



Comparison of BPAP S/T and Average Volume-Assured Pressure Support Modes for Hypercapnic Respiratory Failure in the Emergency Department: A Randomized Controlled Trial

Nurfer Zehra Gören¹, Emre Şancı², Feride Fulya Ercan Coşkun³, Duygu Gürsoylu⁴, Başak Bayram⁵

¹Department of Emergency Medicine, Medical Park Hospital, İzmir University of Economics, İzmir, Turkey

²Department of Emergency Medicine, Kocaeli Derince Training and Research Hospital, İzmit, Turkey

³Department of Emergency Medicine, İzmir Çiğli Training and Research Hospital, İzmir, Turkey

⁴Department of Emergency Medicine, Gölbaşı Şehit Ahmet Özsoy State Hospital, Ankara, Turkey

⁵Department of Emergency Medicine, Dokuz Eylül University School of Medicine, İzmir, Turkey

Background: There is limited research into the utility of average volume-assured pressure support (AVAPS), a volume-assured pressure-controlled mode, especially in patients with hypercapnic respiratory failure.

Aims: This study aimed at a randomized comparison of AVAPS and bilevel positive airway pressure spontaneous/timed (BPAP S/T) modes in non-invasive mechanical ventilation (NIMV) application with hypercapnic respiratory failure patients in the emergency department (ED).

Study Design: Randomized controlled study.

Methods: In this prospective randomized controlled study, 80 patients admitted to ED with hypercapnic respiratory failure requiring NIMV were randomly assigned to AVAPS or S/T groups using the sealed envelope method (33 patients in the S/T group, 47 patients in the AVAPS group). Data of arterial blood gas (ABG), vital parameters, Glasgow Coma Score (GCS), additional treatment needs, and clinical outcomes were evaluated, and the treatment success rates of both groups were compared.

Results: A total of 80 patients, 33 in the S/T and 47 in the AVAPS group, were analyzed in the study. The pH values improved in the AVAPS group compared to the baseline (0.07 [0.04-0.10] vs 0.03 [0.00-0.11]). PaCO₂ (partial pressure of carbon dioxide) excretion was faster in the AVAPS group than in the S/T group in the first hour (10.20 mmHg [6.20-19.20] vs. 4.75 [-] 0.83-16.88). The comparison of blood gas measurements showed no significant differences between the groups regarding the changes in PaCO₂ and pH values over time ($P = .141$ and $P = .271$, respectively). During the ED follow-up, 3 (6.4%) patients in the AVAPS group and 5 (15.2%) patients in the S/T group needed intubation [Relative risk: 0.42 (95% CI: 0.11 to 1.64), $P = .21$].

Conclusion: In this study, improvements in blood gas parameters in the AVAPS group were faster compared to the S/T group; however, we did not find any significant difference between the groups in terms of clinical parameters. The AVAPS mode is as effective and safe as BPAP S/T in treating patients with hypercapnic respiratory failure in the ED.

INTRODUCTION

Non-invasive mechanical ventilation (NIMV) is an effective treatment method in patients with hypoxemic or hypercapnic respiratory failure such as chronic obstructive pulmonary disease (COPD), acute decompensated heart failure, obesity hypoventilation syndrome (OHS), neuromuscular diseases, and pneumonia.^{1,2} This treatment improves vital parameters and arterial blood gas values, resulting in a significant decrease in the need for intubation and related mortality and morbidity rates.^{3,4}

NIMV can be applied with continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BPAP). CPAP aims at reducing the number of adverse respiratory events by providing constant positive pressure support throughout the breathing cycle, while BPAP provides different levels of positive airway pressure during inspiration and expiration. Bilevel pressure support is provided by setting constant expiratory positive airway pressure (EPAP) and inspiratory positive airway pressure (IPAP) values in the spontaneous/timed (S/T) mode.¹

Corresponding author: Emre Şancı, Department of Emergency Medicine, Kocaeli Derince Training and Research Hospital, İzmit, Turkey
e-mail: emresanci@gmail.com

Received: December 30, 2020 Accepted: June 3, 2021 • DOI: 10.5152/balkanmedj.2021.20137

Available at www.balkanmedicaljournal.org

ORCID iDs of the authors: N.Z.G. 0000-0003-0461-2883; E.Ş. 0000-0002-9707-3315; F.F.E.C. 0000-0002-1514-6729; D.G. 0000-0002-2158-3642; B.B. 0000-0003-2084-2646.

Cite this article as:

Gören NZ, Şancı E, Ercan Coşkun FF, Gürsoylu D, Bayram B. Comparison of BPAP S/T and average volume-assured pressure support modes for hypercapnic respiratory failure in the emergency department: A randomized controlled trial. *Balkan Med J.* 2021;38(5):265-271.

Copyright@Author(s) - Available online at <http://balkanmedicaljournal.org/>

Average volume-assured pressure support (AVAPS) is a different mode of NIMV. To achieve the target tidal volume (TV) with AVAPS, variable pressure support is applied during inspiration. For this purpose, the user defines a target TV and lower and upper limits for IPAP and EPAP, thus featuring more comfortable pressure support, which varies according to the patient's condition. In a limited number of studies in the literature carried out using the AVAPS mode in NIMV, AVAPS has been shown to be effective in special patient groups such as OHS and kyphoscoliosis.^{5,6} The status of consciousness improved faster with AVAPS in patients with COPD who had hypercapnic respiratory failure, while improvements in arterial blood gas (ABG) parameters were similar to the S/T mode.² This study aimed to compare the effects of AVAPS and routine S/T modes in NIMV patients admitted to the ED, on their ABG parameters and clinical status.

MATERIAL AND METHODS

Trial Design and Oversight

This study was carried out between October 2016 and June 2017 as a single-center, single-blind, randomized controlled trial in the Emergency Department (ED) of Dokuz Eylül University Hospital. The study was conducted according to the principles outlined in the Declaration of Helsinki and the International Conference on Harmonization Guidance for Good Clinical Practice. The protocol was approved by The Institutional Clinical Research Ethics Committee and The Ministry of Health, Turkish Medicine and Medical Devices Agency (Ethical board number: 71146310 [2016-CE-006]). The study was registered in the clinicaltrials.gov (Clinical Trial Number: NCT03398239). This study was funded by Dokuz Eylül University Scientific Research Projects Dept. (2017.KB.SAG.033).

Patient Population

Patients with shortness of breath, $\text{PaCO}_2 > 45$ mmHg in ABG, and indications of NIMV in the ED were evaluated for enrollment to the study. The inclusion criteria were the presence of one of the following findings: (1) $\text{SpO}_2 < 90\%$ (in room air); (2) $\text{SpO}_2 < 93\%$ despite 6 L/min oxygen application; (3) the use of accessory respiratory muscles; (4) inability to speak in whole sentences due to respiratory distress; (5) respiratory rate > 24 ; or (6) change in mental status. The exclusion criteria were (1) urgent need for intubation; (2) the patient's inability to maintain airway continuity; (3) presence of pneumothorax; (4) trauma; (5) cardiac arrhythmias or suspected MI; or (6) patients with tracheostomy. The consent of all patients enrolled in the study was obtained.

Randomization and Treatment

"Simple randomization" technique was used for the study. For the randomization procedure, 104 (52 for each group) closed envelopes were prepared. The patient group was determined by random selection of an envelope by the physician who made the decision for mechanical ventilation. The patients' physicians determined additional treatment and intervention needs of the patients, without interference.

NIMV patients were routinely monitored noninvasively for cardiac and respiratory parameters (Vismo patient monitor (PVM-2701), Nihon Kohden Corporation, Shinjuku-ku, Tokyo, Japan). An oronasal mask fitting the patient's face (Philips Respironics AF531 single-use oronasal mask) was applied. An intensive care type non-invasive mechanical ventilator (Respironics V60 ventilator, Respironics California Inc, Carlsbad, CA, USA) was used for non-invasive ventilation. At the beginning of the NIMV treatment, the following initial settings were used in the 2 groups.

AVAPS Group: Target TV: 6-8 mL/kg; EPAP: 6 cm H₂O; IPAP: a minimum of 12 cm H₂O and a maximum of 26 cm H₂O mmHG.

S/T Group: EPAP: 6 cm H₂O; IPAP: 12 cm H₂O mmHg at the beginning. IPAP was increased by 2 cm H₂O according to the patient's blood gas and clinical findings, under the physician's decision on patients' needs.

Monitoring and Data Collection

The socio-demographic data of the patients, medical history of previous diseases, NIMV indications, vital parameters (blood pressure, heart rate, SpO_2 , respiratory rate) obtained at the time of admission and at every 30 minutes, rating on the Glasgow Coma Scale (GCS), EPAP, IPAP, and TV values were recorded in the data form. The ABG findings (PaCO_2 , PaO_2 , pH, SpO_2) obtained at the 30th minute and first hour from the patient during monitoring were recorded in the data form. The length of hospital stay, patient outcomes, and the occurrence of a need for transition to another mode or intubation, were all recorded.

Primary and Secondary Outcomes

Primary outcomes: Improvement in PaCO_2 and pH values.

Secondary outcomes: Changing the present mode (transition to the second mode) due to treatment failure or patient's non-compliance; patient's need for intubation; ED outcomes.

Statistical Analysis

In the randomized controlled trial by Claudette et al.² comparing the addition of AVAPS to the BPAP S/T mode with the use of BPAP S/T mode alone in patients with hypercapnic encephalopathy, the effect size was calculated as 0.7578621 with the alpha error as 0.05 and power as 95%, a minimum of total sample size was determined as 94. The sample size was expanded by 10%, considering attritions, and based on this sample size calculation, the present study aimed to recruit 102 patients.

The Statistical Package for Social Sciences version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) statistical software package was used for data analysis. Descriptive statistics were presented with numbers and percentages for categorical variables, while they were presented using mean and standard deviation values for quantitative variables. The Kolmogorov–Smirnov test was used to evaluate the normality of distribution. Differences between the categorical variables in independent groups were tested with Chi-square analysis. The Mann–Whitney *U*-test was used to compare quantitative variables between independent groups. In group comparisons of

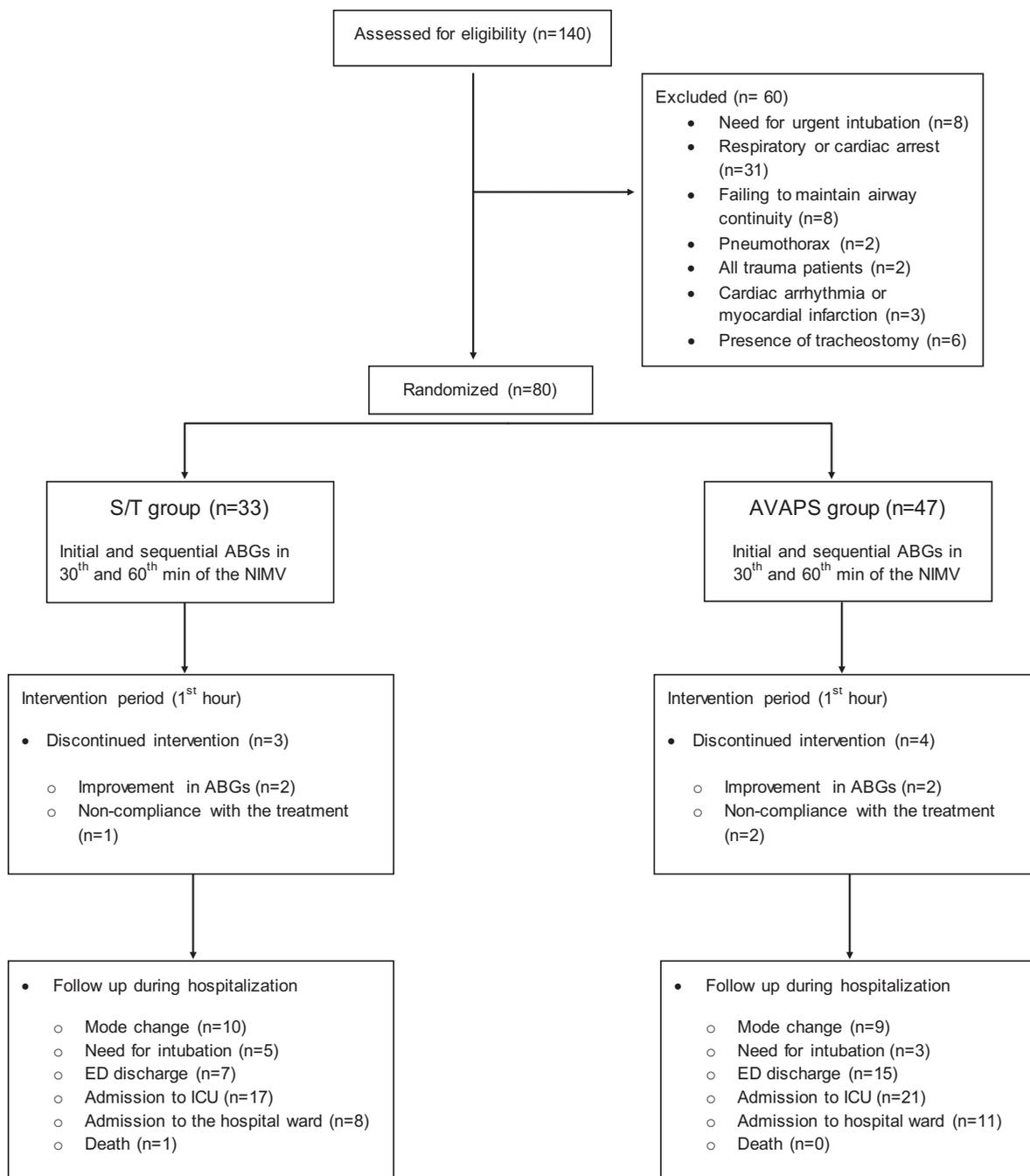


FIG. 1. The flow diagram of the study.

repeated measures (pH, PaCO₂, PaO₂, heart rate, systolic blood pressure, diastolic blood pressure, TV, IPAP, and EPAP), the measurements fitting normal distribution were compared with the repeated measures ANOVA, while ordinal and non-normal distribution data were compared using the Friedman test. The statistical significance was accepted as $P < .05$.

RESULTS

One hundred forty-eight patients were admitted to the ED with hypercapnic respiratory failure during the trial period. Eight patients refused to participate in the study. One hundred forty patients were assessed for eligibility, 60 patients were excluded, and 80 patients enrolled to randomization (Figure 1).

TABLE 1. Comparison of Patient Characteristics, Initial Vital Parameters, and ABG Levels Between the Groups

	S/T group	AVAPS group	P
Age*	78 (68-82)	72 (64-83)	.291
Oxygen saturation*(%)	90 (85-94.75)	89 (83-93)	.249
Systolic blood pressure*(mmHg)	132 (115.5-151.5)	138 (123-165)	.477
Diastolic blood pressure*(mmHg)	77.5 (69.5-91)	82 (70-92.5)	.309
Heart rate*(min)	101 (92.8-117.5)	103 (85-118)	.896
pH	7.28 (7.22-7.34)	7.28 (7.21-7.32)	.187
PaCO ₂ *(mmHg)	64 (55-68.9)	65 (57.8-76.5)	.440
PaO ₂ *(mmHg)	65.5 (56.1-84)	63 (52.3-81.4)	.945
GCS**	14 (10-15)	14 (9-15)	.992

*Values presented as median (IQR).
 **Values presented as median (min-max).
 GCS: Glasgow coma scale.

The mean age of the 80 patients included in the study was 72.7 ± 12.9 years (age range: 21-92), and 50% (n = 40) were male. COPD was the most common comorbid disease (n = 63; 78.8%). The median of pre-treatment of GCS values was 14 (9-15).

The age, comorbid diseases, vital signs, and baseline blood gas parameters of the AVAPS and S/T groups were compared, and no significant difference was found between the groups (Table 1). In the S/T group, 78.8% of the patients had COPD (n = 26) and 54.5% had congestive heart failure (n = 18); while 78.7% had COPD (n = 37), 36.2% had congestive heart failure (n = 17), and 4.3%

had interstitial lung disease (n = 2) in the AVAPS group. Initial and follow-up ABG parameters and vital signs during the treatment were compared and the results have been presented in Table 2.

In the S/T group, the median GCS was 15 (range: 12-15) in the evaluation made after 1 hour; a significant difference was found in repeated measurements (P = .009). Post hoc analysis indicated a significant improvement in the first 30 minutes (P = .002). In the AVAPS group, the median GCS was 15 (range: 13-15) in the evaluation made after 1 hour; a significant difference was found in repeated measurements (P < .001). Post hoc analysis indicated a significant improvement in the first 30 minutes (P = .002). GCS values during treatment have been presented in Table 2.

The blood gas parameters were compared and a significant improvement was observed in pH and PaCO₂ values in the follow-up (P = .006 and P = .005, respectively). Post hoc analysis did show a significant improvement in the pH of the first blood gas control (P = .06). The comparison of ABG parameters during treatment also have been presented in Table 2.

The NIMV treatment of 3 patients in the S/T group was terminated within the first 1 hour by their primary physicians; 2 of these were due to improvement in blood gas parameters, and the third was due to non-compliance with the treatment. The treatment of 4 patients in the AVAPS group was terminated within the first 1 hour by their primary physicians; 2 of these were due to improvement in blood gas and clinical parameters, and the other 2 were due to non-compliance with the treatment.

TABLE 2. Comparison of Vital Signs, ABG, and Ventilator Parameters During Treatment

	Initial	30th min	60th min	P
S/T group				
Heart rate (beats/min)	101 (92.8-117.5)	96.5 (88-116.5)	95 (88-115)	0.169
Systolic blood pressure (mm/hg)	132 (115.5-151.5)	122 (113-148.75)	128 (107-142)	0.341
Diastolic blood pressure (mm/hg)	77.5 (69.5-91)	76 (67.75-88.25)	72 (69-81)	0.858
Oxygen saturation (%)	90 (85-94.75)	93 (90.25-95)	94 (91-96)	0.003
GCS	14(12-15)	15(14-15)	15(14-15)	0.009
pH	7.28 (7.22-7.34)	7.32 (7.28-7.38)	7.33 (7.27-7.41)	0.006
PaCO ₂ (mm/hg)	64.1 (55-68.9)	60.2 (48.2-68.6)	56.3 (47-66)	0.005
PaO ₂ (mm/hg)	65.5 (56.1-84)	83.45 (69.2-125)	80 (69-108)	0.851
AVAPS group				
Heart rate (beats/min)	103 (85-118)	100 (87-112)	94 (85-108)	0.06
Systolic blood pressure (mm/hg)	138 (123-165)	129 (118-145)	123 (112-140)	<0.001
Diastolic blood pressure (mm/hg)	82 (70-92.5)	76 (70-83)	73 (65-80)	0.002
Oxygen saturation (%)	89 (83-93)	94 (89-96)	93 (89-96)	<0.001
GCS	14(13-15)	15(14-15)	15(14-15)	<0.001
pH	7.28 (7.21-7.32)	7.33 (7.28-7.37)	7.34 (7.3-7.39)	0.005
PaCO ₂ (mm/hg)	65 (57.8-76.5)	57 (51-68)	54.1 (45.5-63.7)	<0.001
PaO ₂ (mm/hg)	63 (52.3-81.4)	76.8 (55-95)	72.4 (61-87)	0.088

Values presented as median (IQR).
 GCS: Glasgow come scale.

TABLE 3. Comparison of the Changes in pH and PaCO₂

Differences	S/T group	AVAPS	P
	Median (IQR)	Median (IQR)	
Δ pH ₁ (mmHg)	0.03 (0.00-0.09)	0.04 (0.03-0.08)	.127
Δ pH ₂ (mmHg)	0.00 ([-]0.03-0.05)	0.02 (0.01-0.04)	.06
Δ pH ₃ (mmHg)	0.03 (0.00-0.11)	0.07 (0.04-0.10)	.015
Δ PaCO ₂₍₁₋₂₎ (mmHg)	3.30 (0.10-10.50)	7.60 (2.80-15.0)	.205
Δ PaCO ₂₍₂₋₃₎ (mmHg)	0.40 ([-]0.10-8.0)	2.40 ([-]0.30-9.00)	.11
Δ PaCO ₂₍₁₋₃₎ (mmHg)	4.75 ([-]0.83-16.88)	10.20 (6.20-19.20)	.033

Δ pH₁: pH difference between initial and 30th min ABG.

Δ pH₂: pH difference between 30th min and 60th min ABG.

Δ pH₃: pH difference between initial and 60th min ABG.

Δ PaCO₂₍₁₋₂₎: PaCO₂ difference between initial and 30th min ABG.

Δ PaCO₂₍₂₋₃₎: PaCO₂ difference between 30th min and 60th min ABG.

Δ PaCO₂₍₁₋₃₎: PaCO₂ difference between 30th min and 60th min ABG.

The difference between blood gas parameters evaluated in both groups and the previous measurements (delta values) was compared; there was an increase in pH values in the blood gases obtained after the first hour, with a median pH value of 0.07 (0.04-0.10) in the AVAPS group and 0.03 (0.00-0.11) in the S/T group. There was a significant difference between the groups ($P = .015$).

The improvements in PaCO₂ in blood gas were evaluated and there was a 10.20 (median) (6.20-19.20) mmHg decrease of PaCO₂ in the AVAPS group in the first hour, while there was a 4.75 ([-] 0.83-16.88) mmHg decrease in the S/T group. This indicated a significant difference between the groups ($P = .033$). No significant difference was found between the groups in terms of the changes in PaCO₂ and pH values over time when blood gas measurements were compared with repeated measurements ANOVA ($P = .141$ and $P = .271$, respectively). The comparative results of the changes in pH and PaCO₂ between sequential ABG evaluations have been presented in Table 3.

The length of hospital stay for the S/T group was 323.1 ± 499 hours (range: 17-1952), while it was 189.5 ± 187.1 hours (range: 2-720) for the AVAPS group. There was no significant difference between the groups in terms of the length of hospital stay ($P = .815$).

One patient needed intubation within the first 24 hours, and 1 patient died within 24 hours. Moreover, 38 patients (43.1%) were transferred to the intensive care unit.

During the ED follow-up, 3 (6.4%) patients in the AVAPS group and 5 (15.2%) patients in the S/T group needed intubation [Relative Risk (RR): 0.42 (95% CI: 0.11 to 1.64) $P = .21$]. The treatment of 13 patients (27.7%) in the AVAPS group and 8 patients (24.2) in the S/T group were terminated due to non-compliance with NIMV [RR: 1.14 (95% CI: 0.53 to 2.43) $P = .734$]. Mode change was made in 10 (30.3%) patients in the S/T group and 9 (19.1%) patients in the AVAPS group [RR: 0.69 (95% CI: 0.30 to 1.55) $P = .622$]. The procedure was terminated in 31 (66.0%) patients in the AVAPS group and 20 (60.6%) patients in the S/T group because NIMV was no longer required [RR: 0.86 (95% CI: 0.48 to 1.55) $P = .622$]. The comparative figures of mechanical ventilation success and outcomes in both groups have been presented in Table 4.

DISCUSSION

The AVAPS mode is a recently developed NIMV mode that is rarely used in acute cases.^{7,8} A few clinical studies have reported the mode to actively improve blood gas parameters in acute hypercapnic respiratory failure.^{2,8} Previous studies were conducted in intensive care settings; however, patients with respiratory failure are initially treated in EDs.^{2,8} In the study conducted by Briones Claudett et al., patients with hypercapnic respiratory failure were enrolled in a matched case control study, whereas our study conducted a randomized controlled trial. Furthermore, in this study, patients with hypercapnic respiratory failure had comparatively similar improvements in blood gas parameters, but with faster rates in the AVAPS mode than in BPAP S/T. This might be due to patients' comfort and compliance to the NIMV modes. However, in our study, this has not been evaluated.

NIMV is recommended as a first-line treatment in hypercapnic respiratory failure. In particular, NIMV treatment for COPD and OHS patients improves survival, decreases the need for intubation, and improves blood gas parameters. It is recommended that

TABLE 4. Comparison of Mechanical Ventilation Success and Outcomes in both Groups

	S/T, n (%)	AVAPS, n (%)	Relative risk (95% CI)
Reasons for quitting NIV			
Need for intubation	5 (15.2)	3(6.4)	0.42 (0.11-1.64)
Non-compliance with NIV	8 (24.2)	13 (27.7)	1.14 (0.53-2.43)
Mode change	10 (30,3)	9 (19,1)	0.69 (0.30-1.55)
Termination of NIV due to improvement in health	20 (60.6)	31 (66.0)	0.86 (0.48-1.55)
Emergency Department Outcomes			
Discharge from ED	7 (21.2)	15 (31.9)	1.38 (0.62-3.09)
Admission to intensive care	17 (51.5)	21 (44.7)	0.91 (0.54-1.53)
Admission to hospital ward	8 (24.2)	11 (23.4)	0.97 (0.43-2.20)
Death	1 (3)	0 (0)	0.24 (0.01-5.79)

these patients should be treated in intensive care settings.⁹ However, the use of NIMV in EDs is increasing, and mortality has been reported to decrease with NIMV treatment started in EDs in recent years.¹⁰ There is an increase in treatment success with NIMV and decreased mortality in patients with COPD exacerbations. Although the results of NIMV in intensive care units are slightly better, no differences have been shown on the outcomes in other health care areas.¹¹ In this regard, our study presents that different modes of NIMV can be applied to hypercapnic patients effectively in ED.

Studies show that the AVAPS mode can be used as effectively as the other modes in cases causing respiratory failures such as OHS, COPD, and kyphoscoliosis.¹²⁻¹⁴ In a previous study, the use of AVAPS was evaluated in 81 patients with acute hypercapnic respiratory failure in the ICU, and it was reported to have been used effectively.⁸ In a multicenter study by Briones Claudett et al., ST/T and AVAPS modes were compared in 22 patients with hypercapnic encephalopathy.² In this study, AVAPS was reported to provide better GCS improvements, but there was no significant difference in blood gases.² In our study, significant decreases were observed even in the first 30 minutes of blood gas control, in PaCO₂ of the AVAPS group. When partial carbon dioxide and pH levels, which are the study's primary objective, are considered, rapid and further improvement can be achieved with AVAPS. However, the comparison of both groups did not indicate a significant difference in terms of improvement in blood gas parameters similar to previous studies. NIMV treatment administered with both modes can effectively improve blood gas parameters.

One of the most important problems in hypercapnic respiratory failure is the emergence of consciousness disorder secondary to hypercapnia. Briones Claudett et al. reported that the AVAPS mode provided significant improvement in GCS of patients with hypercapnic encephalopathy.² Similarly, in our study, significant improvement in GCS was observed in patients treated with NIMV using AVAPS and S/T modes. This is an expected result due to the improvement in PaCO₂ levels in patients. Improvement of consciousness is one of the factors that reduce the need for intubation. NIMV treatment initiated in the early period in the ED reduces the need for additional intervention. However, several factors other than initial blood gas parameters, such as the severity of present clinical conditions, comorbid diseases, and the severity of respiratory diseases, may have affected the outcome of patients with hypercapnic respiratory failure.

In-hospital mortality of patients with hypercapnic respiratory failure is relatively high. In the analysis of 2693 patients who were administered NIMV for 2 months in 143 hospitals in the UK, 61% of the patients were diagnosed with COPD, 8% with decompensated heart failure, and 8% with OHS. Among these patients, the mortality of patients with COPD who had deeper acidosis was higher than those who had better pH values (36%, pH <7.26; 26%, pH 7.26-7.35). In this study, while the in-hospital mortality rate of patients receiving NIMV under intensive care conditions was 28%, the mortality rate of patients receiving non-intensive care treatment was reported to be 40%.¹⁵ Of the patients included in our study, 79.8% had COPD, and the mean pH was determined to be

7.27 ± 0.08. Although the patients' pH was low, in-hospital mortality was found to be 26.3%. The patients' pH levels were similar; however, the survival of the patients was found to be significantly better. These findings might have occurred due to the immediate initiation of the NIMV treatment in the ED. Also, the mortality of the patients did not increase despite the long stay in the ED, which may have resulted from the same approach.

Bilevel intensive care ventilators are available in our ED's resuscitation unit, and all physicians and nurses are trained and experienced in invasive and non-invasive ventilation. Due to the limited number of intensive care beds in our hospital and city, patients may have a longer length of stay in our ED. Additionally, to prove the insight and efficacy of this treatment, more studies evaluating the use of NIMV in hypercapnic respiratory failure in critical care areas such as EDs are needed. Our study presented that NIMV can be applied to hypercapnic respiratory failure patients, and both AVAPS and ST/T mode can be applied safely in this regard.

In our study, the mean length of the patients' ED stay was 49.3 ± 52.6 hours. The duration of hospital stay for 13 patients who were referred to external centers could not be determined. The duration of hospital stay for the remaining 67 patients was found to be 10.1 ± 14.5 days. Çiftçi et al. reported that the length of ICU stays in their study was 6.4 ± 2.5 days.⁸ The length of hospital stay in our study was longer than this study.⁸ These results may be due to the fact that the study by Çiftçi et al. was conducted in the patient wards and intensive care unit.⁸

This study has several limitations. Firstly, our study could not reach the targeted number of samples according to the calculations for sample size. Based on our center's prior admissions of hypercapnic patients, we applied for a recruitment window of 1 year, which was granted by the institutional review board; however study did not reach a sufficient number of participants, and therefore, application for an extension was made and was granted for 6 more months. During this time period (including extension), 140 patients were assessed for eligibility and 80 patients were analyzed during the trial. The study was concluded without recruiting more patients upon completing the trial time period approved by the ethics committee and our institution.

This study had also aimed to collect the opinions of the patients' comfort about NIMV methods. However, due to the seriousness of the patients' conditions included in the study and longer stay in ED than expected, this could not be obtained.

In the follow-up of NIMV treatment, the duration of the period for obtaining blood gases was entirely left to the physician's decision. Therefore, the collection of all blood gases could not be carried out regularly from the beginning of the treatment. No intervention was made by the study team except for mode selection at the beginning, and mode changes and settings were made by the primary physicians. The adjustment of the treatment parameters by a single team can improve the results significantly.

Thirteen of the patients included in the study were transferred to intensive care units of other hospitals. Although these patients

survival was evaluated, the length of their hospital stay could not be evaluated.

A faster improvement was observed in pH and PaCO₂ levels with the AVAPS mode compared to BPAP S/T in our study. However, no significant difference was found between the groups in the analysis of repeated measurements. While significant improvement was observed in GCS in both modes, systolic and diastolic blood pressure decreased significantly in the AVAPS group. However, there was no hemodynamic deterioration that occurred in any patient who required termination of NIMV. Although AVAPS is not superior to the routine BPAP S/T mode in patients admitting to the ED with hypercapnic respiratory failure, it is as safe and effective as S/T mode.

The study was presented as an oral presentation at the 6th Eurasian Congress on Emergency Medicine on November 8, 2018-November 11, 2018, Belek, Antalya, Turkey.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Dokuz Eylül University, (Approval No: 71146310 [2016-CE-006]).

Patient Consent for Publication: Informed consent was obtained from the patients.

Author Contributions: Concept - B.B.; Design - B.B., N.Z.G.; Supervision - B.B.; Resources - N.Z.G.; Data Collection and/or Processing - D.G., F.F.E.; Analysis and/or Interpretation - E.Ş., B.B.; Literature Review - N.Z.G., B.B., E.Ş.; Writing - B.B., N.Z.G.; Critical Review - E.Ş., F.F.E., D.G.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: This study was funded by Dokuz Eylül University Scientific Research Projects (2017.KB.SAG.033).

REFERENCES

- Bauman K. A, Hyzy R. C. Non-invasive positive pressure ventilation in acute respiratory failure in adults. Available at: <http://www.uptodate.com/contents/noninvasive-positive-pressure-ventilation-in-acute-respiratory-failure-in-adults#H23>. Accessed November 2, 2020.
- Briones Claudett KH, Briones Claudett M, Chung Sang Wong M, et al. Non-Invasive Mech Vent Average volume assured pressure support (AVAPS) in patients with chronic obstructive pulmonary disease and hypercapnic encephalopathy. *BMC Pulm. Med.* 2013;13:12.
- British Thoracic Society Standards of Care Committee. Non-invasive ventilation in acute respiratory failure. *Thorax.* 2002;57(3):192-211. [CrossRef]
- Kaya A. *Akciğer hastalıkları temel bilgiler, Türk toraks derneği*, S. Poyraz Tibbi Yayıncılık, Ankara; 2008:393-407.
- Murphy PB, Davidson C, Hind MD, et al. Volume targeted versus pressure support non-invasive ventilation in patients with super obesity and chronic respiratory failure: a randomized controlled trial. *Thorax.* 2012;67(8):727-734. [CrossRef]
- Couillard A, Pepin JL, Rabec C, et al. Non-invasive ventilation: efficacy of a new ventilator mode in patients with obesity hypoventilation syndrome. *Rev Mal Respir.* 2015;32(3):283-290. [CrossRef]
- Inonu H., Çelik D. Average volume-assured pressure support (AVAPS) mode in chronic respiratory failure: report of two cases. *Tur Toraks Der.* 2012;13(4):30-33. [CrossRef]
- Çiftçi F, Çiledağ A, Erol S, et al. Evaluation of the feasibility of average volume-assured pressure support ventilation in the treatment of acute hypercapnic respiratory failure associated with chronic obstructive pulmonary disease: A pilot study. *J Crit Care.* 2017;39:232-237. [CrossRef]
- Davidson AC, Banham S, Elliott M, et al. BTS/ICS guideline for the ventilator management of acute hypercapnic respiratory failure in adults. *Thorax.* 2016;71(2):1-35.
- Carteciano MC, Ibrahim I, Chan Y.H., Mahadevan M, Lim TK. Non-invasive ventilation in the emergency department from 2004-2015. *Eur Respir J.* 2016;48:3575. [CrossRef]
- Ram FS, Picot J, Lightowler J, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Systrev.* 2004;1:CD004104.
- Piesiak P, Brzecka A, Kosacka M, Jankowska R. Efficacy of non-invasive volume targeted ventilation in patients with chronic respiratory failure due to kyphoscoliosis. *Adv. Exp. Med. Biol.* 2015;838:53-58.
- Crisafulli E, Manni G, Kidonias M, Trianni L, Clini EM. Subjective sleep quality during average volume assured pressure support (AVAPS) ventilation in patients with hypercapnic COPD: a physiological pilot study. *Lung.* 2009;187(5):299-305. [CrossRef]
- Storre JH, Seuthe B, Fiechter R, et al. Average volume-assured pressure support in obesity hypoventilation: a randomized crossover trial. *Chest.* 2006;130(3):815-821. [CrossRef]
- Davies M. *Report British Thoracic Society NIV Audit 2013*. Available at: <https://www.brit-thoracic.org.uk/document-library/audit-and-quality-improvement/audit-reports/bts-adult-niv-audit-report-2013>. Accessed March 20, 2021.