The Korean Journal of Internal Medicine: 21:1-9, 2006

Is Hypercapnea a Predictor of Better Survival in the Patients who Underwent Mechanical Ventilation for Chronic Obstructive Pulmonary Disease (COPD)?

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Background : There are contradictory reports concerning hypercapnia as a predictor of a better outcome in COPD. This study examined the clinical implications of hypercapnea in COPD patients (M:F = 59:19) who required mechanical ventilation.

Methods : The clinical parameters at the time of MICU admission, the total ventilation time, the APACHE II score and the pulmonary function testing were retrospectively analyzed between the survivors and nonsurvivors.

Results : Univariate analysis showed that compared with the nonsurvivors, the survivors had lower $AaDO_2$ values (59.8±53.5 vs. 105.0±73.3 mmHg, p=0.000), higher $PaCO_2$ values (64.9±16.0 vs. 48.9±17.8 mmHg, p=0.000), lower APACHE II scores (19.0±3.8 vs. 24.1±5.1, p=0.002), the more frequent application of initial noninvasive positive pressure ventilation (44.0 vs. 14.3%, p=0.008), and a lower combined rate of septic shock (4.0 vs. 39.3%, p=0.000). Multivariate analysis revealed that a lower $PaCO_2$ (OR: 0.94, p=0.008), the presence of septic shock (OR: 10.16, p=0.011), a higher APACHE II score (OR: 1.22, p=0.040) and a longer ventilation time (OR: 1.002, p=0.041) were the risk factors for mortality. A lower $PaCO_2$ was also verified as the predictor for mortality by multivariate analysis when excluding septic shock.

Conclusions : Hypercapnia at admission is thought to be an independent predictor of better survival for the COPD patients who require mechanical ventilation.

Key Words : COPD, Hypercapnia, Mechanical ventilation, Respiratory failure, Mortality

INTRODUCTION

Deterioration of lung function that leads to progressive acute respiratory failure in the patients with chronic obstructive pulmonary disease (COPD) requires the administration of mechanical ventilatory support. The mortality rates that have been reported for these patients range between 19% and 46%[1-8]. A number of prognostic factors have been reported for COPD patients, including the APACHE (acute physiology and chronic health evaluation) II score, age, the baseline pulmonary function, the oxygenation status, the number of organ failures, the nutritional status, the severity of the underlying disease and the appropriateness of the medical management[1-10].

It may be that in COPD patients with hypercapnia, if oxygenation is equally maintained regardless of the serum carbon dioxide, a low minute ventilation is required to maintain the optimal arterial oxygenation, and this reflects the less advanced diffusion disturbances or the less severe ventilation-perfusion mismatch compared to the COPD patients with hypocapnea. The results from experimental models of acute

• Received : July 4, 2005
• Accepted : September 2, 2005
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lung injury indicate that hypercapnea can attenuate lung injury via various mechanisms and it may have some therapeutic potential[11-18]. Depending on the $PaCO_2$ level at admission, these physiological and therapeutic differences may affect survival for the COPD patients suffering with acute respiratory failure. However, there are conflicting reports regarding hypercapnia as a predictor for survival in COPD patients[8, 19-22].

The aim of the present study was to determine whether the $PaCO_2$ level at admission was a prognostic indicator for survival in the COPD patients who underwent mechanical ventilatory support.

METHODS AND MATERIALS

Study population

The study retrospectively examined 78 consecutive COPD patients who underwent mechanical ventilation due to their acute respiratory, and they were treated in the medical intensive care unit (MICU) of a university-affiliated hospital from March 1991 to August 2003. The diagnosis of COPD was determined by the clinical criteria and the previously documented airflow limitation (FEV_1 <80% of the predicted value in combination with an FEV_1/FVC <70% that was not fully reversible)[23-26]. We used the clinical criteria, the clinical history with the compatible physical findings and/or evidence of hyperinflation on the chest radiography to support the diagnosis of COPD in the absence of the results for the previous pulmonary function testing[23-26]. A positive bronchodilator response was defined according to the ATS criteria when there was an increase of either the FVC or FEV_1 by 12% or more and an absolute change of 200 mL of either one was documented[27]. The study excluded patients with COPD combined with a tuberculous-destroyed lung, bronchiectasis, kyphoscliosis, malignancy, preexisting tracheostomy and stroke. The application of invasive or noninvasive ventilation was decided upon based on the judgment of the ICU attending physicians. Noninvasive positive pressure ventilation (NPPV) was not tried dor the patients who had respiratory arrest, unstable hemodynamics, problems of airway protection, excessive secretion, anatomic abnormalities that interfered with the mask fit and poor cooperation.

Data collection

We retrospectively analyzed the following data that was collected at the time of MICU admission: the complete blood count and blood chemistry, the radiological findings, the APACHE II scores (first day of MICU), the infection status, the presence of septic shock, the co-existing medical problems and the medication. The blood gas data obtained before the start of mechanical ventilation was also analyzed. In addition, the total ventilation time, the total ICU stay, the total hospital stay and the final outcome (survival or death) during the hospital stay were reviewed. The best results for the pulmonary function testing (PFT) and the baseline arterial blood gas analysis were also obtained when the patient was stable and this was done within the preceding 3 years. For the patients who had a history of frequent mechanical ventilation, the most recent application available was selected. PFT data were available for 64 of the 78 COPD patients, and the baseline arterial blood gas data with the patient in a stable condition were collected for 53 of the 78 COPD patients. The admission route, cor pulmonale, home oxygen therapy and smoking status were noted during the chart review. A detailed smoking history, including the total pack-years of smoking, was obtained for each patient. An ex-smoker was defined as an individual who had stopped smoking for more than one year.

Clinical parameters were analyzed either between the surviving and nonsurviving groups or depending upon the

Table 1. Characteristics of the patients with COPD

Item	Data of COPD patients
Total No.	78
Age	67.6±8.7
Gender (M/F)	59:19 (75.6:24.4%)
Smoking (Sm: Ex-Sm: NonSm)	34:23:18
Admission Route	
OPD	2 (2.6%)
ER	60 (76.9%)
Ward	16 (20.5%)
NPPV	N=26 (33.3%)
MV after initial NPPV apply	19 (73.1%)
only NPPV	7 (26.9%)
Baseline PFT	N=64
FVC (%)	61.6±19.6
FEV_1(%)	31.8±11.1
FEV_1/ FVC (%)	40.3±13.9
BDR	29/50 (58%)
Home O_2 therapy	28/72 (35.9%)
Cor Pulmonale	40/71 (51.3%)
Total Ventilation Time (hour)	251.3±556.6
Total ICU stay (day)	14.5±22.8
Total hospital stay (days)	23.7±27.8
Baseline Blood Gas prior to admission	N=53
$PaCO_2$ (mmHg)	48.3±10.1
$AaDO_2$ (mmHg)	39.2±31.7
PaO_2/FiO_2ratio (mmHg)	310.9±83.1
Blood Gas at the time of admission	N=78
$PaCO_2$ (mmHg)	59.1±18.3
$AaDO_2$ (mmHg)	76.0±64.7
PaO_2/FiO_2ratio (mmHg)	188.8±62.1
APACHE II score	20.8±4.9
Pneumonia at admission	48 (61.5%)
Septic shock at admission	13 (16.7%)
Body Mass Index (kg/m^2)	20.3±3.9

NPPV, noninvasive positive pressure ventilation; BDR, bronchodilator response

Table 2. Comparison of the parameters at the time of MICU admission according to the $PaCO_2$

$PaCO_2$ level	50 mmHg	< 50 mmHg	*p*-value
Total No.	55	23	
Age	67.6±8.8	67.7±8.7	0.544
Male : Female (% of male)	40:15 (72.7%)	19:4 (82.6%)	0.354
Smoking (Sm : Ex-Sm : Non-Sm)	25:14:15	9:9:3	0.630
Home O_2 therapy	22 (26.1%)	6 (40.0%)	0.243
Cor Pulmonale	31/52 (59.6%)	9/19 (47.4%)	0.357
Respiratory Rate (Frequency/min.)	26.3±4.5	27.0±5.4	0.507
Pulmonary function test	N=47	N=17	
FVC (%)	62.6±19.3	58.8±20.9	0.491
FEV_1(%)	31.9±10.2	31.7±13.8	0.963
FEV_1/ FVC (%)	40.9±15.0	38.7±10.8	0.572
BDR (No of positive / total No)	19/34 (55.9%)	10/16 (62.5%)	0.658
Blood Gas at the time of admission	N=55	N=23	
PH	7.32±0.11	7.42±0.10	0.000
$PaCO_2$ (mmHg)	68.4±12.0	37.0±9.2	0.000
$AaDO_2$ (mmHg)	65.9±58.4	100.2±73.4	0.032
PaO_2/FiO_2ratio (mm Hg)	183.1±53.1	202.5±79.3	0.211
Base excess	8.1±8.8	0.3±6.7	0.000
Baseline Gas prior to admission	N=40	N=13	
pH	7.42±0.05	7.44±0.05	0.120
$PaCO_2$ (mmHg)	50.6±9.6	41.4±8.5	0.003
$AaDO_2$ (mmHg)	38.6±32.7	41.3±29.6	0.793
PaO_2/FiO_2ratio (mmHg)	304.4±83.2	331.0±82.7	0.320
Base excess	4.7±3.1	2.5±3.8	0.036
Mechanical Ventilation	N=55	N=23	
NIV at admission	22 (40.0%)	4 (17.4%)	0.053
Total Ventilation Time (hour)	293.4±644.9	150.6±219.6	0.304
Total ICU stay (day)	15.3±26.3	12.6±10.6	0.633
Total hospital stay (day)	25.7±31.2	19.0±17.0	0.331
Previous Mechanical Ventilation	18 (32.7 %)	6 (26.1 %)	0.562
APACHE II score	20.1±3.9	22.4±6.6	0.066
Pneumonia at admission	31 (56.4%)	17 (73.9%)	0.146
Septic shock at admission	6 (10.9%)	7 (30.4%)	0.035
Survival	41 (74.5%)	9 (39.1%)	0.003
Body Mass Index (kg/m^2)	20.8±4.0	19.2±3.3	0.126
Cholesterol (mg/dL)	159.6±41.6	180.1±55.2	0.083
Albumin (g/dL)	3.3±0.6	3.0±0.7	0.067

NPPV, noninvasive positive pressure ventilation; BDR, bronchodilator response

$PaCO_2$ value at admission: the hypercapnic group had ≥50 mm Hg, and the non-hypercapnic group had <50 mmHg. Hypercapnia was defined as a $PaCO_2$ level ≥50 mmHg[28]. PAO_2 (the alveolar oxygen tension) was calculated using the following formula: $PAO_2=(760-47)\times FiO_2-PaCO_2/R$, where R was assumed to be 0.8. The alveolar-arterial PO_2 difference was calculated by subtracting the PaO_2 from the PAO_2. The body mass index (BMI) at the time of admission was calculated as weight (kg) divided by the square of height (m^2).

Data analysis

All the data were analyzed using SPSS version 11.0. All the values are expressed as means±standard deviation (SD), or as the numbers of patients and a percentage. Chi-Square and/or Fisher's exact tests were used for comparison of the categorical data. For the continuous data, Student's *t*-test was used for comparison of the parametric data, and the Mann-Whitney test was used for comparison of the nonparametric data. Multiple logistic regression using the stepwise forward method was used to evaluate the independent risk factors by including all the significant and nearly significant parameters ($p<0.1$) The results of the logistic regression analysis are reported as odds ratios (OR) with 95% confidence intervals (CI). *p*-values less than 0.05 were considered statistically significant.

RESULTS

Baseline characteristics of the patients (Table 1)

Males comprised 75.6% of the study group. The emergency

Table 3. Comparison of the parameters at the time of MICU admission between the survivals and non-survivals

	Survival	Non-survival	*p*-value
Total No.	50	28	
Age	68.1±8.6	66.8±9.1	0.544
Male : Female (% of male)	38:12 (76%)	21:7 (75%)	1.000
Smoking (Sm : Ex-Sm : Non-Sm)	23:13:13	11:10:5	0.892
Home O_2 therapy	20 (40%)	8 (28.6%)	0.313
Cor Pulmonale	25/45 (55.6%)	15/26 (57.7%)	1.000
Respiratory Rate (Frequency/min.)	25.5±4.1	28.3±5.3	0.013
Pulmonary function test	N=45	N=19	
FVC (%)	61.3±18.3	62.4±22.9	0.834
FEV_1(%)	31.7±9.8	32.1±14.1	0.901
FEV_1/ FVC (%)	41.1±14.7	38.5±12.3	0.499
BDR (No of positive / total No)	20/33 (60.6%)	9/17 (52.9%)	0.603
Blood Gas at the time of admission	N=50	N=28	
pH	7.32±0.10	7.39±0.11	0.008
$PaCO_2$ (mmHg)	64.9±16.0	48.9±17.8	0.000
$AaDO_2$ (mmHg)	59.8±53.5	105.0±73.3	0.002
PaO2/FiO2ratio (mmHg)	193.7±61.4	180.0±63.5	0.353
Base excess	6.3±7.0	5.0±11.7	0.582
Baseline Gas prior to admission	N=39	N=14	
pH	7.39±0.05	7.32±0.05	0.213
$PaCO_2$ (mmHg)	48.7±9.8	47.4±11.1	0.686
$AaDO_2$ (mmHg)	36.1±29.9	47.9±36.1	0.237
PaO_2/FiO_2ratio (mmHg)	317.7±86.0	291.9±73.8	0.323
Base excess	4.0±3.4	4.6±3.3	0.617
Mechanical Ventilation	N=50	N=28	
NPPV at admission	22 (44.0%)	4 (14.3%)	0.011
Total Ventilation Time (hour)	145.4±285.3	440.3±823.2	0.076
Total ICU stay (day)	10.5±12.4	21.6±33.5	0.101
Total hospital stay (day)	22.0±17.1	26.8±40.7	0.557
Previous Mechanical Ventilation	15 (30%)	9 (32.2%)	0.844
APACHE II score	19.0±3.8	24.1±5.1	0.000
Pneumonia at admission	28 (56.0%)	20 (71.4%)	0.228
Septic shock at admission	2 (4.0%)	11 (39.3%)	0.000
Body Mass Index (kg/m^2)	20.9±4.0	19.1±3.4	0.058
Cholesterol (mg/dL)	167.0±43.7	162.9±52.4	0.717
Albumin (g/dL)	3.3±0.5	3.0±0.7	0.100

NPPV, noninvasive positive pressure ventilation; BDR, bronchodilator response

room was the admission route to the MICU in 76.9% (60) of the cases. NPPV was first applied in 33.3% (26) of the patients, of whom 73.1% (19) had to be intubated during their MICU stay. The baseline FEV_1 analysis showed that the patients generally had severe airway obstruction (31.8±11.1%) even when they were in a stable state. The baseline blood gas data in the stable state was available for 53 patients, and it showed that the $PaCO_2$ was 48.3±10.1 mmHg and the PiO_2/FiO_2 ratio was 310.9±83.1 mmHg. Home O_2 therapy was administered in 35.9% of the cases (28 of 72 patients).

At the time of admission, the mean APACHE II score was 20.8±4.9. Septic shock was present in 13 (16.7%) of the patients, and 48 (61.5%) patients had pneumonia.

Relationship between the clinical parameters and the $PaCO_2$ (Table 2)

We found that the $PaCO_2$ level was inversely correlated with the APACHE II score (r=-0.313, p=0.005) (Figure 2). Although not statistically significant, the group with higher $PaCO_2$ values ($\geq$50 mmHg) appeared to have lower APACHE II scores (20.1 ±3.9 vs. 22.4±6.6, p=0.066) and more use of NPPV (40.0 vs. 17.4%, p=0.053) than did the group with the lower $PaCO_2$ values (<50 mm Hg). The higher $PaCO_2$ group had more survivors (74.5% vs. 39.1%, p=0.003) and less cases of septic shock (10.9% vs. 30.4%, p=0.035) as compared to the lower group. There was no difference between the two groups in terms of the baseline pulmonary function test results, the total ventilation time or the BMI.

Comparison of the clinical indices between the survivors and non-survivors by univariate analysis (Table 3, 4).

Table 4. Comparison of the parameters at the time of MICU admission between the survivals and non-survivals in the COPD patient group without septic shock.

	Survival	Non-survival	*p*-value
Total No.	48	17	
Age	68.1±8.7	66.2±7.2	0.428
Male : Female (% of male)	36:12 (75.0%)	11:6 (64.7%)	0.415
Smoking (Sm : Ex-Sm : Non-Sm)	22:13:12	6:8:3	0.873
Home O_2 therapy	19 (39.6%)	4 (23.5%)	0.376
Cor Pulmonale	24/44 (54.5%)	9/16 (56.3%)	0.907
Respiratory Rate (Frequency/min.)	25.4±4.2	28.1±5.8	0.050
Pulmonary function test	N=44	N=13	
FVC (%)	61.9±18.0	55.1±19.2	0.243
FEV_1(%)	31.9±9.9	28.5±14.1	0.337
FEV_1/FVC (%)	40.6±14.4	39.1±12.8	0.746
BDR (No of positive / total No)	20/33 (60.6%)	7/11 (63.6%)	1.000
Blood Gas at the time of admission	N=48	N=17	
pH	7.32±0.10	7.42±0.12	0.002
$PaCO_2$ (mmHg)	65.4±15.9	51.6±18.1	0.004
$AaDO_2$ (mmHg)	59.5±54.3	91.7±77.8	0.067
PaO_2/FiO_2ratio (mmHg)	194.8±62.1	180.2±68.8	0.442
Base excess	6.3±7.1	8.2±11.6	0.433
Baseline Gas prior to admission	N=38	N=11	
pH	7.42±0.05	7.44±0.06	0.225
$PaCO_2$ (mmHg)	48.7±9.9	47.1±12.1	0.657
$AaDO_2$ (mmHg)	33.5±25.3	40.3±32.8	0.466
PaO_2/FiO_2ratio (mmHg)	321.6±83.7	303.4±69.2	0.515
Base excess	3.9±3.4	4.3±3.7	0.741
Mechanical Ventilation	N=48	N=17	
NPPV at admission	21 (43.8%)	3 (17.6%)	0.080
Total Ventilation Time (hour)	150.3±290.3	648.1±1008.0	0.061
Total ICU stay (day)	9.9±12.1	30.9±40.3	0.049
Total hospital stay (day)	21.1±15.7	38.0±49.0	0.180
Previous Mechanical Ventilation	14 (29.2%)	6 (35.3%)	0.683
APACHE II score	19.0±3.8	22.1±3.4	0.005
Pneumonia at admission	27 (56.3%)	10 (58.8%)	0.854
Body Mass Index (kg/m^2)	20.9±4.1	19.6±3.6	0.279
Cholesterol (mg/dL)	169.1±43.2	177.0±55.6	0.554
Albumin (g/dL)	3.3±0.5	3.2±0.7	0.413

NPPV, noninvasive positive pressure ventilation; BDR, bronchodilator response

The mortality rate while receiving mechanical ventilation was 29.5% (28/78 patients). The cause of death was identified in 21 patients: respiratory failure (7 cases, 33.3%), septic shock (6 cases, 28.6%), pneumonia (6 cases, 28.6%) and arrhythmia (2 cases, 9.5%).

Age and gender did not differ between the survivors and nonsurvivors, and neither did the baseline PFT including the FVC, FEV_1 and FEV_1/FVC. Although both groups had similar degrees of severe obstructive ventilatory defect (FEV_1; 31.7±9.8% vs. 32.1±14.1%, p=0.901) and identical $PaCO_2$ levels when stable, the survivors had higher $PaCO_2$ values (64.9±16.0% vs. 48.9±17.8%, p=0.002) and lower $AaDO_2$ (59.8±53.5 vs. 105.0±73.3 mmHg, p=0.000) levels at the time of ICU admission compared to the nonsurvivors (Figure 1). The PaO_2/FiO_2 ratio was not different between the two groups.

Regarding the parameters of mechanical ventilation, compared

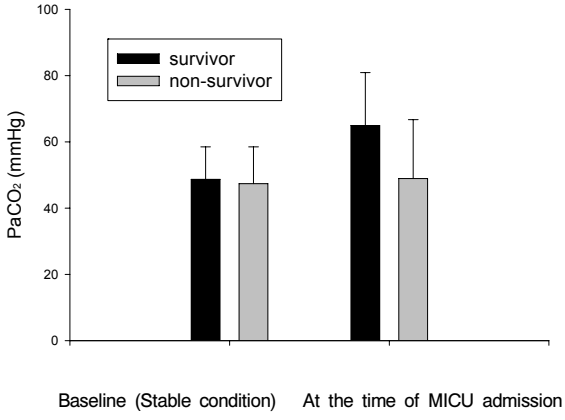

Figure 1. PaCO2 level at a stable condition and at the time of MICU admission.

Table 5. Multivariate Analysis for the Prognostic Factors

Variable	Odds Ratio	95% Confidence Interval	*p*-value
$PaCO_2$ (mmHg)	0.936	0.891-0.983	0.008
Septic Shock	10.160	1.742-71.477	0.011
APACHE II score	1.222	1.009-1.481	0.040
Total Ventilation Time (hour)	1.002	1.000-1.003	0.041

Table 6. Multivariate Analysis for the Prognostic Factors in COPD patients without septic shock

Variable	Odds Ratio	95% Confidence Interval	*p*-value
$PaCO_2$ (mmHg)	0.937	0.890-0.986	0.012
APACHE II score	1.264	1.018-1.569	0.034
Total Ventilation Time (hour)	1.002	1.000-1.003	0.030

to nonsurvivors, the survivors used NPPV more frequently (44.0% vs. 14.3%, p=0.011), and they appeared to have longer ventilation times, although this latter difference was not found to be statistically significant (440.3±823.2 vs. 145.4±285.3 h, p=0.076). There were no significant differences for the ICU stay, the total hospital stay and the number of previous mechanical ventilations between the survivors and nonsurvivors.

The survivors had lower APACHE II scores (19.0±3.8 vs. 24.1±5.1, p=0.000) and fewer cases of septic shock (4.0 vs. 39.3%, p=0.228). Although the BMI appeared to be higher in the survivors, this difference was not statistically significant (20.9± 4.0 vs. 19.1±3.4, p=0.058). In the analysis with excluding the patients with septic shock, the survivors had a lower pH, a higher $PaCO_2$ and a longer ICU stay than did the non-survivors.

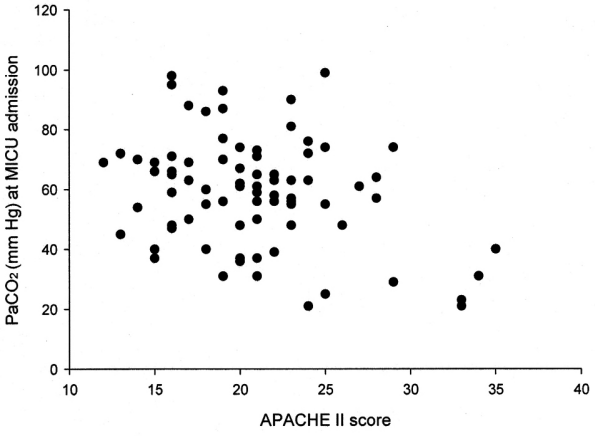

Figure 2. Correlation between the $PaCO_2$ and the APACHE II score at the time of MICU admission (r=-0.313, p=0.005).

Multivariate analysis for the prognostic factors (Table 5, 6)

Multiple logistic regression analysis that included the variables whose p-values were less than p<0.1 showed that a low $PaCO_2$ as well as the presence of septic shock, a high APACHE II score and a long total ventilation time were the independent prognostic factors for a worse outcome in the COPD patients who underwent mechanical ventilation. Multiple logistic regression analysis for the COPD patients without septic shock also demonstrated that not only were a high APACHE II score and a long total ventilation time independent prognostic factors, but a low $PaCO_2$ was also an independent prognostic factor.

DISCUSSION

This study showed that hypercapnia at admission was an independent predictor for better survival in the COPD patients who underwent mechanical ventilation. In addition, the study found that septic shock, a high APACHE II score and a long ventilation time were independent factors for a worse prognosis.

The $PaCO_2$ levels prior to the start of mechanical ventilation were analyzed in the present study. This approach was taken since the $PaCO_2$ levels can be altered by the tidal volumes from a mechanical ventilator or by other therapeutic measures designed to relieve airway obstruction during the ICU stay, and such $PaCO_2$ level changes are thought to make the carbon dioxide levels less reliable as a prognostic marker.

The principal finding of this study is that elevated systemic carbon dioxide tension at the time of MICU admission was linked to better survival, and this was despite that both the survivors and nonsurvivors had similar pulmonary function and $PaCO_2$ levels during their stable condition. This study also demonstrated that the $PaCO_2$ levels were inversely correlated with the APACHE II scores, and that the higher $PaCO_2$ group had a lower $AaDO_2$ compared to the lower $PaCO_2$ group. Because septic shock that causes hyperventilation and hypocapnia could have been a confounding factor in our study,

we analyzed our subjects with excluding the patients without septic shock. This result also showed that hypocapnia was an independent factor for a worse outcome by the multivariate analysis. The findings suggest that high carbon dioxide levels can be an independent marker for survival before mechanical ventilation is applied in the clinical context of a COPD patient with respiratory failure.

There are conflicting data in the literature regarding hypercapnia as a predictor for survival in COPD patients[8, 19-22]. There is a concern that acidosis and hypercapnia may carry the risk of pulmonary vasoconstriction and pulmonary hypertension[29-33]. Many in vivo and in vitro experimental models have demonstrated that hypercapnia causes no harm, and indeed it directly ameliorates lung injury after ischemic-reperfusion, free radical exposure and ventilator-induced lung damage[11-18]. There are additional reports that hypercapnic acidosis attenuates several aspects of the inflammatory response, and that acidosis per se has a cytoprotective effect[34-43]. Indeed, hypercapnic acidosis is reported to alleviate ischemia-induced injury, and even in the heart and brain[44-49]. Elevation of the systemic carbon dioxide tension has been considered as a negligible side-effect that is the consequence of limiting alveolar stress for lung-protective ventilation, and permissive hypercapnia (acceptance of increased concentrations of carbon dioxide in mechanically-ventilated patients) has been found to increase survival[50-53]. Conversely, hypocapnia, which is related to many acute illnesses, is thought to reflect the underlying hyperventilation. However, we could not say that our results indirectly support the above-mentioned studies. Moreover, the present study was unable to determine whether acidosis or hypercapnia has the greater beneficial effect because the effects of pH and pCO2 were not separately analyzed.

Hypercapnia has been reported in clinical studies to result in a better prognosis for COPD and interstitial fibrosis patients[19, 20]. We have also observed that a higher $PaCO_2$ level could be an independent parameter of better survival in respiratory failure patients with tuberculosis-destroyed lungs[54].

With reference to hypocapnia, it has been suggested that low $PaCO_2$ levels identical to those observed during hypoxia indicate a condition that requires a higher degree of ventilation to maintain the oxygenation, and this suggests the presence of more advanced diffusion disturbances or a more advanced ventilation-perfusion mismatch[20, 54]. There is also a possibility that some degree of hypoventilation related to hypercapnia could delay respiratory muscle fatigue and improve the survival rate[19].

An issue for this study was the classification of COPD into emphysema and chronic bronchitis. Hypercapnia linked to a better COPD prognosis may be attributed to the possibility that late stage emphysema may have played a role, and this was more common in the hypocapnic group[19]. We were unable to separate the COPD patients into emphysema and chronic bronchitis groups because the HRCT data was not available.

While NPPV is known to reduce mortality in COPD patients[55, 56], the application of NPPV in this retrospective study was not randomized and multivariate analysis did not identify the independent benefits of NPPV. In this study, the mortality rate of all the patients who received mechanical ventilation while in MICU was 29.5%. The reported mortality rates for the COPD patients while they received mechanical ventilation due to acute respiratory failure range between 19% and 46%[1-9]. This wide range in the reported mortality may reflect differences in the severity of organ dysfunction and the different inclusion criteria for each study.

The data for the present study were collected over 10 years. Recent advances in mechanical ventilation strategies may be a confounding factor for the parameters such as the total ventilation time and survival. However, differing mechanical ventilation strategies were not considered in the analysis as the study focused on the initial manifestations at the time of MICU admission.

In conclusion, to the best of our knowledge, the present study is the first to show data indicating that hypercapnia is an independent predictor for survival in the COPD patients who undergo mechanical ventilation. In addition, the study showed that shock, a high APACHE II score and a long ventilation time were also independent prognostic factors.

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