

Updates on the Management of Chronic Hypercarbic Respiratory Failure

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PCCM Updates

November 4, 2021

Hello!



A million years ago...



A few years ago...

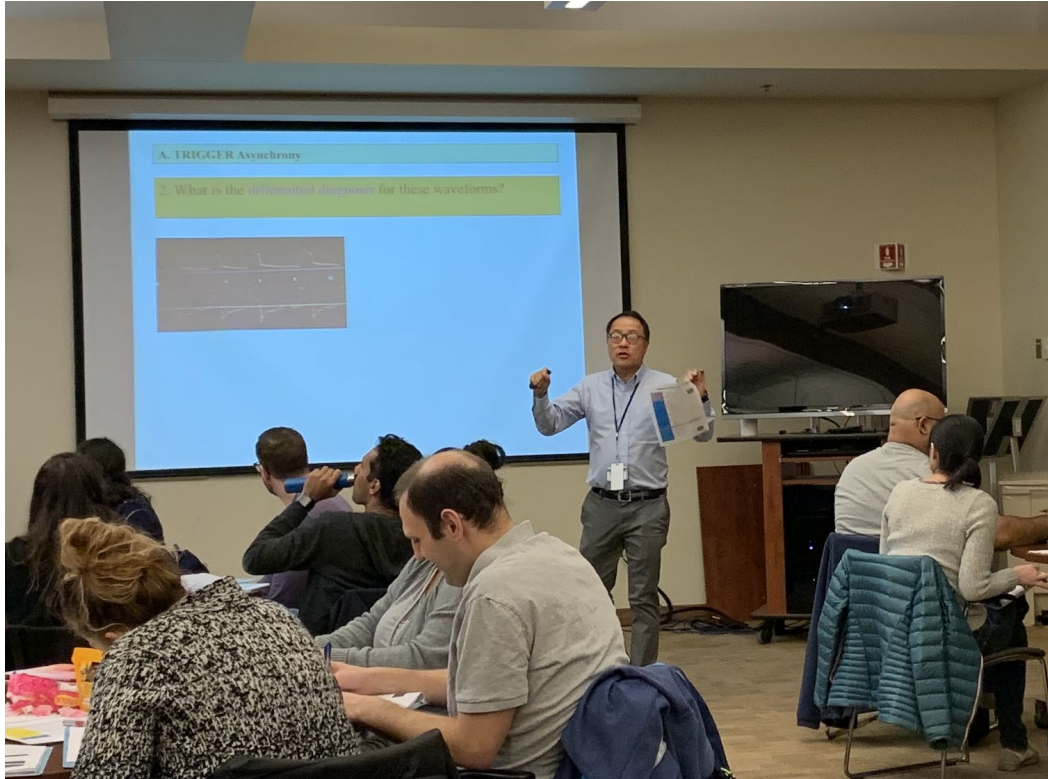


A few months ago...

Vent Course: Nov 8-10 (next week!)



National Institutes
of Health



Goals and objectives

- Discuss the pathophysiology behind three common forms of hypercarbic respiratory failure
 - COPD
 - OHS
 - NM disease (ALS)
- Describe the role of non-invasive ventilation in each of these disease states
- Provide updates on new literature

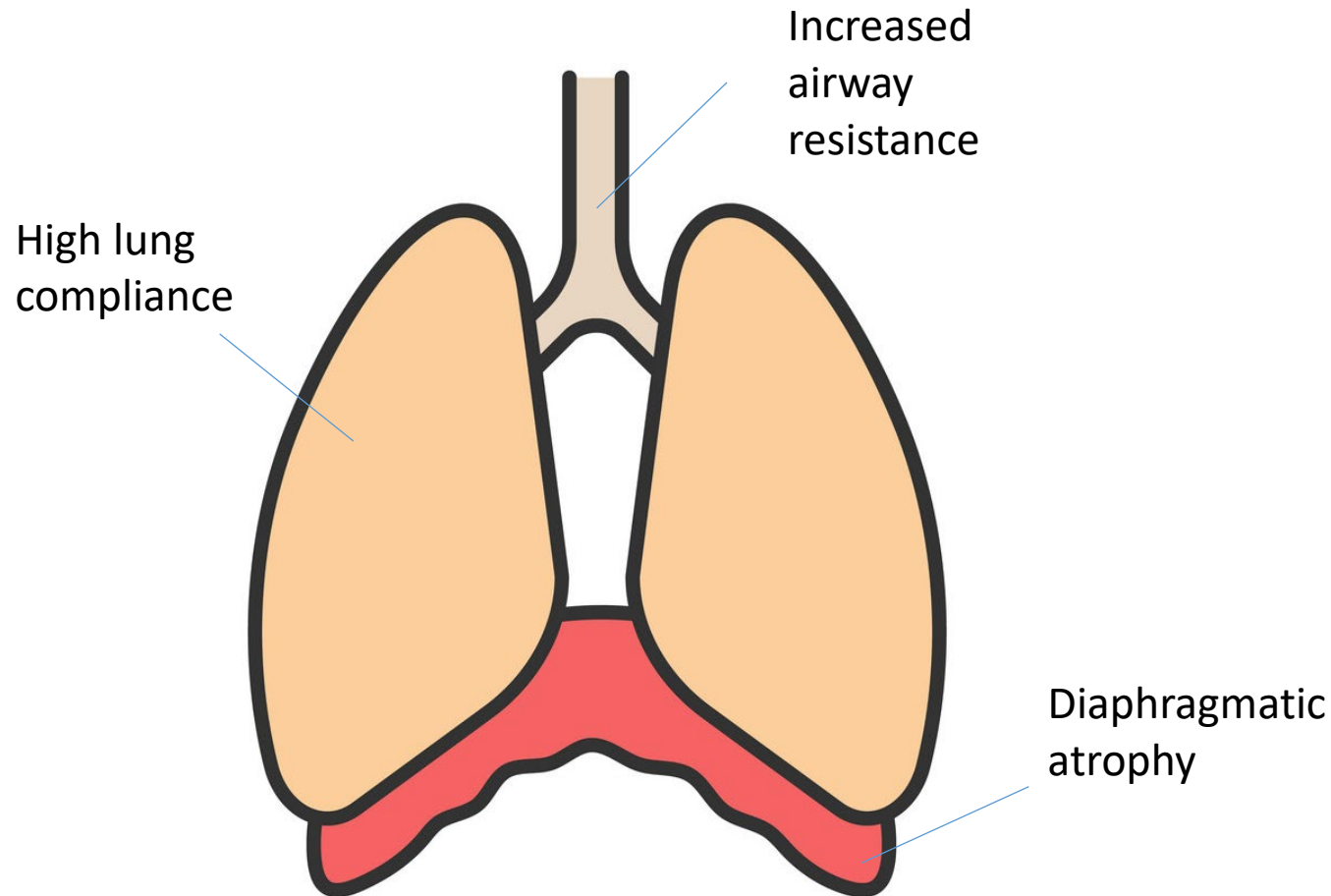
Case 1

A 65-year-old man, former smoker, with a history of Chronic Obstructive Pulmonary Disease (COPD) presents to clinic for evaluation of nocturnal ventilation. He was admitted with an acute exacerbation of COPD (AECOPD) three months prior, requiring non-invasive ventilation with BPAP while in the intensive care unit. Since discharge, he has returned to his baseline functional status and is currently enrolled in pulmonary rehab. PSG in the interim demonstrated an oxygen saturation of <88% for 25 minutes with an Apnea Hypopnea Index of 3 events/hour.

Pulmonary function testing reveals an FEV₁ 38% predicted. Labs from the day of this visit demonstrate a PaCO₂ of 60mm Hg.

Is there a role for NIV in the management of this patient?

NIV in COPD



- Increased respiratory muscle load
 - (pressure-time product)
- Hypoxemia and hypercarbia can give way to worsening diaphragmatic muscle dysfunction
- Chronic hypercapnia may suppress innate immunity

Coleman et al. Ann Am Thorac Soc 2019; 16(9):1091-1098.

Low-Intensity Noninvasive Ventilation

	Casanova <i>et al.</i> (10)	Clini <i>et al.</i> (11)	McEvoy <i>et al.</i> (12)
Design	RCT	RCT	RCT
N	44	86	144
Age, yr	24 vs. 20	47 vs. 39	72 vs. 72
BMI, kg/m ²	68 vs. 64	66 vs. 64	69 vs. 67
FEV ₁ , %	25 vs. 25	25 vs. 26	25.4 vs. 25.5
FEV ₁ , % predicted	31 vs. 29	31 vs. 27	23.1 vs. 25
PaO ₂ , mm Hg	57.5 vs. 55.7	49.5 vs. 50	52.5 vs. 54.8
PaCO ₂ , mm Hg	52 vs. 50	55.5 vs. 54	54.4 vs. 52.6
Mode	Bilevel-S	Bilevel-S/T	Bilevel-S
IPAP/EPAP, cm H ₂ O	12/4	14/2	13/5
Adherence, (h/day)	5.9	9.2	4.5
Acclimatization	2 d	10 d	3–4 d
Outcome	No improvement in acute COPD exacerbations, hospital admissions, intubations, or mortality	No improvement in hospitalizations or readmissions	Improved sleep quality and overnight hypercapnia, decrease in QoL

$$V_t \propto (IPAP-EPAP)/R \times T_i$$

Definition of abbreviations: Bilevel-S = no backup rate; Bilevel-S/T = backup rate; BMI = body mass index; COPD = chronic obstructive pulmonary disease; EPAP = expiratory positive airway pressure; FEV₁ = forced expiratory volume in 1 second; IPAP = inspiratory positive airway pressure; Pa_{CO₂} = carbon dioxide tension; PaO₂ = arterial oxygen tension; QoL = quality of life; RCT = randomized controlled trial; SaO₂ = arterial oxygen saturation.

Coleman et al. Ann Am Thorac Soc 2019; 16(9):1091-1098.

	Low-Intensity Noninvasive Ventilation			High-Intensity Noninvasive Ventilation		
	Casanova <i>et al.</i> (10)	Clini <i>et al.</i> (11)	McEvoy <i>et al.</i> (12)	Struik <i>et al.</i> (21)	Köhnlein <i>et al.</i> (20)	Murphy <i>et al.</i> (22)
Design	RCT	RCT	RCT	RCT	RCT	RCT
N	44	86	144	201	195	116
Age, yr	24 vs. 20	47 vs. 39	72 vs. 72	100 vs. 101	93 vs. 102	59 vs. 57
BMI, kg/m ²	68 vs. 64	66 vs. 64	69 vs. 67	63.5 vs. 63.9	64.4 vs. 62.2	67.1 vs. 66.4
FEV ₁ , %	25 vs. 25	25 vs. 26	25.4 vs. 25.5	24.8 vs. 24.6	24.5 vs. 24.8	22.2 vs. 21.5
FEV ₁ , % predicted	31 vs. 29	31 vs. 27	23.1 vs. 25	26 vs. 26	27 vs. 26	22.9 vs. 24
PaO ₂ , mm Hg	57.5 vs. 55.7	49.5 vs. 50	52.5 vs. 54.8	57.8 vs. 59.3	57.8 vs. 58.5	59 vs. 59
PaCO ₂ , mm Hg	53 vs. 50	55.5 vs. 54	54.4 vs. 52.6	Bilevel-S/T	Bilevel-S/T	Bilevel-S/T
Mode	Bilevel-S	Bilevel-S/T	Bilevel-S	19.2/4.8	21.6/4.8	24/4
IPAP/EPAP, cm H ₂ O	12/4	14/2	13/5	6.3	5.9	4.7
Adherence, (h/day)	5.9	9.2	4.5	3–4 d	5–6 d	5–6 d
Acclimatization	2 d	10 d	3–4 d	No change in exacerbations, improvement in daytime PaCO ₂	Improvement in mortality, PaCO ₂ , SaO ₂ , and FEV ₁	Decrease COPD readmissions
Outcome	No improvement in acute COPD exacerbations, hospital admissions, intubations, or mortality	No improvement in hospitalizations or readmissions	Improved sleep quality and overnight hypercapnia, decrease in QoL			

Definition of abbreviations: Bilevel-S = no backup rate; Bilevel-S/T = backup rate; BMI = body mass index; COPD = chronic obstructive pulmonary disease; EPAP = expiratory positive airway pressure; FEV₁ = forced expiratory volume in 1 second; IPAP = inspiratory positive airway pressure; PaCO₂ = carbon dioxide tension; PaO₂ = arterial oxygen tension; QoL = quality of life; RCT = randomized controlled trial; SaO₂ = arterial oxygen saturation.

Coleman et al. Ann Am Thorac Soc 2019; 16(9):1091-1098.

NIV in COPD

- Kohnlein et al (2014)
 - Investigated the effect of long-term NPPV, targeted to reduce hypercapnia, on survival in patients with advanced, stable hypercapnic COPD.
 - Looked at stable GOLD Stage IV COPD with PaCO₂ of 51.9 mm Hg or higher and a pH > 7.35.
 - Patients randomly assigned to standard therapy vs NIV for at least 12 months
 - NIV targeted to reduce baseline PaCO₂ by at least 20% or to achieve PaCO₂ < 48.1 mmHg.
 - Primary outcome: 1 year mortality

Kohnlein et al. Lancet Respr Med 2014;2:698-705.

NIV in COPD

- “High-intensity” BPAP
 - Mean IPAP/EPAP 21.6/4.9

	3 months	6 months	9 months	12 months
Overall	0.8 (3.5)	2.1 (5.7)	0.9 (4.0)	2.6 (8.6)
Non-invasive positive pressure ventilation group	0.2 (1.1)	1.4 (4.7)	1.3 (4.9)	2.2 (10.2)
Control group	1.5 (4.9)	3.0 (6.9)	0.4 (1.9)	3.1 (5.4)

Values are mean (SD).

Table 2: Emergency hospital admissions per patient by follow-up period and treatment group

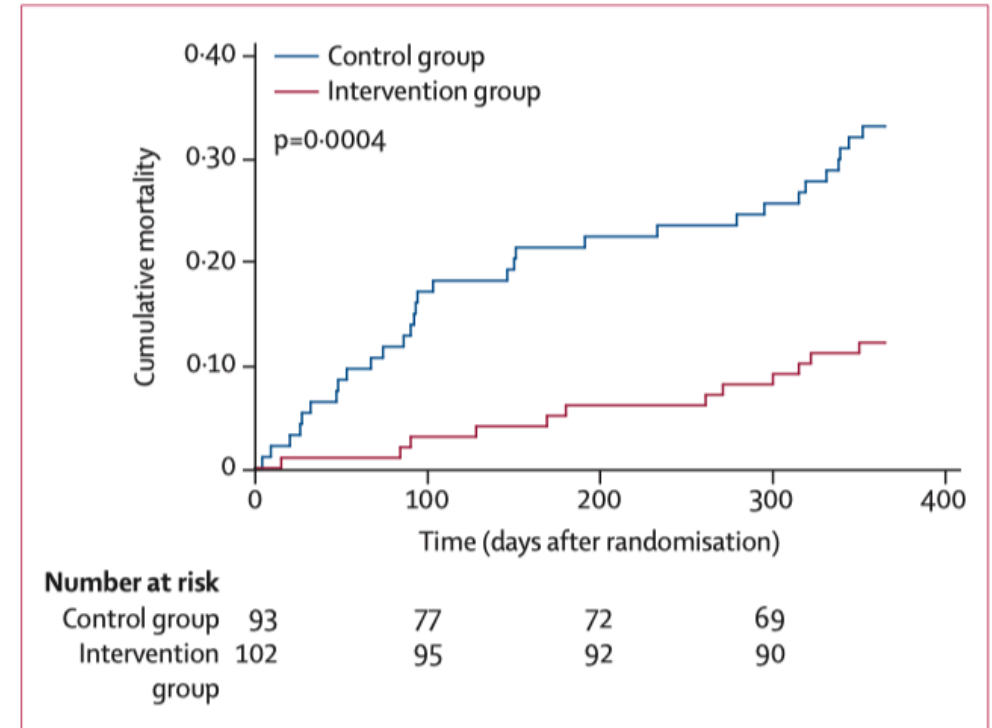


Figure 2: Kaplan-Meier estimate of cumulative all-cause mortality during the first year after randomisation (primary outcome)

The p value results from a log-rank test of the between-group difference.

Kohnlein et al. Lancet Respr Med 2014;2:698-705.

II. Severe COPD

ABG PaCO₂ is \geq 52 mm Hg while patient is awake and breathing the prescribed FiO₂.



Sleep oximetry study demonstrates oxygen saturation \leq 88% for \geq 5 cumulative minutes of nocturnal recording time (minimum recording time of 2 hours), done while breathing oxygen at 2 liters per minute (LPM) or the patient's usual FiO₂ (whichever is higher).







Prior to initiating therapy, sleep apnea and treatment with CPAP has been considered and ruled out. (Note: Formal sleep testing is not required if there is sufficient information in the medical record to demonstrate that the patient does not suffer from some form of sleep apnea [obstructive sleep apnea (OSA), central sleep apnea (CSA) and/or complex sleep apnea (CompSA)] as the predominant cause of awake hypercapnia or nocturnal arterial oxygen desaturation).

E0470


- E0470— aka BiPAP S
- ResMed: AirCurve 10S, AirCurve V-Auto
 - Resironics: Dreamstation BiPAP

NIV in COPD

E0471

 <p>LOW PRICE</p>		 <p>LOW PRICE</p>	
<p>ResMed AirCurve 10 St BILEVEL Machine w/ HumidAir 3.0 ★★★★★ 1 BiPAP</p>	<p>ResMed AirCurve 10 St BILEVEL Machine w/ HumidAir - Certified Refurbished BiPAP</p>	<p>ResMed AirCurve 10 VPAP St with HumidAir/Heated Tube 4.5 ★★★★★ 47 BiPAP More size options</p>	<p>AirCurve 10 St with HumidAir and ClimateLineAir 37307 by ResMed</p>
<p>\$2,500.00 \$139.27 below typical Sistemma Free delivery</p>	<p>\$1,899.00 My Medical Outlet Free delivery by Wed, Nov 17</p>	<p>\$2,399.99 \$92.39 below typical MajorCPAP Free delivery by Wed, Nov 17</p>	<p>\$2,935.00 Help Medical Supplies Free delivery by Thu, Nov 11</p>
<p>Compare prices from 4 stores</p>	<p>Compare prices from 2 stores</p>	<p>Compare prices from 2 stores</p>	<p>Compare prices from 2 stores</p>

Home Ventilator



Philips Respironics Trilogy Evo Ventilator
Portable

\$17,500.00
Peoples Care Medical Supply
Google Guarantee

Case 2

A 33-year-old female, never smoker, with a past medical history of pre-diabetes presents to clinic after her primary care doctor noted an elevated serum bicarbonate of 32 mEq/L on routine labs. Her vitals are notable for a body mass index (BMI) of 40.

Pulmonary function testing reveals a mildly restrictive pattern with a low ERV and preserved DLCO. Labs from the day of this visit demonstrate a PCO_2 of 50 mm Hg.

Is there a role for NIV in the management of this patient?

NIV in Chronic OHS

- Obesity Hypoventilation Syndrome (OHS)
 - Definition: Obesity (BMI ≥ 30 kg/m²), daytime hypercapnia (PaCO₂ ≥ 45 mm Hg) not attributable to other causes of hypoventilation.
 - 90% have concurrent OSA (nearly 70% have severe)
 - American Thoracic Society (ATS) Clinical Practice Guidelines for patients with confirmed OHS
 - + severe OSA: CPAP titration and treatment
 - If inadequate treatment, change to NIV
 - + no OSA or mild/moderate OSA: NIV initiation and treatment with consideration of bariatric surgery
 - Per the ATS, if admitted with acute on chronic hypercarbic respiratory failure in the setting of OHS, patients should be discharged with NIV

Mokhlesi et al. Am J Respir Crit Care Med 2019. 200(3):e6-e24.

NIV in Chronic OHS

[Sleep Original Research]

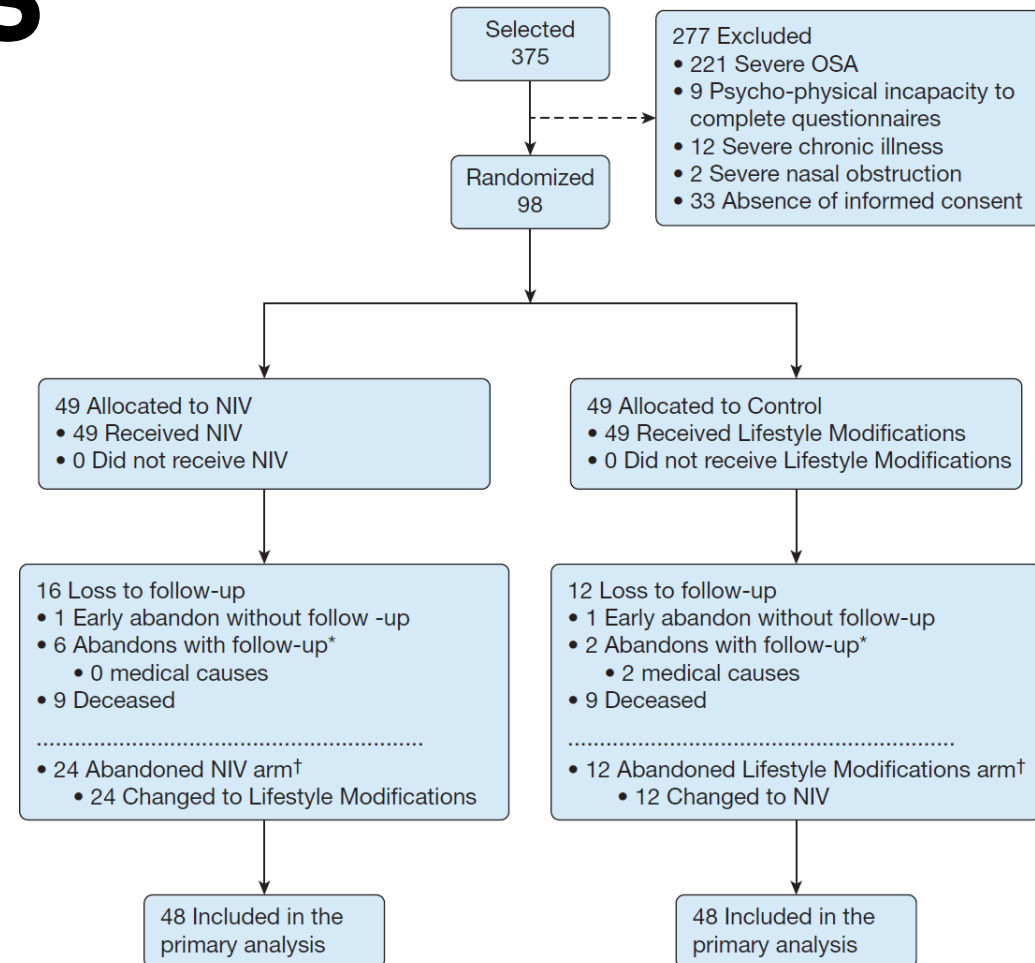


Long-term Noninvasive Ventilation in Obesity Hypoventilation Syndrome Without Severe OSA

The Pickwick Randomized Controlled Trial



- VAPS vs lifestyle modification
- Inclusion: untreated OHS, mild-to-moderate OSA
- Exclusion: severe OSA, other sleep conditions, chronic nasal obstruction
- Primary endpoint: hospitalization days per year
- Secondary endpoint: hospital resource utilization, CV events, mortality, ABG data



Masa et al Chest 2020; 158(3):1176-1186.

NIV in Chronic OHS

- Primary outcome: Hospitalization days per year
 - Lifestyle modification group: 2.6 +/- 5.31d vs NIV: 2.71 +/- 4.52d (ns)
- Secondary outcomes:
 - Hospital resource utilization: dec in hospital admissions, ER visits among NIV
 - CV events: ns
 - Mortality: ns
 - Cause of mortality in the NIV group: CV events (67%)
 - Cause of mortality in the lifestyle modification group: respiratory failure (44%)

Masa et al Chest 2020; 158(3):1176-1186.

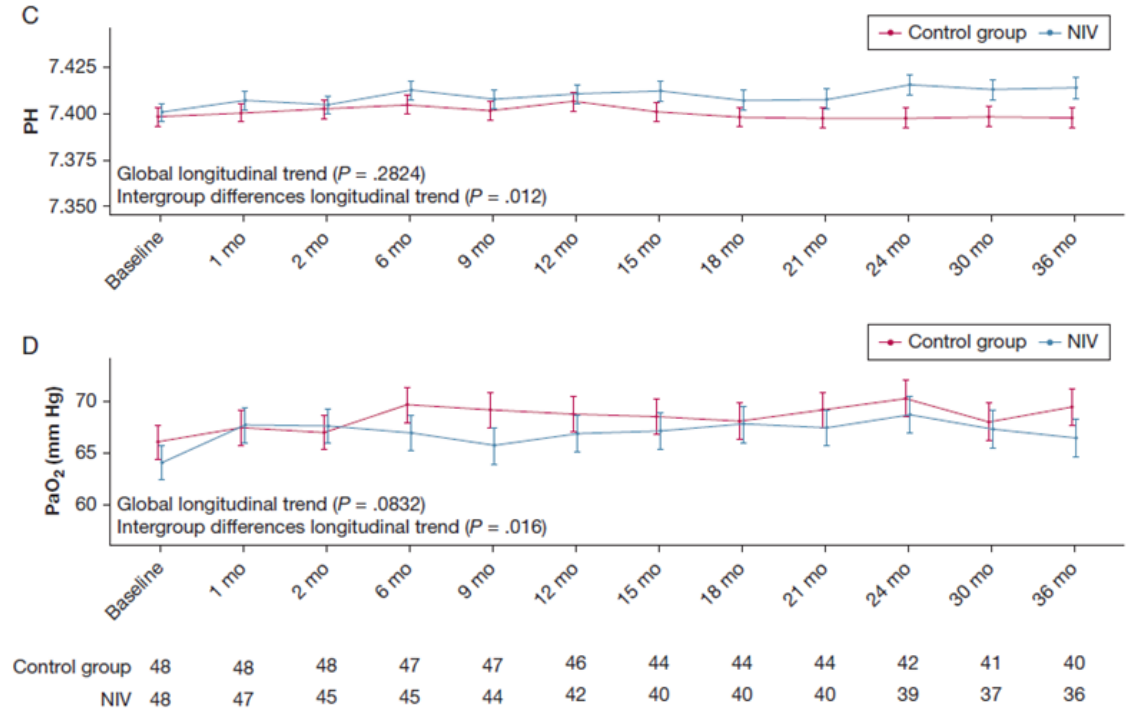
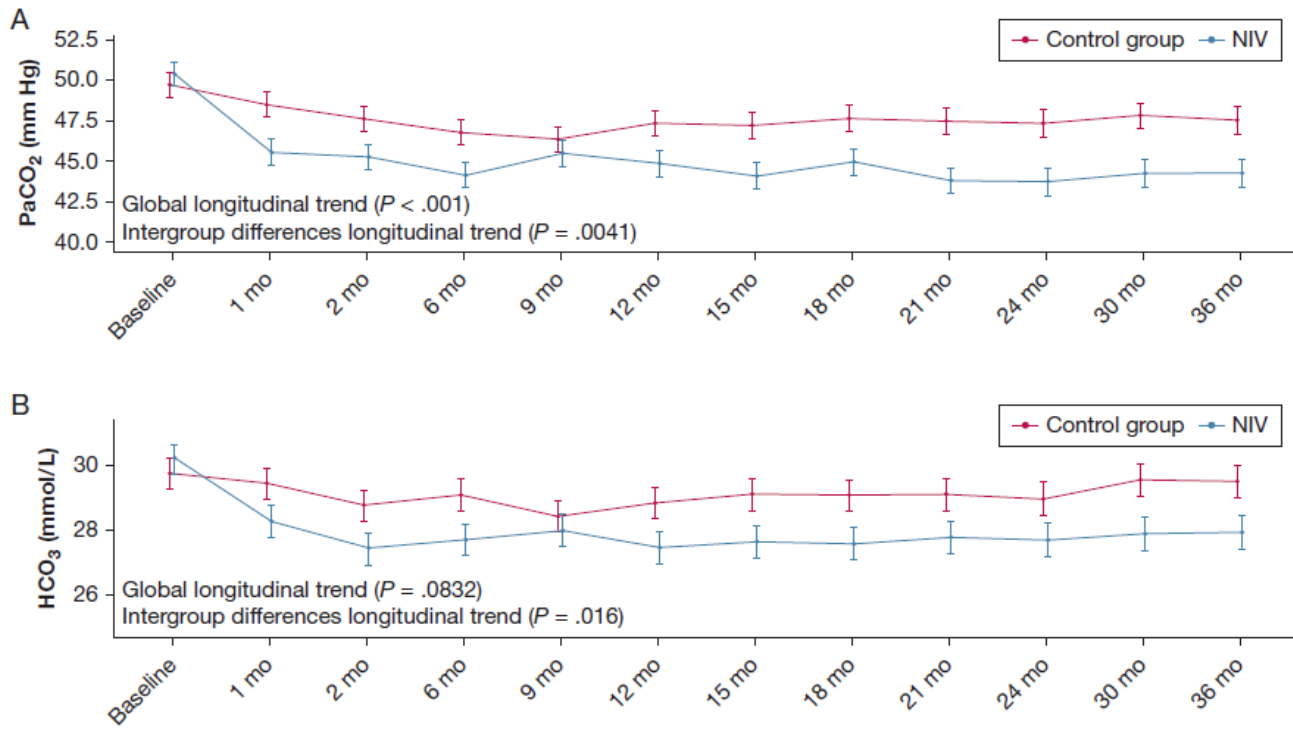


Figure 2 - A-D, Adjusted longitudinal changes of arterial blood gases during follow-up (mean and 95% CI). P values correspond to longitudinal changes for treatments and for intergroup control and NIV comparison from linear mixed-effects regression model: (A) PaCO₂ changes, (B) HCO₃⁻ changes, (C) pH changes, and (D) PaO₂ changes. HCO₃⁻ = bicarbonate. See Figure 1 legend for expansion of other abbreviation.

NIV in Chronic OHS

- Moral of the story for OHS without severe OSA?
 - Need more data
 - PAP adherence!!



Case 3

A 60-year-old man with a recent diagnosis of ALS presents to clinic. He complains of some recent upper extremity weakness and denies any bulbar symptoms. He notes frequent morning headaches and frequent arousals at night. He also reports some mild exertional dyspnea, though denies any shortness of breath at rest.

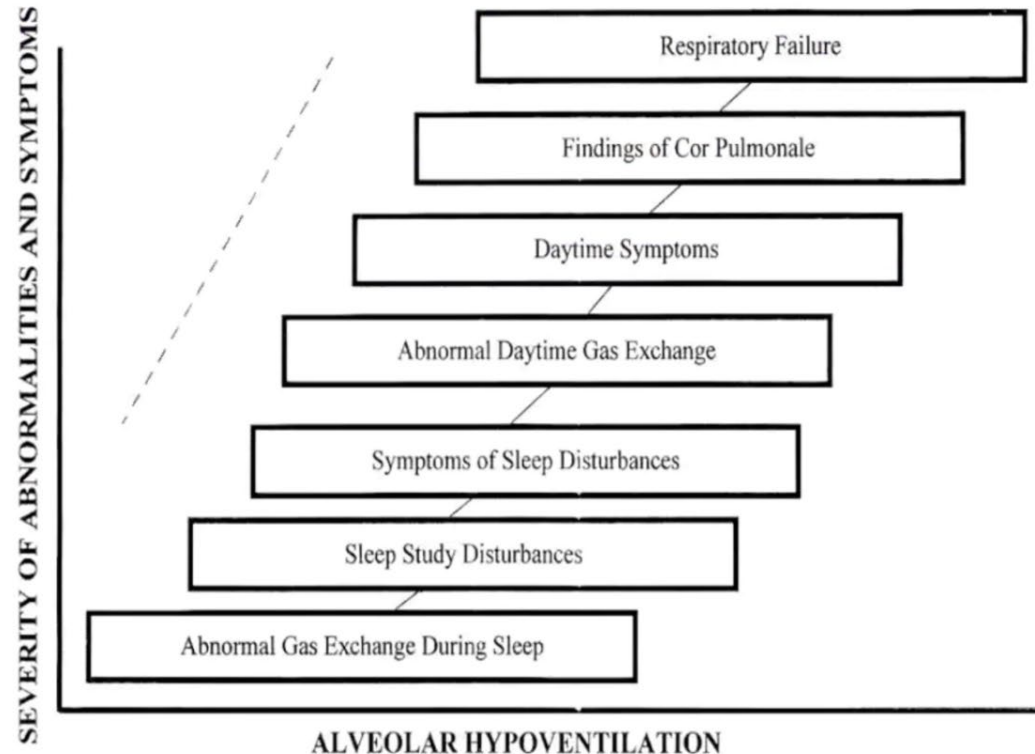
A nocturnal oximetry study is obtained, which demonstrates desaturations below 88% for 45 minutes.

Is there a role for NIV in the management of this patient?

NIV in Neuromuscular Disease

- ALS

Muscle weakness progresses to involve the diaphragm → sleep disruption, respiratory insufficiency, respiratory failure



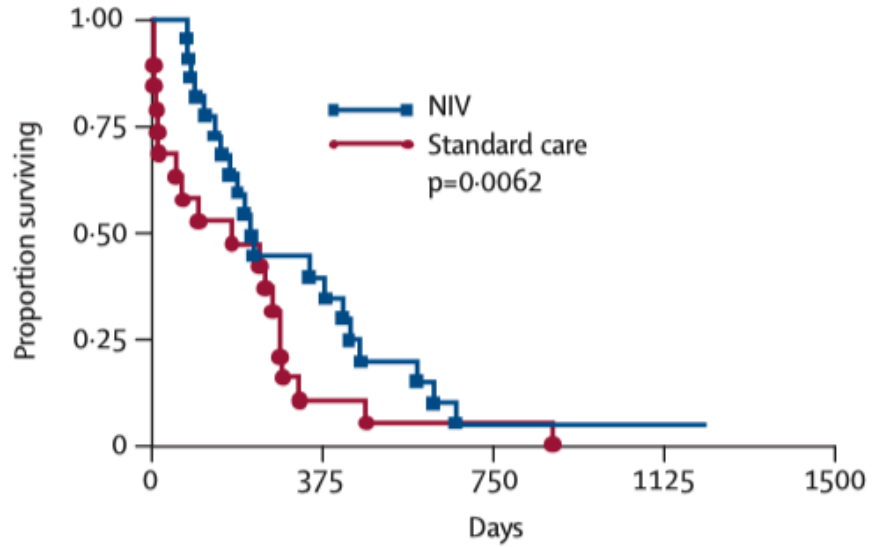
Chest, Volume 116(2), August 1999, 521-534

Cooksey et al. Sleep Med Clin 15(2020):527-538.

NIV in Neuromuscular Disease

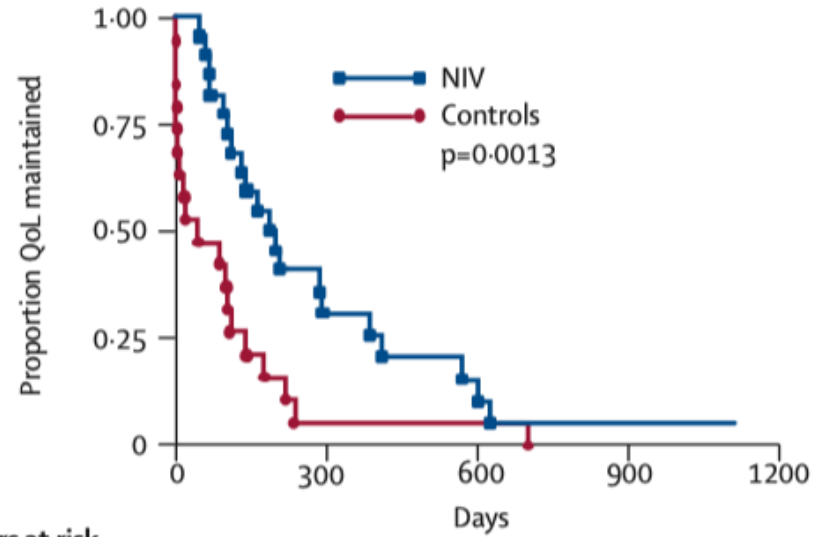
- Bourke et al (2006)
 - Investigated the impact of NIV on quality of life and survival in ALS
 - Looked at patients with ALS and reassessed every 2 months for the onset of respiratory symptoms (orthopnea with MIP <60% of predicted or symptomatic hypercapnia)
 - Randomly assigned to NIV (BPAP S/T) or standard of care
 - Primary outcomes: quality of life outcome measures, survival

Bourke et al. Lancet Neurol 2006;5:140-147.



Numbers at risk

NIV	22
Standard care	19



Numbers at risk

NIV	22
Standard care	19

Bourke et al. Lancet Neurol 2006;5:140-147.

NIV in Neuromuscular Disease

Annals of the American Thoracic Society

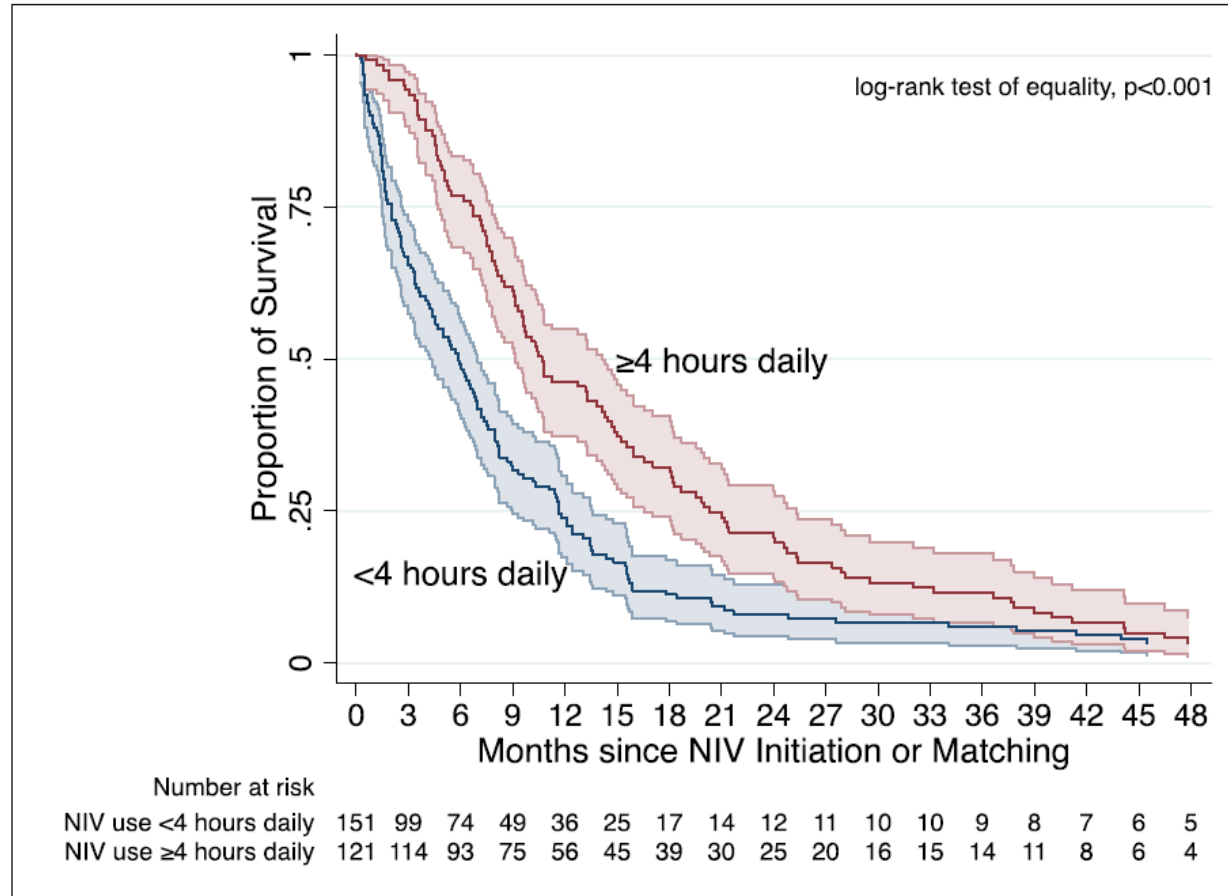
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Noninvasive Ventilation Use Is Associated with Better Survival in Amyotrophic Lateral Sclerosis

- Retrospective cohort study
- Inclusion: diagnosis of ALS
- Exclusion: initiation of NIV prior to enrollment, history of trach
- Primary endpoint: time from NIV prescription (or matched date) until death

Ackrivo et al. Ann Am Thorac Soc. 2021 Mar;18(3):486-494.

NIV in Neuromuscular Disease



- Results:

- ≥ 4 hours vs <4 hours
- Limb-onset ALS vs bulbar ALS

Ackrivo et al. Ann Am Thorac Soc. 2021 Mar;18(3):486-494.

Recap

- Reviewed three common causes of chronic hypercarbic respiratory failure
- Described the role of NIV in severe COPD with chronic hypercarbia, obesity hypoventilation with and without severe OSA, and neuromuscular disease through the lens of ALS

Thank you!

- Happy to answer questions!

Works Consulted

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