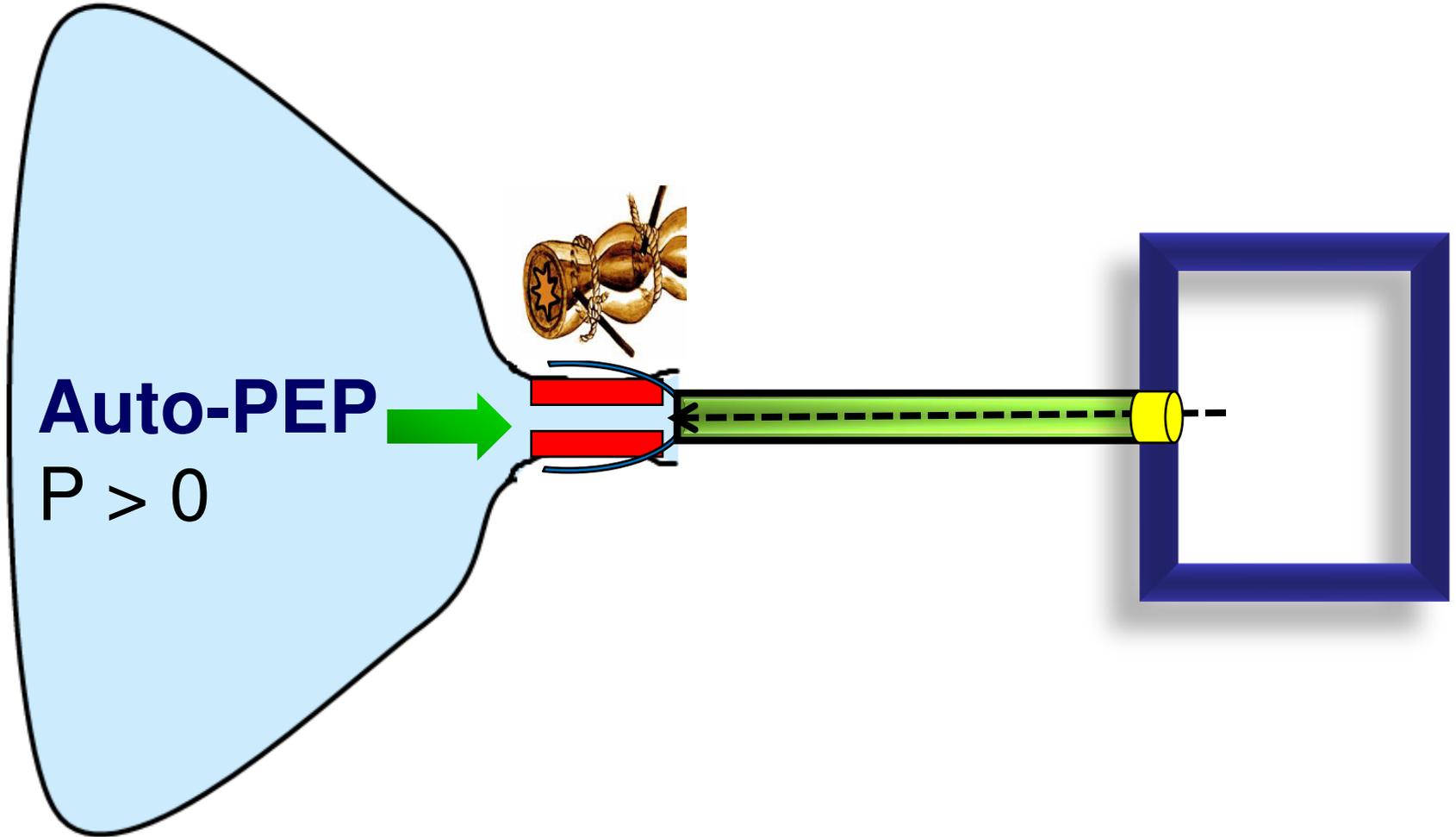
BIPAP



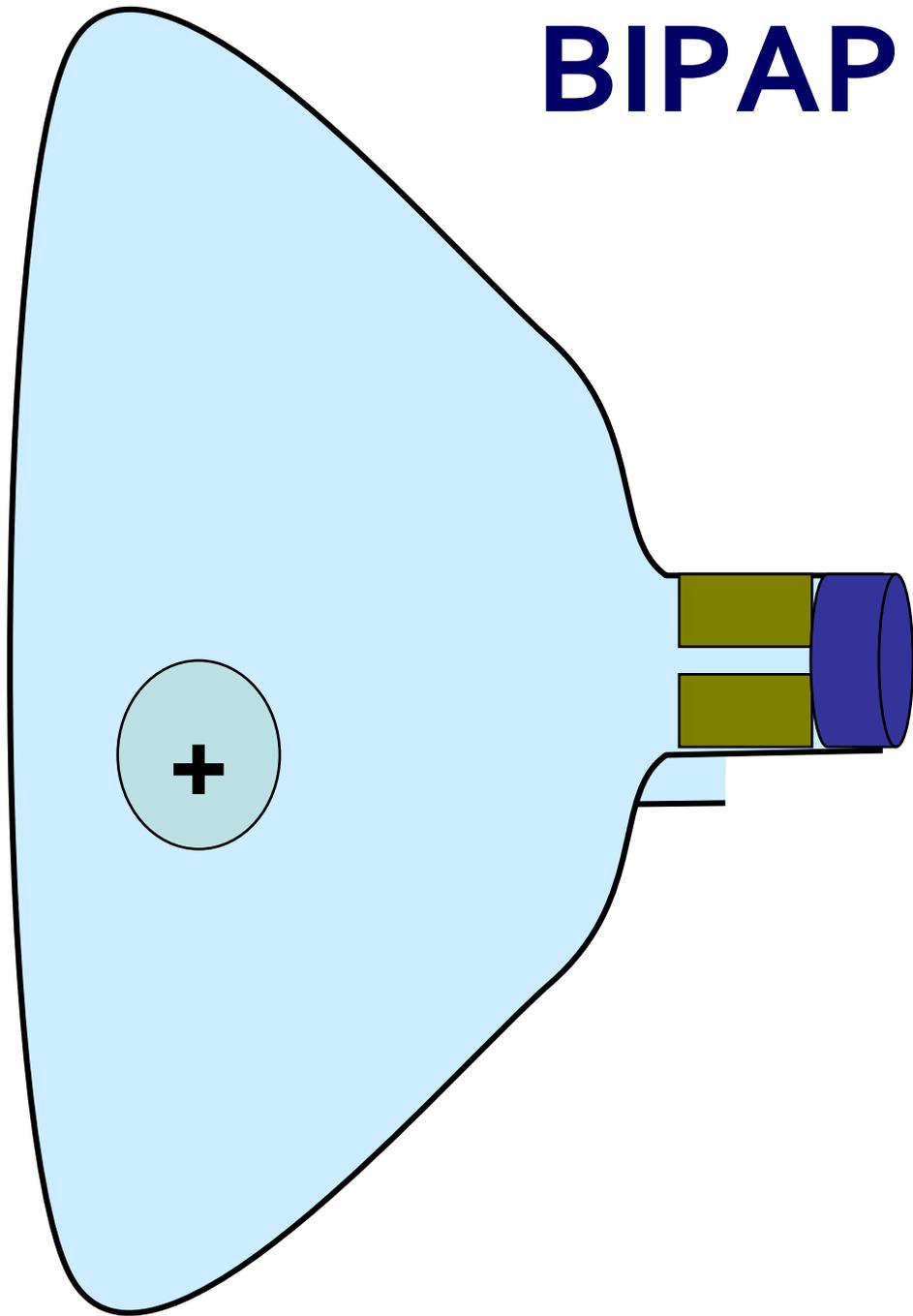
BIPAP



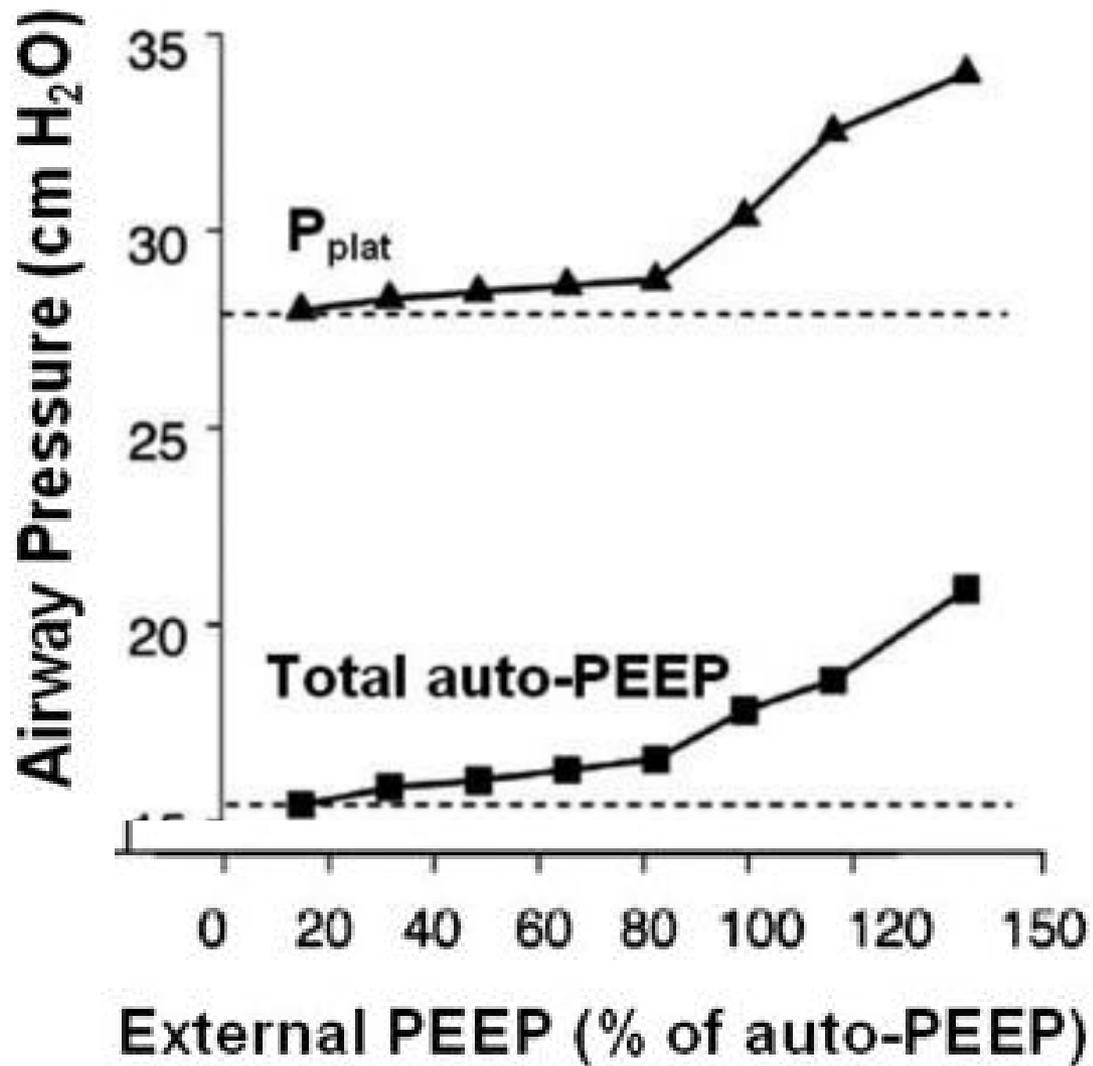
BIPAP

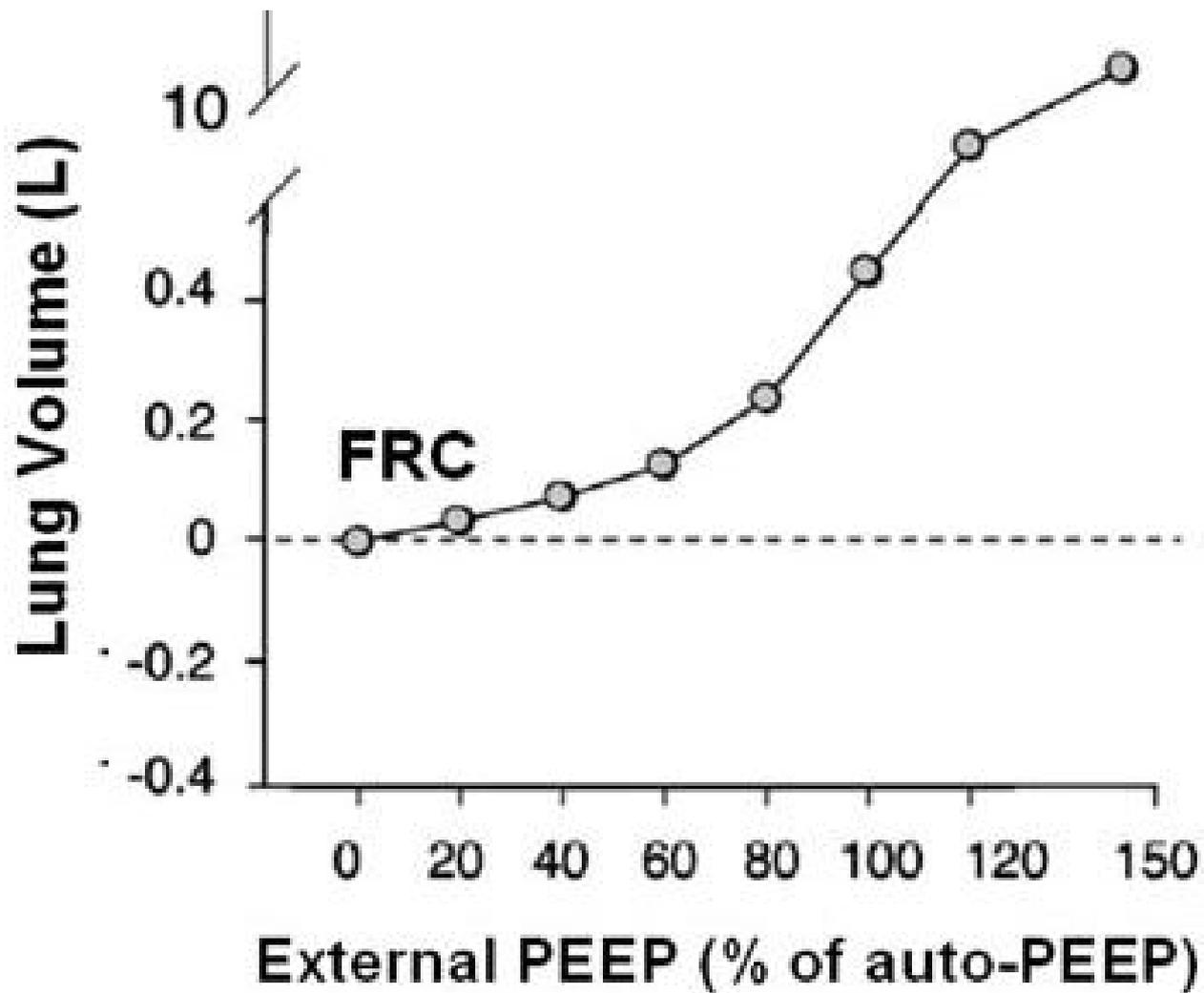


BIPAP et AAG

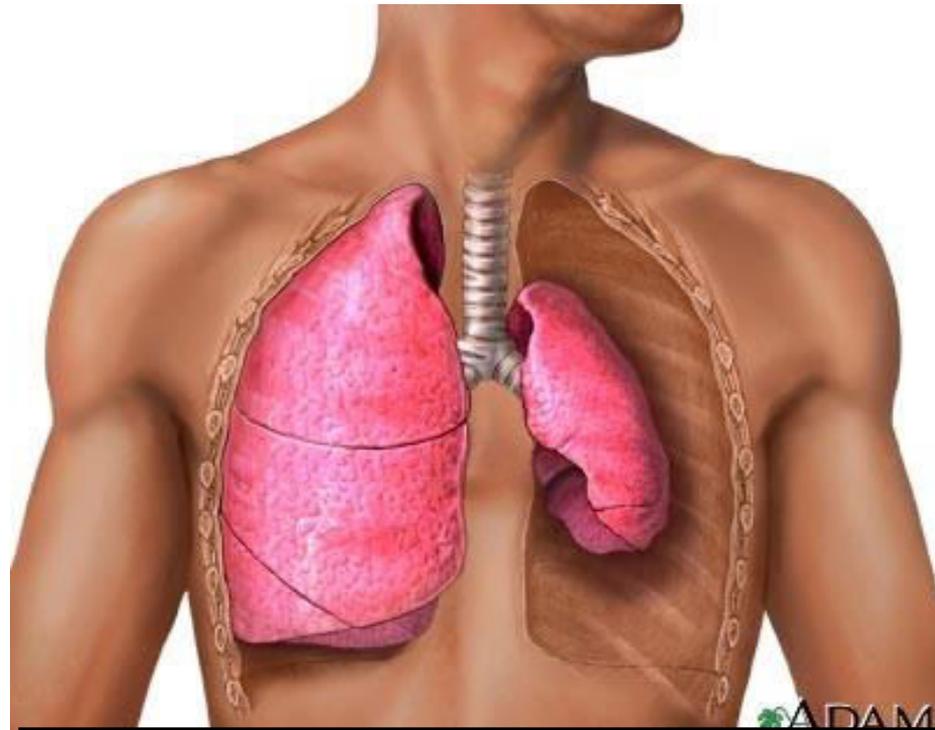


**Distension
Alvéolaire +++**





Caramenz MP et al Crit Care Med. 2005 Jul;33(7):1519-28.



**Risque
Barotraumatique**

Donc...

- ◆ la physiopathologie de l'AAG apporte des arguments contre l'utilisation de la VNI
- ◆ Sur le plan pratique???

Types d'études

1. Cas cliniques
2. Études Rétrospectives
3. Études Prospectives randomisées (6)
4. Méta-analyse (1)
5. Review papers + Editorials

La ventilation non invasive dans l'asthme aigu grave, une nouvelle attitude thérapeutique ?

À propos de deux cas

F Thys¹, J Roeseler², E Marion¹, A El Gariani¹, E Danse¹,
P Meert¹, PF Laterre², P Matte², L Jacquet², MS Reynaert²

TABLEAU I. Observation n° 1 : deuxième crise bronchospastique,

Observation 1:

- ◆ **Patiente de 68 ans**
- ◆ **ATCD de BPCO depuis 15 ans**
- ◆ **pH : 7.14; PaCO₂: 84 mmHg; HCO₃: 21 mmol/l**

Use of Noninvasive Ventilation in Adult Patients With Acute Asthma Exacerbation

Aarthi Ganesh, MD,^{1*} Sundeep Shenoy, MD,² Viral Doshi, MD,³
Muhammad Rishi, MD,⁴ and Janos Molnar, MD⁵

Table 3. Outcomes of the analysis.

Characteristics	Successful NIV	Failed on NIV	<i>P</i>
Duration of ventilation (d)	0	3.68	0.000
Length of ICU (d)	0.89	4.00	0.002
Length of hospital (d)	3.92	6.79	0.016

Numbers in parentheses are expressed in percentage.

Table 2. Clinical and laboratory parameters at admission.

Characteristics	Successful NIV	Failed on NIV	<i>P</i>
APACHE	7.8 ± 4	8.8 ± 2	0.305
A—a gradient (mm Hg)	153 ± 126	128 ± 171	0.484
pH	7.33	7.29	0.128
pCO ₂ (mm Hg)	54.5	62.6	0.06
pO ₂ (mm Hg)	148.71	171.79	0.51
FiO ₂ (%)	20.42	46.21	0.019
HCO ₃ (mEq/L)	27.13	28.13	0.37

CLINICAL INVESTIGATIONS

Ethical Dilemmas in a Randomized Trial of Asthma Treatment: Can Bayesian Statistical Analysis Explain the Results?

MARK T. HOLLEY, MD, THOMAS K. MORRISSEY, MD, PHD,
DAVID C. SEABERG, MD, BEKELE AFESSA, MD,
ROBERT L. WEARS, MD, MS

- ◆ Etude Américaine prospective randomisée
- ◆ Lieu: Urgences (HU Florida)
- ☉ **Critères d'inclusion:**
- ◆ AAG ne répondant pas aux B2 mimétiques
- ◆ age ≥ 18 ans; FR ≥ 30 /min; DEP $\leq 70\%$ valeur de base;
- ◆ Signes de lutte respiratoire

Critères de jugement

◆ Primaires:

- ◇ Recours à la VM invasive (sur des critères bien définis)
- ◇ Durée de séjour

◆ Secondaires:

- ◇ Amélioration des signes respiratoires
- ◇ Amélioration des signes Spirométriques

- ◆ Réduction significative du taux de VMI: 7.5 % à 2.5% (5%) avec une puissance de l'étude de 80 %
- ◆ Échantillon prévue: **518 patients**

TABLE 1. Patient Characteristics (Mean \pm Standard Deviation) Are Similar between Groups upon Study Entrance

	BiPAP* Group	No-BiPAP Group
Age (years)	34.4 \pm 9.8	39.7 \pm 9.2
Respiratory rate (breaths/min)	28.3 \pm 4.8	26.6 \pm 8.4
Systolic blood pressure (mm Hg)	142.9 \pm 20.3	141.3 \pm 29.6
Diastolic blood pressure (mm Hg)	84.9 \pm 17.1	89.3 \pm 17.8
Pulse rate (beats/min)	114.2 \pm 18.2	121.2 \pm 18.0
Pulse oximetry value (%)	86.6 \pm 28.9	88.9 \pm 23.6
Peak flow rate (L/min)	184.2 \pm 90.0	210.0 \pm 129.9
Arterial pH	7.35 \pm 0.04	7.32 \pm 0.06
PaCO ₂ (torr)	39.8 \pm 10.6	44.1 \pm 11.9
PaO ₂ (torr)	121.2 \pm 62.6	101.8 \pm 44.8
Arterial oxygen saturation (%)	95.4 \pm 4.7	93.8 \pm 7.2

Paramètres	Groupe VNI (+) N: 19	Groupe VNI (-) N: 16	p
Ventilation Invasive	1	2	<0.05
Durée de séjour	46 heures	74 heures	<0.05
Critères secondaires	NS	NS	NS
Coût de séjour	6041 £	7572 £	<0.05

TABLE 2. Secondary Outcome Measures (Mean \pm Standard Deviation) Are Similar between Groups at Three and 12 Hours after Study Entrance

	BiPAP* Group 3 Hours	No-BiPAP Group 3 Hours
Respiratory rate (breaths/min)	24.7 \pm 6.8	20.3 \pm 5.8
Systolic blood pressure (mm Hg)	133.7 \pm 17.8	140.6 \pm 30.8
Diastolic blood pressure (mm Hg)	75.7 \pm 13.2	81.1 \pm 25.5
Pulse rate (beats/min)	109.1 \pm 11.7	135.3 \pm 74.4
Pulse oxymetry (%)	98.1 \pm 2.2	96.4 \pm 4.6
Peak flow rate (L/min)	241.0 \pm 93.5	184.3 \pm 117.9

*BiPAP = bilevel positive airway pressure.

Mais.....

- ◆ Pas de corticothérapie avant l'inclusion!!!

- ◆ Page 1132: The study was prematurely terminated secondary to this physician treatment bias.

se

A Pilot Prospective, Randomized, Placebo-Controlled Trial of Bilevel Positive Airway Pressure in Acute Asthmatic Attack*

Arie Soroksky, MD; David Stav, MD; and Isaac Shpirer, MD

- ◆ Étude prospective randomisée
- ◆ Lieu: urgences d'un hôpital universitaire
- ◆ Critères d'inclusion: clinique et spirométriques ($DEP \leq 60\%$)

A Pilot Prospective, Randomized, Placebo-Controlled Trial of Bilevel Positive Airway Pressure in Acute Asthmatic Attack*

Arie Soroksky, MD; David Stav, MD; and Isaac Shpirer, MD

- ◆ Deux groupes: VNI (+) et VNI(-)
- ◆ mêmes traitements!!!
- ◆ Critères de jugement:
 - ◇ primaires: Augmentation du DEP de + 50 % (après 3h)
 - ◇ Secondaires: * Hospitalisation
 - * Recours à la VMI

Paramètres	VNI (+) (N:15)	VNI (-) (N:15)	p
Age (ans)	34 ± 8	32 ± 9	NS
DEP (% prédite)	37 ± 10	34 ± 10	NS
Délai de la crise	2.6 ± 2	2 ± 1.7	NS
pH	7.41 ± 0.04	7.40 ± 0.02	NS
PCO2	34 ± 3	34 ± 5	NS
PaO2	83 ± 38	85 ± 29	NS
FR	35 ± 2	33 ± 1.7	NS

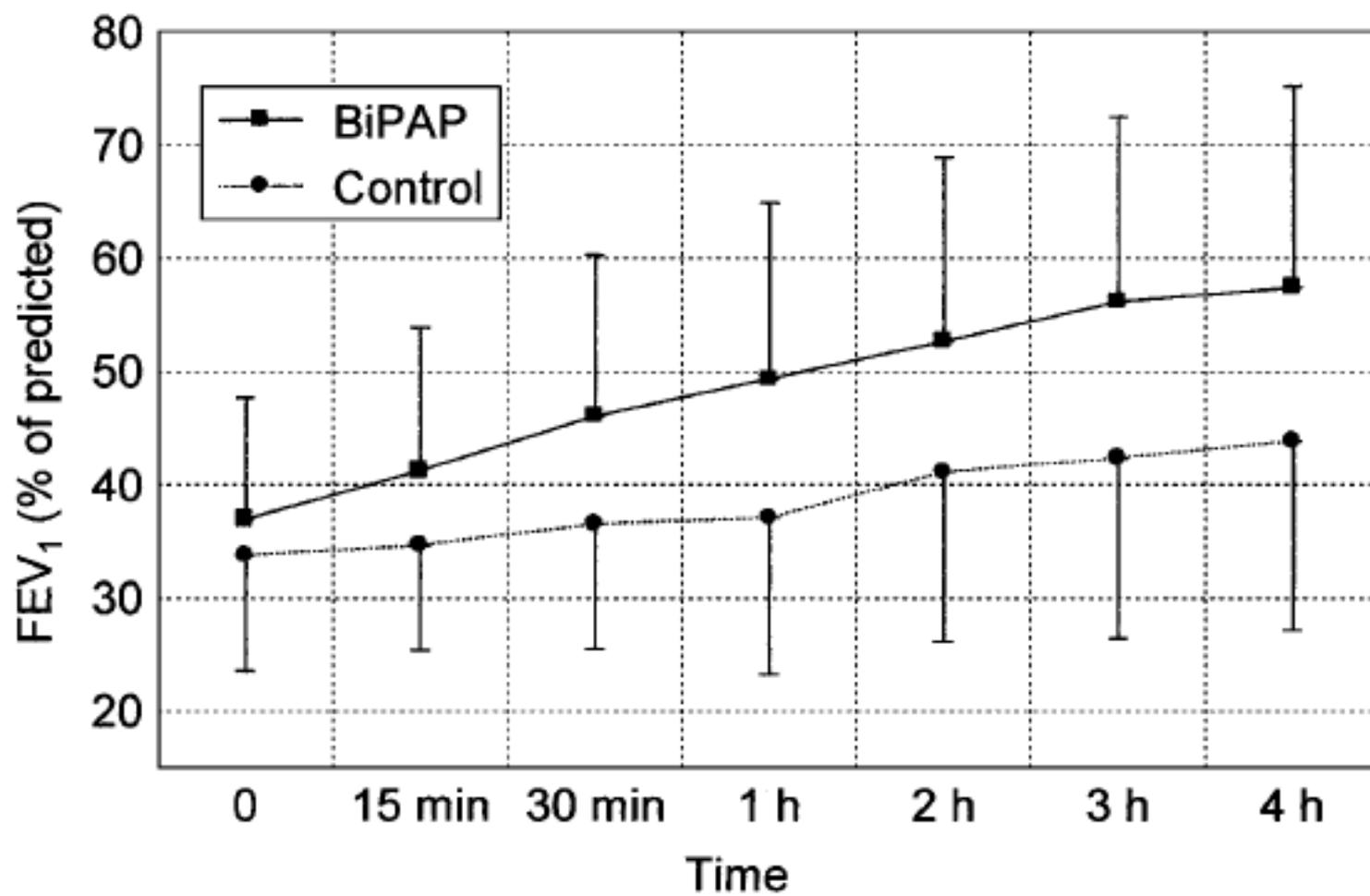


FIGURE 2. Change in FEV₁ in BPV group (BiPAP) and control group during 4 h.

Table 5—Characteristics of the Hospitalized Patients*

Parameters	BPV Group	Control Group	p Value
Patients who reached primary end points,† No.	12	3	< 0.004
Patients hospitalized,‡ No./total	3/17	10/16	0.013
Days of hospitalization§	4 ± 0	2.5 ± 1.4	
FEV ₁ on hospital admission	24.67 ± 9.5	28.4 ± 7.63	NS
PEFR on hospital admission	22.33 ± 1.53	31.4 ± 12.9	0.057
FVC on hospital admission	35.67 ± 7.02	40 ± 10.6	NS

Mais.....

Table 2—Treatment in the Emergency Department*

Parameters	BPV Group	Control Group
IV methylprednisolone†	15	12
IV hydrocortisone, mg‡	186.66 ± 124.6	158.66 ± 127.4
Nebulizations with ipratropium and salbutamol,§ No.	11	9
Inspiratory positive airway pressure	13.06 ± 0.45	1
Expiratory positive airway pressure	4.06 ± 0.45	1

Mais.....

- Doses de B2 mimétiques non standardisées
- Dose de bromure d'ipratropium à 0.25 mg!!!
- Critères d'hospitalisation non définis!!!

Page 1025: Although the study was blinded....., a limitation of the study was that we did not succeed in blinding it from the investigating team.

Original Research

A Prospective Randomized Controlled Trial on the Efficacy of Noninvasive Ventilation in Severe Acute Asthma

Dheeraj Gupta MD DM, Alok Nath MD DM, Ritesh Agarwal MD DM,
and Digamber Behera MD

- ◆ Étude prospective randomisée 18 mois
- ◆ Lieu: Service de Réanimation respiratoire
- ◆ Critères d'inclusion: clinique et spirométriques

Original Research

A Prospective Randomized Controlled Trial on the Efficacy of Noninvasive Ventilation in Severe Acute Asthma

Dheeraj Gupta MD DM, Alok Nath MD DM, Ritesh Agarwal MD DM,
and Digamber Behera MD

- ◆ Deux groupes: VNI (+) et VNI(-)
- ◆ mêmes traitements (B2, Atrovent, Corticothérapie et Mg++) +++
- ◆ Critères de jugement:
- ◇ primaires: Augmentation du DEP de + 50 % (après 3h); durée de séjour (ICU+ Hospital stay)
- ◇ Secondaires: * les paramètres cliniques, gazométriques
 - * Recours à la VMI ou
 - * VNI pour le groupe VNI (-)

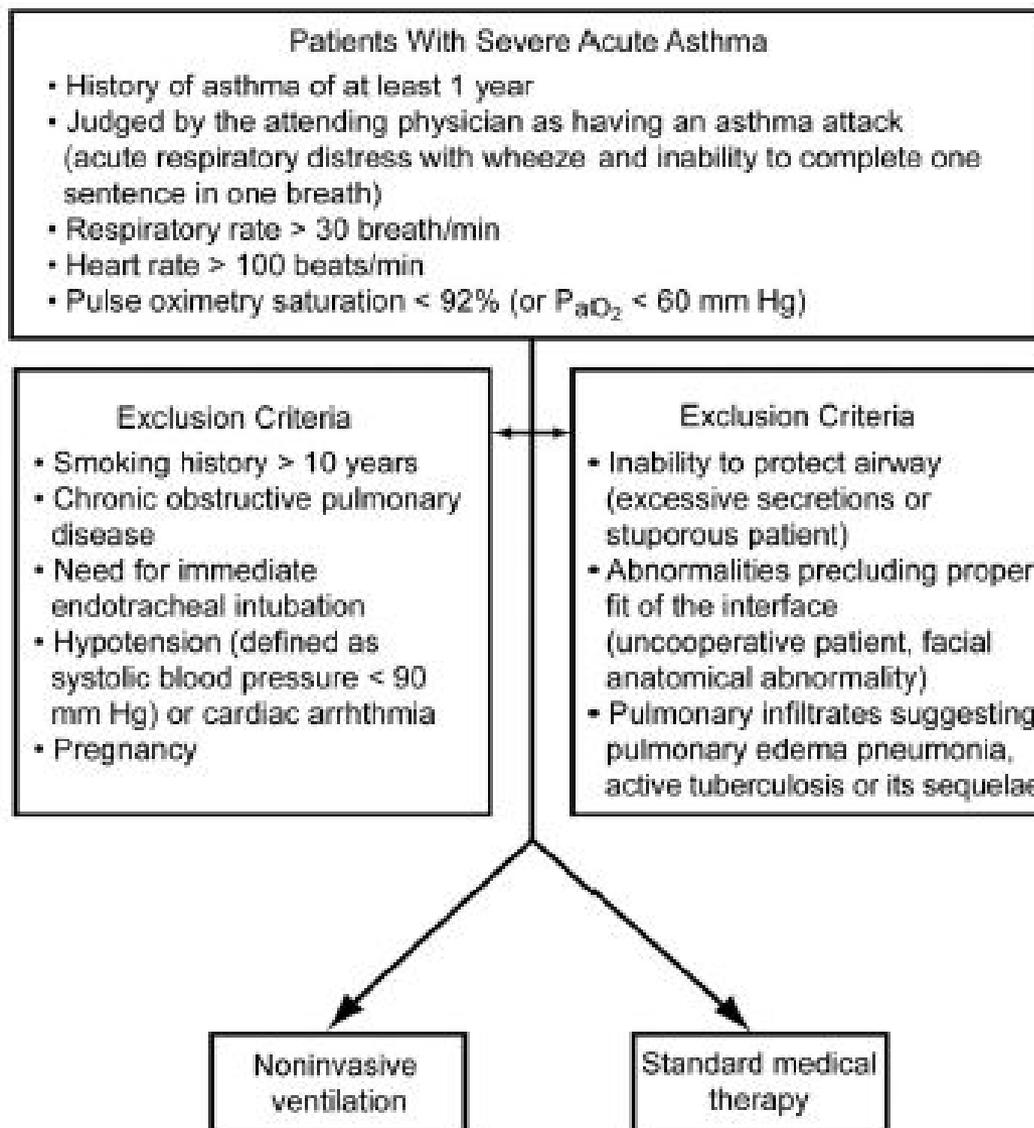


Fig. 1. Flowchart of inclusion and exclusion process.

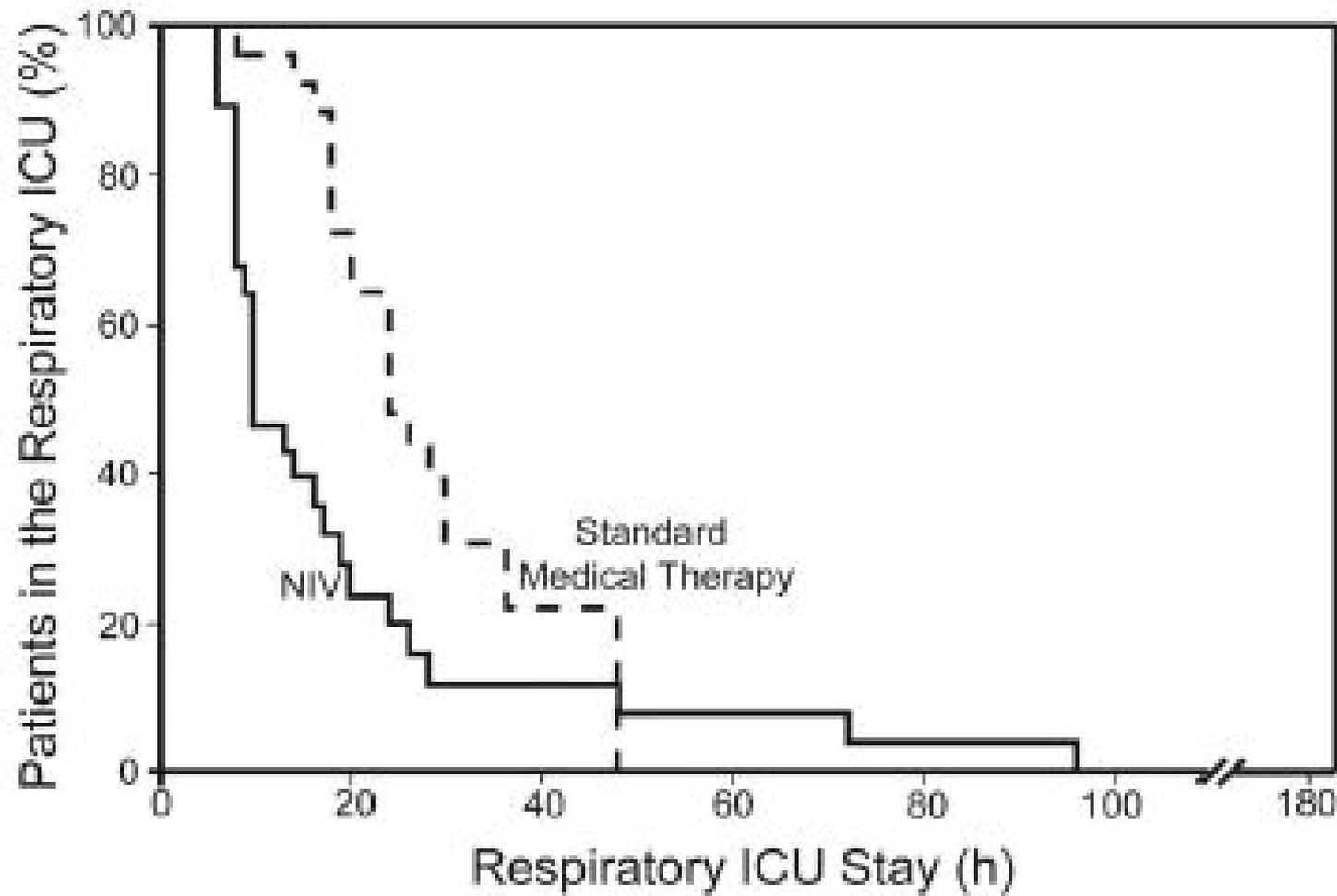
Paramètres	VNI (-) (N:25)	VNI (+) (N:28)	p
Age (ans)	41±12	46 ± 16	0.26
DEP (% prédite)	24.4 ± 12	21.6 ± 6	0.67
Délai de la crise	3.2 ± 2	3.4 ± 2	0.91
FR	38(32-42)	36(32-40)	0.60
pH	7.43 ± 0.04	7.42 ± 0.06	0.70
PCO2	35 ± 8	37 ± 8	0.41
PaO2/FiO2	298	281	0.33
Number of Guina criteria(9)	8(7-9)	8 (8-9)	0.64

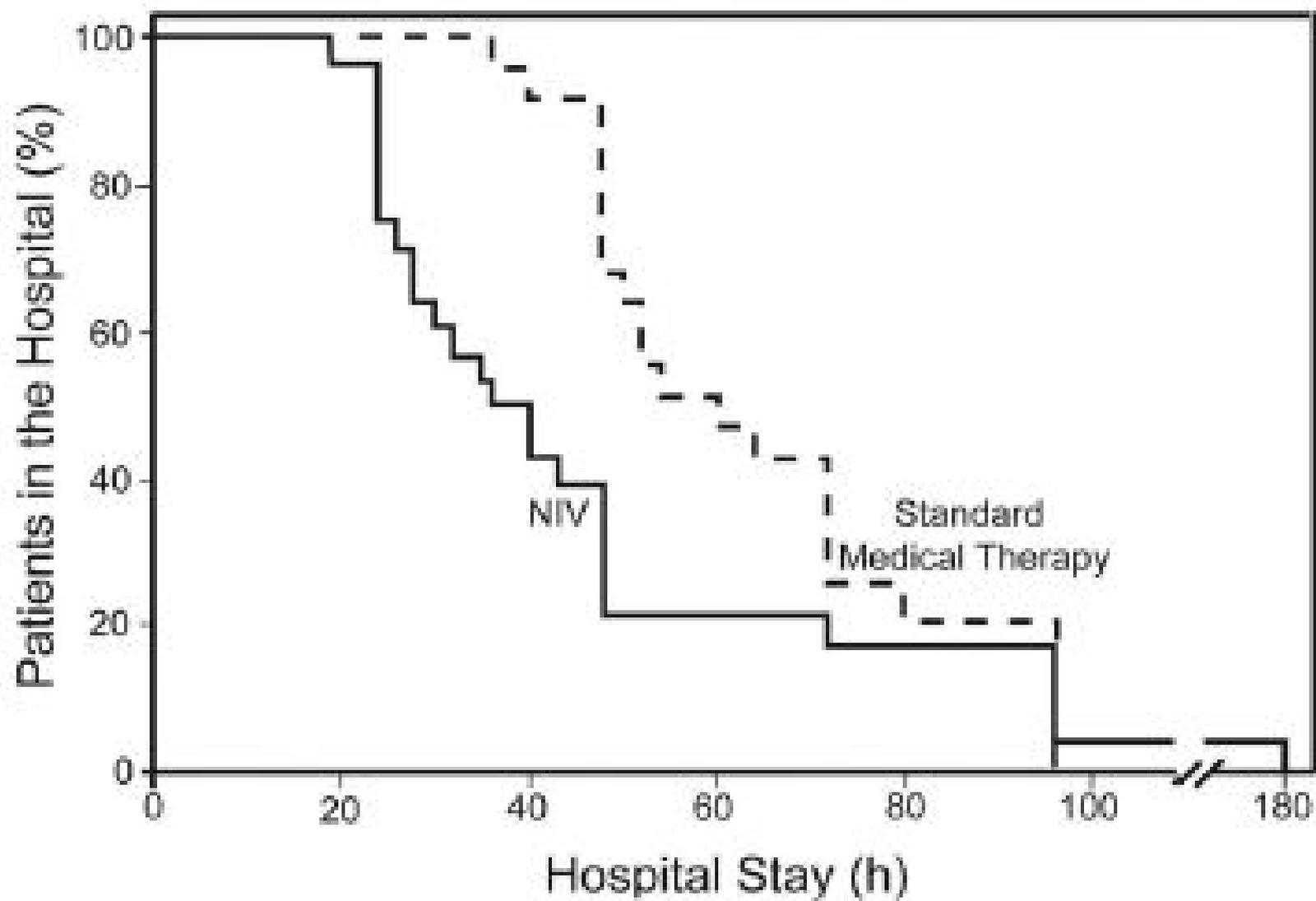
Table 3. Outcomes

	Standard Medical Therapy (<i>n</i> = 25)	NIV (<i>n</i> = 28)	<i>P</i>
Primary Outcomes			
≥ 50% improvement in FEV ₁ over baseline (<i>n</i> , %)			
At 1 h	11 (44)	10 (36)	.62
At 2 h	12 (48)	15 (54)	.70
At 4 h	16 (64)	24 (86)	.08
ICU stay (median and IQR h)	24 (18–36)	10 (8–20)	.01
Hospital stay (median and IQR h)	54 (48–72)	38 (24–48)	.01
Secondary Outcomes			
Time to disappearance of accessory muscle use (mean ± SD h)	3.2 ± 1.7	2.3 ± 1.4	.06
Dose of inhaled salbutamol (mean ± SD mg)	42.8 ± 10.4	31.2 ± 14.5	.008
Dose of inhaled ipratropium (mean ± SD mg)	7.6 ± 2.2	5.2 ± 2.8	.007
Failure of primary therapy (<i>n</i> , %)	4 (16)	2 (7)	.35

FEV₁ = forced expiratory volume in the first second

IQR = interquartile range





Mais.....

Avez-vous pris en charge un AAG avec?

- ◆ FR: 38/min
- ◆ pouls à 120/min
- ◆ Pouls paradoxal à 22mmhg
- ◆ DEP: 22% de la théorique
- ◆ signes de lutte respiratoire
- ◆ number of Guina criteria : 8
- ◆ évolution depuis plus que 3 heures

pH: 7.43
**PaCO₂:
35 mmHg**

Mais.....

- ◆ Faible puissance de l'étude: 332 patients sont nécessaire pour avoir des résultats

Page 542: The absence of blinding and lack of predefined discharge criteria may have caused the observed difference in stay between the 2 groups.

standardisée

Noninvasive Ventilation Coupled With Nebulization During Asthma Crises: A Randomized Controlled Trial

Valdecir C Galindo-Filho MSc, Daniella C Brandão MSc, Rita de Cássia S Ferreira MSc,
Maria José C Menezes, Paulo Almeida-Filho MSc, Verônica F Parreira PhD,
Tayse N Silva MSc, Maria da Glória Rodrigues-Machado PhD, Elizabeth Dean PhD,
and Armêle Dornelas de Andrade PhD

RESPIRATORY CARE • FEBRUARY 2013 VOL 58 NO 2

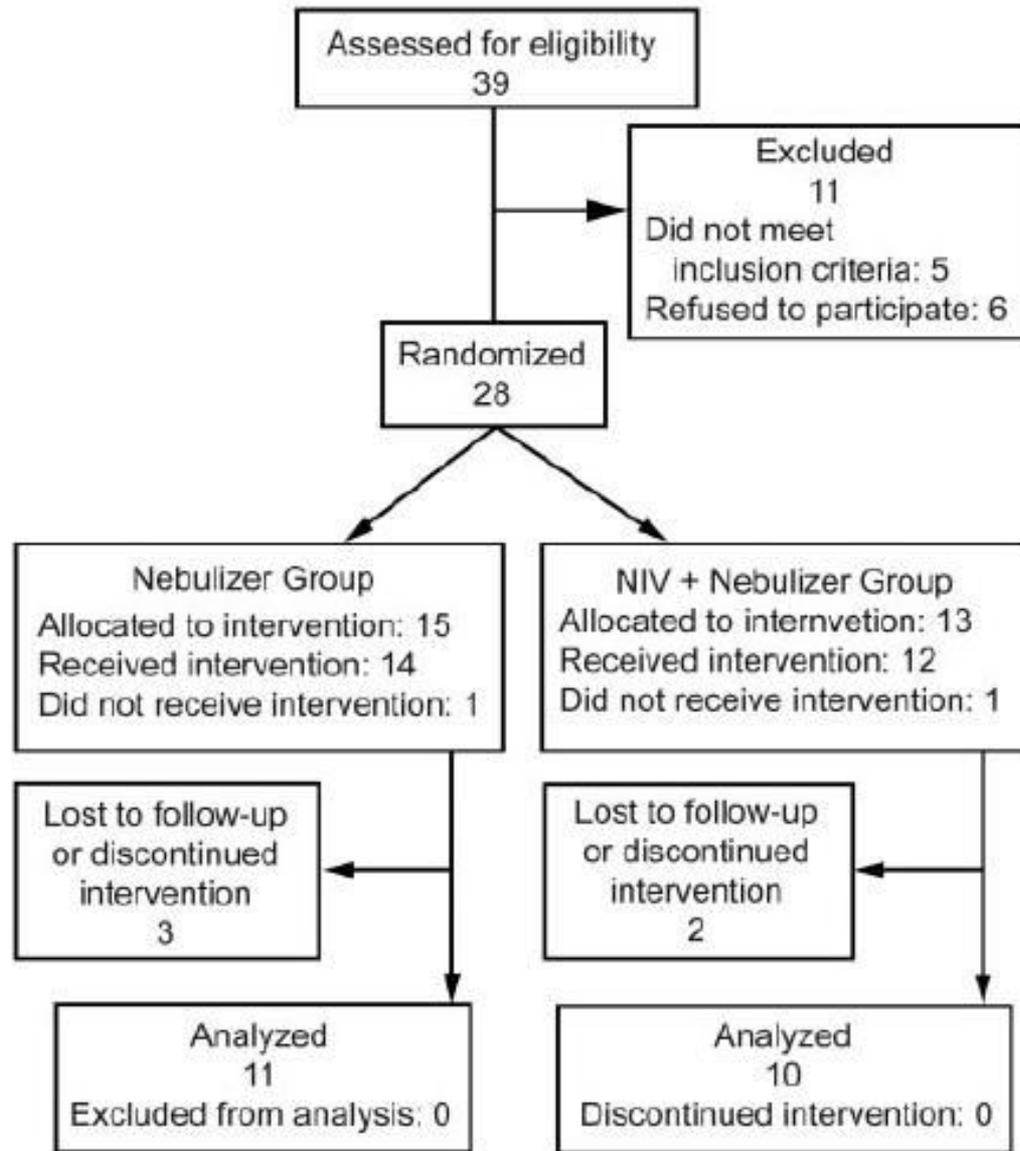


Fig. 1. Flow diagram of the study.

Table 1. Anthropometric and Cardiopulmonary Characteristics

	Nebulizer Control Group (<i>n</i> = 11)	NIV + Nebulizer Group (<i>n</i> = 10)	<i>P</i>
Age, y	44.2 ± 10.3	49.5 ± 8.93	.58
Male/female, no.	4/7	2/7	
BMI, kg/m ²	26.4 ± 3.46	27.9 ± 4.76	.57
Breathing frequency, breaths/min	29.2 ± 1.40	30.2 ± 2.04	.22
S _{pO₂} , %	95.4 ± 1.74	95.6 ± 1.50	.69
V _T , L	0.37 ± 0.09	0.35 ± 0.07	.67
V _E , L	10.6 ± 2.45	10.7 ± 2.23	.90
Heart rate, beats/min	83.4 ± 11.4	79.2 ± 12.79	.59
Systolic blood pressure, mm Hg	126.4 ± 16.4	125.8 ± 13.89	.50
Diastolic blood pressure, mm Hg	84.5 ± 10.3	81.0 ± 10.22	.57
FEV ₁ , % predicted	44.2 ± 18.7	51.3 ± 11.5	.44
FEV ₁ , L	1.18 ± 0.45	1.28 ± 0.23	.53
FVC, % predicted	43.1 ± 18.7	50.2 ± 11.3	.74
FVC, L	1.49 ± 0.52	1.59 ± 0.50	.73
PEF, % predicted	41.6 ± 10.3	40.4 ± 9.7	.70
PEF, L/min	158.7 ± 45.55	140.19 ± 47.64	.49
FEF _{25-75%} , % predicted	31.8 ± 11.9	38.5 ± 7.2	.12
FEF _{25-75%} , L	1.03 ± 0.56	1.20 ± 0.44	.45
Inspiratory capacity, % predicted	55.4 ± 15.5	59.9 ± 15.8	.79
Inspiratory capacity, L	1.16 ± 0.37	1.26 ± 0.52	.38

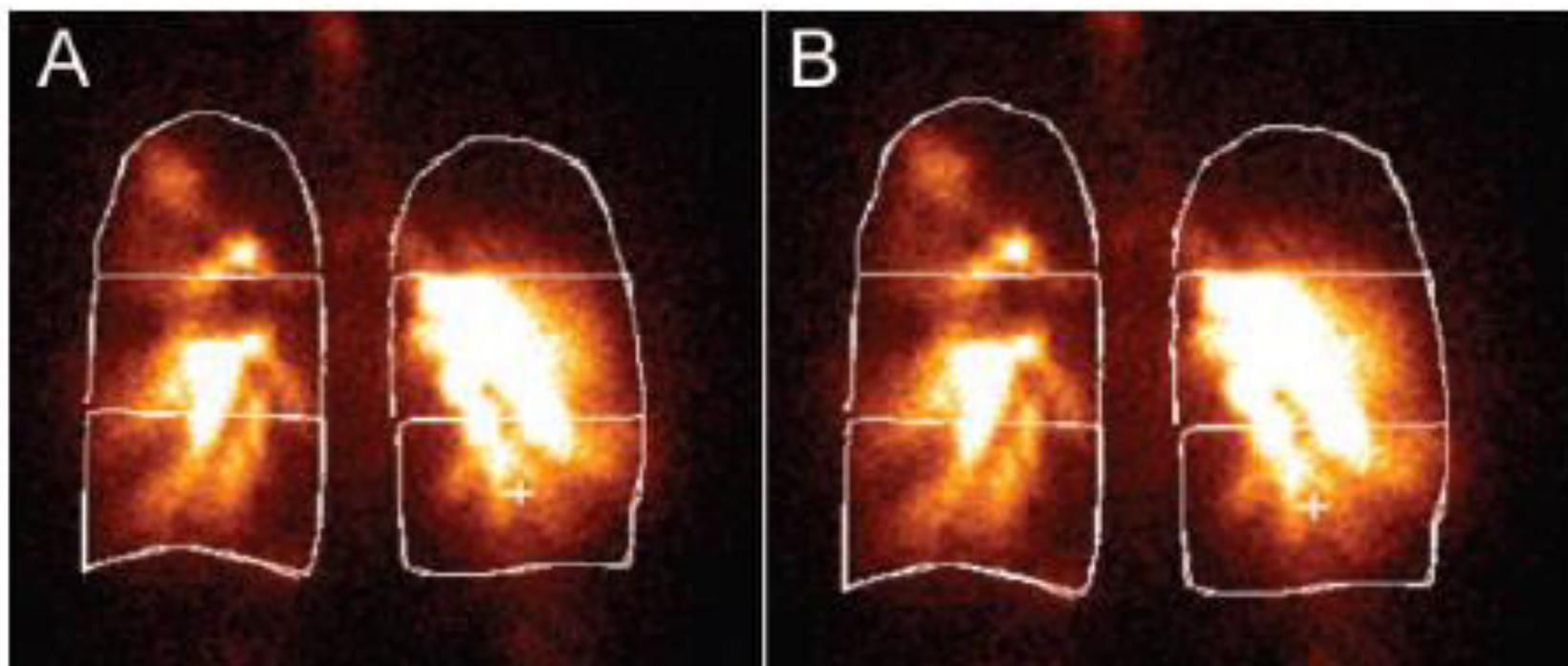


Fig. 2. Heterogeneous deposition pattern in scintigraphic images of subjects with asthma, with a predominance of radio-aerosol deposition in the central region in a subject in the control group (A) and another in the noninvasive ventilation + nebulizer group (B).

Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma (Review)

Lim WJ, Mohammed Akram R, Carson KV, Mysore S, Labiszewski NA, Wedzicha JA, Rowe BH, Smith BJ



**THE COCHRANE
COLLABORATION®**

Brandao 2009

De Miranda 2004

Filho 2009

Gupta 2010

Soroksky 2003

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma

Results

Severe asthma exacerbation therapy: noninvasive positive-pressure ventilation+usual medical care versus usual medical care.

Outcome	Quality of Evidence (GRADE)	Relative Effect (95% CI)	Number of Participants (Studies)
Mortality	Very low	Unable to meta-analyze	86 (2 studies)
Intubation	Low	RR 4.48 (0.23–89.13)	86 (2 studies)
Length of hospital stay	Very low	Unable to meta-analyze data	86 (2 studies)
Length of ICU stay	—	Unable to meta-analyze data	83 (2 studies)
Treatment failure	—	RR 0.73 (0.21–2.53)	86 (2 studies)
No. of admissions	Very low	RR 0.28 (0.09–0.84)	33 (1 study)

—, evidence not graded.

This review of studies has highlighted the paucity of data that exist to support the use of NPPV in patients in status asthmaticus. As such this course of treatment remains controversial despite its continued use in current clinical practice. Larger, prospective randomised controlled trials of rigorous methodological design are needed to determine the role of NPPV in patients with asthma.

Systematic Review Snapshot

TAKE-HOME MESSAGE

There is limited evidence to recommend use of noninvasive positive-pressure ventilation in patients with respiratory failure from severe asthma exacerbations.

Results

Severe asthma exacerbation therapy: noninvasive positive-pressure ventilation+usual medical care versus usual medical care.

Outcome	Quality of Evidence (GRADE)	Relative Effect (95% CI)	Number of Participants (Studies)
Mortality	Very low	Unable to meta-analyze	86 (2 studies)
Intubation	Low	RR 4.48 (0.23–89.13)	86 (2 studies)
Length of hospital stay	Very low	Unable to meta-analyze data	86 (2 studies)
Length of ICU stay	—	Unable to meta-analyze data	83 (2 studies)
Treatment failure	—	RR 0.73 (0.21–2.53)	86 (2 studies)
No. of admissions	Very low	RR 0.28 (0.09–0.84)	33 (1 study)

—, evidence not graded.

Noninvasive Ventilation in Severe Acute Asthma?
Still Far From the Truth

**Ventilation non invasive et AAG?
Encore loin de la réalité!**

Non pour la VNI lors de l'AAG pour Différentes Raisons

1. Bases physiopathologiques contre
2. Absence d'études prospectives
randomisées avec méthodologie correcte
en faveur de cette thérapeutique

Non pour la VNI lors de l'AAG pour Différentes Raisons

3. AAG n'est pas une exacerbation de BPCO:

- * Évolution plus rapidement favorable s/s TTT
- * Pas collapsus bronchique à l'expiration
- * Bouchon muqueux+++
- * Hyperréactivité bronchique +++
- * Hypersudation importante+++

Non pour la VNI lors de l'AAG pour
Différentes Raisons

Traitement AAG:

1. Oxygénothérapie
2. B2 mimétiques
3. Corticoïdes
4. Sulfate de Mg⁺⁺

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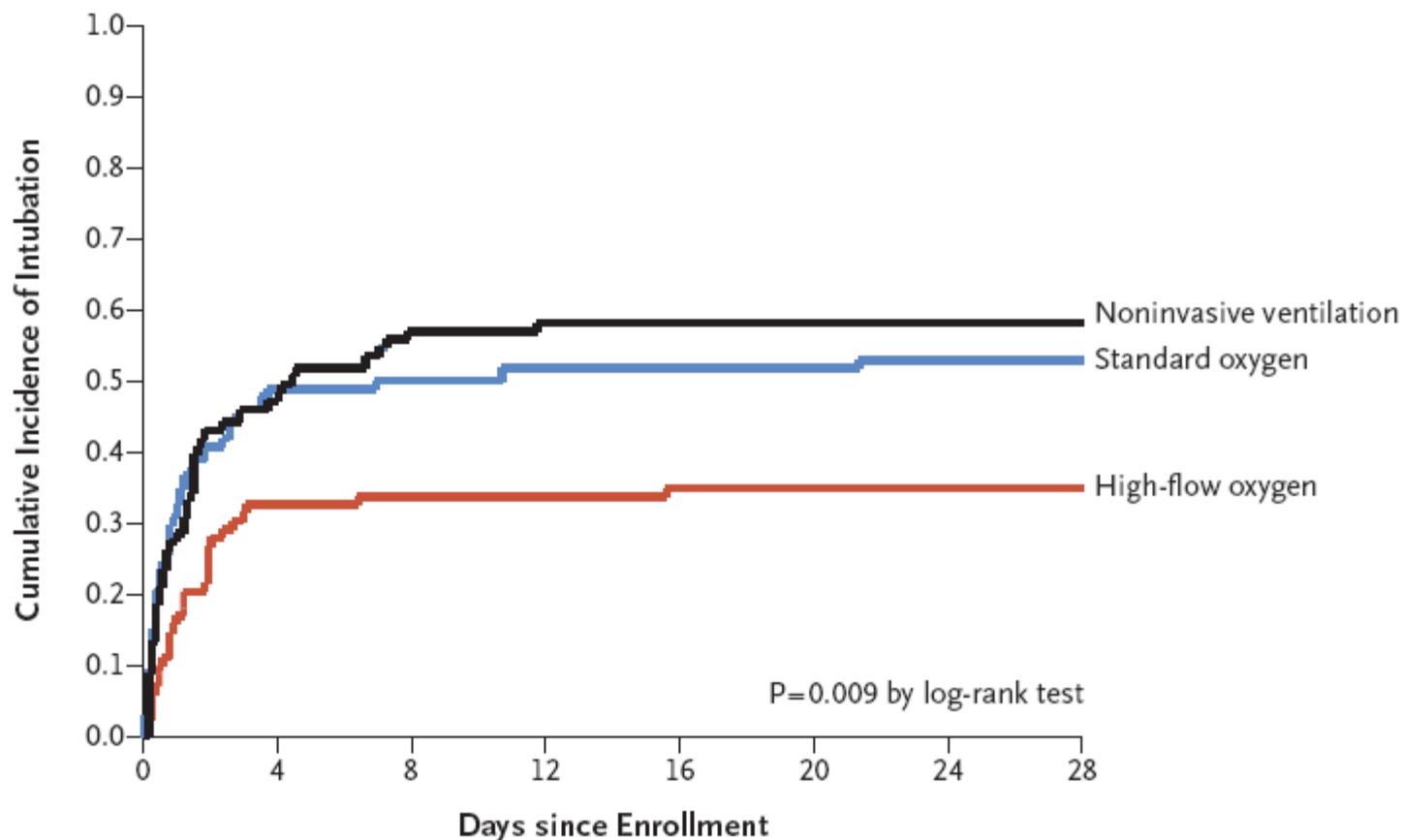
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JUNE 4, 2015

VOL. 372 NO. 23

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic
Respiratory Failure

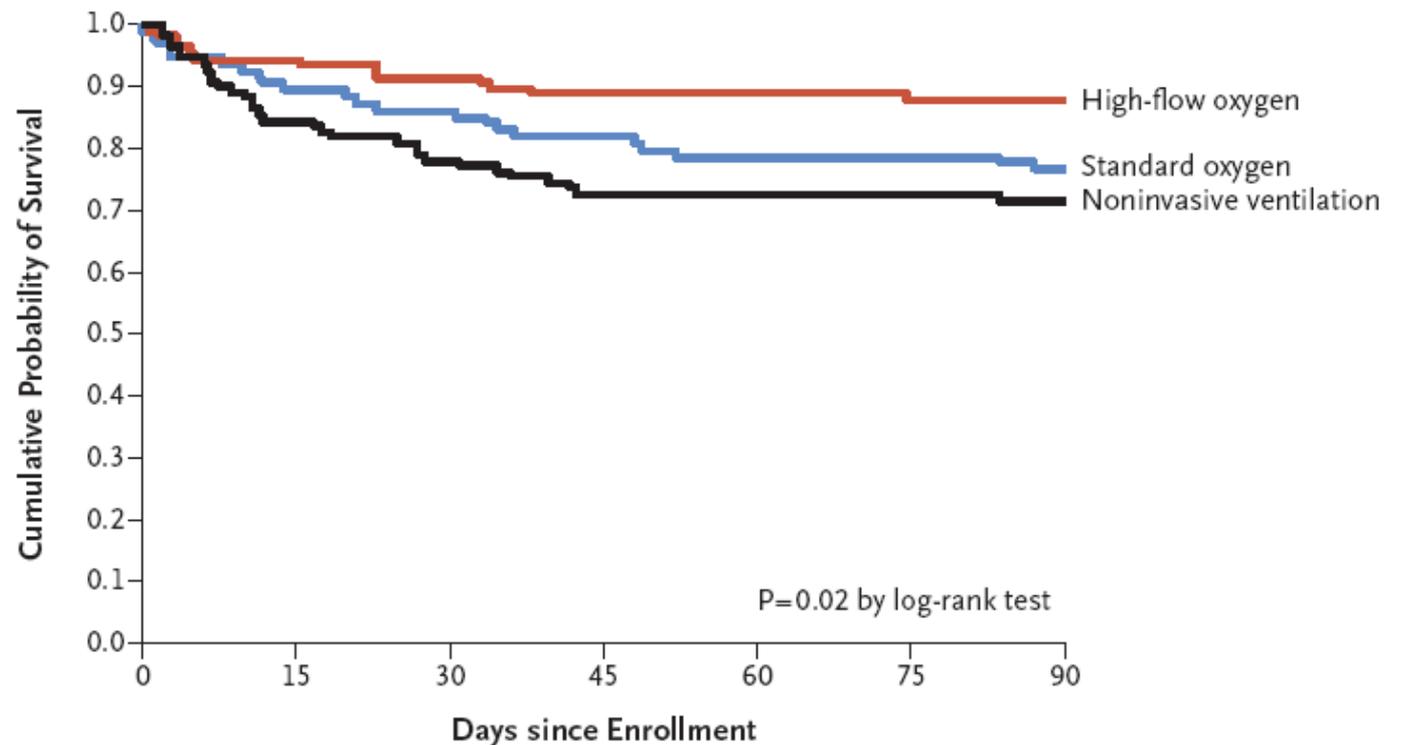
for the FLORALI Study Group and the REVA Network*

B Patients with a $\text{PaO}_2:\text{FiO}_2 \leq 200$ mm Hg**No. at Risk**

High-flow oxygen	83	55	54	54	53	53	53	53
Standard oxygen	74	37	35	34	34	34	33	33
Noninvasive ventilation	81	41	34	32	32	32	32	32

Figure 2. Kaplan–Meier Plots of the Cumulative Incidence of Intubation from Randomization to Day 28.

Results in the overall population and in patients with a $\text{PaO}_2:\text{FiO}_2$ of 200 mm Hg or less are shown. $\text{PaO}_2:\text{FiO}_2$ denotes the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen.

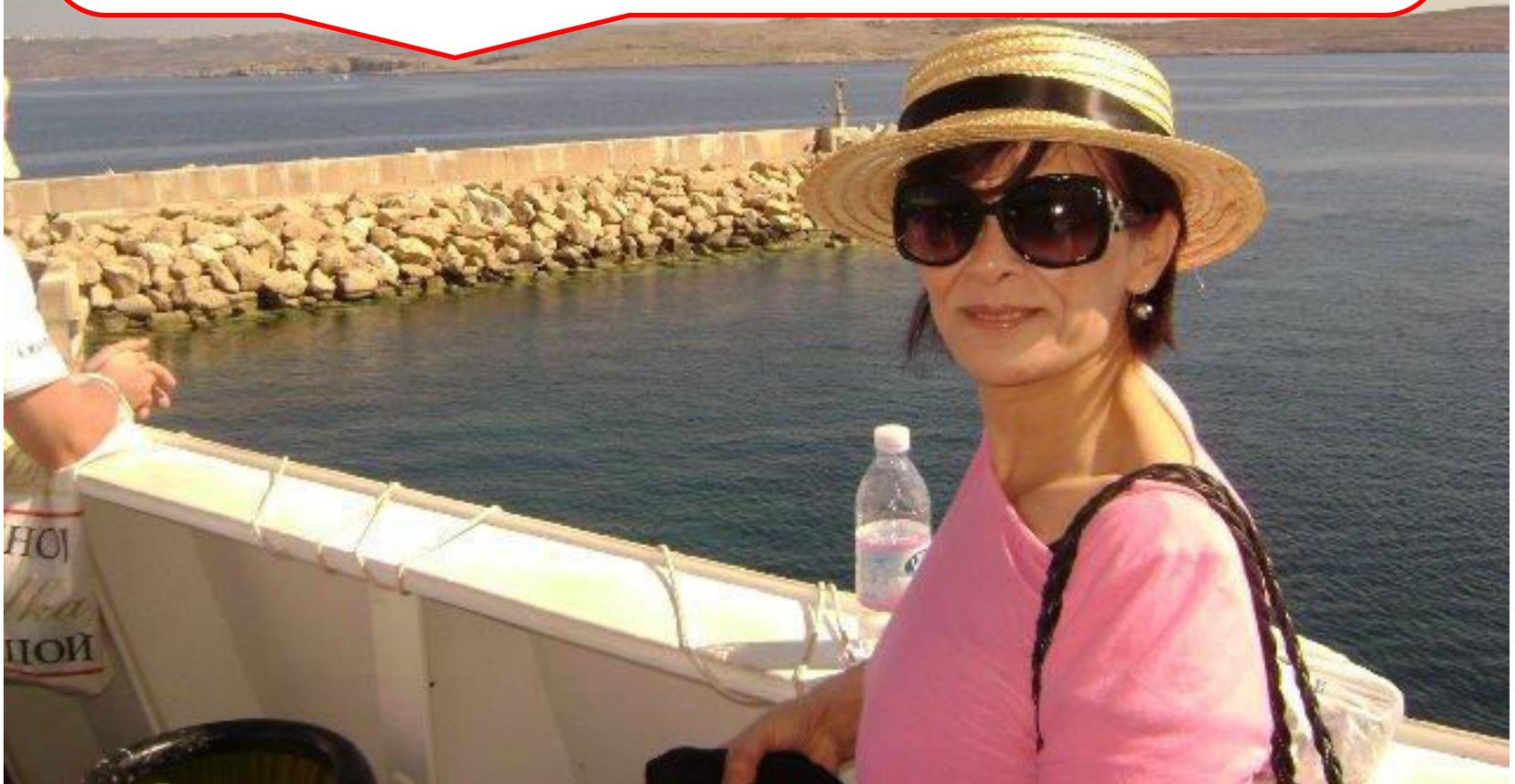


No. at Risk

High-flow oxygen	106	100	97	94	94	93	93
Standard oxygen	94	84	81	77	74	73	72
Noninvasive ventilation	110	93	86	80	79	78	77

Figure 3. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.

NON, NON, NON...



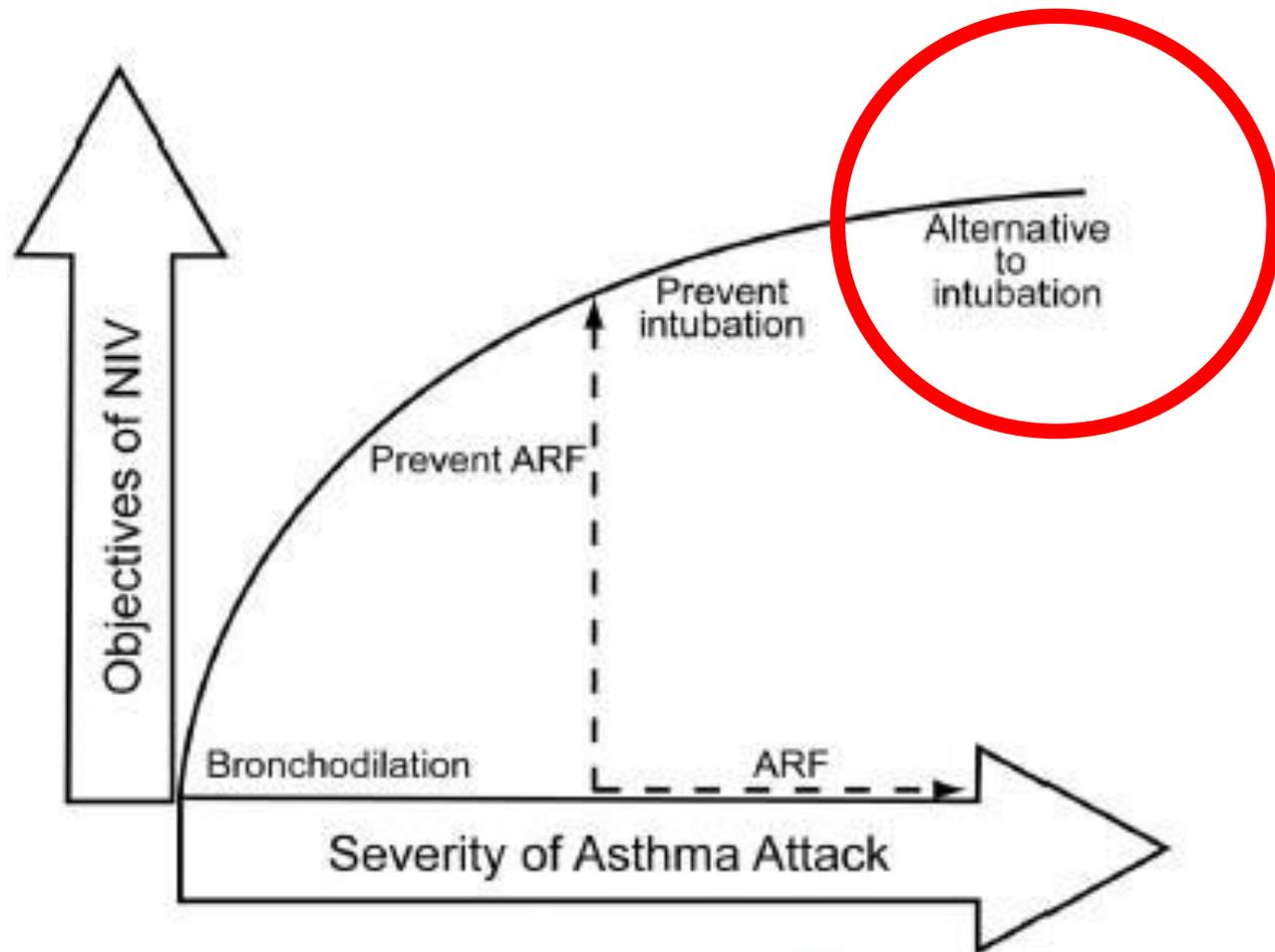


Fig. 1. Potential goals of noninvasive ventilation (NIV) in severe acute asthma. ARF = acute respiratory failure.

**Merci pour votre
Attention**