

## Recent Predictive Parameters for Successful Weaning from Mechanical Ventilation in Critically Ill Patients

Osama Abdel-Hay Kasem, Ahmed Mohamed Abdel-Galeel, Mohamed Abdel-Gawad  
Abdel-Halim Abo El-Suod, Ahmed Hesham El-Sayed Hemdan\*

Department of Anesthesia and Intensive Care, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

\*Corresponding author: Ahmed Hesham El-Sayed Hemdan, Mobile: (+20)01144885689,

E-Mail: ahmadelhalapy@gmail.com

### ABSTRACT

**Background:** Removal of patients from mechanical ventilation (MV) has been termed liberation, discontinuation, withdrawal and most commonly weaning. Weaning covers the entire process of liberating the patient from mechanical support and from the endotracheal tube. Although weaning from MV is successful in most cases, the first attempt fails in 20% of patients. In addition, weaning accounts for over 40% of the total MV time, the proportion varying in function of the etiology of respiratory failure.

**Objective:** The aim of this study was to evaluate the recent protocols of successful weaning from mechanical ventilation of critically ill patients, depending on central venous oxygen saturation, ultrasonographic assessment of diaphragmatic movement, and serial arterial blood gases to assess failure rate 48 hours after weaning. **Patients and methods:** This prospective randomized study included a total of 90 mechanically ventilated Egyptian patients of both sexes, ASA (I-II) attending at least for 48 hours at intensive care unit, Al-Azhar University Hospitals. The included subjects were divided into three groups depending on method of monitoring; group A: serial arterial blood gases, group B: Central venous oxygen saturation and group C: Ultrasonographic assessment of diaphragmatic movement pre and post spontaneous breathing trial. All patients were subjected to daily monitoring of the following weaning parameters: static and dynamic compliances and inspiratory resistance, intrinsic positive end expiratory pressure (Auto PEEP) and Maximum inspiratory pressure (MIP).

**Results:** There is highly statistically significant difference between patients as regard weaning outcome. As the group depended on normal ultrasonographic assessment of diaphragmatic movement, had the largest number of patients with successful weaning.

**Conclusion:** Normal ultrasonographic assessment of diaphragmatic movement proved to be the most important criteria for successful weaning from mechanical ventilation.

**Keywords:** Weaning, Mechanical ventilation, TTE, ICU

### INTRODUCTION

Use of mechanical ventilation is often lifesaving <sup>(1)</sup>. Mechanical ventilation is indicated when the patient's spontaneous ventilation is inadequate to sustain life. In addition, it is indicated as a measure to control ventilation in critically ill patients and as prophylaxis for impending collapse of other physiologic function. Physiologic indications include respiratory or mechanical insufficiency and ineffective gas exchange <sup>(2)</sup>.

The ventilator discontinuation process is an essential component of overall ventilator management. Undue delay leads to excess stay, iatrogenic lung injury, unnecessary sedation and even higher mortality. On other hand, premature withdrawal can lead to muscle fatigue, dangerous gas exchange impairment, loss of air entry protection and a higher mortality <sup>(3)</sup>.

Approximately 30% of patients treated with mechanical ventilation experience difficult or prolonged weaning <sup>(4)</sup>. For these patients, organizational and clinician factors influence the duration and success of weaning. Because of the risk of further prolongation of mechanical ventilation, reintubation, and increased mortality, identification of potentially modifiable factors that

cause delays in weaning, unsuccessful weaning trials, and unsuccessful attempts in extubation is needed <sup>(5)</sup>.

Conceptually, weaning from mechanical ventilation includes both the assessment of a patient's readiness to breathe independently and the systematic reduction of ventilatory support. A variety of weaning strategies have been used to assess weaning. In the past, determining a patient's readiness to be weaned were based on the judgments of individual physicians, who considered objective indicators of gas exchange, respiratory mechanics, and the patient's ability to protect the airway. Use and evaluation of these indicators often resulted in wide variations in weaning practices among providers. More recently, the use of weaning protocols has markedly reduced the duration of mechanical ventilation. The key to successful weaning may be that protocol is used, rather than specifically how the protocol is constructed or what method of weaning is used <sup>(5)</sup>.

Mixed venous oxygen saturation (SvO<sub>2</sub>), which requires invasive measurements via right heart catheterization, and the easier to obtain central venous oxygen saturation (ScvO<sub>2</sub>), are two

indices closely associated with global tissue oxygenation<sup>(6)</sup>.

Ultrasound of multiple organ systems is becoming more commonplace in the intensive care unit (ICU) setting. Ultrasound has been used to identify cardiac, respiratory or diaphragmatic risk factors of weaning failure<sup>(7)</sup>. Further, ultrasound may be helpful in providing a visual assessment of cardiorespiratory state at different phases of weaning. Therefore, a combined structured transthoracic echocardiogram (TTE), lung and diaphragm ultrasound examination added to conventional clinical predictors could be a useful tool to increase the accuracy in predicting weaning outcome and extubation failure<sup>(8)</sup>.

The aim of this work was to study recent protocols of successful weaning from mechanical ventilation of critically ill patients, using central venous oxygen saturation, ultrasonographic assessment of diaphragmatic movement, and serial arterial blood gases to assess failure rate 48 hours after weaning.

## PATIENTS AND METHODS

This prospective randomized study included a total of 90 mechanically ventilated Egyptian patients of both sexes, ASA (I-II) attending at least for 48 hours at intensive care unit, Al-Azhar University Hospitals (El-Hussein and Bab El-Sharia). **Approval of the local Ethics Committee of the Faculty of Medicine, Al-Azhar University and a written informed consent from the highest close relatives of all the subjects were obtained.** This study was conducted between January 2016 and December 2017.

All patients were subjected to:

- Detailed medical history (from patients if possible or relatives)
- Full general and local examination.
- Monitoring the patients by continuous ECG monitoring, non-invasive blood pressure, and pulse oximetry.
- Central venous line inserted through the right internal jugular guided by U/S.
- Arterial cannulation through the radial artery for sampling.
- Basic laboratory investigations as complete blood count, random blood sugar, liver and kidney function tests, to exclude ineligible cases.
- Advanced laboratory investigations as (ABG electrolyte levels Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>++</sup>, Ca<sup>++</sup>, and phosphorus) as needed.
- Daily chest x-ray.

**Inclusion criteria:** Critically ill mechanically ventilated patients, ASA (I-II) in intensive care

unit at least for 48 hours scheduled for exventilation and extubation.

### Exclusion criteria:

- ASA ≥ III.
- Geriatrics and pediatrics patients below 18 years and above 65 years old.
- GCS > 8/15.
- Brain stem death.
- Neuromuscular diseases e.g.: Guillain Barre Syndrome.
- Phrenic nerve paralysis e.g.: cervical transection above T<sub>3</sub>.
- Multi-organ failure syndrome.

### Techniques:

All patients were also subjected to daily monitoring of the following weaning parameters:

#### (1) *Static and dynamic compliances and inspiratory resistance*

By the aid of the end inspiratory occlusion technique, a constant inspiratory flow of the volume controlled mode was applied to a relaxed patient and allowing an end inspiratory pause more than 0.5 second after cessation of the inspiratory flow.

***Compliance and resistance were calculated (During complete relaxation) as:***

$$\text{Static compliance } C = \frac{\text{tidal volume}}{\text{Plateau pressure} - \text{PEEP}}$$

$$\text{Dynamic compliance } C = \frac{\text{tidal volume}}{\text{Peak pressure} - \text{PEEP}}$$

$$\text{Total Inspiratory Resistance} = \frac{\text{peak pressure} - \text{plateau pressure}}{\text{Peak inspiratory flow}}$$

#### (2) *Intrinsic positive end expiratory pressure (Auto PEEP):*

By the aid of end expiratory occlusion technique which lasts about 5 sec during complete relaxation, leading to the cessation of gas flow and the obtained pressure equilibrates with alveolar pressure at end expiration (auto PEEP).

#### (3) *Maximum inspiratory pressure (MIP):*

It is the maximum inspiratory pressure the cooperative patient can generate against a closed valve. It assesses primarily the muscle function and excludes severe muscle weakness. The mean of three readings was taken.

**Randomization:** Randomization was done through opaque and well-sealed envelopes. The sequence generation was done by computer. Number was written on envelope and group was written on the card within it along with the serial

number. When patients come, envelope was opened to see the group to be allotted.

#### Study groups:

Ninety patients were randomly allocated in three equal groups;

- **Group A:** Serial arterial blood gases.
- **Group B:** Central venous oxygen saturation.
- **Group C:** Ultrasonographic assessment of diaphragmatic movement pre and post spontaneous breathing trial.

Any patient on mechanical ventilation should be considered for weaning if she/he fulfilled the readiness criteria;

- The underlying cause for mechanical ventilation has been treated and the patient is improving.
- The patient is hemodynamically stable on no pressers.
- The patient is able to initiate spontaneous inspiratory efforts.
- The patient should be afebrile (temp < 38 °C), stable metabolic status (PH > 7.25), adequate hemoglobin (Hb > 8-10 g/dL), and adequate mentation (e.g., arousable, Glasgow coma scale > 13).
- Normal electrolyte (Na, K, Ca).

#### In each group the method of weaning trial was either by:

- (1) Gradual withdrawal of pressure support: at the beginning we sit the minimum pressure support at a level that achieves rapid shallow breathing index below 105/breath /min/L then we gradually withdrew the pressure support 2 cm H<sub>2</sub>O every 2 hours.
- (2) An abrupt t- piece trial. The choice of the method is according to the physician judgment.

**The weaning trials in each group were considered failing if the patient developed one of the following:** Signs of increased work of breathing, respiratory rate > 35 / minute, anxiety, deterioration of conscious level ,worsening of arterial blood gases(SaO<sub>2</sub> < 85%; PO<sub>2</sub> < 50–60 mm Hg; pH< 7.32) or vital signs instability.

**When no signs of failure appeared for two hours and the patient was capable of protecting his or her airways and clearing secretions, extubation was performed.**

**The trial was considered successful if** the patient remained off any ventilatory support and with no signs of failure for more than 24 hours.

Patient who did not fulfill criteria of extubation but was capable of remaining off the

mechanical ventilation for a period more than 24 hours was also considered as being successfully weaned.

**When signs of failure appeared,** full ventilatory support was reinstated promptly either by increasing the level of pressure support or using assist control mode according to patient ventilator synchrony and comfort assessment.

**After investigating and correcting any reversible cause behind the weaning trial failure,** the next trial was not attempted before the lapse of 24 hours of rest.

**The next weaning trials** were performed by the same protocol of the previous trial according to the group the case belongs.

#### In each group we finally evaluated the following:

- Success rate of discontinuation trials.
- Incidence of re-intubation (even after 24 hours after discontinuation)
- Ventilation time
- Occurrence of ventilator associated complications
- Mortality (even after 24 hours after discontinuation)

#### Statistical Analysis

All the observed parameters and results were carefully recorded and analyzed statistically. Data were fed to the computer and analyzed using IBM SPSS software package version 23.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level (P-values less than 0.05 were considered significant, P-values more than 0.05 were considered non-significant).

**The used tests were: Chi-square test:** For categorical variables, to compare between different groups. **Monte Carlo correction:** Correction for chi-square when more than 20% of the cells have expected count less than 5. **F-test (ANOVA):** For normally distributed quantitative variables, to compare between more than two groups.

#### RESULTS

According to demographic characteristics, there was no statistically significant difference between patients as regard age, gender, and BMI as shown in (table: 1) (P. value>0.05).

**Table (1) Demographic characteristics of the studied patients.**

	Group A (n=30)	Group B (n=30)	Group C (n=30)	p-value
<b>Age (years):</b>				
<b>(Range): Mean ± SD</b>	(19-65) 46.98±15.33	(18-65) 47.86±15.94	(19-64) 47.41±15.64	0.751
<b>Gender: n (%)</b>				
<b>Male (68)</b>	23 (76.7)	21 (70)	24 (80)	0.211
<b>Female (22)</b>	7 (23.3)	9 (30)	6 (20)	
<b>BMI (kg/m<sup>2</sup>):</b>				
<b>(Range) Mean ± SD</b>	(18-29) 22.51±6.34	(18-30) 22.90±5.11	(19-30) 23.11±6.64	0.355

ANOVA test was used. Data expressed as n (%) and (Range) Mean ± SD, P. value>0.05 is insignificant.

Group A: Serial arterial blood gases.

Group B: Central venous oxygen saturation.

Group C: Ultrasonographic assessment of diaphragmatic movement.

BMI (Body Mass Index) = weight/ length<sup>2</sup>.

According to heart rate examination, there was no statistically significant difference between patients (P. value>0.05). But there was highly significant difference in heart rate before and after extubation, as the heart rate of the studied patients was highest during extubation as shown in (table: 2) (P. value<0.05).

**Table (2) Heart Rate (HR) of the studied patients before and after extubation.**

	Group A (n=30)	Group B (n=30)	Group C (n=30)	p-value
<b>HR 0</b>	(72-88) 80.41±6.24	(73-88) 80.20±7.32	(72-89) 81.01±7.19	0.257
<b>HR 1</b>	(73-88) 80.50±7.36	(72-89) 81.21±7.11	(73-89) 81.31±7.22	
<b>HR 2</b>	(96-111) 104.01±6.64	(95-111) 103.52±6.32	(96-110) 103.81±6.19	
<b>HR 3</b>	(88-101) 94.41±6.33	(87-101) 94.50±6.34	(88-100) 94.21±5.77	
<b>HR 4</b>	(82-98) 90.41±7.54	(83-98) 90.20±7.39	(82-99) 90.21±8.17	
<b>HR 5</b>	(72-88) 80.43±7.33	(73-88) 80.22±7.34	(72-89) 81.61±7.54	
<b>p-value</b>	0.001*			

ANOVA test was used. Data expressed as (Range) Mean ± SD, \* P. value<0.05 is significant, and >0.05 is insignificant.

HR0: Heart Rate during ventilation (at baseline).

HR1: Heart Rate 5 minutes before extubation.

HR2: Heart Rate during extubation.

HR3: Heart Rate 5 minutes after extubation.

HR4: Heart Rate 10 minutes after extubation.

HR5: Heart Rate 15 minutes after extubation.

According to mean arterial blood pressure, there was no statistically significant difference between patients (P. value>0.05). But there was highly significant difference in mean arterial blood pressure before and after extubation, as the mean arterial blood pressure of the studied patients was highest during extubation as shown in (table: 3) (P. value<0.05).

**Table (3) Mean Arterial Blood pressure (MAP) of the studied patients before and after extubation.**

	Group A (n=30)	Group B (n=30)	Group C (n=30)	p-value
<b>MAP 0</b>	(68-98) 80.22±17.14	(69-99) 81.28±17.13	(68-99) 80.98±16.11	0.143
<b>MAP 1</b>	(82-99) 90.45±7.09	(83-99) 90.13±7.18	(82-99) 90.12±6.75	
<b>MAP 2</b>	(87-101) 95.43±4.33	(88-101) 95.52±4.54	(88-100) 95.13±4.37	
<b>MAP 3</b>	(82-98) 90.41±6.74	(83-98) 90.20±6.39	(82-98) 90.21±7.17	
<b>MAP 4</b>	(72-97) 80.43±16.34	(73-97) 79.22±16.87	(72-98) 80.61±15.65	
<b>MAP 5</b>	(69-98) 80.38±17.52	(68-98) 80.91±16.25	(68-98) 80.20±17.41	
<b>p-value</b>	0.001*			

ANOVA test was used. Data expressed as (Range) Mean ± SD, \* P. value<0.05 is significant, and >0.05 is insignificant.

MAP0: Mean Arterial Blood pressure during ventilation (at baseline).

MAP1: Mean Arterial Blood pressure 5 minutes before extubation.

MAP2: Mean Arterial Blood pressure during extubation.

MAP3: Mean Arterial Blood pressure 5 minutes after extubation.

MAP4: Mean Arterial Blood pressure 10 minutes after extubation.

MAP5: Mean Arterial Blood pressure 15 minutes after extubation.

According to respiratory rate, there was no statistically significant difference between patients (P. value>0.05). But there was highly significant difference in respiratory rate before and after extubation, as the respiratory rate of the studied patients was highest during extubation as shown in (table: 4) (P. value<0.05).

**Table (4) Respiratory Rate (RR) of the studied patients before and after extubation.**

	Group A (n=30)	Group B (n=30)	Group C (n=30)	p-value
<b>RR 0</b>	(16-21) 18.55±2.13	(16-20) 18.12±2.55	(15-21) 18.76±2.23	0.866
<b>RR 1</b>	(16-20) 18.12±1.56	(15-21) 18.76±1.25	(16-21) 18.55±2.17	
<b>RR 2</b>	(24-29) 26.23±2.29	(24-30) 26.31±3.57	(24-30) 26.45±3.26	
<b>RR 3</b>	(20-26) 22.55±3.13	(20-26) 22.12±3.55	(21-25) 22.76±2.23	
<b>RR 4</b>	(18-22) 20.55±1.12	(18-22) 20.55±1.24	(18-22) 20.55±1.11	
<b>RR 5</b>	(16-21) 18.55±2.24	(16-20) 18.12±2.57	(15-21) 18.76±2.21	
<b>p-value</b>	0.001*			

ANOVA test was used. Data expressed as (Range) Mean ± SD.

\* P. value<0.05 is significant, and >0.05 is insignificant.

RR0: Respiratory Rate during ventilation (at baseline).

RR1: Respiratory Rate 5 minutes before extubation.

RR2: Respiratory Rate during extubation.

RR3: Respiratory Rate 5 minutes after extubation.

RR4: Respiratory Rate 10 minutes after extubation.

RR5: Respiratory Rate 15 minutes after extubation.

At the end of the study we have found that, there is highly statistically significant difference between patients as regard weaning outcome. As group C has the largest number of patients which had successful weaning as shown in (table: 5) (P. value<0.05).

**Table (5) Weaning outcome of the studied patients.**

	Group A (n=30)	Group B (n=30)	Group C (n=30)	p-value
<b>Weaning outcome: n (%)</b>				
<b>Successful weaning (47)</b>	11 (33.3)	13 (46.7)	23 (80)	0.001*
<b>Failed weaning (43)</b>	19 (66.7)	17 (53.3)	7 (20)	

ANOVA test was used. Data expressed as n (%).

\* P. value<0.05 is significant.

## DISCUSSION

Removal of patients from mechanical ventilation (MV) has been termed liberation, discontinuation, withdrawal and most commonly weaning<sup>(9)</sup>. Weaning covers the entire process of liberating the patient from mechanical support and from the endotracheal tube<sup>(10)</sup>.

Weaning from mechanical ventilation requires dynamic and collaborative decision making to minimize complications and avoid delays in transition to extubation and effective collaboration requires open, extensive, and coordinated communication as well as shared team goals and will result in improved quality of care, patient safety and discharge outcomes<sup>(11)</sup>.

Predicting extubation outcome and preventing extubation failure is, therefore, an important task. Various weaning parameters have been suggested to be useful, e.g., central venous oxygen saturation (ScvO<sub>2</sub>), ultrasonographic assessment of diaphragmatic movement, and serial arterial blood gases (ABG)<sup>(12)</sup>.

The purpose of our work was to study factors affecting successful weaning from mechanical ventilation of critically ill patients, using central

venous oxygen saturation, ultrasonographic assessment of diaphragmatic movement, and serial arterial blood gases to assess failure rate 48 hours after weaning.

This study was carried out on 90 mechanically ventilated Egyptian patients of both sexes ASA (I-II) in intensive care unit at least for 48 hours. The patients were randomly allocated in three equal groups; Group A: Serial arterial blood gases, Group B: Central venous oxygen saturation, and Group C: Ultrasonographic assessment of diaphragmatic movement pre and post spontaneous breathing trial.

In our study, the patients' baseline characteristics and physiological variables at the beginning of the weaning were similar. The process of randomization favored a balance between the study groups, making them comparable. This finding goes in accordance with a study done by **Cassiano *et al.***<sup>(13)</sup>, who reported that, the baseline characteristics of their study groups were nearly similar.

The patient's age in the current study was ranged from 18 to 65 years with mean age 47 years. This goes in accordance with a study done by **Miu *et al.***<sup>(14)</sup>, who demonstrated that, the subjects were 49.5-year-old.

In the current study, there was no significant difference between the study groups regarding the age. This finding matches with a study done by **Corbellini et al.** <sup>(15)</sup>, who demonstrated that, comparisons according to age showed no statistically significant differences between their study groups.

In our study, the patient's BMI was ranged from 18 to 30 kg/m<sup>2</sup> with mean 22.5 kg/m<sup>2</sup> with no significant difference between the study groups. Also, **Theerawit et al.** <sup>(16)</sup>, demonstrated the same results.

**Al-Banna et al.** <sup>(12)</sup>, revealed no significant statistical relationship between BMI and the weaning trials from mechanical ventilation among the studied sample. This finding is in congruence with the results of a published study conducted by **Anzuoto et al.** <sup>(17)</sup> who found no differences in the duration of mechanical ventilation, or the duration of weaning from mechanical ventilation in relation to body mass index categories.

In our study, the duration of ventilation was ranged from 3-7 days with the mean 5 days, with no significant difference between the study groups. This goes in accordance with a study done by **Miu et al.** <sup>(14)</sup>.

In the current study, the time of SBT extubation was ranged from 31-60 minutes with the mean 45 minutes with no significant difference between the study groups. **Tenza-Lozano et al.** <sup>(18)</sup>, made a study on 69 patients and reported similar results.

**Ely et al.** <sup>(19)</sup>, demonstrated that patients who underwent daily assessment of weaning parameters have been more successful during extubation and higher survival rates.

In the current study, we found that, the main cause of mechanical ventilation was respiratory failure and the main co-morbidity associated with mechanical ventilation was COPD, with no significant difference between the study groups. This result matches with several studies as, **Dres et al.** <sup>(20)</sup>, **Cassiano et al.** <sup>(13)</sup> and **Tenza-Lozano et al.** <sup>(18)</sup>.

In the current study, the pressure support level was ranged from 6-8 CmH<sub>2</sub>O with the mean 6.5 CmH<sub>2</sub>O, PEEP was ranged from 3-6 CmH<sub>2</sub>O with the mean 4.5 CmH<sub>2</sub>O, and tidal volume was ranged from 6-8 ml/kg with the mean 6.5 ml/kg with no significant difference between the study groups. Also, **Cassiano et al.** <sup>(13)</sup>, and **Dres et al.** <sup>(20)</sup>, reported similar results.

In the current study, there was no statistically significant difference between patients according to heart rate examination. But there was highly significant difference in heart rate before and after extubation, as the heart rate of the studied patients was significantly increased during extubation (at time of weaning), and we found the same result regarding respiratory rate and arterial blood pressure. **Shen et al.** <sup>(21)</sup>, made a comparative study on twenty-four patients,

and reported the same results in the 12 patients in the success group.

At the end of this study, we found that, there is highly statistically significant difference between patients regarding weaning outcome. As group C whom depending on normal ultrasonographic assessment of diaphragmatic movement had the largest number of patients which had successful weaning. **Ali and Mohamad** <sup>(22)</sup>, made a prospective cohort study on 60 patients and reported similar results.

Successful weaning depends on several factors: muscle strength, cardiac, respiratory and metabolic. Acquired weakness in mechanical ventilation is a growing important cause of weaning failure. With the development of ultrasonography, diaphragmatic dysfunction can be evaluated with ultrasound in weakness patients to predict weaning outcomes <sup>(23)</sup>.

In our study, we found that, group A and B whom depending on normal arterial blood gases and normal central venous oxygen saturation respectively had less number of patients which had successful weaning.

This result matches with **Pawson and DePriest** <sup>(24)</sup>, who reported that, ABG measurement does not appear to be a precondition to extubation following a clinically successful spontaneous breathing trial.

Also, **Chittawattanasarat et al.** <sup>(25)</sup>, reported that, ScvO<sub>2</sub> does not predict successful weaning from mechanical ventilators and extubation in critically ill patients.

## CONCLUSION

**According to the present results, we conclude that:**

- Appropriate randomization favored a balance between the study groups, making them comparable and give suitable results.
- Normal ultrasonographic assessment of diaphragmatic movement proved to be the most important criteria for successful weaning from mechanical ventilation.
- Factors as (age, gender, BMI, causes of ventilation, co-morbidities with ventilation, normal arterial blood gases (ABG) and normal central venous oxygen saturation (ScvO<sub>2</sub>) does not predict nor affect weaning outcome from mechanical ventilation.

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