Critical Review Form
Therapy

Acet Öztürk NA, Aydın Güçlü Ö, Demirdöğen et al. AVAPS-NIV treatment in hypercapnic respiratory failure with insufficient response to fixed-level PS-NIV. Tuberk Toraks. 2022 Dec;70(4):324-333.

Objectives: **To test the hypothesis "that COPD patients with AHRF who did not show the desired reduction in $PaCO_2$ with fixed-level PS-NIV might benefit from AVAPS mode. The primary objective of our study is to evaluate the performance of AVAPS-NIV on $PaCO_2$ measurements. Secondary outcomes are the effects of AVAPS-NIV treatment on length of stay and intubation rates." (p. 325)**

Methods: **This observational study included patients admitted to the non-ICU pulmonary ward of the Bursa Uludağ University Hospital, a tertiary care hospital in Turkey, with acute exacerbations of COPD. Respiratory support was considered for patients presenting with hypercapnic respiratory failure – defined as an arterial pH ≤ 7.35 and $PaCO_2$ > 45 mmHg – or with a respiratory rate > 24 breaths/minute despite optimal medical treatment. Exclusion criteria included contraindications for NIV, pneumothorax, PE, difficulty with secretion clearance, upper airway obstruction, ventricular arrhythmia, myocardial ischemia, hemodynamic instability despite fluid resuscitation, facial deformities, recent surgery to the head or upper GI system, lack of cooperation, or altered consciousness not due to hypercapnia.**

All patients received fixed-level pressure support NIV upon admission for 18 hours/day initially and disconnected for an hour for each meal. Patients who did not reach clinical and laboratory stability under fixed pressure support (GCS = 15, respiratory rate < 24, O_2 saturation ≥ 90%, and normalized arterial pH with $PaCO_2$ reduction) were switched to the AVAPS mode of NIV. After reaching 12-14-hour/day of NIV support without any deterioration, pressure support was also decreased. Stable patients under the AVAPS mode of NIV treatment were re-assigned to use PS mode.

A total of 35 patients were included with a mean age of 70.7 years; 74.3% were male and 11.4% were current smokers.

Critical Review Form: Therapy	
Guide	Comments
Are the results valid?	

Did experimental and control groups being the study with a similar prognosis?	
Were patients randomized?	No. This was a cohort study in which results were compared among those who responded to fixed-level pressure support with those who did not respond and hence required AVAPS.
Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be "randomized" to a particular group?	N/A
Were patients analyzed in the groups to which they were randomized?	No. Again, the comparisons were made between those who responded appropriately to initial treated with fixed-level pressure support and those who eventually required treatment with AVAPS.
Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. "Patients who needed a change in NIV mode to AVAPS (Group 2) had similar age, comorbidities, history of NIV use, pneumonia in chest x-ray, and laboratory parameters such as leukocyte count, brain natriuretic peptide and C-reactive protein with patients who continued PS-NIV (Group 1)." (p. 328)
Did experimental and control groups retain a similar prognosis after the study started?	
Were patients aware of group allocation?	Yes, although it seems unlikely that performance bias on the part of patients would have affected outcomes.
Were clinicians aware of group allocation?	Yes, and it is possible that performance bias on the part of clinicians could have affected outcomes.
Were outcome assessors aware of group allocation?	Presumably yes. The authors make no mention blinding of outcome assessors or how this would have been accomplished.
Was follow-up complete?	Yes. All outcomes were measured during the index hospitalization and hence would have been available from the records.
What are the results?	
How large was the treatment effect?	• After a median 28.0 (range 16.5–95.0) hours of PS-NIV treatment, 14 (40%) of patients showed no improvement or worsening of $PaCO_2$ and were switched to AVAPS mode. • Arterial $PaCO_2$ and pH levels significantly improved after AVAPS-NIV administration: o After 4.0 (3.0–10.0) hours of AVAPS-NIV treatment, $PaCO_2$ showed a -9.52 (-23.9–4.2)% change and after 19.5 (9.0–24.0) hours of AVAPS-NIV treatment, $PaCO_2$ showed -11.4 (-22.0 – -0.5) % improvement. o Within Group 2, using AVAPS-NIV for 19.5 (9.0–24.0) hours created a significantly better $PaCO_2$ change rate than using PS-NIV for 21.0 (10.0–24.0) hours [-11.4 (-22.0 – -0.5) vs 8.2 (-5.3–19.5), p= 0.02]. • Higher Charlson comorbidity index [OR= 1.74 (95% CI= 1.02–2.97)] and higher $PaCO_2$ upon admission [OR= 1.18 (95% CI= 1.03–1.35)] were significantly related to an increased risk of AVAPS-NIV requirement.
How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?)	See above.
How can I apply the results to patient care?	
Were the study patients similar to my patient?	Uncertain. This study was conducted in the non-ICU inpatient pulmonology unit at a single hospital in Turkey, where ethnic and racial differences could affect disease processes such as COPD. The authors

	provide very little information on medical comorbidities in these patients making direct comparison even more difficult (external validity).
Were all clinically important outcomes considered?	No. The primary outcome measures were based on changes in surrogate lab values rather than patient-centered outcomes.
Are the likely treatment benefits worth the potential harm and costs?	Uncertain. This was not a true therapy study as billed in the article, but rather a cohort study in which patients who did not improve with treatment A (fixed pressure NIV) were switched to treatment B (AVAPS). Comparisons between nonresponders and responders provides very little useful clinical information. It does appear that AVAPS may be a safe rescue mode for patients with acute exacerbations of COPD not responding to fixed pressure NIV, but this is based on anecdotal evidence. This study does not address the efficacy or safety of using AVAPS as the initial mode of ventilation for these patients.

Limitations:

1. **There was no blinding of patients of clinicians and no mention of blinding of outcome assessors.**
2. **The authors relied primarily on surrogate outcomes rather than patient-centered outcomes.**
3. **This study was conducted at a single hospital in Turkey, where ethnic and racial differences could affect disease processes such as COPD. The authors provide very little information on medical comorbidities in these patients making direct comparison even more difficult (external validity).**
4. **This was not a true therapy study, but rather a cohort study in which patients who did not improve with treatment A (fixed pressure NIV) were switched to treatment B (AVAPS). Comparisons between nonresponders and responders provides very little useful clinical information and this study does not address the efficacy or safety of using AVAPS as the initial mode of ventilation for these patients.**

Bottom Line:

This cohort study suggests that among patients with acute exacerbations of COPD with hypercapnic respiratory failure who fail to improve on traditional fixed pressure support NIV, switching to AVAPS mode may be beneficial at improving pH and $PaCO_2$.