Maximum Inspiratory Pressure: Can it Be A Helpful Parameter for Predicting Successful Weaning in Chronic Obstructive Pulmonary Disease Patients?

Maksimum İnspiratuar Basınç: Kronik Obstrüktif Akciğer Hastalığı Olan Hastalarda İnvaziv Ventilatörden Ayırma Başarısını Tahminde Yardımcı Bir Parametre Olabilir mi?

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ABSTRACT Objective: To evaluate the predictive value of maximum inspiratory pressure (MIP) besides rapid and shallow breathing index (RSBI) in the weaning of chronic obstructive pulmonary disease (COPD) patients. **Material and Methods:** Fifty-six COPD patients with acute exacerbation and type II respiratory failure requiring invasive mechanical ventilation for more than 24 hours were enrolled in this study. Extubation was planned if the patients tolerated pressure support mode for at least two hours and spontaneous breathing during a 30 minutes T-piece trial. Breathing frequency, exhaled tidal volume, rapid and shallow breathing index (RSBI), minute ventilation (Vmin), MIP and vital capacity measurements were recorded prior to extubation. Patients were divided into two groups according to weaning success (WS) and failure. WS was defined as 48 hours of independence from mechanical ventilation after extubation. **Results:** Although RSBI values between two groups were not significantly different, there were statistically significant differences between the two groups in terms of MIP (30 vs 18 cmH2O; p= 0.008) and Vmin (10.40 vs 8.25; p= 0.032). Patients with a MIP value greater than or equal to 25 cm H2O had greater WS when compared to those with values lower than 25 cm H2O. **Conclusion:** RSBI alone seems not reliable enough to predict weaning outcome in COPD patients with type II respiratory failure due to acute exacerbation. Supported with MIP, better results may be achieved to predict weaning outcome.

Key Words: Weaning; pulmonary disease, chronic obstructive; respiration, artificial

ÖZET Amaç: KOAH'lı hastalarda invaziv ventilatörden ayırma başarısını tahminde, hızlı yüzeyel soluma indeksinin (RSBI) yanında, maksimum inspiratuar basıncın (MIB) değerini araştırmaktır. **Gereç ve Yöntemler:** Yirmi dört saatten fazla invazif ventilatör gereksinimi olan, tip II solunum yetmezliği bulunan, akut alevlenmeli 56 KOAH hastası çalışmaya alındı. Hastalar en az iki saat boyunca basınç destek modunu ve 30 dakika boyunca T-parçası ile spontan solunumu tolere edebildiklerinde ekstübasyon planlandı. Solunum sayısı, ekshale tidal volüm, RSBI, dakika ventilasyonu (Vmin), MIB ve vital kapasite ölçümleri ekstübasyon öncesinde kaydedildi. Hastalar invaziv ventilatörden ayırma başarısı ve başarısızlığına göre iki gruba ayrıldı. Ekstübasyon sonrası en az 48 saat mekanik ventilasyon ihtiyacı olmaması başarı olarak tanımlandı. **Bulgular:** Her iki grup arasında RSBI değerleri farklı değildi ancak MIB (30 ve 18 cmH2O; p= 0.008) ve Vmin (10.40 ve 8.25; p= 0.032) değerleri arasında anlamlı fark görüldü. Yirmi beş cm H2O'ye eşit veya daha fazla MIB değeri olan hastalarda ayırma başarısı, bu değeri 25 cm H2O'den düşük olan hastalara göre daha fazlaydı. **Sonuç:** Tip II respiratuar yetmezliği olan akut alevlenmeli KOAH hastalarında başarılı ayırma tahmini için RSBI tek başına yeterli değildir. MIB ile destekleğinde ayırma başarısını değerlendirmek için daha iyi sonuçlar elde edilebilir.

Anahtar Kelimeler: Ayırma; akciğer hastalığı, kronik obstrüktif; solunum, suni

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Weaning from mechanical ventilator is an important step in the treatment of acute respiratory failure. Each day passed under mechanical ventilation (MV) weakens the respiratory muscles and diminishes the chance for successful weaning.[1] Moreover, the risk of developing ventilator associated pneumonia (VAP) increases with prolonged MV days.[2] On the counterpart, early or unplanned extubation is associated with sensibly higher mortality.[3,4] Therefore the importance of the timing for weaning and extubation is crucial. Even slight differences in terms of success rates of different weaning indices may be of great importance in terms of morbidity and mortality.

Many procedures were set up in order to predict the outcome of weaning in the last 20 years. With the continuing evolution of technology, multi-processor ventilators integrated new measured or calculated parameters considered as potential predictors of successful weaning. Although promising results of these parameters, medical characteristics of patients enrolled in most studies were non-homogenous. Since parameters were tested separately in non-homogenous patient groups, divergent results were obtained and engendered controversies on their usefulness.

Rapid and shallow breathing index (RSBI) was found to be the most accurate predictor of weaning outcome.[5] Again, this index was originally evaluated in a non-homogeneous patient population. Considering that inspiratory muscle strength is markedly diminished in COPD patients, it seems rational to think that indices evaluating the muscle strength such as vital capacity (VC), minute ventilation (Vmin), maximum inspiratory pressure (MIP) and inspiratory airway occlusion pressure at 0.1 sec (P0.1), should be more reliable predictors of weaning outcome in this group of patients. Therefore, RSBI may not necessarily lead to successful extubation for COPD patients.

In this prospective study, we aimed to evaluate the predictive value of MIP and RSBI in weaning of COPD patients.

MATERIAL AND METHODS

Fifty-six COPD patients with acute exacerbation and type II respiratory failure, requiring invasive mechanical ventilation for more than 24 hours were enrolled in this prospective study for over a six months period, in the Intensive Care Unit (ICU) of Dr. Suat Seren Chest Diseases and Thoracic Surgery Hospital, İzmir, Turkey. All patients were previously hospitalized and followed-up for more than two years in our institution. COPD diagnosis was based on clinical history, chest radiography and pulmonary function tests according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. All patients had severe COPD with a FEV1< 50% and FEV1/FVC<70%.[6]

The study protocol was approved by the Institutional Review Board. An informed consent was obtained from each patient or next of kin.

All patients were first admitted in the Emergency Department. The main causes of COPD exacerbation were pneumonia (n= 8), congestive heart failure (n= 12) and infectious exacerbations of chronic obstructive pulmonary disease (n= 36).

Most of them were intubated (86%) soon after their arrival and then transferred to the ICU in less than two hours. The rest of the patients were intubated in the ICU. Upon arrival to the ICU, endotracheal tubes with internal diameters smaller than 8.0 mm were replaced with tubes of this caliber. All patients were sedated with intravenous (IV) propofol perfusion on their first day in the ICU. The sedation was maintained until PaO_2/FiO_2 ratio reached 200. COPD patients with type II respiratory failure on acute exacerbation received aggressive treatment based on antibiotics, corticosteroids, bronchodilators, diuretics and inotropes if needed. As soon as they met the weaning criteria, they were taken into the weaning trial without delay. Treatment of acute exacerbation of COPD in our ICU typically includes bronchodilator therapy consisting of nebulized salbutamol and ipratropium bromide given at regular intervals, usually every 4-6 hours, intravenous corticosteroids (hydrocortisone, 100 mg every 6h), and systemic antibiotics, when indicated. All patients received enteral feeding solutions (Jevity Plus, Abbott Laboratories, USA) with an energy content of 20 to 30 kcal/kg if possible. All patients were ventilated with a Galileo ventilator (Hamilton-Medical, Bonaduz, Switzerland). Pressure controlled (PCV) mode was preferred until triggering was satisfactory. Pressures and breaths per minute were set in the controlled mode ventilation and changed regularly in order to diminish $PaCO_2$ gradually. Pressure support (PS) mode was selected as rapidly as possible for patient comfort.

Prior to weaning, all patients were hemodynamically stable and optimization of volume status and electrolytes and treatment of comorbidities such as high blood pressure, arrhythmia and exacerbation of COPD were achieved with appropriate drugs.

The decision to attempt a weaning trial was made according to the criteria similar to those of the ACCP-ACCCM-AARC Weaning Guidelines:[7] patient hemodynamically stable for at least six hours under PS ventilation with 10 cm H_2O support, 5 cm H_2O level of positive end expiratory pressure (PEEP), $FiO_2 \leq 0.40$, triggering less than 30 breaths per minute and a PaO_2 / FiO_2 ratio ≥ 250. Two hours before the weaning trial, enteral feeding was stopped. After two hours, residual gastric content was suctioned. A fiberoptic bronchoscopy was performed to ensure that the endotracheal tube was free of mucus plug.

The weaning procedure consisted of 30 minutes spontaneous breathing with a T-piece and 6 L min^{-1} O_2. A final blood gas analysis was performed and if PaO_2/FiO_2 ratio was maintained over or equal to 250, $PaCO_2$ < 60 mmHg and pH > 7.30, the patient was extubated. Patients with deteriorated clinical condition or blood gases in this step were considered as not ready for weaning (NR) and were reoriented to intensive physiotherapy. These patients were not re-evaluated again in this study. If the patient did not need mechanical ventilation (MV) more than 48 hours after extubation, the trial was considered as a successful weaning (WS), and otherwise weaning failure (WF).

Demographic characteristics (age, gender, history) as well as acute physiology and choronic health evaluatiın (APACHE II) and simplified acute physiology (SAPS) scores are recorded for each patient in our ICU. Clinical data (e.g., body temperature, arterial blood pressure, blood gases, blood biochemistry and ventilatory parameters) were recorded on the daily basis. Eligible patients were disconnected from the ventilator and a T-piece with a flow of oxygen at 6 L min^{-1} was attached to the endotracheal tube for 30 minutes. After this period, the flow sensor of the ventilator, which is also a pneumotachograph, was connected between the T-piece and the end of the endotracheal tube. The ventilator's RS232 serial port was connected to a computer, on which a homemade software recorded real-time flow, pressure and volume data. After calibration of the flow sensor, measures of RSBI and MIP as well as minute ventilation (Vmin) and vital capacity (VC) were performed for all patients by his/her primary physician who was unaware of the study. When stable and quiet ventilation was assured, the respiratory rate and the average of tidal volumes over one minute were noted. RSBI was calculated as the ratio of respiratory rate to the average tidal volume (f/Vt).

The patients were informed on the procedure. The T-piece was removed and a unidirectional valve was mounted to the flow sensor. The inspiratory pressures were recorded for 30 seconds by the computer. Then the T-piece was resumed. After five minutes of rest, the same maneuver was repeated to verify the reproducibility. The maximum inspiratory pressure recorded was accepted as the MIP value.

Minute volume was measured by the time RSBI measurement was made. The vital capacity was calculated as the average of volumes after five maximal inspiratory efforts plus the maximal functional residual capacity measured while patients were having MIP maneuvers. Vital capacity to body weight ratio (VC/BW) was calculated using the last known weight of the patient.

After the measurements, the patient was extubated and received oxygen through a facial mask.

Statistical Analysis

Numeric (scale) data are presented as medians (minimum-maximum). Medians between two groups were compared by Mann-Whitney U tests. Binominal data are presented in proportions and compared using Chi-square or Fisher's exact test. All data were processed with SPSS 16.0 for Windows (LEAD Technologies Inc., USA) and NCSS (Hintze J., Number Cruncher Statistical Systems, Kaysville, Utah, USA). The standard formulae were used to calculate the predictive power of the threshold values for each index: Sensitivity = true positive/(true positive + false negative), Specificity = true negative/ (true negative + false positive) and Diagnostic accuracy = (true positive + true negative)/ (true positive + true negative + false positive + false negative). The definition of a true positive was a successful weaning when the index predicted a WS while a true negative was a weaning failure when the index predicted a WF. SPSS was used to generate receiver operating characteristic (ROC) curves and calculate the sensitivity and specificity for a range of cutoff points for the RSBI, MIP and Vmin data.

RESULTS

Of fifty-six patients, 14 (25 %) were considered as not ready for weaning (NR). Of the remaining forty-two patients, 33 were successfully weaned (78.6%). Group B accounted nine unsuccessful weaning patients (21.4 %). Patient demographics and arterial blood gas analysis results of extubation were reported on Table 1 for each group. Patients in both group were similar in terms of age, sex ratio, APACHE II and SAPS scores measured on the first day of mechanical ventilation in the ICU and days of mechanical ventilation until the day of weaning trial (MV days).

The median MIP values were significantly different between the two groups (Table 2, Figure 1). RSBI was under 105 breaths $min^{-1} L^{-1}$ in all patients, a value that was considered as the cut-off value for successful weaning by Tobin et al.[5] Moreover, five of the nine patients in group B (WF group) had a value under 50 breaths $min^{-1} L^{-1}$, and finally the medians of RSBI of the two groups were not statistically different (Table 2, Figure 2). Considering a cut-off value of 25 cm H_2O (Lower confidence limit of the median, 95% of CI), only one patient in group B presented a MIP value over this cut-off value. MIP demonstrated better outcome prediction than RSBI, even with values of 50 breaths $min^{-1} L^{-1}$. A sensitivity of 81.8 % and a specificity of 88.9% were calculated for MIP, whereas

TABLE 1: Demographic data of patients according to weaning success and failure.

	WS (n = 33)	WF (n = 9)	p
Age (years)	65 (46-77)	76 (59-81)	0.121
Sex (M/F)	21/12	5/4	0.710
APACHE II	17.00 (6-29)	17.00 (14-19)	0.816
SAPS	40.00 (30-64)	39.00 (38-56)	0.641
FEV1 (L)	1.2 (0.7-1.8)	1 (0.9-1)	0.352
FEV1/FVC (%)	56 (41-65)	49 (47-50)	0.264
pH	7.40 (7.31-7.59)	7.38 (7.35-7.48)	0.598
$PaCO_2$ (mmHg)	54 (40-76)	54 (45-68)	0.960
PaO_2 (mmHg)	83 (60-98)	87 (67-98)	0.281

WS= weaning success, WF= weaning failure, APACHE II= acute physiology and chronic health evaluation, SAPS= simplified applied physiology score, FEV1= forced expiratory volume in one second, FVC= forced vital capacity, $PaCO_2$= partial pressure of carbon dioxide in arterial blood, PaO_2= partial pressure of oxygen in arterial blood. Data are presented as median (minimum-maximum).

TABLE 2: Comparison of the respiratory parameter of two groups. Data are presented as medians (minimum-maximum).

	WS (n = 33)	WF (n = 9)	P
RSBI	43 (19-91)	33 (27-86)	0.908
Vmin	10.40 (7.30-15.20)	8.25 (5.50-9.00)	0.032
MIP	30 (18-50)	18 (12-30)	0.008
VC/BW	10.50 (6.00-18.30)	6.35 (4.00-14.60)	0.154
MV (days)	2 (1-4)	2 (1-10)	0.768

WS=weaning success, WF=weaning failure, RSBI=rapid and shallow breathing index, Vmin=minute volume, MIP=maximum inspiratory pressure, VC/BW=vital capacity to body weight ratio, MV=mechanical ventilation.

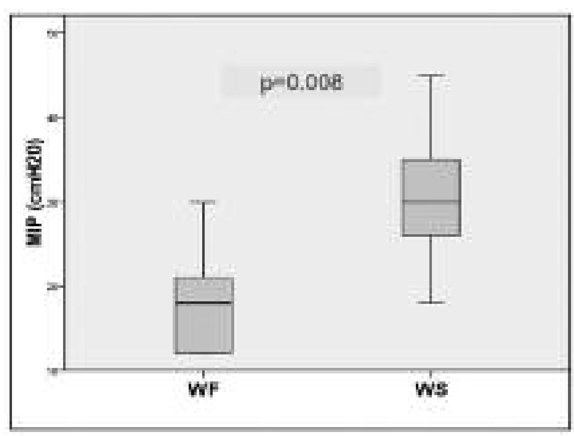

FIGURE 1: Boxplots of the MIP values of the two groups. The line in the middle of the box indicates the median, the upper and lower end of the box indicate the upper and lower quartile, and the upper and lower end of the error bar indicate the maximum and minimum.

MIP= maximum inspiratory pressure, WF= weaning failure, WS= weaning success.

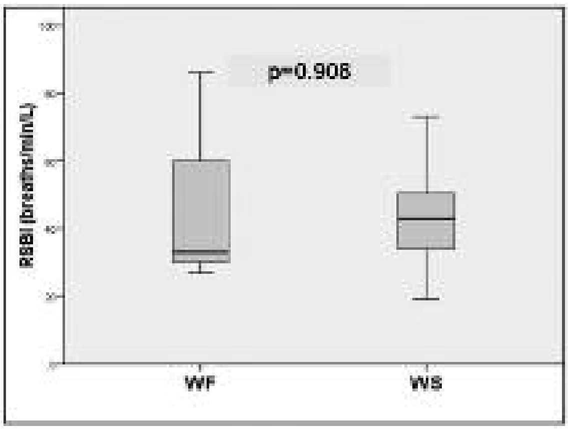

FIGURE 2: Boxplots of the RSBI values of the two groups. The line in the middle of the box indicates the median, the upper and lower end of the box indicate the upper and lower quartile, and the upper and lower end of the error bar indicate the maximum and minimum.

RSBI= rapid shallow breathing index, WF= weaning failure, WS= weaning success.

TABLE 3: Sensitivity, specificity and diagnostic accuracy of weaning predictors for different threshold levels.

	RSBI	MIP	Vmin	
Threshold value for WS	≤ 50	≥ 25	≤ 8.6	≥ 10
Sensitivity	75.8 %	81.8 %	15.1 %	66.7 %
Specificity	44.4 %	88.9 %	55.6 %	100 %
Diagnostic accuracy	69.0 %	83.3 %	23.8 %	73.8 %

RSBI=rapid and shallow breathing index, Vmin=minute volume, MIP=maximum inspiratory pressure.

for RSBI, these parameters were 75.8% and 44.4%, respectively (Table 3).

For another index, Vmin, the median value was found significantly different between the two groups, and a threshold value of 8.6 L min^{-1} was used in order to calculate its predictive significance.[8] The sensitivity and the specificity of Vmin were 15.1% and 55.6%, respectively. If instead of this threshold value, a mean value for Vmin (10 L min^{-1}) was considered as a threshold value predicting WS, the sensitivity and specificity of Vmin would be 66.7% and 100% respectively (Table 3).

DISCUSSION

This study suggests that MIP measurements may be a good predictor of weaning success in severe COPD patients besides RSBI.

Many authors reported valuable data related to weaning predictors,[9-13] but only few of the published research were performed on homogenous population of patients with similar etiologies of respiratory failure. This may in part explain the controversies on the significance of these predictors. In this study, only COPD patients with acute exacerbation and requiring mechanical ventilation were enrolled.

Physicians are most reluctant to use invasive methods for the ventilatory support in COPD patients. Moreover, non-invasive mechanical ventilation is more effective in assisting these patients during acute exacerbation episodes and it reduces the need for intubation.[14,15] However, in severe cases, patients with acute exacerbation may not benefit from non-invasive techniques and require sedation and invasive strategies.[15] Physicians know how difficult is to wean COPD patients from the ventilator, especially when the duration of MV is prolonged. On the other hand, premature extubation and reintubation have an independent associations with increased risk for death and prolonged ICU stay.[3] Hence, there is a need for a reliable predictor of successful weaning applicable to severe COPD patients.

Since the publication of Yang and Tobin, many authors tested RSBI in various populations of patients.[5,16,18] In many of these publications, efficiency of RSBI has been proven. In COPD patients, however, RSBI with its proposed threshold value of 105 breaths min^{-1} L^{-1} was not found to be the best predictor of outcome.[8] Instead, while some authors proposed lower threshold values for better weaning outcome prediction, some others proposed to use other indices like the airway occlusion pressure after onset of inspiration (P0.1), P0.1/maximal inspiratory pressure (P0.1/MIP), the oxygen cost of breathing and compliance-rate-oxygenation-pressure index (CROP).[8,19-22]

It seems rational to think that the determinant for successful weaning of each etiological group of patients may be different. Correspondingly, to estimate weaning outcome, it seems adequate that the attending physician prefers using indices evaluating the limiting factors in each case. Even for a specific group of patients such as severe COPD patients, physicians may feel the need to use different indices for short term versus long term ventilated patients, for patients with tracheotomy or for type I versus type II respiratory failure patients. Some authors refute the use of weaning outcome predictors, or recommend using more than one predictor for more accurate results.[23,24]

Although easy to use, old indices such as respiratory rate (RR), Vmin and Vt/Body Weight, seem to be abandoned because of their insufficient accuracy. New indices such as P0.1, P0.1/MIP, maximal inspiratory pressure (PImax), occlusion pressure and CROP have their reputations, but they require new generation ventilators. RSBI, an easy-to-use and ventilator independent predictor of weaning, was very promising in that way. However, in the present study, even with a severe lowering of the threshold value to 50 breaths min^{-1} L^{-1}, its predictive value was limited. Variation of respiratory mechanics in COPD patients, such as relatively low RR, tolerance of higher $PaCO_2$ and lower PaO_2, may partially explain these results.

According to Yang and Tobin, the threshold value of Vmin for predicting weaning outcome was ≤ 15 $L.min^{-1}$.[5] According to Sahn et al., a Vmin < 10 $L.min^{-1}$ was associated with the weaning success, and the authors concluded that higher values of Vmin (> 15 to 20 L min^{-1}) would help identifying patients who were unlikely to be liberated, but lower values were not helpful in predicting success.[25] In the present study, four of 33 patients (12.1%) in the WS group had a Vmin > 15 L min^{-1} and median Vmin was significantly higher in the WS group when compared to WF group. This difference in Vmin may be related to the fact that COPD patients must not only ventilate their alveoli, but also the increased dead-spaces. Despite the difference between means, the sensitivity and the diagnostic accuracy of Vmin were low (66.7% and 73.8%, respectively). Nevertheless, if recalculated for a new threshold level of 10 $L.min^{-1}$, the specificity of Vmin was 100%. On the other hand, all WF patients had a Vmin less than 10 L min^{-1}. This value, however, should be considered cautiously since the number of patients was too small to be a representative sample.

In the present study, MIP seems to be more reliable than RSBI or other indices alone in predicting weaning outcome of COPD patients. Severe form of COPD usually causes a state of chronic respiratory muscle compromise because of the incomplete alveolar emptying at the end of expiration leading to dynamic hyperinflation, intrinsic positive end-expiratory pressure, flattened diaphragm, recruitment of accessory respiratory muscles, and changes in the shape of the rib cage.[26] The mesurement of MIP is the most widely used and is a simple way to gauge respiratory muscle strength and to quantify its severity.[27-29] The measurement of MIP indicates the state of respiratory muscles, and it may also provide clinicians with a further and helpful tool in evaluation of muscle strength of COPD patients before weaning procedure. Although different threshold values for MIP were stipulated by different authors, the lower limit of the 95% confidence interval, for instance 25 cm H_2O was taken as the threshold value in this study.

One of the weaknesses of the study is that no values of auto positive end expiratory pressure (PEEP) were provided because of technical limitations. Auto PEEP is known to severely hamper weaning in COPD patients. Dynamic hyperinflation and auto-PEEP are common problems in patients receiving full or partial ventilatory support, as well as in those ready to be weaned from the ventilator. 5 cm H2O level of PEEP was adjusted to overcome auto-PEEP in this study.

The interesting point of this study was the relatively short duration of MV compared to more severely infected patients. There was no difference in MV days in both groups. Even with short duration of MV, MIP seems to have a better predictive value than RSBI in COPD patients.

CONCLUSION

This study demonstrated that, MIP with a threshold value of 25 cm H2O seems to have a high predictive value for the successful weaning in COPD patients with acute exacerbation and type II respiratory failure necessitating mechanical ventilation.

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