Assessment of risk factors responsible for difficult weaning from mechanical ventilation in adults

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Received 3 June 2012; accepted 13 June 2012
Available online 29 January 2013

Abstract

Objective: The aim of this work is to identify the most important risk factors responsible for difficult weaning from mechanical ventilation in adult patients.

Design: A prospective cohort study.

Setting: Respiratory Intensive care unit of Alexandria main University Hospitals.

Patients: Thirty one patients requiring mechanical ventilation with difficult weaning according to Brochard’s classification.

Methods: After failure of weaning on PSV mode of mechanical ventilation, the patient is reevaluated to detect the risk factors responsible for difficult weaning.

Results: Eighteen patients (58%) were successfully weaned and thirteen (42%) failed weaning trials and finally died. Of the thirty-one studied cases, 16 (52%) were males. Mean age of the studied patients was 57.7 ± 15 and mean BMI was 30 ± 7.9. Twenty-one patients (67.7%) required prolonged mechanical ventilation and ten (32%) required less than 14 days. Mean of Rapid Shallow Breathing Index measured during SBT was 56 ± 9 breaths/min per L among cases who were successfully weaned from MV and 122 ± 19 breaths/min per L among those who failed weaning trials. Mean CROP index value was 38.7 ± 11 ml/breath per min among cases who were successfully weaned and of significantly lower value 7.5 ± 2.6 ml/breath per min among those who failed weaning trials & finally died, (p = 0.00). In the present work; risk factors that found to be responsible for failure of weaning trials were recent infections (pulmonary and/or extra-pulmonary) that were detected in all the studied cases (100%), disturbances in the trace elements & electrolytes in 26 cases (83.8%), cardio-

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.
vascular dysfunctions in 18 (58%), psychological problems in 12 (38.7%), endocrin disturbances in the form of hypothyroidism in 3 (9.6%), nutritional deficiency in 27 (87%), neuromuscular dysfunctions in 14 (45%) and other additional co-morbid problems as hepatic or renal impairment in 15 patients (48%). In the present work; EMG & nerve conduction study was done to 19 cases with difficult weaning. The results showed 26% with normal picture, 63% with moderate to severe axonal sensory motor peripheral neuropathy and 10.5% with a picture of myopathy. Regarding the effect of neuromuscular dysfunctions on the outcome of MV, in the present study, 33% of the patients with polyneuropathy failed weaning trials and finally died ($p = 0.798$). The present study stresses on the importance of neuromuscular assessment in all cases with difficult weaning as this may be an important contributing factor for difficult weaning and prolonged mechanical ventilation.

**Conclusion:** All potential causes of ventilator dependency should be identified when a patient is difficult-to-wean. Then, a plan should be developed that uses a multidisciplinary team approach to correct the reversible causes of weaning failure and facilitates weaning thereafter.

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**Introduction**

Weaning is the progressive decrease of the amount of support that a patient receives from the mechanical ventilator [1]. Discontinuation from mechanical ventilation is usually started only after the underlying disease process that necessitated mechanical ventilation has significantly improved or is resolved [2]. As many as 20% of mechanically ventilated patients, however, will fail their first attempt at weaning, and more than 40% of the total duration of MV is spent in the weaning process [3,4]. Prolonged MV is associated with a host of complications (e.g., infection, gastrointestinal bleeding, and deep venous thrombosis) [5]. On the other hand, premature extubation followed by reintubation is associated with increased morbidity and mortality [6].

Weaning from MV depends on the strength of respiratory muscles, the load applied to those muscles, and the respiratory drive to breathe. Respiratory failure may occur because of any of these. This could happen secondary to inadequate resolution of the initial problem that rendered the patient on MV, a rise of a new problem, a ventilator-associated complication, or a combination of these factors [5]. Weaning success is defined as extubation and the absence of ventilatory support 48 h following the extubation. Weaning failure is defined as one of the following: Failed spontaneous breathing trials (SBT); reintubation and/or resumption of ventilatory support following successful extubation; or death within 48 h following extubation.

The process of initial weaning from the ventilator involves a two-step strategy. It begins with an assessment regarding readiness for weaning, which is then followed by SBT as a diagnostic test to determine the likelihood of successful extubation [7].

Many risk factors affect the weaning process. Over the past several years, there has been controversy about the timing and role of tracheostomy in the ICU in reducing the development of VAP and delayed weaning [8–10]. Placing mechanically ventilated patients in a semi-recumbent body position (45°) has been demonstrated to reduce the incidence of VAP more than 75% compared with those placed in a completely horizontal position (0°) [11]. In a study by Ibrahim, et al., comparing early and late enteral feeding in medical ICU patients receiving mechanical ventilation, there was no mortality difference between the early and late enteral feeding groups. However, the group of patients who were fed earlier had a greater incidence of VAP and longer ICU stay [12]. Another study concluded that the administration of early enteral feeding in patients at high risk of death is likely to be beneficial [13].

A new classification of patients into three groups is proposed, as suggested by Brochard during the International Consensus Conference, according to the difficulty and length of the weaning process [14]:

- **Simple weaning:** Patients who proceed from initiation of weaning to successful extubation on the first attempt without difficulty.
- **Difficult weaning:** Patients who fail initial weaning and require up to three SBT or as long as 7 days from the first SBT to achieve successful weaning.
- **Prolonged weaning:** Patients who fail at least three weaning attempts or require more than 7 days of weaning after the first SBT.

**Patients and methods**

This study included 31 patients requiring mechanical ventilation with difficult weaning according to Brochard’s classification [14] (Patients who fail initial weaning and require up to three SBT or as long as 7 days from the first SBT to achieve successful weaning), selected from Alexandria University hospitals. All patients were accompanied by first degree relatives who were able to write down their consent to participate in this study. Ethical Committee of Alexandria faculty of medicine approved this study.

**Selection criteria**

- Patients who need mechanical ventilation for medical reasons.
- Patient fulfilling the parameters for weaning, (7) with failed spontaneous breathing trial.

**Exclusion criteria**

- Patients with central nervous system disorders as cerebrovascular stroke, brain tumors and encephalopathy.
- Traumatic lesions that necessitate mechanical ventilation.
• Post-operative patients who need mechanical ventilation.
• Patients less than eighteen year old.
• Patients who discharged before seven days after the first attempt of weaning will be excluded from this study.
• Patients who are mechanically ventilated due to malignant lung tumors either primary or secondary.

History taking, general examination, vital signs, thorough chest examination, neurologiological evaluation (Glasgow Coma Score), [15] and assessment of Body Mass Index (BMI): weight/height in m². Plain chest X-ray was done for radiological evaluation. Electrocardiogram (ECG) and arterial gasometry and acid base state were done.

Then after failure of weaning on PSV mode of mechanical ventilation which is proved by the previous data, the patient is reevaluated to detect the risk factors responsible for difficult weaning:

• Drug history during the period of ICU stay including corticosteroids, sedatives, and aminoglycosides.
• Cardiovascular system evaluation:
  ■ New ECG to detect any recent myocardial ischemia.
  ■ ECHO for assessment of left ventricular systolic and diastolic function, measurement of mean pulmonary artery pressure and EF%.
• Neuromuscular evaluation: EMG and nerve conduction (motor nerve conduction study of median and peroneal nerves, sensory nerve conduction study of ulnar and superficial peroneal nerves and Electromyogram (EMG) of biceps, extensor digitorum, vastus medialis and tibialis anterior muscles for suspected patients of muscle weakness) which was done to selected cases.
• Radiological assessment: by plain X-ray chest and CT scan (if needed) for evaluation of signs of pulmonary barotraumas (e.g.: pneumothorax, interstitial emphysema, pneumomediastinum, subcutaneous emphysema), atelectrauma, hyperinflation, radiological infiltrates, etc.), and new parenchymal infiltrates.
• Thyroid function tests: (free T3, free T4 and TSH serum levels).
• Assessment of some serum electrolytes: Potassium (k+), Calcium (Ca + 2), Phosphorus (Ph) and Magnesium (Mg) levels.
• Blood and urine cultures (if needed) to search for a source of recent infection.
• Second tracheal aspirate culture for aerobic & anaerobic bacteria and fungi.
• Follow up of the routine hematological profile (CBC, renal and hepatic functions) after failure of weaning.

In revising the existing literature, PMV has been defined as > 14 days, [16] of mechanical ventilation. In the present study, prolonged mechanical ventilation was considered as duration ≥ 14 days. For those patients who failed weaning after 14 days of MV, tracheostomy was done to guard against the occurrence of complications as trachea-esophageal fistula.

Data were analysed using Statistical Package for the Social Sciences (SPSS) Version 18.0 for Windows (SPSS Inc, Chicago, IL, USA). A p value of < 0.05 was considered significant. Quantitative data was expressed using range, mean and standard deviation while Qualitative data was expressed in frequency and percent. Qualitative data was analyzed using Chi-square test also exact tests such Fisher exact and Monte Carlo was applied. Chi-square test used to test for association between categorical variables. Quantitative data was analyzed using student t-test. Linear correlation was used for the test of different correlations.

Results

The present study included thirty-one patients with difficult weaning from mechanical ventilation. During follow up of the studied patients, 18 (58%) were successfully weaned and 13 (42%) failed weaning trials and finally died. Of the 31 studied cases, 16 (52%) were males and 15 (48%) were females. Mean age of the studied patients was 57.7 ± 15 and mean BMI was 30 ± 7.9. Regarding smoking history, 15 patients (48%) were smokers and 16 (52%) were non-smokers. About the presence of co-morbid illness reported on admission; 6 patients (19.3%) had no co-morbid illness, 11 (35%) had single disease and 14 (45%) had two or more co-morbid illnesses.

Nine patients (69%) with AECOPD were successfully weaned and 4 (31%) failed weaning trials & finally died. Two patients (40%) with ILD were successfully weaned and 3 (60%) failed weaning. Among the studied patients with OHS, 3 (75%) failed weaning trials and one (25%) was successfully weaned. All the studied cases with OSAS and hypoventilation were successfully weaned. There were two patients with ARDS; one (50%) was successfully weaned. Also one patient with bronchiectasis (50%) was successfully weaned. The studied case with pulmonary embolism (100%) failed weaning trials and finally died. While the patient with thalassemia major & pleural effusion (100%) was successfully weaned. Statistically there was no significant relationship between the outcome of MV in the studied cases and the primary diagnosis (P > 0.05). Twenty-one patients (67.7%) required prolonged mechanical ventilation and ten (32%) required less than 14 days. Among the studied cases: eight (61.5%) with AECOPD, three (60%) with ILD, three (75%) with OHS, two (66.7%) with OSA & hypoventilation, one (50%) with bronchiectasis and all the patients (100%) with ARDS required prolonged MV. Also the two cases with thalassemia major and pulmonary embolism required prolonged mechanical ventilation.

All the patients with AECOPD developed infections either pulmonary or extra-pulmonary. Cardiovascular dysfunctions were found in six patients (64.1%). Six patients (64.1%) showed neuromuscular dysfunction by EMG and nerve conduction study. Electrolyte disturbances developed in 12 patients (92%) and malnutrition was observed in 11 cases (84.6%). Two patients (15.4%) developed psychological problems and 7 (53.8%) showed other factors as renal and/or hepatic impairment. Tracheal aspirate cultures taken on admission were sterile in 61.5% of patients. Whereas tracheal aspirate cultures taken after weaning failure, revealed pseudomonas aeruginosa, klebsiella and MRSA (30.8% each). While blood cultures revealed pseudomonas aeruginosa, klebsiella and MRSA (10% each) and the remaining 70% were sterile.

All the cases with ILD developed infections. Cardiovascular dysfunctions were detected in four patients (80%). EMG and nerve conduction study showed neuromuscular dysfunction in one patient (50%). Four patients (80%) developed psychological problems and three (60%) had electrolyte disturbances. All the studied cases with ILD (100%) developed...
malnutrition during ICU stay. Other factors as renal and hepatic impairment were observed in one patient (20%).

All the cases with OHS developed infections and three patients (75%) showed cardiovascular dysfunctions. Neuromuscular dysfunction was detected in two cases (100%) by EMG and nerve conduction study. Three patients (75%) suffered from psychological problems and all the patients developed electrolyte disturbances (100%). Hypothyroidism was detected in two patients (50%). And malnutrition was observed in two cases (50%) during ICU stay. Three patients (75%) showed other factors as renal and/or hepatic impairment. All the cases with ARDS & hypoventilation developed infections, cardiovascular dysfunctions and malnutrition during ICU stay. Neuromuscular dysfunction was detected in two patients (66.7%) by EMG and nerve conduction study. Two cases (66.7%) showed other factors as renal and/or hepatic impairment.

All the cases with ARDS developed infections, electrolyte disturbances and malnutrition. One patient (50%) suffered from psychological problems and hypothyroidism was detected in one patient (50%). No neuromuscular or cardiovascular dysfunctions were found. All the cases with bronchiectasis (100%) developed infections (pulmonary and/or extra-pulmonary) and malnutrition. EMG and nerve conduction study showed neuromuscular dysfunctions in 50%, electrolyte disturbances were observed in 50% and cardiovascular dysfunctions in 50% of cases. One patient (50%) suffered from psychological problems during ICU stay. The case with thalassemia major & pleural effusion suffered from psychological problems during ICU stay. The patient also developed pulmonary infections, electrolyte disturbances and malnutrition. About the case with pulmonary embolism; pulmonary infection, electrolyte disturbances, cardiovascular dysfunctions, malnutrition, and renal impairment were observed during the period of MV. EMG and nerve conduction study showed neuromuscular dysfunctions (in the form of axonal sensory motor peripheral neuropathy).

Measuring some serum electrolytes revealed, mean Na of 136 mEq/L (median, 137; range, 122–144) on admission, of 138 mEq/L (median, 138; range, 132–143) just before the start of weaning trial, and of 137 mEq/L (median, 139; range, 126–149). Whereas mean K was of 3.9 mEq/L (median, 3.8; range, 3–4) just before the start of weaning trials, and of 3.6 mEq/L (median, 3.6; range, 2.7–4.6) after failure of weaning. Both Na and K did not significantly change during the period of MV (P > 0.05). There was a significant relation between respiratory rate, RSBI, and CROP index measured during the second weaning trial on PSV and the outcome of mechanical ventilation (Table 1). The incidence of some of risk factors for difficult weaning in the studied patients are shown in Table 2.

Fifteen patients received corticosteroids for duration ≥14 days; eight (53.3%) were successfully weaned & seven (46.7%) failed weaning trials. And in relation to the duration of MV; 12 (80%) required duration of MV ≥14 days & three (20%) required < 14 days. Among the studied patients who received aminoglycosides during ICU stay, five (71.4%) were successfully weaned & two (28.6%) failed weaning trials and finally died. While in relation to the duration of MV, four patients (57.1%) required duration of MV ≥14 days & three (42.9%) required < 14 days. There was no significant relationship between aminoglycosides intake and the outcome & duration of MV (P > 0.05). Fourteen cases received sedatives drugs during the period of MV. As regarding the outcome of MV, seven patients (50%) were successfully weaned and seven (50%) failed weaning trials & finally died. While in relation to the duration of MV, ten patients (71.4%) required duration of MV ≥14 days & four (28.6%) required < 14 days. There was no significant relationship between sedative drug intake and the outcome & duration of MV, (P > 0.05).

In the present study tracheostomy was done to nine patients; one (11.1%) was successfully weaned and eight (88.9%) failed weaning trials and finally died. While those cases in which tracheostomy was not done (since they did not meet the needed criteria for tracheostomy or due to refusal of the relatives); 17 (77.3%) were successfully weaned from MV and 5 (22.7%) failed weaning trials & finally died. There was a significant relationship between tracheostomy and the outcome of MV (p = 0.001). There was no significant relation between EMG and nerve conduction study findings and the outcome & duration of MV is demonstrated in Table 3. The most common microorganisms in urine, blood and second tracheal aspirate cultures among patients who were successfully weaned and those who failed weaning trial & finally died are demonstrated in Table 4. Risk factors of failure of weaning and final death among the studied patients arranged in descending order according to their significance to the outcome of mechanical ventilation in Table 5.

Table 1 Relation between respiratory rate, RSBI, and CROP index measured during the second weaning trial on PSV and the outcome of mechanical ventilation.

<table>
<thead>
<tr>
<th>Outcome of MV</th>
<th>Mann–Whitney U (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final weaning</td>
<td>Failed weaning &amp; death</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>19 ± 2.6</td>
</tr>
<tr>
<td>RSBI</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>14–23</td>
<td>19.5</td>
</tr>
<tr>
<td>27–35</td>
<td>30</td>
</tr>
</tbody>
</table>

By Mann–Whitney U. (P) < 0.05 represents significant difference. (* denotes significance). RSBI: rapid shallow breathing index. CROP: compliance (C), respiratory rate (R), arterial oxygenation (O), and maximal inspiratory pressure (P).
Discussion

The discontinuation or withdrawal process from mechanical ventilation is an important clinical issue. [17,18] This process is termed “ventilator weaning” (implying a gradual process), or “discontinuation”. All potential causes of ventilator dependency should be identified when a patient is difficult-to-wean. Then, a plan should be developed that uses a multidisciplinary team approach to correct the reversible causes of weaning failure and facilitates weaning thereafter.

The present study included 31 patients with difficult weaning from mechanical ventilation. They are screened to identify the risk factors responsible for difficult weaning. Among the studied patients, 16 (52%) were males and 15 (48%) were female. During assessment of the readiness to wean, some parameters were used including; respiratory rate, RSBI, and CROP index. The present study showed improvement of these parameters during SBT after correction of some of the risk factors causing difficult weaning, ($p = 0.000$).

Mean of RSBI (Rapid Shallow Breathing Index) measured during SBT was 56 ± 9 breaths/min per L among cases who were successfully weaned from MV and 122 ± 19 breaths/min per L among those who failed weaning trials. Yang and Tobin [19] conducted a prospective cohort study and reported that an RSBI of 100 breaths/min per L was better than nine...
other weaning predictors when used to discriminate between the likelihood of weaning success or failure. The rate of weaning success was 56%. RSBFI predicted weaning success with a sensitivity and specificity of 97 and 64%, respectively. The positive predictive value and negative predictive value were 78 and 95%, respectively. While a meta-analysis of more than 60 potential predictors of weaning outcome found that the RSBFI performs poorly as a predictor of weaning outcome [20,21]. However, this result is probably not valid because there was marked heterogeneity of the pretest probability (i.e., the prevalence of successful weaning) [22]. The likely causes of the heterogeneity are test-referral bias and spectrum bias.

Regarding CROP index as an integrative test; it is used also to assess the readiness for weaning from mechanical ventilation. In the present study; mean CROP index value was 38.7 ± 11 ml/breath per min among cases who were successfully weaned and of significantly lower value 7.5 ± 2.6 ml/breath per min among those who failed weaning trials & finally died, (p = 0.00). A study adopted by Yang and Tobin [19] examined the CROP index prospectively; the positive and negative predictive values were 71 and 70%, respectively.

Concerning respiratory rate; it is considered as one of the rapid bed side tests to assess the readiness for weaning from mechanical ventilation. We found statistically significant relationship between respiratory rate and the outcome of mechanical ventilation (mean was 19 f/min among patients who were successfully weaned and 30 f/min among those who failed weaning, p = 0.00). Vallverdu et al. [23] also found that there is a statistically significant relationship between respiratory rate and the outcome of mechanical ventilation (mean was 25 among successful weaning and 29 failed ABT, p < 0.05). Menzeis et al. [24] found some other results.

In revising the existing literature, PMV has been variously defined as > 24 h, [25,26] > 2 days, [27] > 14 days, [16] or > 29 days [28] of mechanical ventilation or, alternatively, the need for post-ICU mechanical ventilator support [29]. In the present study, prolonged mechanical ventilation was considered as duration ≥ 14 days. With follow up of our studied patients; 18 (58%) were successfully weaned and 13 (42%) failed weaning trials and finally died. Other studies found that, hospital survival for adult PMV patients in the short-term acute care (STAC) hospital setting ranges from 39 to 75%, depending on the patient population and definition for PMV [30,31]. And hospital survival in various non-STAC hospital settings varies from 50% in many series [32–35] to as high as 94%, depending in part on admission criteria and likelihood of transfer to a different facility when patients become acutely ill.

Difficult weaning from mechanical ventilation proved to be multifactorial. In the present work; risk factors that found to be responsible for failure of weaning trials were recent infections (pulmonary and/or extra-pulmonary) that were detected in all the studied cases (100%), disturbances in the trace elements & electrolytes in 26 cases (83.8%), cardiovascular dysfunctions in 18 (58%), psychological problems in 12 (38.7%), endocrine disturbances in the form of hypothyroidism in 3 (9.6%), nutritional deficiency in 27 (87%), neuromuscular dysfunctions in 14 (45%) and other additional co-morbid problems as hepatic or renal impairment in 15 patients (48%).

While among those cases who failed weaning and died at the end; 4 (30.7%) were diagnosed as acute exacerbation of Chronic Obstructive Pulmonary Diseases, 3 (23%) as Interstitial Lung Diseases, 3 (23%) as Obesity Hypoventilation Syndrome, one (7.7 %) as bronchiectasis, one (7.7 %) as ARDS and one (7.7 %) as pulmonary embolism. There was no significant relation between the primary diagnosis and the outcome of mechanical ventilation. (p = 0.5). This may be due to small sample size. Similar findings were reported by Menzeis et al. [24] who found no statistically significant relationship between the cause of acute respiratory failure and the outcome of mechanical ventilation.

In the present work, new parenchymal infiltrates in chest X-ray were detected in 13 cases (41.9%); 8 (61.5%) failed weaning & died finally and 5 (38.5%) were successfully weaned and there was no significant relation between the appearance of new infiltrates in chest X-ray as a part of assessment for lower respiratory tract infection and the outcome of MV, (P > 0.05). Kollef, et al. [36] studied 314 patients admitted to the ICU and required MV for more than 5 days & reported that 34 (39.1%) patients with late-onset VAP died during hospitalization.

In the present work; EMG & nerve conduction study was done to 19 cases with difficult weaning. The results showed 26% with normal picture, 63% with moderate to severe axonal sensory motor peripheral neuropathy and 10.5% with a picture of myopathy. De Jonghe, et al. [37] reported that neuromuscular weakness is a common occurrence in patients who are critically ill, developing in ≥ 25 % of patients who are in the intensive care unit (ICU) and ventilated for at least seven days. They reported, four independent variables associated with the occurrence of clinical motor weakness. The number of days with dysfunction in at least two organs before awakening was significantly higher in ICU acquired paresis patients than in the controls, suggesting that the duration, rather than the severity, of multiple-organ dysfunction plays a significant role in ICU acquired paresis. They found a strong association between administration of corticosteroids and the occurrence of ICU acquired paresis. The duration of mechanical ventilation before awakening was also significantly associated with the occurrence of ICU acquired paresis. Surprisingly, female sex was found to be independently associated with a higher rate of ICU acquired paresis in their study. Concerning the relation between neuromuscular dysfunctions and the duration of MV, in the present study 50% of the cases with myopathy

<table>
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<tr>
<th>Table 5 Showing parameters which are considered risk factors of failure of weaning and final death among the studied patients by univariate analysis arranged in descending order according to their significance to the outcome of mechanical ventilation.</th>
<th>Chi-square test/Mann Whitney U test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open surgical tracheostomy</td>
<td>0.001a</td>
</tr>
<tr>
<td>Duration of CVC</td>
<td>0.015b</td>
</tr>
<tr>
<td>Mean Hb level</td>
<td>0.026b</td>
</tr>
<tr>
<td>Psychological problems during ICU stay</td>
<td>0.027a</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.03b</td>
</tr>
<tr>
<td>Serum Mg</td>
<td>0.035b</td>
</tr>
<tr>
<td>Gender</td>
<td>0.048g</td>
</tr>
<tr>
<td>Electrolytes disturbance</td>
<td>0.05g</td>
</tr>
<tr>
<td>a Chi-square test.</td>
<td></td>
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<tr>
<td>b Mann Whitney U test.</td>
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</table>
Assessment of risk factors responsible for difficult weaning from mechanical ventilation in adults

Follow up of the studied patients with difficult weaning from mechanical ventilation revealed: Respiratory rate, RBSI, and CROP index are considered accurate parameters that can be used to assess the readiness for weaning from mechanical ventilation while the patient is on PSV mode.

Much attention should be paid for assessment, early detection and management of these risk factors to achieve successful weaning. These factors include: Infections both pulmonary and extra-pulmonary, Cardiovascular dysfunctions, Electrolytes and trace elements disturbances, Psychological problems (anxiety and depression), Inadequate nutrition, Metabolic factors, Endocrinal dysfunctions as hypothyroidism, Drug therapy during the ICU sat as corticosteroids, aminoglycosides and sedatives, Neuromuscular dysfunctions including peripheral neuropathy and critical illness myopathy acquired during ICU stay.

Prolonged use of invasive devices (urinary and central venous catheters) is usually associated with higher incidence of infection and longer duration of mechanical ventilation. Open surgical tracheostomy may be a contributing factor for weaning failure and higher mortality among the studied cases.

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