

# CURSO DE VMNI

## NIPPON 2026



### VMNI nas exacerbações de DPOC



Elsa Fragoso  
*Pneumologista, ULSSM*



# A VNI tem um papel determinante nas exacerbações de DPOC

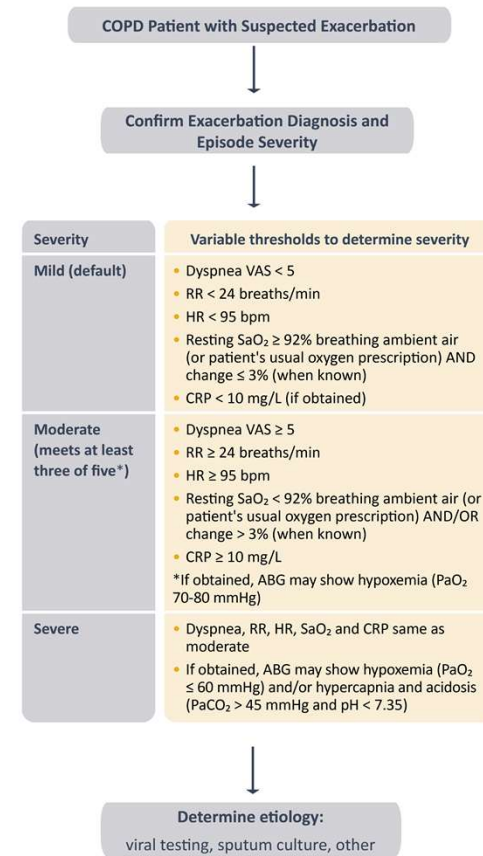
- A DPOC é a 3ª causa de morte a nível global
- As exacerbações agudas de DPOC (EADPOC) causam frequentemente insuficiência respiratória global aguda (ou crónica agudizada) e admissão em UCI
- A intubação traqueal (IOT) associa-se a internamentos mais prolongados, maior mortalidade e aumento dos custos
- A VNI tornou-se o suporte respiratório *gold standard* no doente com EADPOC grave e IRG descompensada

# O doente com insuficiência respiratória aguda é, por definição, um doente grave



## Classification of the Severity of COPD Exacerbations

Figure 4.2



Adapted from: The Rome Proposal, Celli et al. (2021) Am J Respir Crit Care Med. 204(11): 1251-8.

Abbreviations: VAS visual analog dyspnea scale; RR respiratory rate; HR heart rate; SaO<sub>2</sub> oxygen saturation; CRP C-reactive protein; ABG arterial blood gases; PaO<sub>2</sub> arterial pressure of oxygen; PaCO<sub>2</sub> arterial pressure of carbon dioxide.

# Alterações fisiopatológicas na EADPOC

## A lógica por detrás da VNI

EADPOC grave: broncoespasmo agravado, taquipneia

Dispneia e insuflação pulmonar dinâmica

Aumento do trabalho respiratório (WoB) por mecânica ventilatória desfavorável

Falência de bomba ventilatória

Acidémia respiratória

# Alterações fisiopatológicas na EADPOC

## A lógica por detrás da VNI

EADPOC grave: broncoespasmo agravado, taquipneia

Dispneia e insuficiência respiratória

Aumento do trabalho ventilatório

Falência de bomba ventilatória

Acidémia respiratória

A VNI reduz o WoB, melhora as trocas gasosas e corrige o pH

# Effects of Noninvasive Ventilation on Pulmonary Gas Exchange and Hemodynamics during Acute Hypercapnic Exacerbations of Chronic Obstructive Pulmonary Disease

ORLANDO DIAZ, RAQUEL IGLESIA, MIQUEL FERRER, ELISABETH ZAVALA, CRISTINA SANTOS, PETER D. WAGNER, JOSEP ROCA, and ROBERT RODRIGUEZ-ROISIN

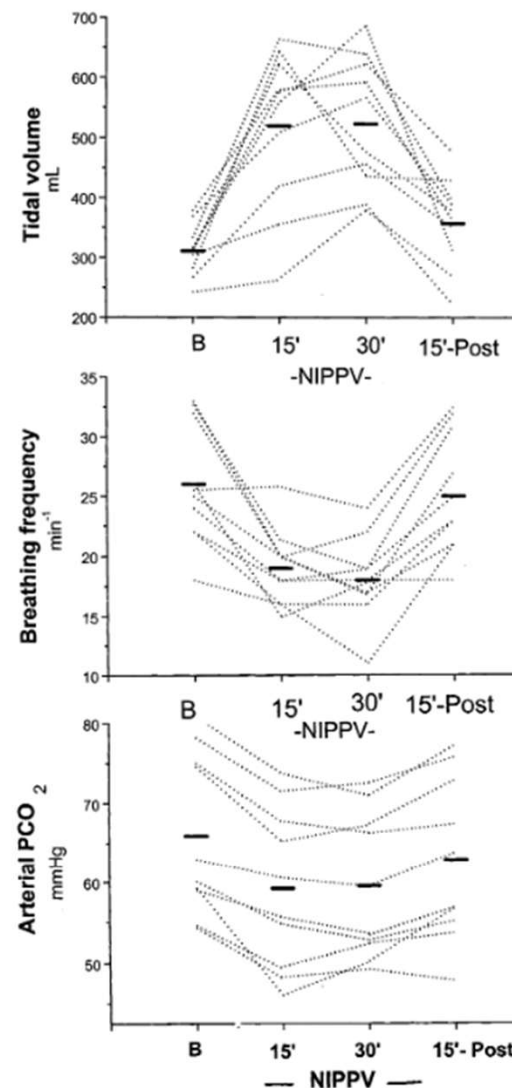
Servei de Pneumologia i Alergia Respiratòria and UCI Quirúrgica, Hospital Clínic, Departament de Medicina, Universitat de Barcelona, Barcelona, Spain; and Section of Physiology, University of California–San Diego, La Jolla, California

TABLE 1  
GENERAL CLINICAL CHARACTERISTICS OF THE PATIENTS AT ADMISSION

Patient No.	Age (yr)	FEV <sub>1</sub> (L) (% predicted)	FEV <sub>1</sub> /FVC (%)	Pa <sub>O2</sub> (mm Hg)	Pa <sub>CO2</sub> (mm Hg)	pHa	F <sub>I</sub> O <sub>2</sub>	PSV (cm H <sub>2</sub> O)	PEEP (cm H <sub>2</sub> O)
1	69	0.51 (19)	38	48	89	7.23	0.24	14	0
2	54	0.54 (17)	28	57	75	7.33	0.24	12	4
3	61	0.88 (31)	55	44	59	7.39	0.21	10	5
4	72	2.14 (74)	62	53	73	7.32	0.21	10	4
5	71	1.41 (51)	48	45	66	7.25	0.21	10	3
6	72	0.77 (26)	34	47	54	7.39	0.21	10	3
7	57	1.59 (45)	55	39	66	7.36	0.21	15	0
8	79	0.58 (21)	36	34	60	7.32	0.21	12	3
9	78	0.29 (11)	23	34	93	7.20	0.21	14	4
10	70	0.93 (31)	32	35	76	7.31	0.21	13	3
Mean	68	0.93 (31)	41	44	71	7.31	0.22	12	3
SD	8	0.59 (20)	13	8	13	0.06	0.01	2	2

Definition of abbreviations: pHa = arterial pH; F<sub>I</sub>O<sub>2</sub> = fraction of inspired oxygen; PSV = pressure support ventilation; PEEP = positive end-expiratory pressure.

Spirometric data were measured during stable clinical conditions or during recovery (33). PSV and PEEP levels were measured at baseline.



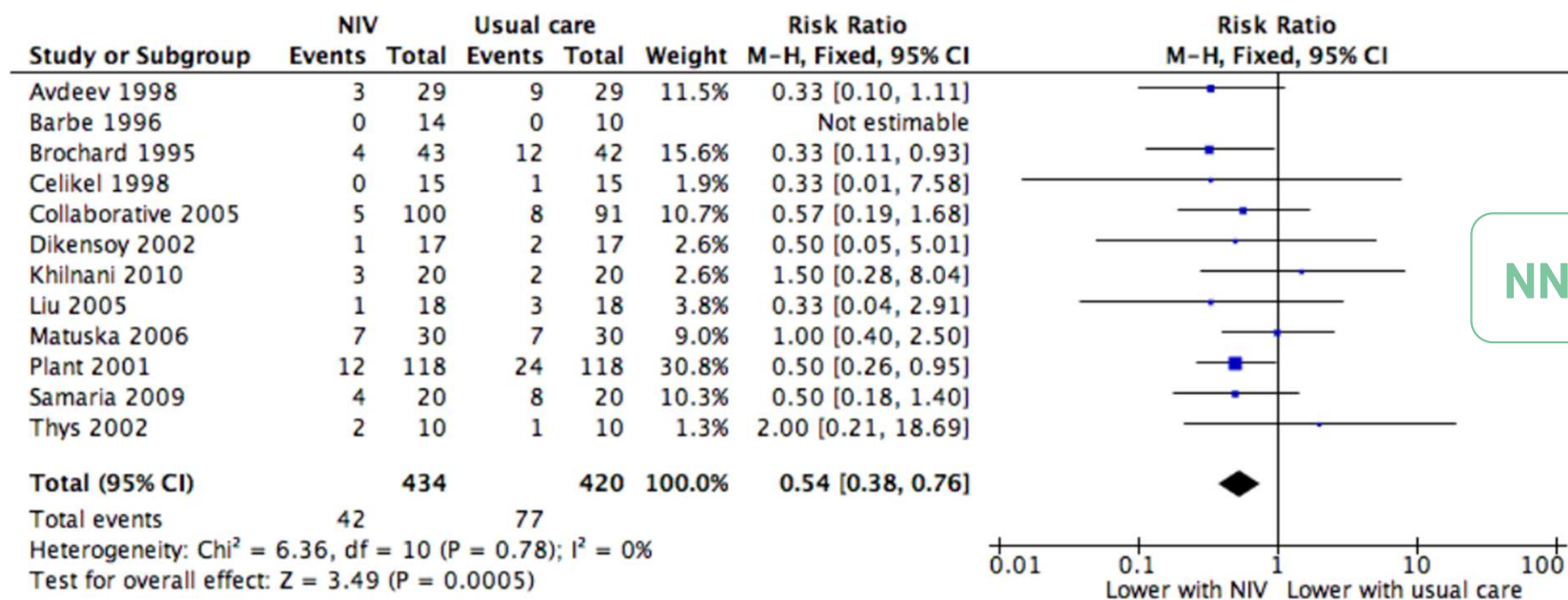
CURSO DE VNI  
NIPPON 2026

# A VNI na EADPOC grave é uma intervenção com benefício comprovado

Vários ensaios clínicos desde o início dos anos 1990 demonstram que a VNI é uma intervenção de 1ª linha na EADPOC com IRG aguda

# A VNI reduz a mortalidade em 46%

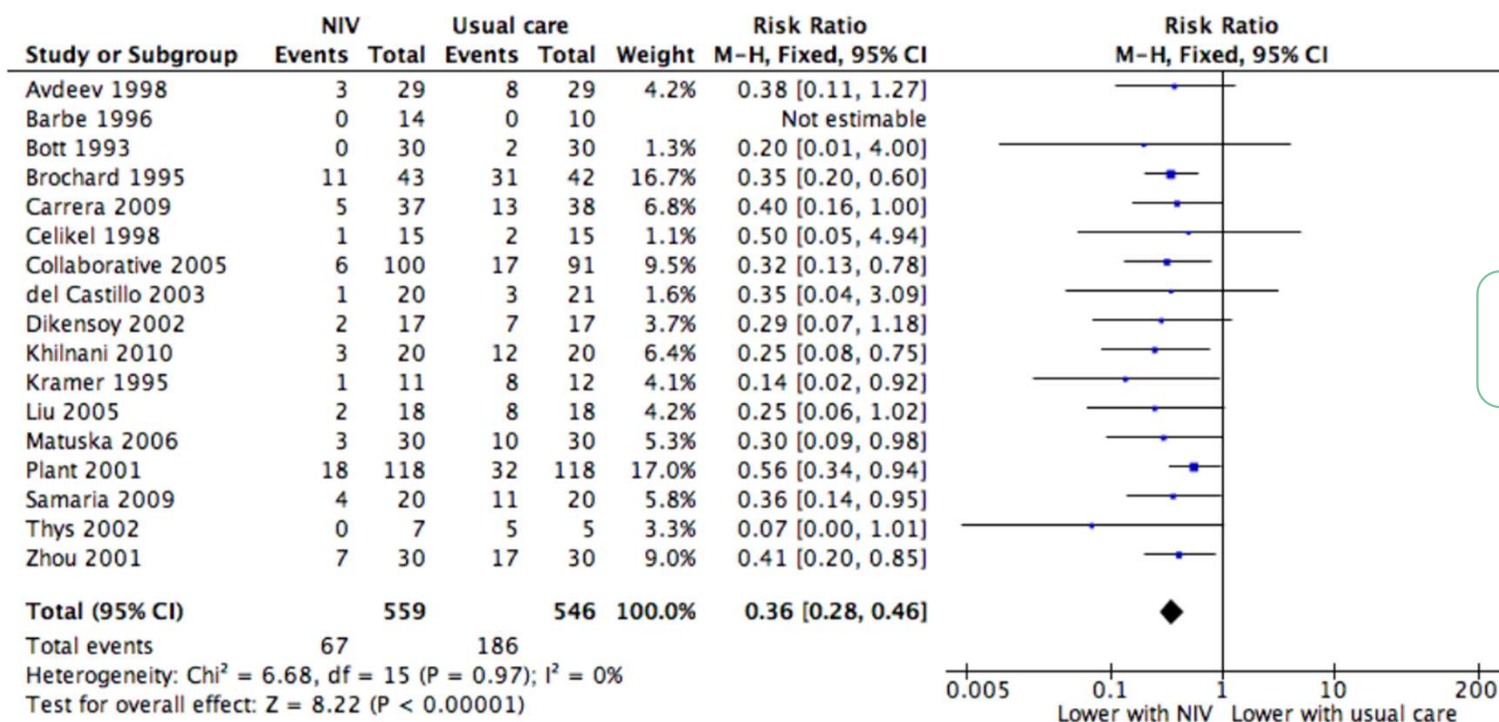
Figure 3. NIV vs usual care (overall) - Mortality



NNT 12

# A VNI reduz a necessidade de IOT em 64%

Figure 6. NIV vs usual care (overall) - Need for endotracheal intubation



NNT 5

# A VNI altera a história natural da EADPOC grave

- Redução da demora média hospitalar
  - Sobretudo nos doentes com acidémia mais grave (pH <7.30)
- Redução das complicações não relacionadas com a VNI
  - Falência multiorgânica
  - Pneumonia associada ao ventilador
- Melhoria do pH e PaO<sub>2</sub> na 1ª hora de suporte ventilatório
- Resultados consistentes em vários cenários
  - Enfermaria *versus* SMI
  - Acidémia menos grave (pH 7.30 – 7.35) *versus* mais grave (pH <7.30)

# A VNI iniciada precocemente na enfermaria de Pneumologia é segura e reduz a mortalidade

O principal determinante do sucesso são equipas treinadas

- 236 doentes com EADPOC com acidémia ligeira a moderada (pH 7.25-7.35) internados em enfermarias de Pneumologia
  - 2 braços (1:1): *standard of care* versus VNI + *standard of care*

Critérios de IOT cumpridos em 27.1% (SOC) versus 15.3% (VNI),  $p=0.02$

Mortalidade hospitalar 20.3% (SOC) versus 10.2% (VNI),  $p=0.05$

A VNI conduziu a melhoria mais rápida do pH na 1ª hora e maior ↓ da FR às 4h

# Estudos de vida real: o impacto da VNI versus VMI

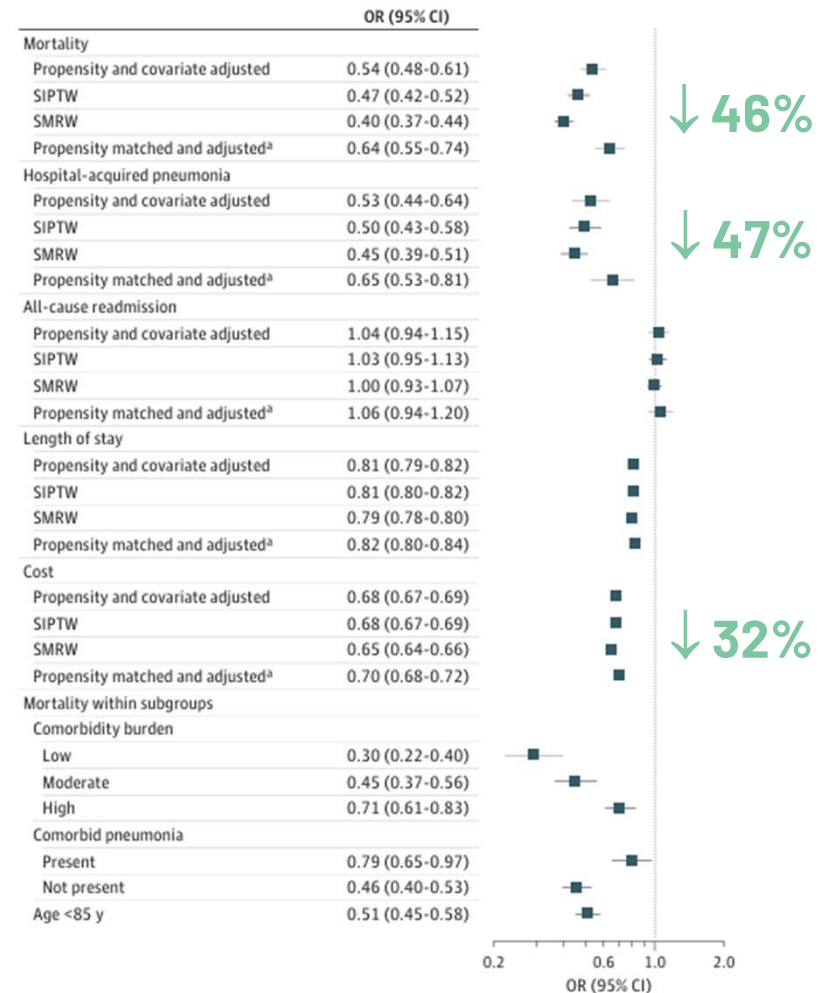
- Estudo de coorte retrospectivo (2008-2011)
- 25 628 admissões por EADPOC com necessidade de suporte ventilatório (primeiras 24-48h) em 420 hospitais dos EUA
- 70%: abordagem inicial VNI

↓ 1.6 dias de internamento

Risco de readmissão (todas as causas ou EADPOC) aos 30 dias pós-alta semelhante

10,408 (VMI) versus 15,677 USD (VNI)

Figure 2. Association Between Noninvasive Ventilation and Outcomes



# Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

Bram Rochweg  | Laurent Brochard | Mark W. Elliott [Show More](#) 

European Respiratory Journal 2017 50(2): 1602426; DOI: <https://doi.org/10.1183/13993003.02426-2016>

TABLE 2 Recommendations for actionable PICO questions

Clinical indication <sup>#</sup>	Certainty of evidence <sup>¶</sup>	Recommendation
Prevention of hypercapnia in COPD exacerbation	⊕⊕	Conditional recommendation against
Hypercapnia with COPD exacerbation	⊕⊕⊕⊕	Strong recommendation for
Cardiogenic pulmonary oedema	⊕⊕⊕	Strong recommendation for
Acute asthma exacerbation		No recommendation made
Immunocompromised	⊕⊕⊕	Conditional recommendation for
<i>De novo</i> respiratory failure		No recommendation made
Post-operative patients	⊕⊕⊕	Conditional recommendation for
Palliative care	⊕⊕⊕	Conditional recommendation for
Trauma	⊕⊕⊕	Conditional recommendation for
Pandemic viral illness		No recommendation made
Post-extubation in high-risk patients (prophylaxis)	⊕⊕	Conditional recommendation for
Post-extubation respiratory failure	⊕⊕	Conditional recommendation against
Weaning in hypercapnic patients	⊕⊕⊕	Conditional recommendation for

<sup>#</sup>: all in the setting of acute respiratory failure; <sup>¶</sup>: certainty of effect estimates: ⊕⊕⊕⊕, high; ⊕⊕⊕, moderate; ⊕⊕, low; ⊕, very low.

# A VNI está indicada na EADPOC grave sem resposta à terapêutica médica e titulação de O<sub>2</sub> otimizadas

**TABLE 1 ]** Severity of AECOPD in Hospitalized Patients Classified by Clinical Signs

Severity	Clinical Signs
No respiratory failure	Respiratory rate: $\leq 24$ breaths/min; heart rate $< 95$ beats/min; no use of accessory respiratory muscles; no change in mental status; hypoxemia improved with supplemental oxygen via Venturi mask 24%-35% inspired oxygen ( $F_{IO_2}$ ); no increase in $P_{aCO_2}$
Acute respiratory failure—non-life-threatening	Respiratory rate: $> 24$ breaths/min; using accessory respiratory muscles; no change in mental status; hypoxemia improved with supplemental oxygen via Venturi mask $> 35\%$ $F_{IO_2}$ ; hypercarbia, ie, $P_{aCO_2}$ increased compared with baseline or elevated 50-60 mm Hg
Acute respiratory failure—life-threatening	Respiratory rate: $> 24$ breaths/min; using accessory respiratory muscles; acute change in mental status; hypoxemia not improved with supplemental oxygen via Venturi mask or requiring $F_{IO_2} > 40\%$ ; hypercarbia, ie, $P_{aCO_2}$ increased compared with baseline or elevated $> 60$ mm Hg or the presence of acidosis ( $pH \leq 7.25$ )

AECOPD = acute exacerbation of COPD.

**Candidato ideal: IRG com pH 7.25–7.35, PaCO<sub>2</sub>  $\geq$ 50–60 mmHg, dispneia moderada a grave com tiragem e taquipneia persistentes ( $>24$ – $30$ /min)**

# VNI na EADPOC: Contra-indicações

TABLE 3 ] Absolute and Relative Contraindications to NIV

<b>Absolute</b>
Need for emergent intubation (eg, cardiac, or respiratory arrest, severe respiratory distress, unstable cardiac arrhythmia)
<b>Relative</b>
Acutely life-threatening nonrespiratory organ failure associated with severe encephalopathy (Glasgow Coma Scale < 10, severe upper GI bleeding, or hemodynamic instability)
Facial or neurological surgery, trauma, or deformity
Significant airway obstruction such as tracheal tumor or laryngeal mass
Inability of the patient to cooperate, protect airway, or clear secretions precipitating a high aspiration risk
Anticipated prolonged need for mechanical ventilation ( $\geq$ 4-7 d)
Recent esophageal or gastric anastomosis
Inability to fit the interface or NIV mask appropriately
Insufficient staffing support

NIV = noninvasive ventilation.

**Algumas contra-indicações podem ser ultrapassadas com equipas treinadas**

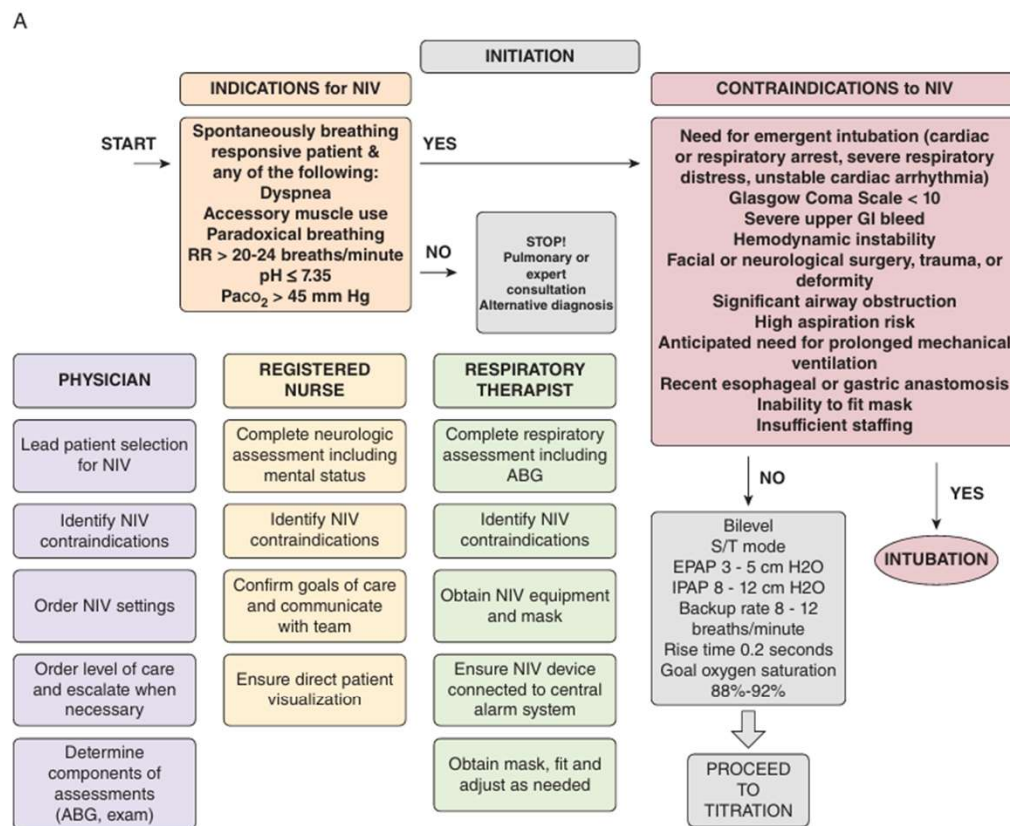
# VNI na EADPOC: factores preditivos de falência

**TABLE 2 ]** Predictors of Potential NIV Failure

Inability to protect airway	Hypotension (SBP < 90 mm Hg)
Reduced level of consciousness	Age > 40 y
Asynchronous breathing	Shock of any etiology
Edentulism	Glasgow Coma Scale < 11
Severe agitation	Acute Physiology and Chronic Health Evaluation (APACHE) II score $\geq$ 29
Profuse secretions	Established acute respiratory distress syndrome
Tachypnea $\geq$ 30 breaths/min	pH < 7.25 (worsening acidosis on ABG)

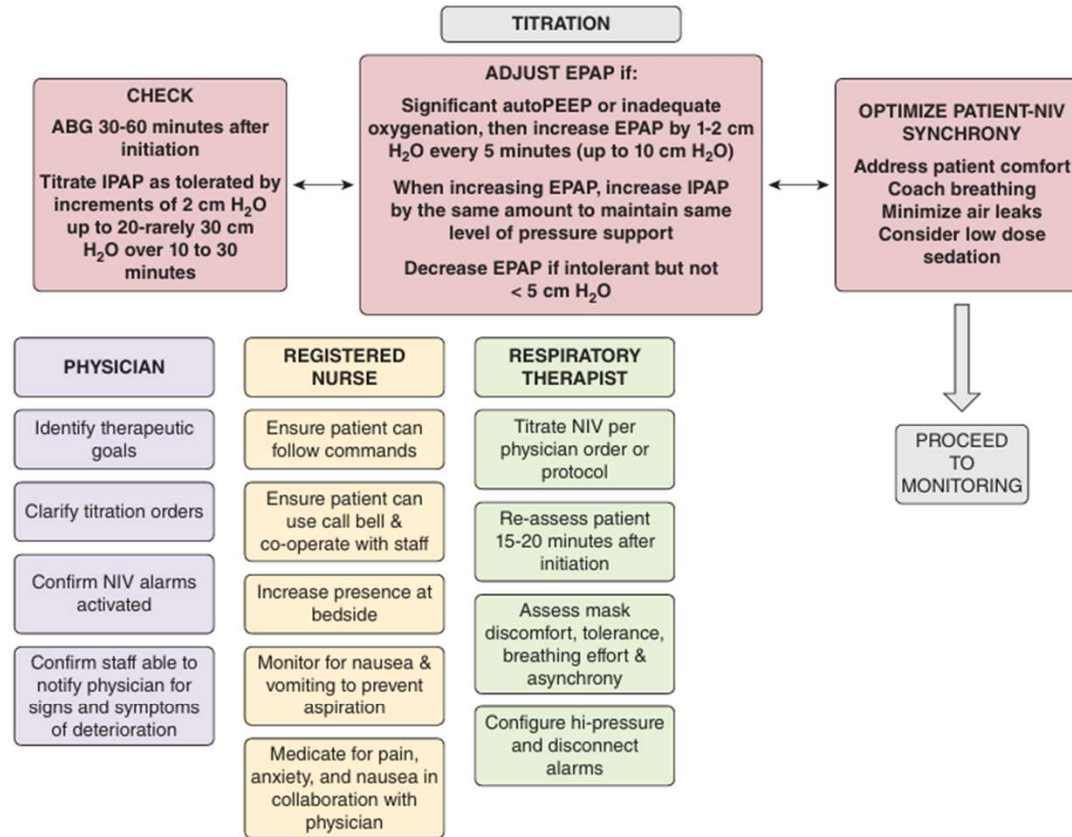
ABG = arterial blood gas; NIV = noninvasive ventilation; SBP = systolic BP.

# Implementação da VNI: decisões e ajustes iniciais

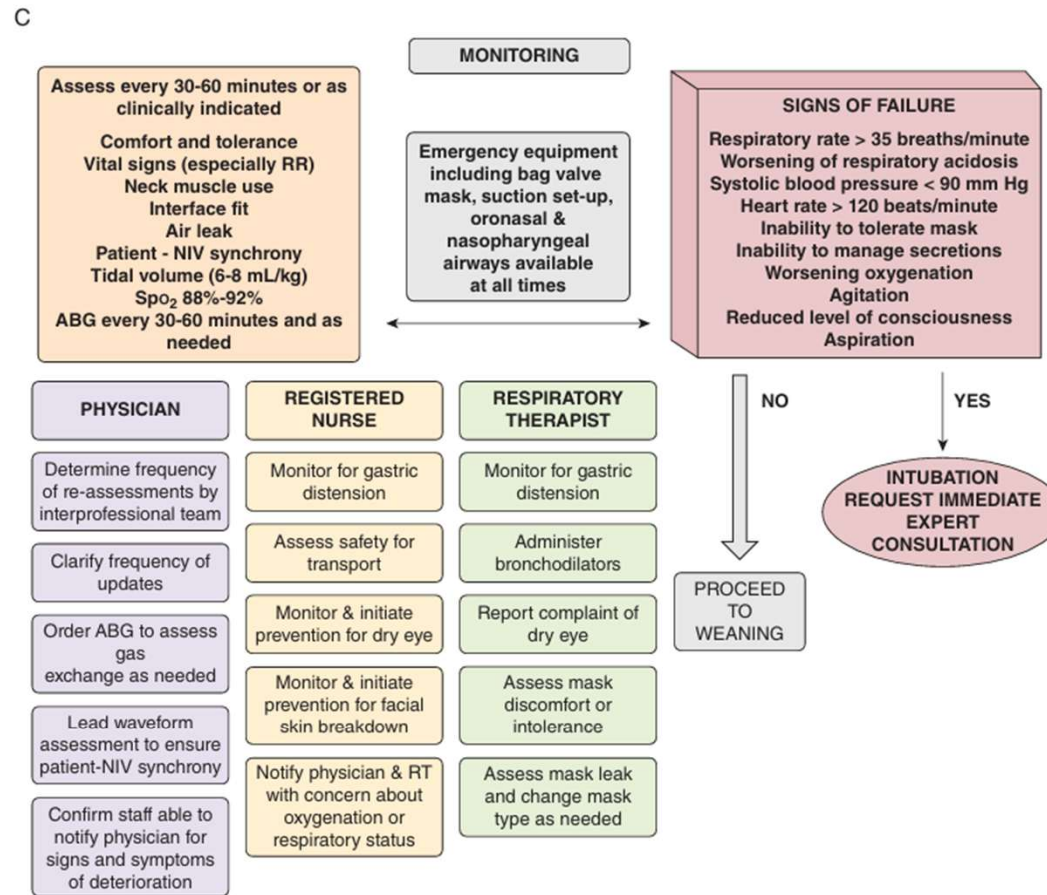


# Implementação da VNI: titulação do suporte

B

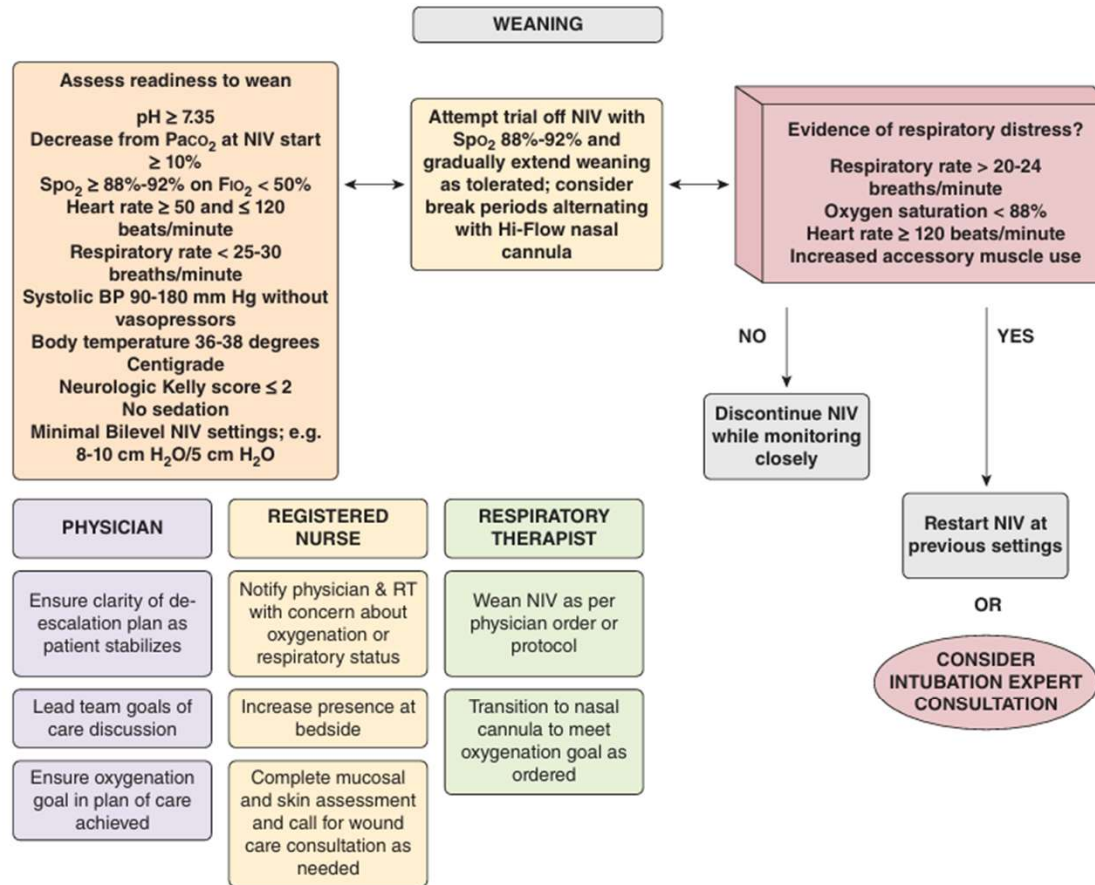


# Implementação da VNI: monitorização



# Implementação da VNI: desmame

D



# O sucesso da VNI na EADPOC requer uma equipa multidisciplinar coordenada num ambiente calmo



# O doente que não se adapta: aprender a reconhecer as assincronias

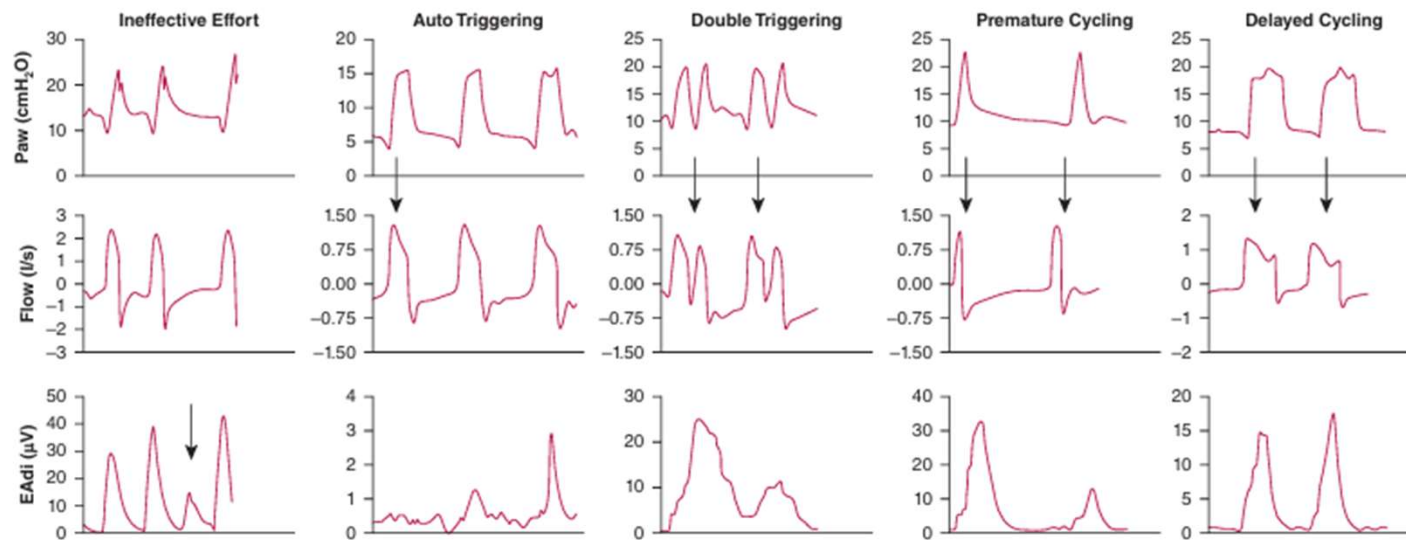


Figure 2 – Noninvasive ventilation asynchrony. Arrows highlight the asynchronous events. Paw = airway pressure; EAdi = electrical activity of the diaphragm. Reprinted from Longhini et al.<sup>37</sup> doi:10.3389/fmed.2022.1119924.

# O doente que não se adapta: como lidamos com as assincronias?

A desadaptação ventilatória por assincronia é um dos factores determinantes de falência da VNI

TABLE 4 ] Noninvasive Ventilation Asynchrony

Type of Asynchrony	What Is It?	What Causes It?	How Do You Treat It?
Ineffective triggering	Patient effort fails to trigger a breath	Weak respiratory effort High intrinsic PEEP Inappropriately set trigger sensitivity	Lower trigger sensitivity Check for autoPEEP
Auto triggering	Mechanical insufflation not triggered by any patient inspiratory effort	Wrongly sensed triggering efforts including: Disturbances in airway pressure Disturbances in flow Air leaks	Check sensitivity Check for air leak Check trigger type
Double triggering	Breath stacking = second breath taken before delivery of first breath completed	Most common in low tidal volume ventilation, and high minute ventilation requirements (metabolic acidosis, high dead space)	Increase tidal volume
Reverse triggering	Reflex contraction most often induced by mechanical ventilation	Entrainment of patient's intrinsic respiratory rhythm from the brainstem respiratory centers to periodic mechanical insufflations from NIV	Optimal treatment unknown Reduce sedation Increase or decrease set rate
Premature cycling	Interruption of the ventilator insufflation anticipating patient effort termination	Disproportionately shorter inspiratory time (I-time) of machine in comparison with patient neural I-time	Increase inspiratory time
Delayed cycling	Mechanical assistance is longer than patient effort and extends into patient expiration	Air leaks prevent achievement of expiratory trigger threshold and insufflation cycling-off	Identify source of air leak, ie, interface (mask), loose tubing
Flow asynchrony	Ventilator flow delivery insufficient to meet patient demands	Leaks Inappropriate rise time Inappropriate tidal volume Inappropriate PEEP	Correct air leaks Adjust rise time Increase flow Use NIV machine with leak compensation software Switch mode of ventilation
Auto-PEEP	Positive pressure remains in the alveoli at the end of the exhalation phase of respiratory cycle leading to increased lung volumes, reduced venous return, and potential hemodynamic compromise	Untreated obstructive lung disease Not enough time to exhale	Treat underlying obstruction Increase inspiratory flow Decrease respiratory rate Decrease tidal volume Apply extrinsic PEEP

NIV = noninvasive ventilation; PEEP = positive end-expiratory pressure.

Farmer MJS, Callahan CD, Hughes AM, Riska KL, Hill NS. Applying Noninvasive Ventilation in Treatment of Acute Exacerbation of COPD Using Evidence-Based Interprofessional Clinical Practice. *Chest*. 2024; 165(6): 1469-1480. doi: 10.1016/j.chest.2024.02.040. Epub 2024 Feb 28

# Complicações associadas à VNI

- Úlceras de pressão
- Secura das mucosas
  - Epistáxis, congestão nasal, dor nos seios perinasais
  - Irritação ocular
  - Atelectasias por rolhões de secreções
- Distensão gástrica; aerocolia
- Claustrofobia
- Ansiedade
- *Delirium*
- Barotrauma

**Muitas destas complicações podem ser evitadas com equipas treinadas e ventiladores específicos de VNI de última geração**

# VNI na EADPOC

O doente com grande dependência de suporte ventilatório



- VNI com humidificação
- Rotação de interfaces
- Procinéticos e fármacos para reduzir aerocolia
- RR intensiva nas pausas da VNI
- Alternância entre suportes (HFNO)
- Considerar sonda para alimentação

# Pode a oxigenoterapia de alto fluxo (HFNO) ser uma opção na EADPOC com IRG descompensada?

- RCT *open-label* de não-inferioridade
- 225 doentes com EADPOC (1:1), pH 7.25-7.35 e  $\text{PaCO}_2 \geq 50$  mmHg
- Admissão em UCI
- Endpoint primário: falência do tratamento (IOT ou mudança de braço)

**Falência de 25.7% (HFNO) versus 14.3% (VNI)  
(IC 95% 0.25-21.20,  $p=0.033$ )**

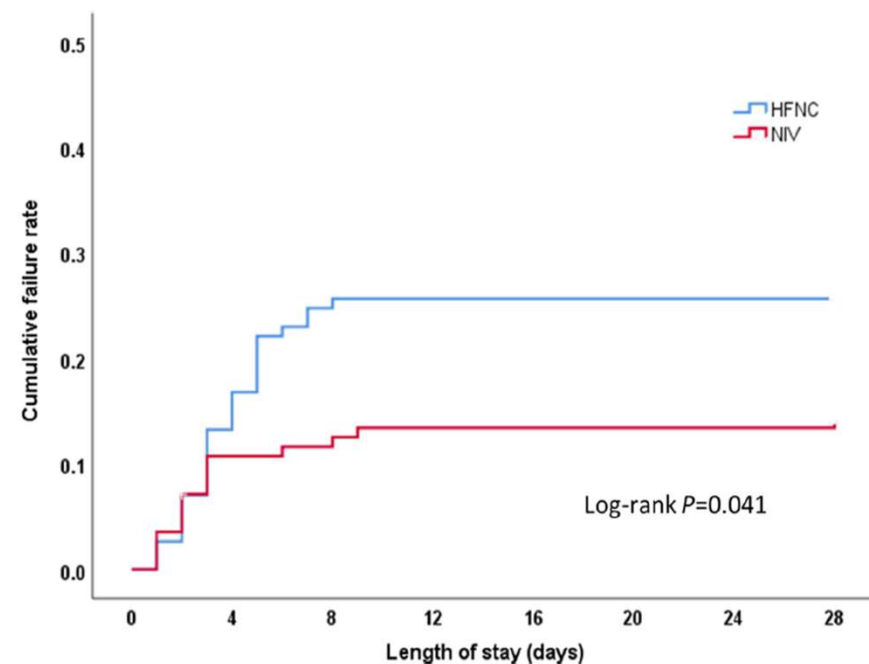


Fig. 2 Kaplan-Meier curve analysis for cumulative failure rate. HFNC: High-flow nasal cannula oxygen therapy; NIV: Non-invasive ventilation

# Pode a oxigenoterapia de alto fluxo (HFNO) ser uma opção na EADPOC com IRG descompensada?

**Table 3** Secondary endpoints in the HFNC and NIV groups

	HFNC (n=113)	NIV (n=112)	p value
Invasive ventilation	16 (14.2)	6 (5.4)	0.026
Treatment switch	13 (11.5)	10 (8.9)	0.524
Length of stay in ICU, days	7 (6–9)	9 (6–11)	0.059
Length of stay in hospital, days	10 (8–13)	11 (9–13)	0.228
28-day mortality, n (%)	11 (9.7)	8 (7.1)	0.485

HFNC High-flow nasal cannula oxygen therapy; NIV Non-invasive ventilation; ICU Intensive care unit

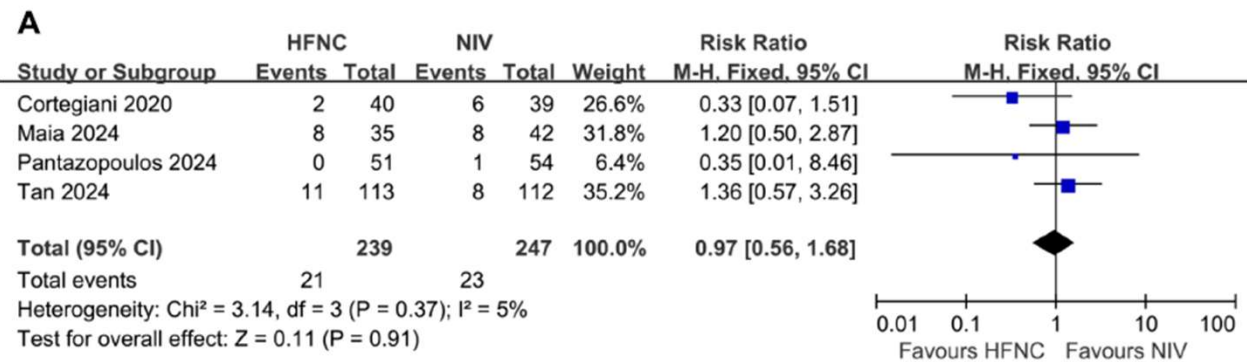
**Table 5** Other characteristics in the HFNC and NIV groups

	HFNC (n=113)	NIV (n=112)	P value
Duration of HFNC or NIV (hours)	85.9±30.5	78.7±33.8	0.312
Day 1 (hours)	13.2±4.5	9.9±3.5	<0.001
Day 2 (hours)	16.3±4.1	12.8±3.9	0.005
Day 3 (hours)	15.9±6.4	14.8±8.6	0.068
Day 4 (hours)	14.9±6.5	13.6±8.5	0.075
Day 5 (hours)	12.8±4.9	11.4±7.9	0.125
Dyspnea score	2 (2–4)	2 (1–3)	0.085
Airway care interventions, per day	5 (3–7)	8 (6–10)	<0.001
Comfort score	7 (6–8)	6 (5–7)	<0.001
Treatment intolerance	1 (0.9)	5 (4.5)	0.210
Nasal facial skin breakdown, n (%)	3 (2.7)	10 (8.9)	0.044

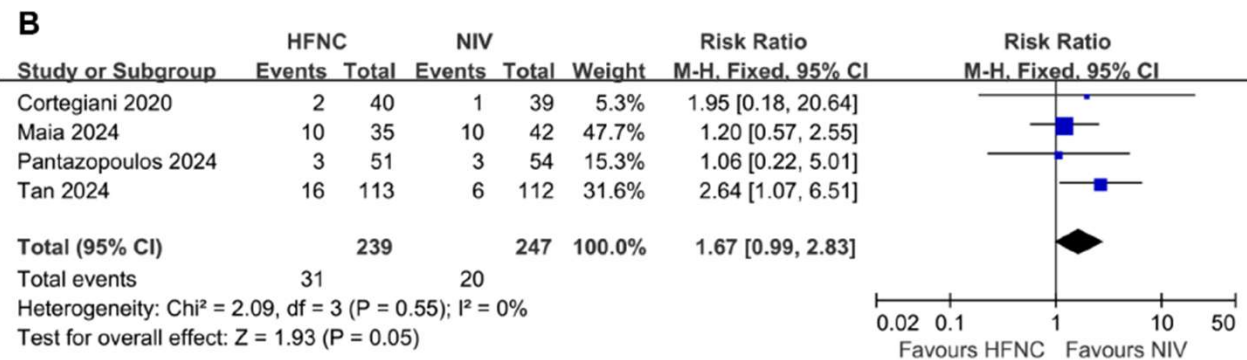
HFNC High-flow nasal cannula oxygen therapy; NIV Non-invasive ventilation; ICU Intensive care unit

# A HFNO é inferior à VNI no doente com EADPOC grave e IRG descompensada

MORTALIDADE  
POR TODAS AS  
CAUSAS

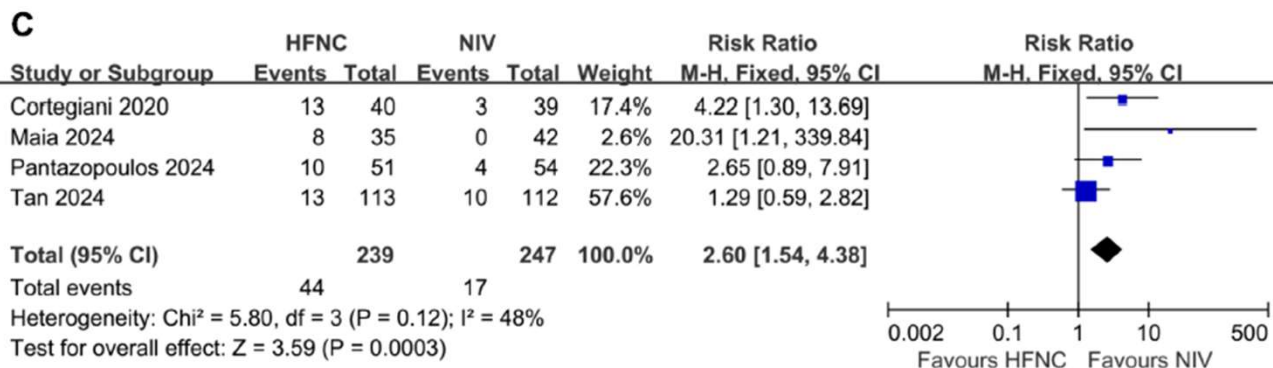


TAXA DE IOT

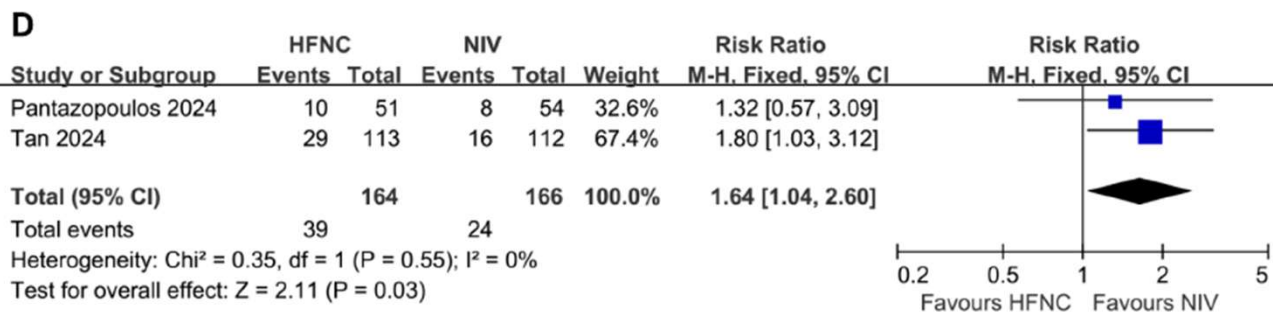


# A HFNO é inferior à VNI no doente com EADPOC grave e IRG descompensada

MUDANÇA DE TRATAMENTO



FALÊNCIA DE TRATAMENTO



# VNI em alternância com HFNO: o melhor de dois mundos

## VNI

↓↓↓ WoB

Recrutamento alveolar +++  
Correcção mais eficaz da  
PaCO<sub>2</sub> e pH  
Aquecimento e  
humidificação  
(equipamentos específicos)



## HFNO

Maior conforto  
Facilidade de utilização  
Aquecimento e humidificação  
Promoção da *clearance* de  
secreções, prevenção de  
atelectasias (em conjunto com  
RR)

Recrutamento alveolar +  
↓ WoB  
↓ Espaço morto

Prevenção de úlceras de pressão  
Drenagem brônquica mais eficaz  
Melhor tolerância

## VNI na EADPOC: Mensagens finais

- A VNI nas exacerbações graves de DPOC com acidemia respiratória reduz a mortalidade e a necessidade de IOT versus terapêutica *standard of care* otimizada
- É uma intervenção efectiva em vários cenários se aplicada precocemente e de forma apropriada
  - SU, enfermaria e UCI
- O sucesso da VNI implica a selecção do doente adequado, início atempado e monitorização por uma equipa experiente
- As equipas multidisciplinares treinadas garantem uma implementação com elevado nível de qualidade

# Referências

1. Venkatesan P. GOLD COPD report: 2026 update. *The Lancet Respiratory Medicine*. Published online November 2025:S2213260025004321. doi:[10.1016/S2213-2600\(25\)00432-1](https://doi.org/10.1016/S2213-2600(25)00432-1)
2. Qin JQ, Wang G, Liao Y, Shang W, Han D. High flow nasal therapy versus noninvasive ventilation for AECOPD with acute hypercapnic respiratory failure: a meta-analysis of randomized controlled trials. *Annals of Intensive Care*. 2025;15. doi:[10.1186/s13613-025-01480-w](https://doi.org/10.1186/s13613-025-01480-w)
3. Tan D, Wang B, Cao P, et al. High flow nasal cannula oxygen therapy versus non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: a randomized controlled non-inferiority trial. *Critical Care*. 2024;28. doi:[10.1186/s13054-024-05040-9](https://doi.org/10.1186/s13054-024-05040-9)
4. Farmer M, Callahan C, Hughes A, Riska K, Hill N. How I Do It Applying non-invasive ventilation in treatment of acute exacerbation of chronic obstructive pulmonary disease using evidence-based interprofessional clinical practice. *Chest*. Published online February 1, 2024. doi:[10.1016/j.chest.2024.02.040](https://doi.org/10.1016/j.chest.2024.02.040)
5. Longhini F, Bruni A, Garofalo E, et al. Monitoring the patient-ventilator asynchrony during non-invasive ventilation. *Front Med*. 2023;9:1119924. doi:[10.3389/fmed.2022.1119924](https://doi.org/10.3389/fmed.2022.1119924)
6. Rochweg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J*. 2017;50(2):1602426. doi:[10.1183/13993003.02426-2016](https://doi.org/10.1183/13993003.02426-2016)
7. Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA, Smith BJ. Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. Cochrane Airways Group, ed. *Cochrane Database of Systematic Reviews*. 2017;2017(7). doi:[10.1002/14651858.CD004104.pub4](https://doi.org/10.1002/14651858.CD004104.pub4)
8. Lindenauer P, Stefan M, Shieh M, Pekow P, Rothberg M, Hill N. Outcomes associated with invasive and noninvasive ventilation among patients hospitalized with exacerbations of chronic obstructive pulmonary disease. *JAMA internal medicine*. 2014;174 12:1982-1993. doi:[10.1001/jamainternmed.2014.5430](https://doi.org/10.1001/jamainternmed.2014.5430)
9. Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet (London, England)*. 2009;374:250-259. doi:[10.1016/s0140-6736\(09\)60496-7](https://doi.org/10.1016/s0140-6736(09)60496-7)
10. Lightowler J, Wedzicha J, Elliott M, Ram F. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. *BMJ : British Medical Journal*. 2003;326:185. doi:[10.1136/bmj.326.7382.185](https://doi.org/10.1136/bmj.326.7382.185)
11. Keenan SP, Sinuff T, Cook DJ, Hill NS. Which Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease Benefit from Noninvasive Positive-Pressure Ventilation?: A Systematic Review of the Literature. *Ann Intern Med*. 2003;138(11):861-870. doi:[10.7326/0003-4819-138-11-200306030-00007](https://doi.org/10.7326/0003-4819-138-11-200306030-00007)
12. Plant P, Owen J, Elliott M. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *The Lancet*. 2000;355:1931-1935. doi:[10.1016/s0140-6736\(00\)02323-0](https://doi.org/10.1016/s0140-6736(00)02323-0)
13. Doherty M, Greenstone M. Survey of non-invasive ventilation (NIPPV) in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) in the UK. *Thorax*. 1998;53:863-866. doi:[10.1136/thx.53.10.863](https://doi.org/10.1136/thx.53.10.863)
14. Diaz O, Iglesia R, Ferrer M, et al. Effects of Noninvasive Ventilation on Pulmonary Gas Exchange and Hemodynamics during Acute Hypercapnic Exacerbations of Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med*. 1997;156(6):1840-1845. doi:[10.1164/ajrccm.156.6.9701027](https://doi.org/10.1164/ajrccm.156.6.9701027)
15. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive Ventilation for Acute Exacerbations of Chronic Obstructive Pulmonary Disease. *N Engl J Med*. 1995;333(13):817-822. doi:[10.1056/NEJM199509283331301](https://doi.org/10.1056/NEJM199509283331301)