Original Article

Non-invasive ventilation for acute respiratory failure: pressure support ventilation *vs.* pressure-controlled ventilation

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Background: The best ventilator mode for patients receiving non-invasive ventilation (NIV) has not been clarified. This study compared the effectiveness of two pressure-targeted modes, i.e., pressure support ventilation (PSV) and pressure-controlled ventilation (PCV), in patients receiving NIV.

Methods: This was a prospective multicentre observational study of NIV use for acute respiratory failure (ARF) in adult patients. We compared the two pressure-targeted modes in terms of NIV success and complication rates.

Results: Among 176 patients receiving NIV, 88 patients were included in the study (PCV mode, n=29; PSV mode, n=59). The study population had a median age of 73.0 years and median body mass index of 20.8 kg/m^2. The applied inspiratory positive airway pressure (IPAP) was higher in patients with PCV than in those with PSV [18.0 cmH_2O (15.0–20.5 cmH_2O) *vs.* 15.0 cmH_2O (12.0–17.0 cmH_2O), respectively, P=0.001]. More patients with PCV received sedatives and experienced dry mouth than those with PSV; however, the incidences of large leaks were low in both groups (n=5 *vs.* n=2, respectively). With regard to NIV outcomes, 24 (27.2%) patients experienced NIV failure and 13 (14.8%) died in hospital. PSV mode was a significant factor for NIV success [odds ratio (OR), 2.303; 95% confidence interval (CI), 1.216 to 4.360] in multivariate analyses and this association remained significant in a 1:1 matched cohort (n=29 per group).

Conclusions: In contrast to PCV mode, PSV mode was significantly associated with NIV success in the intensive care unit setting, particularly when large leaks were not a major concern. Nevertheless, further well-designed multicenter, protocol-driven randomized controlled trials are warranted.

Keywords: Non-invasive ventilation (NIV); acute respiratory failure (ARF); treatment outcome

Submitted Nov 11, 2019. Accepted for publication Feb 21, 2020.
doi: 10.21037/jtd.2020.03.27
View this article at: http://dx.doi.org/10.21037/jtd.2020.03.27

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Introduction

Non-invasive ventilation (NIV) has been widely used as the first-line strategy for improving oxygenation and ventilation in patients with acute respiratory failure (ARF) in the intensive care unit (ICU), with various applications in clinical practice, such as to facilitate early weaning from invasive mechanical ventilation (IMV) (1,2), for respiratory support after surgery (3), during certain procedures (4) or as palliative therapy (5). Its beneficial effects have been demonstrated in patients with acute hypercapnic respiratory failure (AHRF) (6), but questions remain regarding its efficacy for hypoxaemic respiratory failure, particularly *de novo* respiratory failure (7,8).

An NIV machine can deliver either pressure- or volume-targeted ventilation (9). Compared to volume-targeted ventilation, pressure-targeted ventilation has advantages of compensating for leaks and limiting high airway pressure (2,10-12). However, the most appropriate mode for NIV has not been clearly established. Pressure support ventilation (PSV), a flow-cycled mode, is widely used in many centres for AHRF. However, in the presence of large leaks, it can prolong inspiratory time, resulting in patient-ventilator asynchrony (12). By contrast, with assisted pressure-controlled ventilation (APCV), a time-cycled mode, the maximum inspiratory time can be set, theoretically achieving effective CO_2 removal and promoting better synchrony.

Only a few studies have reported comparisons of the two pressure-targeted NIV modes, and no significant differences were detected (12). This multicentre prospective observational study was performed to compare the two modes (PSV *vs.* PCV) in terms of NIV success and complication rates in the ICU setting.

Methods

Study population

This was a prospective multicentre observational study conducted in 20 ICUs of university-affiliated hospitals in South Korea from June 1, 2017, to February 28, 2018, and some of the data were previously reported (13). Adult patients (age >18 years) who were admitted to the ICUs and received NIV treatment (at least 2 h) for ARF were prospectively enrolled in the study. Among the indications for NIV, AHRF indicates respiratory failure in patients with chronic lung disease (obstructive or restrictive), and *de novo* ARF usually indicates respiratory failure in patients without chronic lung disease, mostly those with hypoxaemic respiratory failure, such as pneumonia, post-operative respiratory failure, sepsis or acute respiratory distress syndrome (ARDS) (14,15). Among all patients initially included in the study, we excluded patients with do-not-resuscitate (DNR) orders and finally selected only patients treated with PCV or PSV mode.

The ethics committees of all participating hospitals approved this study, as did the Hallym University Institutional Review Board (approval no. 2017-I044). Informed consent was obtained from all enrolled patients or their legal surrogates.

Data collection and outcomes

We collected patient demographic information and the following data: comorbidities, underlying lung diseases, primary indications for NIV, and Richmond Agitation Sedation Score (RASS) and Sequential Organ Failure Assessment (SOFA) immediately before starting NIV. We also assessed the results of arterial blood gas analyses as well as vital signs before and 2 h after commencement of NIV. We investigated the type of NIV machine [i.e., invasive mechanical ventilator (IMV) with NIV module, IMV without NIV module, or home mechanical ventilator (MV)] and the interface (i.e., oronasal, nasal or total facial mask, helmet). In addition, the NIV settings [fractional inspired oxygen (FiO_2), inspiratory positive airway pressure (IPAP), expiratory positive airway pressure (EPAP), and tidal volume] and their median durations (hours/day) were also investigated.

Treatment success and failure rates, complications from NIV treatment and ICU and in-hospital mortality rates were investigated as patient outcomes. Treatment success indicated successful weaning from NIV (i.e., a minimal duration of 24 h without NIV); the overall duration of NIV was determined by the physician in charge based on clinical improvement and arterial blood gas results. Treatment failure was defined as: (I) endotracheal intubation and invasive MV; (II) tracheostomy; and (III) hopeless discharge with NIV device. The following criteria were used for endotracheal intubation: (I) loss of consciousness; (II) hemodynamic instability (i.e., systolic blood pressure <90 mmHg despite fluid or need for vasopressors); and (III) worsening of respiratory distress under NIV (i.e., respiratory rate >40 breaths/minute or SpO_2 remaining below 90% despite FiO_2 100%). Patients who died within 24 h of NIV weaning were also classified as NIV failures.

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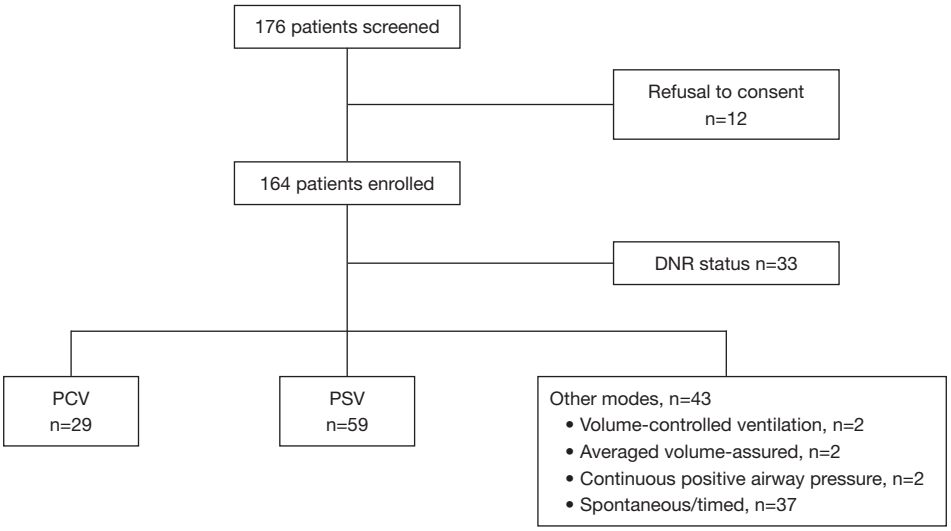

Figure 1 Flow chart of enrolled patients. DNR, do not resuscitation; PCV, pressure-controlled ventilation; PSV, pressure-support ventilation.

Large leaks were defined as leak flow >60 L/min or when the attending physician considered it too large to allow the treatment to continue.

The primary outcomes in this study were comparisons of NIV success and complication rates between patients treated with PCV *vs.* PSV mode. Secondary outcomes were risk factors for NIV success and in-hospital mortality rates.

Statistical analyses

All categorical variables are presented as numbers with percentages, and all continuous variables are presented as medians with interquartile ranges. Mann-Whitney U test was used to compare continuous variables, and the chi-square or Fisher's exact test was used to compare categorical variables. Logistic regression analyses were performed using covariates with P<0.10 in univariate analyses to identify independent factors for NIV success (and in-hospital mortality); we employed a backward stepwise selection method based on the likelihood ratio. To reduce selection bias and confounding effects, we also performed matched analysis. We matched the patients with nearest-neighbor matching method, in a 1:1 ratio (PCV *vs.* PSV), for severity and other baseline variables which were significantly different between the two groups. All statistical analyses were performed using R, version 3.3.1, (R Foundation Inc.; http://cran.r-project. org/). In all analyses, P<0.05 was taken to indicate statistical significance.

Results

Study population

During the study period, 176 patients with ARF receiving NIV in the ICUs were initially included. After excluding 88 patients (withholding of consent, n=12; DNR order, n=33; other NIV modes, n=43), 88 patients (PCV, n=29; PSV, n=59) were included (*Figure 1*). The median age of the study population was 73.0 years (66.3–79.0 years), and 39 (44.3%) patients were female (*Table 1*). Eight patients had active cancer and five were in an immunocompromised state other than cancer. As the primary indication for NIV, AHRF was the most common (n=43, 48.9%), followed by post-extubation respiratory failure (PERF, n=33) and *de novo* ARF (n=10). Obstructive lung disease was the most common underlying lung disease (n=51), and a total of 20 patients (22.7%) received at least one sedative, among which remifentanil was the most commonly used (n=12).

NIV machine and interfaces

IMV with NIV mode was used in 95.5% of the patients, IMV without NIV mode was used in one patient and a home ventilator was used in three patients (*Table 2*). The orofacial mask was the most common interface used (86.4%), and there were no significant differences in NIV machine or interfaces used between the PCV and PSV groups. NIV time (h/day) and NIV days were also similar between the

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Table 1 Comparison of baselines characteristics

Characteristics	PCV (n=29)	PSV (n=59)	P
Age, years	74.0 (64.5 to 78.0)	73.0 (67.0 to 80.0)	0.797
Sex, male/female	15/14	20/39	0.193
Body mass index, kg/m^2	20.2 (16.2 to 24.9)	21.4 (18.4 to 25.9)	0.077
SOFA[a]	4.0 (3.0 to 6.0)	3.0 (2.0 to 5.0)	0.164
RASS[a]	0.0 (–1.0 to 0.5)	0.0 (–1.0 to 1.0)	0.255
Comorbidities			
Heart	10 (34.5)	12 (20.3)	0.150
Chronic kidney disease	2 (6.9)	8 (13.6)	0.487
Liver cirrhosis	1 (3.4)	2 (3.4)	1.000
Cerebrovascular accidents	5 (17.2)	5 (8.5)	1.000
Active cancer	3 (10.3)	5 (8.5)	1.000
Immunocompromised	1 (3.4)	4 (6.8)	1.000
Underlying lung conditions			0.947
Normal	6 (20.7)	15 (25.4)	
Obstructive	17 (58.6)	34 (57.6)	
Restrictive	5 (17,2)	8 (13.6)	
Undetermined	1 (3.4)	2 (3.4)	
Reasons for NIV start			
AHRF	16 (55.2)	27 (45.8)	0.407
De novo RF	3 (10.3)	7 (11.9)	1.000
PERF	9 (31.0)	24 (40.7)	0.380
CPE	1 (3.4)	1 (1.7)	1.000
Hypercapnia	25 (86.2)	41 (69.5)	0.118
Lactate, mmol/L*	0.9 (0.6 to 1.5)	1.3 (0.9 to 1.8)	0.046
Use of HFNC*	9 (31.0)	21 (40.4)	0.403

Data are presented as median (interquartile range) or number (percentage). [a], pre-NIV value; *, pre-NIV values. AHRF, acute hypercapnic respiratory failure; COPD, chronic obstructive pulmonary disease; CPE, cardiogenic pulmonary edema; HFNC, high flow nasal cannula; NIV, non-invasive ventilation; PCV, pressure controlled ventilation; PERF, post-extubation respiratory failure; PSV, pressure support ventilation; RF, respiratory failure; RASS, Richmond agitation and sedation scale; SOFA, sequential organ failure assessment.

two groups. However, during NIV treatment, more patients in the PCV group used sedatives than in the PSV group [12 (41.4%) *vs.* 8 (13.6%), respectively, P=0.003]. Applied inspiratory positive airway pressure (IPAP) was significantly higher in the PCV group than the PSV group [18.0 cmH_2O (15.0–20.5 cmH_2O) *vs.* 15.0 cmH_2O (12.0–17.0 cmH_2O), respectively, P=0.001]. There were no differences in arterial blood gas parameters (in both pre-NIV and post-2-h-NIV periods) between the two groups. However, pre-NIV respiratory rate tended to be higher in the PCV group (*Table 3*). With regard to the differences (i.e., delta values) between pre-NIV and post-2-h-NIV periods, the arterial blood gas parameters and vital signs were similar between the PCV and PSV groups (data not shown).

NIV outcomes and complications

NIV success was achieved in 64 (72.7%) patients; among

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Table 2 Comparison of NIV treatments and outcomes between PCV and PSV groups

Treatments and outcomes	PCV (n=29)	PSV (n=59)	P
NIV machine			0.795
IMV with NIV mode	28 (96.6)	56 (94.9)	
IMV without NIV mode	0 (0.0)	1 (1.7)	
Home ventilator	1 (3.4)	2 (3.4)	
Interfaces			0.315
Orofacial mask	26 (89.7)	50 (84.7)	
Helmet	2 (6.9)	7 (11.9)	
Nasal mask	1 (3.4)	2 (3.4)	
NIV settings			
IPAP, cmH_2O	18.0 (15.0 to 20.5)	15.0 (12.0 to 17.0)	0.001
EPAP, cmH_2O	5.0 (5.0 to 6.0)	5.0 (4.0 to 6.0)	0.801
Tidal volume, mL	454.4 (364.3 to 538.7)	400.0 (311.3 to 524.8)	0.208
Change of NIV machine	4 (13.8)	7 (11.9)	1.000
Change of interface	3 (10.3)	6 (10.2)	1.000
Use of sedatives	12 (41.4)	8 (13.6)	0.003
Complications during NIV	6 (20.7)	12 (20.3)	0.969
Skin erythema	1 (3.4)	8 (13.6)	0.261
Abdominal distension	1 (3.4)	3 (5.1)	1.000
Dry mouth	4 (13.8)	0 (0.0)	0.010
Aspiration	3 (10.3)	2 (3.4)	0.326
Claustrophobia	0 (0.0)	1 (1.7)	1.000
Nasal congestion	1 (3.4)	0 (0.0)	0.330
Large leaks	2 (6.9)	5 (8.5)	1.000
NIV duration, hours/day	17.0 (3.8 to 24.0)	12.0 (4.0 to 20.0)	0.308
NIV, days	2.0 (1.0 to 3.5)	2.0 (1.0 to 5.0)	0.431
ICU, days	14.0 (7.5 to 21.0)	11.0 (6.0 to 17.0)	0.191
NIV success	16 (55.2)	48 (81.4)	0.020
ICU survival	25 (86.2)	56 (94.9)	0.212
Hospital survival	22 (75.8)	53 (89.8)	0.111

Data are presented as median (interquartile range) or number (percentage). EPAP, expiratory positive airway pressure; ICU, intensive care unit; IMV, invasive mechanical ventilator; IPAP, inspiratory positive airway pressure; NIV, non-invasive ventilation; PCV, pressure-controlled ventilation; PIP, peak inspiratory pressure; PSV, pressure support ventilation.

them, 15 patients were weaned off NIV in the general ward. The PSV group had a higher NIV success rate than the PCV group (81.4% *vs.* 55.2%, P=0.020; *Table 2*). Among 24 (27.3%) patients with NIV failure, 20 were intubated and received invasive ventilation, and four underwent tracheostomy. The most common reasons for NIV failure were the lack of arterial blood gas improvement (n=9) or absence of clinical improvement (n=7; *Table 4*). With

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Table 3 Comparison of vital signs and arterial blood gas between PCV and PSV groups

Variables	PCV (n=29)	PSV (n=59)	P
Pre NIV			
pH	7.36 (7.32 to 7.42)	7.40 (7.32 to 7.45)	0.318
P_aO_2/FiO_2, mmHg	198.8 (140.0 to 243.0)	225.0 (162.5 to 299.0)	0.189
P_aCO_2, mmHg	59.0 (48.6 to 67.0)	52.0 (40.8 to 66.7)	0.196
Systolic blood pressure, mmHg	128.0 (113.0 to 145.5)	135.0 (116.0 to 150.0)	0.374
Heart rate, min^{-1}	94.0 (84.0 to 107.0)	95.0 (81.0 to 109.0)	0.591
Respiratory rate, min^{-1}	26.0 (22.5 to 31.5)	24.0 (20.0 to 28.0)	0.074
Body temperature, ℃	36.9 (36.7 to 37.4)	36.8 (36.5 to 37.1)	0.219
Lactate, mmol/L	0.9 (0.6 to 1.5)	1.3 (0.9 to 1.8)	0.046
Post NIV (2 h)			
pH	7.41 (7.35 to 7.45)	7.42 (7.40 to 7.47)	0.608
P_aO_2/FiO_2, mmHg	226.6 (166.8 to 278.0)	226.9 (169.8 to 299.2)	0.567
P_aCO_2, mmHg	48.7 (45.0 to 61.5)	47.0 (40.4 to 61.3)	0.633
Systolic blood pressure, mmHg	121.0 (106.0 to 142.5)	130.0 (116.5 to 145.0)	0.114
Heart rate, min^{-1}	90.0 (81.5 to 105.0)	92.5 (80.0 to 101.7)	0.971
Respiratory rate, min^{-1}	25.0 (20.5 to 28.0)	23.0 (19.0 to 27.0)	0.285
Body temperature, ℃	36.8 (36.6 to 37.4)	36.9 (36.5 to 37.1)	0.498
Lactate, mmol/L	1.0 (0.6 to 1.6)	1.3 (0.9 to 1.8)	0.228

Data are presented as median (interquartile range). NIV, non-invasive ventilation; PCV, pressure-controlled ventilation; PSV, pressure support ventilation.

Table 4 Reasons for NIV failure (n=24)

Reasons for NIV failure	AHRF (n=11)	De novo RF (n=6)	PERF (n=6)	CPE (n=1)
Inadequate efficacy	7	4	4	1
Lack of ABGA improvement	3	2	3	1
Absence of clinical improvement	4	2	1	0
Interface intolerance	4	0	0	0
Large leak	0	1	1	0
Agitation	0	1	0	0
Copious secretion	0	0	1	0

ABGA, arterial blood gas analysis; AHRF, acute hypercapnic respiratory failure; CPE, cardiogenic pulmonary edema; ICU, intensive care unit; NIV, non-invasive ventilation; PERF, post-extubation respiratory failure; RF, respiratory failure.

regard to the primary indications for NIV, *de novo* ARF was more frequent in patients with NIV failure than in those with NIV success (25.0% *vs.* 6.3%, respectively, P=0.022; *Table S1*). A total of 18 (20.5%) patients experienced complications associated with NIV treatment; skin erythema was the most common and large leaks were reported in seven patients (*Table 2*). However, dry mouth was more frequent in the PCV group than the PSV group

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Table 5 Univariable and multivariable analyses for predictors of NIV success*

Variables	OR†	P	OR (95% CI)#	P
Immunocompromised	0.079	0.027	0.034 (0.002 to 0.577)	0.019
Change of NIV machine	0.250	0.039	–	–
Large leaks	0.246	0.082	–	–
De novo RF	0.200	0.021	0.141 (0.022 to 0.891)	0.037
Use of sedatives	0.825	0.044	–	–
PSV *vs.* PCV	3.545	0.012	2.302 (1.216 to 4.360)	0.010
Post-2 h-NIV HR	0.978	0.090	–	–
Post-2 h-NIV RR	0.886	0.009	0.865 (0.772 to 0.970)	0.013
NIV days	1.558	0.008	1.548 (1.036 to 2.312)	0.033

*, Hosmer-Lemeshow test: chi-square =9.562 and P=0.297; †, univariable analysis; #, multivariable analysis. CI, confidence intervals; HR, heart rate; OR, odds ratio; PCV, pressure-controlled ventilation; PSV, pressure support ventilation; RR, respiratory rate; RF respiratory failure.

(13.8% *vs.* 0.0%, respectively, P=0.010).

Risk factors for NIV outcomes

In univariate analyses, nine variables were associated with NIV success (P<0.10; *Table S1*). In multivariate analyses, five variables (immunocompromised condition, *de novo* respiratory failure, post-2-h-NIV respiratory rate, NIV days, and PSV mode) were significantly associated with NIV success, and PSV mode showed an OR of 2.302 (95% CI, 1.216–4.360) for NIV success (*Table 5*). However, 75 (85.2%) patients survived to discharge (*Table S2*); 15 (62.5%) patients in the NIV failure group (n=24) survived. In multivariate analyses, PERF and low post-2-h-NIV heart rate were significantly associated with survival until discharge (*Table S3*).

For the analysis of matched data, the two groups (PSV *vs.* PCV) were matched for age, gender, SOFA, pre-NIV lactate, reasons for NIV, IPAP levels, and use of sedatives (i.e., 29 pairs). The baseline characteristics were well balanced between the two groups (*Tables S4-S6)*. In the multivariate analysis, where seven variables were finally included, PSV mode was a significant factor for NIV success (OR, 4.080; 95% CI, 1.020–16.321; *Table S7)*.

Discussion

This study yielded several interesting results. First, PSV mode was associated with the use of lower IPAP levels than PCV mode in patients receiving NIV for ARF in the ICU setting. Second, the frequency of sedative use and the occurrence of dry mouth were higher in the PCV group than the PSV group. Finally, the OR of NIV success in the PSV group was double that in the PCV group; this association remained significant in the matched cohort.

The present study was small sized and study population was heterogeneous; both NIV failure and mortality rates varied depending on the causes of ARF (i.e., AHRF, *de novo* ARF, PERF and cardiogenic pulmonary oedema; *Table S2*). However, to date, few studies have compared the two pressure-targeted modes in patients receiving NIV for ARF. Previously, NIV failure and mortality rates were reported to be higher in patients with *de novo* ARF (i.e., 37–51.6% and 28.2–35.8%, respectively) (16-18) than in those with AHRF, PERF or receiving NIV for facilitation of IMV weaning (6,19-25). Both NIV failure and mortality rates were less than 30% in the latter three groups. Hence, the NIV outcomes in our cohort seemed to be comparable to those in previous studies. In our cohort, however, the use of NIV for facilitation of IMV weaning was not identified as a separate category from the PERF group. Besides, the NIV success group included patients who were transferred to the general ward in a stable condition with the NIV device in place (n=15); all patients were ultimately weaned off NIV and afterwards, two died.

Patients treated with other modes, mostly Spontaneous/Time (S/T) mode, were excluded from the present study because the aim was to compare the PCV and PSV modes among patients with NIV treatment. However, the rate of NIV success was also significantly higher in patients with

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PSV mode than other modes [81.4% (48/59) *vs.* 62.8% (27/43), respectively, P=0.032]. These results suggest that NIV mode where the cycle variable depends on the patient's inspiratory effort may be better or more suitable for patients with ARF in the ICU setting. However, Kirakli *et al.* reported that PCV mode may be more effective for eliminating CO_2 compared to PSV mode and may be better tolerated in patients requiring high inspiratory flow rate in the presence of leaks (12). In the presence of large leaks, patients with PSV mode may experience difficulty terminating inspiratory phase, leading to patient-ventilator asynchrony. In the present study, although we did not obtain detailed data on the inspiratory times or air leaks, the frequency of large leaks was low in both groups (n=2 in PSV mode *vs.* n=5 in PCV mode). This may have mitigated the negative effects of PSV.

Interestingly, the level of IPAP was higher in the PCV group than the PSV group. Although data are not shown, IPAP was significantly correlated with pre-NIV $PaCO_2$ (r=0.333 and P=0.002) and pre-NIV pH (r=−0.297 and P=0.005). Therefore, it is likely that patients with high $PaCO_2$ were treated with a high level of IPAP using PCV mode. Patients with PCV mode required sedatives and experienced dry mouth more frequently, which may be explained by their high levels of IPAP. However, it should be noted that although the goal of NIV application is to increase alveolar ventilation leading to decreased work of breathing, the high pressure support levels (to increase alveolar ventilation) may not be useful (or may rather be harmful) because they are not associated with the recruitment of the poorly ventilated area (12,26).

The higher NIV success rate with PSV mode may have been due to better patient-ventilator synchrony compared to PCV mode. However, we do not have any specific data supporting the association. Instead, as initial SOFA score and pre-NIV $PaCO_2$ were lower and pre-NIV PaO_2/FiO_2 was higher in the PSV group, it is possible that the lower disease severity influenced the lower level of IPAP and higher rate of NIV success (27). In addition, as mentioned above, the occurrence of large leaks, which can compromise patient-ventilator synchrony with PSV mode, was uncommon in our patients. However, importantly, some different baseline characteristics and the observational nature of our study suggest that our data were prone to have selection bias (or confounding effects). To control this effect, we matched patients for several baseline variables, including severity score, and found that the association of PSV mode with NIV success remained significant in the matched cohort. Nonetheless, considering the small sample size and potential confounders, there might be overfitting of the multivariate models.

The present study has some limitations. First, there may have been unintended bias in the results because our study was not randomised and sample size was small. Again, we cannot exclude confounding effects entirely. Second, we did not use a protocol driven algorithm for NIV treatment. Hence, the selection of mode or change of NIV machine was determined at the discretion of participating physicians, and the practice for NIV treatment varied among the participating hospitals. Third, a large number of patients who consented to the study were initially excluded, and there were multiple indications for NIV treatments (i.e., heterogeneity of study population). Fourth, uniquely, the variation of body mass index was smaller, compared to that of other studies (28-30), which could limit the generalisability of the study. This must be taken into consideration when interpreting our results. Fifth, despite the significant association with NIV success, the PSV mode was not associated with hospital survival. Although the hospital (and ICU) survival rate was numerically lower in PCV group *vs.* PSV group, further studies with a larger sample size will be needed to clarify this. Sixth, for the majority of patients (96.6%), an IMV machine was used for NIV instead of a dedicated NIV machine, and in particular, four patients used dissimilar NIV machine. Finally, we could not investigate the long-term outcomes among patients. However, to date, there have been few studies comparing the two pressure-targeted modes among patients receiving NIV for ARF. Hence, our results are meaningful and may prompt future studies on interesting topics. For example, it may be possible to find subgroups that are best fit for PSV mode (or PCV mode) through future well-designed studies.

Conclusions

In conclusion, we found that PSV mode was significantly associated with higher rate of NIV success than PCV mode in the ICU setting, particularly when the occurrence of large leaks is not a major concern. However, the mode was not associated with better hospital survival. Future large-scale, protocol-driven, randomised controlled trials are needed to confirm our results.

Acknowledgments

The authors sincerely thank the following investigators

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of Korean NIV study group for the participation in this study: Jin Woo Kim (The Catholic University of Korea, Uijeongbu St. Mary's Hospital), Jong Hoo Lee (Jeju National University Hospital), Tae Oak Kim (Chonnam National University Hospital), Seung Yong Park (Chonbuk National University Hospital), M.D Won-Il Choi (Kyeimyung University Dongsan Hospital), and Yun Su Sim (Hallym University Kangnam Sacred Heart Hospital).
Funding: None.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jtd.2020.03.27). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The ethics committees from all participating hospitals approved this study, as did the Hallym University Institutional Review Board (approval no. 2017-I044). Informed consent was obtained from all enrolled patients or their legal surrogates.

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Cite this article as: Nam H, Cho JH, Park TS, Kim SW, Kang HK, Shin YM, Hwang JJ, Lee K, Ha JH, Lee YS, Chang Y, Park S; on behalf of Korean NIV Study Group. Non-invasive ventilation for acute respiratory failure: pressure support ventilation *vs.* pressure-controlled ventilation. J Thorac Dis 2020;12(5):2553-2562. doi: 10.21037/jtd.2020.03.27

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Supplementary

Table S1 Comparisons between patients with NIV success and those with NIV failure

Patient characteristics and outcomes	NIV failure (n=24)	NIV success (n=64)	P
Age, years	74.0 (66.3 to 77.8)	72.5 (65.5 to 80.0)	0.837
Sex, male/female	16/8	38/26	0.532
Body mass index, kg/m^2	20.2 (16.4 to 25.3)	20.8 (18.0 to 25.4)	0.549
SOFA[a]	4.0 (3.0 to 7.0)	3.0 (2.0 to 5.0)	0.125
RASS[a]	0.0 (–1.0 to 1.0)	0.0 (–1.0 to 1.0)	0.965
Comorbidities			
Heart disease	8 (33.3)	14 (21.9)	0.269
Chronic kidney disease	3 (12.5)	7 (10.9)	1.000
Liver cirrhosis	1 (4.2)	2 (3.1)	1.000
Cerebrovascular accidents	2 (8.3)	8 (12.5)	0.721
Active cancer	4 (16.7)	4 (6.3)	0.206
Immunocompromised	4 (16.7)	1 (1.6)	0.018
Underlying lung conditions			0.441
Normal	7 (29.2)	14 (21.9)	
Obstructive	12 (50.0)	39 (60.9)	
Restrictive	5 (20.8)	8 (12.5)	
Undetermined	0 (0.0)	3 (4.7)	
Reasons for NIV start			
AHRF	11 (45.8)	32 (50.0)	0.728
De novo RF	6 (25.0)	4 (6.3)	0.022
PERF	6 (25.0)	27 (42.2)	0.138
CPE	1 (4.7)	1 (1.7)	0.473
Hypercapnea (>45 mmHg)[a]	19 (79.2)	47 (73.4)	0.580
Lactate, mmol/L*	1.0 (0.6 to 1.6)	1.25 (0.83 to 1.67)	0.248
Use of HFNC*	10 (43.5)	20 (34.5)	0.450
NIV machine			0.931
IMV with NIV mode	23 (95.8)	61 (95.3)	
IMV without NIV mode	0 (0.0)	1 (1.5)	
Home ventilator	1 (4.2)	2 (3.1)	
Interfaces			0.287
Orofacial mask	20 (83.3)	56 (87.5)	
Helmet	2 (8.3)	1 (1.6)	
Nasal mask	2 (8.3)	7 (10.9)	
NIV settings			
PSV/PCV	11/13	48/16	0.020
IPAP, cmH_2O	16.5 (13.3 to 21.0)	16.0 (12.3 to 18.0)	0.170
EPAP, cmH_2O	5.0 (4.3 to 6.0)	5.0 (5.0 to 6.0)	0.922
PIP, cmH_2O	16.0 (14.0 to 21.0)	16.0 (13.0 to 18.0)	0.288
Tidal volume, mL	449.0 (305.3 to 591.5)	402.5 (347.5 to 521.0)	0.732
Change of NIV machine	6 (25.0)	5 (7.8)	0.063
Change of Interface	3 (12.5)	6 (9.4)	0.700
Use of sedatives	9 (37.5)	11 (17.2)	0.051
Post-NIV (2 h)			
pH	7.33 (7.43 to 7.45)	7.41 (7.36 to 7.47)	0.784
P_aO_2/FiO_2, mmHg	228.0 (152.0 to 305.0)	222.0 (180.6 to 289.0)	0.784
PCO_2, mmHg	48.0 (40.9 to 57.0)	48.7 (41.4 to 62.5)	0.672
Systolic blood pressure, mmHg	128.0 (114.0 to 146.0)	127.5 (113.3 to 143.5)	0.541
Heart rate, min^{-1}	94.0 (87.0 to 114.0)	90.0 (79.0 to 99.5)	0.068
Respiratory rate, min^{-1}	27.0 (21.0 to 31.0)	22.0 (19.0 to 26.0)	0.018
Body temperature, ℃	36.8 (36.4 to 37.4)	36.9 (36.6 to 37.2)	0.650
Complications during NIV	5 (20.8)	13 (20.3)	1.000
Skin erythema	0 (0.0)	9 (14.1)	0.107
Abdominal distension	1 (4.2)	3 (4.7)	1.000
Dry mouth	1 (4.2)	3 (4.7)	1.000
Aspiration	2 (8.3)	3 (4.7)	0.611
Claustrophobia	0 (0.0)	1 (1.6)	1.000
Nasal congestion	1 (4.2)	0 (0.0)	0.273
Large leaks	4 (16.7)	3 (4.7)	0.085
NIV duration, hours/day	8.5 (2.3 to 21.7)	12.0 (5.5 to 21.5)	0.130
NIV days	1.0 (1.0 to 2.0)	3.0 (1.0 to 5.0)	0.001
ICU survival	17 (70.8)	64 (100.0)	<0.001
Hospital survival	15 (62.5)	60 (93.8)	0.001

Data are presented as median (interquartile range) or number (percentage). [a], pre-NIV value; *, pre-NIV values. AHRF, acute hypercapnic respiratory failure; COPD, chronic obstructive pulmonary disease; CPE, cardiogenic pulmonary edema; EPAP, expiratory positive airway pressure; HFNC, high flow nasal cannula; ICU, intensive care unit; IMV, invasive mechanical ventilator; IPAP, inspiratory positive airway pressure; NIV, non-invasive ventilation; PERF, post-extubation respiratory failure; PIP, peak inspiratory pressure; RF, respiratory failure; RASS, Richmond agitation and sedation scale; SOFA, sequential organ failure assessment.

Table S2 NIV and hospital outcomes by reasons for NIV use

Reasons for NIV use	NIV failure	ICU mortality	Hospital mortality	Length of ICU stay (days)
AHRF (n=43)	11 (25.6)	4 (9.3)	9 (20.0)	9.0 (5.0 to 20.0)
De novo RF (n=10)	6 (60.0)	2 (20.2)	2 (20.0)	14.5 (5.3 to 20.0)
PERF (n=33)	6 (18.2)	0 (0.0)	1 (3.0)	13.0 (8.0 to 20.0)
CPE (n =2)	1 (50.0)	1 (50.0)	1 (50.0)	2.0 and 41.0

Data are presented as median (interquartile range) or number (percentage). AHRF, acute hypercapnic respiratory failure; CPE, cardiogenic pulmonary edema; ICU, intensive care unit; NIV, non-invasive ventilation; PERF, post-extubation respiratory failure; RF, respiratory failure.

Table S3 Univariable and multivariable analyses for predictors of hospital survival*

Variables	OR[†]	P	OR (95% CI)[#]	P
RASS	1.511	0.076	–	–
Active cancer	0.238	0.092	–	–
PERF	8.930	0.027	13.412 (1.193 to 150.743)	0.035
Post-2 h-NIV HR	0.959	0.018	0.944 (0.893 to 0.998)	0.044
Post-2 h-NIV RR	0.872	0.054	–	–
NIV success	3.852	0.001	–	–
Length of ICU stay	0.960	0.018	–	–

*, Hosmer-Lemeshow test: chi-square =6.445 and P=0.597; [†], univariable analysis; [#], multivariable analysis. CI, confidence intervals; OR, odds ratio; HR, heart rate; ICU, intensive care unit; NIV, non-invasive ventilation; RR, respiratory rate; PERF, post-extubation respiratory failure.

Table S4 Comparison of baseline characteristics between the two matched groups*

Characteristics	PCV (n=29)	PSV (n=29)	P
Age, years	74.0 (64.5 to 78.0)	74.0 (66.0 to 79.5)	0.907
Sex, male/female	15/14	18/11	0.426
Body mass index, kg/m^2	20.2 (16.2 to 24.9)	20.7 (18.7 to 25.5)	0.086
SOFA[a]	4.0 (3.0 to 6.0)	3.0 (2.0 to 5.0)	0.141
RASS[a]	0.0 (−1.0 to 0.5)	0.0 (−1.0 to 1.0)	0.256
Comorbidities			
Heart disease	7 (24.1)	10 (34.5)	0.387
Chronic kidney disease	2 (6.9)	4 (13.8)	0.670
Liver cirrhosis	1 (3.4)	1 (3.4)	1.000
Cerebrovascular accidents	5 (17.2)	3 (10.3)	0.706
Active cancer	3 (10.3)	2 (6.9)	1.000
Immunocompromised	1 (3.4)	0 (0.0)	1.000
Underlying lung conditions			0.659
Normal	6 (20.7)	8 (27.6)	
Obstructive	17 (58.6)	18 (62.1)	
Restrictive	5 (17.2)	2 (6.9)	
Undetermined	1 (3.4)	1 (3.4)	
Reasons for NIV start			
AHRF	16 (55.2)	15 (51.7)	0.792
De novo RF	3 (10.3)	4 (13.8)	1.000
PERF	9 (31.0)	10 (34.5)	0.780
CPE	1 (3.4)	0 (0.0)	1.000
Hypercapnea	25 (86.2)	23 (79.3)	0.487
Lactate, mmol/L[†]	0.9 (0.6 to 1.5)	0.3 (0.0 to 1.2)	0.614
Use of HFNC[†]	9 (31.0)	9 (31.0)	1.000

Data are presented as median (interquartile range) or number (percentage). *, matched for age, gender, SOFA, pre-NIV lactate, reasons for NIV, IPAP, and use of sedatives; [†], pre-NIV values. AHRF, acute hypercapnic respiratory failure; COPD, chronic obstructive pulmonary disease; CPE, cardiogenic pulmonary edema; HFNC, high flow nasal cannula; NIV, non-invasive ventilation; PCV, pressure controlled ventilation; PERF, post-extubation respiratory failure; PSV, pressure support ventilation; RF, respiratory failure; RASS, Richmond agitation and sedation scale; SOFA, sequential organ failure assessment.

Table S5 Comparison of NIV treatments and outcomes between the two matched groups*

Treatments and outcomes	PCV (n=29)	PSV (n=29)	P
NIV machine			0.839
IMV with NIV mode	28 (96.6)	27 (93.1)	
IMV without NIV mode	0 (0.0)	1 (3.4)	
Home ventilator	1 (3.4)	1 (3.4)	
Interfaces			0.377
Orofacial mask	26 (89.7)	22 (75.9)	
Helmet	2 (6.9)	5 (17.2)	
Nasal mask	1 (3.4)	2 (6.9)	
NIV settings			
IPAP, cmH_2O	18.0 (15.0 to 20.5)	16.0 (13.5 to 18.5)	0.083
EPAP, cmH_2O	5.0 (5.0 to 6.0)	5.0 (4.5 to 6.5)	0.558
Tidal volume, mL	454.4 (364.3 to 538.7)	400.0 (330.0 to 522.0)	0.509
Change of NIV machine	4 (13.8)	3 (10.3)	1.000
Change of interface	3 (10.3)	4 (13.8)	1.000
Use of sedatives	12 (41.4)	8 (27.6)	0.269
Complications during NIV	6 (20.7)	7 (24.1)	0.753
Skin erythema	1 (3.4)	5 (17.2)	0.194
Abdominal distension	1 (3.4)	2 (6.9)	1.000
Dry mouth	4 (13.8)	0 (0.0)	0.112
Aspiration	3 (10.3)	1 (3.4)	0.611
Claustrophobia	0 (0.0)	0 (0.0)	1.000
Nasal congestion	1 (3.4)	0 (0.0)	1.000
Large leaks	2 (6.9)	2 (6.9)	1.000
NIV duration, hours/day	17.0 (3.8 to 24.0)	17.0 (6.7 to 22.5)	0.987
NIV days	2.0 (1.0 to 3.5)	2.0 (1.0 to 5.0)	0.604
ICU days	14.0 (7.5 to 21.0)	11.0 (6.5 to 17.0)	0.279
NIV success	16 (55.2)	25 (86.2)	0.009
ICU survival	25 (86.2)	29 (100.0)	0.112
Hospital survival	22 (75.8)	26 (89.7)	0.164

*, matched for age, gender, SOFA, pre-NIV lactate, reasons for NIV, IPAP, and use of sedatives. Data are presented as median (interquartile range) or number (percentage). EPAP, expiratory positive airway pressure; ICU, intensive care unit; IMV, invasive mechanical ventilator; IPAP, inspiratory positive airway pressure; NIV, non-invasive ventilation; PCV, pressure-controlled ventilation; PIP, peak inspiratory pressure; PSV, pressure support ventilation.

Table S6 Comparison of vital signs and arterial blood gas between the two matched groups*

Variables	PCV (n=29)	PSV (n=29)	P
Pre NIV			
pH	7.36 (7.32 to 7.42)	7.38 (7.29 to 7.44)	0.901
P_aO_2/FiO_2, mmHg	198.8 (140.0 to 243.0)	215.0 (163.0 to 255.8)	0.294
P_aCO_2, mmHg	59.0 (48.6 to 67.0)	61.8 (45.9 to 73.2)	0.828
Systolic blood pressure, mmHg	128.0 (113.0 to 145.5)	140.0 (115.0 to 152.5)	0.437
Heart rate, min^{-1}	94.0 (84.0 to 107.0)	88.0 (77.5 to 105.5)	0.194
Respiratory rate, min^{-1}	26.0 (22.5 to 31.5)	24.0 (19.0 to 29.0)	0.125
Body temperature, ℃	36.9 (36.7 to 37.4)	36.9 (36.4 to 37.1)	0.258
Lactate, mmol/L	0.9 (0.6 to 1.5)	0.3 (0.0 to 1.2)	0.614
Post NIV (2 h)			
pH	7.41 (7.35 to 7.45)	7.39 (7.31 to 7.43)	0.494
P_aO_2/FiO_2, mmHg	226.6 (166.8 to 278.0)	210.0 (168.3 to 273.0)	0.858
P_aCO_2, mmHg	48.7 (45.0 to 61.5)	53.3 (43.5 to 67.9)	0.287
Systolic blood pressure, mmHg	121.0 (106.0 to 142.5)	130.0 (114.0 to 143.5)	0.297
Heart rate, min^{-1}	90.0 (81.5 to 105.0)	99.0 (77.0 to 103.5)	0.624
Respiratory rate, min^{-1}	25.0 (20.5 to 28.0)	24.0 (19.0 to 26.5)	0.538
Body temperature, ℃	36.8 (36.6 to 37.4)	37.0 (36.6 to 37.2)	0.975
Lactate, mmol/L	1.0 (0.6 to 1.5)	0.8 (0.0 to 1.3)	0.843

Data are presented as median (interquartile range). *, matched for age, gender, SOFA, pre-NIV lactate, reasons for NIV, IPAP, and use of sedatives. NIV, non-invasive ventilation; PCV, pressure-controlled ventilation; PSV, pressure support ventilation.

Table S7 Univariate and multivariate analyses in the matched cohort (PCV, n=29; PSV, n=29) for predictors of NIV success*

Variables	OR[†]	P	OR (95% CI)[#]	P
Heart disease	0.316	0.061	–	–
Pre-NIV RR	0.907	0.043	–	–
Post-2h-NIV HR	0.975	0.086	–	–
IPAP	0.839	0.035	0.802 (0.661 to 0.972)	0.025
PSV *vs.* PCV	5.078	0.013	4.080 (1.020 to 16.321)	0.047
Use of sedatives	0.326	0.062	0.221 (0.052 to 0.941)	0.047
NIV days	1.315	0.097	–	–

*, matched for age, gender, SOFA, pre-NIV lactate, reasons for NIV, IPAP, and use of sedatives (Hosmer-Lemeshow test: chi-square =5.994 and P=0.540); [†], univariate analysis; [#], multivariate analysis. CI, confidence interval; HR, heart rate; OR, odds ratio; PCV, pressure-controlled ventilation; PSV, pressure support ventilation; RR, respiratory rate.