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Liberation from mechanical ventilation in critically ill patients: Korean Society of Critical Care Medicine Clinical Practice Guidelines

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Background: Successful liberation from mechanical ventilation is one of the most crucial processes in critical care because it is the first step by which a respiratory failure patient begins to transition out of the intensive care unit and return to their own life. Therefore, when devising appropriate strategies for removing mechanical ventilation, it is essential to consider not only the individual experiences of healthcare professionals, but also scientific and systematic approaches. Recently, numerous studies have investigated methods and tools for identifying when mechanically ventilated patients are ready to breathe on their own. The Korean Society of Critical Care Medicine therefore provides these recommendations to clinicians about liberation from the ventilator.

Methods: Meta-analyses and comprehensive syntheses were used to thoroughly review, compile, and summarize the complete body of relevant evidence. All studies were meticulously assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method, and the outcomes were presented succinctly as evidence profiles. Those evidence syntheses were discussed by a multidisciplinary committee of experts in mechanical ventilation, who then developed and approved recommendations.

Results: Recommendations for nine PICO (population, intervention, comparator, and outcome) questions about ventilator liberation are presented in this document. This guideline includes seven conditional recommendations, one expert consensus recommendation, and one conditional deferred recommendation.

Conclusions: We developed these clinical guidelines for mechanical ventilation liberation to provide meaningful recommendations. These guidelines reflect the best treatment for patients seeking liberation from mechanical ventilation.

Key Words: critical illness; guidelines; mechanical ventilation; ventilator weaning

Guideline

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SUMMARY OF RECOMMENDATIONS

Question 1: In critically ill patients receiving ventilation, does a mechanical ventilation weaning protocol increase the success rate of ventilator liberation?
For critically ill patients on mechanical ventilation, we recommend the use of a mechanical ventilation weaning protocol (recommendation B, conditional recommendation, moderate certainty in the evidence).

Question 2-1: Is pressure support ventilation (PSV) recommended over the T-piece during spontaneous breathing trial (SBT) in adult patients receiving mechanical ventilation?
Either PSV or the T-piece can be applied during SBT when planning to wean adult patients from mechanical ventilation (recommendation B, conditional recommendation, low certainty in the evidence).

Question 2-2: Is PSV recommended over the T-piece during SBT in adult patients at high risk of extubation failure?
Either PSV or the T-piece can be applied during SBT in adult patients at high risk for extubation failure (recommendation B, conditional recommendation, very low certainty in the evidence).

Question 3: Is a cuff leak test (CLT) recommended before extubation of mechanically ventilated patients?
A CLT can be performed, at the discretion of the clinician, prior to extubation of adult patients receiving mechanical ventilation who are at high risk of developing post-extubation stridor (PES) (recommendation B, conditional recommendation, low certainty in the evidence).

Question 4: Are steroids recommended before extubation in mechanically ventilated patients with a failed CLT?
To prevent PES and reintubation, we recommend that mechanically ventilated adult patients who have failed a CLT receive an administration of steroids before extubation (recommendation B, conditional recommendation, moderate level of evidence).

Question 5: Is it recommended to compute the Rapid Shallow Breathing Index (RSBI) before extubating mechanically ventilated adult patients?
The RSBI can be computed at the discretion of the clinician (recommendation B, conditional recommendation, low certainty in the evidence).

Question 6: Is inspiratory muscle training (IMT) recommended for critically ill adult patients on mechanical ventilation?
We recommend IMT for critically ill adult patients on mechanical ventilation to increase the success rate of weaning from mechanical ventilation (recommendation B, conditional recommendation, low certainty in the evidence).

Question 7: Is early physical rehabilitation recommended for critically ill patients on mechanical ventilation?
We recommend early rehabilitation for critically ill adult patients to increase the success rate of weaning from mechanical ventilation (recommendation B, conditional recommendation, low level of evidence).

Question 8-1: Is a high-flow nasal cannula (HFNC) recommended over conventional oxygen therapy (COT) for adult patients undergoing planned extubation?
For successful weaning from mechanical ventilation, we recommend HFNC over COT in adult patients undergoing planned extubation (recommendation B, conditional recommendation, moderate certainty in the evidence).

Question 8-2: Is non-invasive ventilation (NIV) recommended over COT for adult patients undergoing planned extubation?
For successful weaning from mechanical ventilation, we recommend NIV over COT in adult patients undergoing planned extubation who are at high risk for weaning failure (recommendation B, conditional recommendation, moderate certainty in the evidence).

Question 8-3: Is HFNC recommended over NIV for adult patients undergoing planned extubation?
For adult patients undergoing planned extubation, either HFNC or NIV can be applied at the discretion of the clinician

KEY MESSAGES

- We have developed clinical guidelines on mechanical ventilation liberation to provide meaningful recommendations to clinicians.
- These guidelines reflect the best treatment for patients seeking liberation from mechanical ventilation.

(recommendation E, expert consensus recommendation, very low certainty in the evidence).

Question 9: Should an early tracheostomy be performed to successfully wean adult patients from mechanical ventilation?

For patients expected to require prolonged mechanical ventilation, it is recommended that early tracheostomy not be performed (recommendation I, conditional deferred, low certainty in the evidence).

INTRODUCTION

Mechanical ventilation is omnipresent in intensive care units (ICUs) [1]. Every year, more than 1 million patients globally undergo mechanical ventilation for acute respiratory failure and other disease entities [2]. One of the most critical decisions clinicians face in managing these critically ill patients is how and when to liberate them from invasive ventilation. Prolonged mechanical ventilation carries risks of ventilator-associated lung injury, ventilator-associated pneumonia, diaphragm dysfunction, increased in-hospital mortality, and increased lengths of ICU and hospital stays [3,4]. On the other hand, premature extubation attempts can lead to reintubation, increased rates of ventilator-associated pneumonia, and other adverse outcomes [5].

In 1987, Hall and Wood [6] proposed that the ultimate objective is not to wean patients from mechanical ventilation, but rather to liberate them from it . They argued that the term "weaning," which simply denotes the removal of the tube and transition to oral feeding, inadequately captures the pain, challenges, and struggles of both patients being liberated from mechanical ventilation and the healthcare professionals caring for them. The process of liberation from mechanical ventilation involves complex challenges, such as regulating sedation and pain; appropriately managing delirium; and addressing ventilator-associated pneumonia and ventilator-induced lung injury, neuromuscular complications associated with critical illness, weakness of the diaphragm muscle, inadequate nutritional support, and sleep deprivation. It is a multifaceted process that demands dedication and emotional support from healthcare professionals as patients navigate issues that hinder the liberation process. Therefore, when devising appropriate strategies for liberation from mechanical ventilation, it is essential to consider not the individual experiences of healthcare professionals, but also scientific and systematic evidence.

In the decades since Hall and Wood's pronouncement, many studies have investigated methods and tools for identifying the readiness of mechanically ventilated patients for successful liberation [7-9]. However, no relevant recommendations have been proposed in Korea since the original publication of the Guidelines for Liberation from Mechanical Ventilation in 2010 [10].

Therefore, the Korean Society of Critical Care Medicine (KSCCM) has developed these clinical guidelines on mechanical ventilation liberation. These guidelines recommend the best possible treatments for patients seeking liberation from mechanical ventilation.

MATERIALS AND METHODS

Introduction

These clinical practice recommendations were developed using a *de novo* approach by KSCCM. The systematic review used for the *de novo* development followed the Cochrane methodology. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology was adopted to assess the level of evidence and determine the grade of each recommendation (Supplementary Material 1).

Deriving the Key Questions

The key questions (KQs) reflect processes involved in weaning patients from mechanical ventilation, including predictors and methods for success, and were prioritized based on content that could be clinically important or controversial to the users of these guidelines. Subsequently, the KQs deemed to warrant a final recommendation were selected by consensus among the development committee members.

Literature Search

The literature search formula was established by deriving preliminary search terms through discussions between methodology experts and the development committee members in charge of each KQ. The working committee members proposed search terms, and drafts of search formulas reflecting those proposals were prepared for each clinical question using PubMed. The search terms were selected based on terms related to mechanical ventilation and weaning from mechanical ventilation. The search strategy was prepared by selecting natural language and considering control and words similar to the content of each KQ. Searches were conducted in Medline (PubMed), Embase, Cochrane Library, and KoreaMed.

Rationale for Literature Selection

For the selection process, two development committee members were assigned to each KQ, and duplicates search results were eliminated. Literature selection was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. The complete selection process is included in the appendix. The inclusion and exclusion criteria for each KQ were derived based on PICO (population, intervention, comparator, and outcome [benefit and harm]).

Quality and Level of Evidence in the Primary Articles

The level of evidence for each KQ was assessed in two aspects: the quality of the individual primary articles and the single level of evidence presented by all the articles combined. Two reviewers independently assessed the quality of the primary articles for each KQ, and disagreements were resolved by consensus among the responsible committee members and the methodology expert. Cochrane's Risk of Bias 2.0 was used for randomized controlled trials (RCTs), and the Risk of Bias for Nonrandomized Studies 2.0 was used for nonrandomized studies.

Level of Evidence and Grading of Recommendations

The level of evidence was assessed using the GRADE methodology based on discussions between a methodology expert and individual committee members to ensure the objectivity of the level of evidence assessment and application of the same evaluation criteria throughout the recommendations. The direction and strength of each recommendation were determined by the four factors considered in the GRADE methodology: level of evidence, effect size (weighing of benefits and harms), patient values and preferences, and resources.

Meta-analysis

A meta-analysis was performed when unexplained heterogeneity or two or more outcomes were reported in the included studies. However, when the studies had different designs, they were not combined, and meta-analyses were performed separately. In addition, under suspicion of duplication of research data, only the study published most recently or involving the largest sample size was included in the final meta-analysis.

RESULTS

KQ 1. Protocol for liberation from mechanical ventilation

Question 1: In critically ill patients receiving ventilation, does a mechanical ventilation weaning protocol increase the success rate of ventilator liberation?

Recommendation

For critically ill patients on mechanical ventilation, we recommend the use of a mechanical ventilation weaning protocol (recommendation B, conditional recommendation, moderate certainty in the evidence).

Remarks: In studies published to date, no differences have been reported to depend on who (doctors, nurses, or respiratory therapists) applies the weaning protocols for mechanical ventilation, but it is necessary to develop weaning protocols suitable for each institution.

Values and Preference

This recommendation places a high value on decreasing the duration of mechanical ventilation, weaning time, and length of ICU stay.

Background

Mechanical ventilation is an important part of critical care in patients with respiratory failure. However, unnecessarily prolonged mechanical ventilation results in various complications, such as tracheal injuries, barotrauma, and ventilator-associated pneumonia, which can increase in-hospital mortality [3]. If the cause of respiratory failure is being treated and improving, reducing the patient's level of sedation, increasing their waking consciousness (spontaneous awakening trial), and assessing their readiness for withdrawal from mechanical ventilation daily with a SBT is recommended [11]. The criteria for patients to be weaned from mechanical ventilation are: respiratory rate <35/min, adequate oxygenation (FiO_2 ≤40% and positive end-expiratory pressure [PEEP] ≤8 cm H_2O, oxygen saturation >90%, or PaO_2/FiO_2 ratio >150), adequate cough reflex, conscious status on the Richmond Agitation-Sedation Scale from –2 to +1 (an awake state, no use of continuous sedation, and no or minimal use of vasopressors) [12]. Patients admitted for traumatic brain injury, those diagnosed with peripheral neuromuscular disease, and those who refused reintubation were excluded from the relevant study [12]. The

criteria for extubation failure are a respiratory rate ≥35 /min, use of accessory muscles of respiration, oxygen saturation <90%, (FiO_2 0.4 or at least 6 L/min of supplemental oxygen), heart rate ≥140 beats/min, systolic blood pressure <90 mm Hg or >180 mm Hg, cyanosis, skin mottling, and decreased level of consciousness.

Previously, ICU physicians evaluated the patient's condition and then went through the process of mechanical ventilation weaning and extubation. However, ICU physicians are generally unable to continuously evaluate a single patient, and so the process was affected by the physician's schedule. Therefore, it has been reported that ICU nurses or respiratory therapists should use mechanical ventilation weaning protocols to shorten the mechanical ventilation period and ICU length of stay [13,14].

Summary of Evidence

Our literature search strategy returned 972 studies after duplicate removal; of them, 680 studies were screened, and 161 articles were reviewed. In that way, we identified six RCTs and nine observational cohort studies evaluating the effects of mechanical ventilation weaning protocols [15-32]. In our meta-analysis, we found no significant statistical differences in unsuccessful weaning between patients in the RCTs whose care teams followed a weaning protocol and patients treated without a weaning protocol (risk ratio [RR], 0.93; 95% confidence interval [CI], 0.73–1.20; P=0.59), and no statistical difference was found in the before and after studies (RR, 0.75; 95% CI, 0.51–1.10; P=0.14). A sensitivity analysis conducted with six before and after studies showed the same results (RR, 0.84; 95% CI, 0.65–1.08; P=0.17). Patients in the RCTs whose care teams followed a weaning protocol had a significantly shorter duration of mechanical ventilation than those treated without a weaning protocol (mean difference [MD], –25.34 hours; 95% CI, –42.4 to –8.38; P=0.003), and the before and after studies demonstrated similar results between the two groups (MD, –2.35 days; 95% CI, –4.10 to –0.60; P=0.009). A sensitivity analysis conducted with seven before and after studies showed the same result (MD, –2.31 days; 95% CI, –2.99 to –1.63; P<0.001). Patients in the RCTs whose care teams followed a weaning protocol had a significantly shorter weaning time than those treated without a weaning protocol (MD, –38.60 hours; 95% CI, –69.20 to –7.99; P=0.01). The RCTs also showed a significantly shorter ICU length of stay in patients whose care teams followed a weaning protocol (MD, –1.49 days; 95% CI, – 2.65 to –0.33; P=0.01). However, the before and after studies showed a decreasing trend of ICU length of stay in patients whose care teams followed a weaning protocol, but no significant difference between the two groups (MD, –3.24 days; 95% CI, –6.52 to –0.77; P=0.05). ICU mortality in the RCTs was lower but the difference between the groups was not statistically significant (RR, 0.83; 95% CI, 0.59–1.17; P=0.30). However, when all studies were considered together, patients whose care teams followed a weaning protocol had significantly lower ICU mortality (RR, 0.57; 95% CI, 0.42–0.77; P=0.0003).

In summary, the present meta-analysis shows following a weaning protocol is associated with a decreased duration of mechanical ventilation (25 hours), weaning time (39 hours), and length of ICU stay (1.49 days). However, there is no significant correlation between the use of a mechanical ventilation weaning protocol and the incidence of ventilator-associated pneumonia or ICU mortality. It is essential to implement a mechanical ventilation weaning protocol tailored to the situation of each hospital. ICU doctors should treat and manage critically ill patients, but it is difficult for them to consistently provide bedside monitoring during weaning from mechanical ventilation. Therefore, ICU nurses and respiratory therapists play a vital role in applying the mechanical ventilation weaning protocol. However, the number of ICU nurses and respiratory therapists can vary widely depending on the size and severity of cases in the ICU of each hospital. For example, the number of ICU nurses varies from 2.5 to 5 patients per nurse, and respiratory therapists are rarely found in ICUs except in large tertiary hospitals. Thus, the mechanical ventilation weaning protocol should be established and implemented to accommodate the specific ICU situation in each hospital. For practical applications, additional ICU nurses or respiratory therapists might be required, which can increase labor costs. In conclusion, we recommend that each hospital tailor a mechanical ventilation weaning protocol to its specific circumstances and implement it with critically ill patients on mechanical ventilation.

KQ 2. PSV vs. the T-piece in patients during SBTs

Question 2-1: Is PSV recommended over the T-piece during SBT in adult patients receiving mechanical ventilation?

Question 2-2: Is PSV recommended over the T-piece during SBT in adult patients at high risk of extubation failure?

Recommendation

(1) Either PSV or the T-piece can be applied during SBTs in adult patients being weaned from mechanical ventilation (recommendation B, conditional recommendation, low certainty in the evidence).

Remarks: In usual practice, an SBT with PSV or the T-piece is performed for 30 minutes to 2 hours before attempting extubation.

(2) Either PSV or the T-piece can be applied during SBTs of adult patients at high risk for extubation failure (recommendation B, conditional recommendation, very low certainty in the evidence).

Remarks: High risk factors for extubation failure are failure of a first SBT, old age (≥65 years), chronic respiratory disease, chronic heart disease, and head trauma.

Values and Preference

There is insufficient evidence to recommend any method during an SBT. The proper method of SBT should be decided in consideration of each patient's condition, as assessed in a careful evaluation by the clinician.

Background

Delayed extubation and prolonged mechanical ventilation lead to ventilator-associated pneumonia and are associated with increased lengths of stay and both in-hospital and ICU mortality [33]. On the other hand, extubation failure also increases morbidity and in-hospital and ICU mortality in patients receiving mechanical ventilation [34-36]. Therefore, it is critical to determine the proper method of SBT to accelerate extubation and increase the success rate of ventilator weaning [37].

In most studies, SBT with PSV or the T-piece was conducted for 30 minutes to 2 hours before attempting extubation. When the SBT was conducted with PSV, a low inspiratory pressure, such as 5–8 cm H_2O, was applied, and PEEP was not applied or applied at ≤ 5 cm H_2O. In all studies, successful extubation/weaning was defined as the absence of reintubation within 48–72 hours after extubation, except for one study that defined successful weaning as the absence of death or reintubation within 7 days after extubation [38]. Although a recent guideline recommended PSV over the T-piece during SBT [39], the number of studies supporting that recommendation was small, and conflicting results have been published. Moreover, no recommendation for patients at high risk of extubation failure has been made. Therefore, we compared PSV with the T-piece and investigated which method was associated with better clinical outcomes in adult patients undergoing SBT. In addition, we performed subgroup analyses of patients at high risk of extubation failure to determine the proper method of SBT in this high-risk group.

Summary of Evidence

Among the 1,393 studies returned by our search, 30 were reviewed, and 14 were included in the meta-analyses (supplemental data: literature search strategy figure). Of them, 11 were RCTs [12,40-49], and the remaining were a post-hoc study [50], a prospective cohort study [38], and a retrospective cohort study [51]. In our meta-analyses of the RCTs, we found no significant differences between the PSV and T-piece groups in terms of successful extubation/weaning (RR, 1.01; 95% CI, 0.94–1.09; P=0.33) or reintubation (RR, 0.97; 95% CI, 0.69–1.37; P=0.86). Likewise, in in RCTs, the length of stay in the hospital and ICU did not differ between the two methods (MD, 0.88 days; 95% CI, –0.51 to 2.27; P=0.21 and MD, –0.06 days; 95% CI, –0.86 to 0.74; P=0.88). In addition, patients in the RCTs who received PSV showed a trend toward lower hospital and ICU mortality, but the differences were not statistically significant (RR, 0.97; 95% CI, 0.69–1.37; P=0.86 and RR, 0.86; 95% CI, 0.64–1.11; P=0.85, respectively). However, only a few studies were included in the meta-analyses for hospital mortality (n=8) and ICU mortality (n=7), so the lower tendencies for mortality in the PSV group could not be adequately evaluated.

The subgroup analyses for patients at high risk of extubation failure included seven studies: five RCTs [12,41,45,46,49], a post-hoc study [50], and a retrospective cohort study [51]. The definition for the group at high-risk of extubation failure was different in each study: patients with old age (≥65 years), chronic heart disease, or chronic lung disease (n=2) [3,33], with failure of their first SBT (n=2) [41], with both chronic obstructive pulmonary disease (COPD) and failure of the first SBT(n=1) [45], with head trauma (n=1) [49], and with persistent atrial fibrillation (n=1) [51]. In the subgroup analyses of patients from the RCTs at high risk of extubation failure, we found no differences between the PSV and T-piece groups in terms of successful extubation/weaning (RR, 1.04; 95% CI, 0.90–1.20; P=0.59), reintubation (RR, 1.09; 95% CI, 0.84–1.42; P=0.51), in-hospital and ICU mortality (RR, 2.00; 95% CI, 0.67–5.94; P=0.21 and RR, 0.93; 95% CI, 0.62–1.42; P=0.75, respectively), or ICU length of stay (MD, –0.91 days; 95% CI, –2.69 to 0.88; P=0.32).

In summary, our meta-analysis shows no statistically sig-

nificant differences between PSV and the T-piece in terms of successful extubation/weaning, reintubation, hospital and ICU mortality, or hospital and ICU lengths of stay, independent of a high risk of extubation failure. In a recent guideline, the American Thoracic Society and American College of Chest Physicians suggested that the initial SBT be conducted with inspiratory pressure augmentation (5–8 cm H_2O) rather than without (T-piece or continuous positive airway pressure) in acutely hospitalized patients ventilated for more than 24 hours (conditional recommendation, moderate quality of the evidence) [39]. Their recommendation was based on a pooled meta-analyses of a few studies (2 to 4), which showed that conducting the SBT with pressure augmentation was more likely to be successful (RR, 1.11; 95% CI, 1.02–1.18) (n=3), produced a higher rate of extubation success (RR, 1.09; 95% CI, 1.02–1.18) (n=4), and was associated with a trend toward lower ICU mortality (RR, 0.74; 95% CI, 0.45–1.24) (n=2) [39]. However, the results of our meta-analysis are consistent with those from a recent large-scale RCT, which showed no significant differences in major clinical outcomes, including 28-day ventilator-free days [22]. Therefore, in this guideline, we suggest that either PSV or the T-piece can be applied during SBT when planning to wean adult patients from mechanical ventilation. In addition, we suggest that either PSV or the T-piece can be applied during SBT in the high-risk group as well, because we found no significant differences between the two methods in patients at high risk of extubation failure. However, caution should be exercised because the definition of the group at high-risk for extubation failure was different in each study. Therefore, we suggest that the proper method of SBT should be decided individually based on each patient's condition, as assessed in a careful evaluation by the clinician. Furthermore, these recommendations might change depending on the results of an ongoing, large-scale RCT [52].

KQ 3. Cuff leak test

Question 3: Is a CLT recommended before extubation of mechanically ventilated patients?

Recommendation

A CLT can be performed prior to extubation in adult patients who are at high risk of developing PES, at the discretion of the clinician (recommendation B, conditional recommendation, low certainty in the evidence).

Remarks: The risk factors for PES are being female, duration of intubation >6 days, large endotracheal tube and high cuff pressure, traumatic intubation, and reintubation after unplanned extubation.

Values and Preference

This recommendation places a high value on minimizing the incidence of PES and reintubation and a lower value on the burden associated with performing the CLT.

Background

Although endotracheal intubation is a critical procedure in patients requiring respiratory support, it can cause mucosal inflammation and edema of the larynx due to mechanical injury from the endotracheal tube. Laryngeal edema is likely to occur in patients intubated for more than 36 hours [53]. After extubation, laryngeal edema can narrow the upper airway, causing PES, which has an incidence between 6% and 37% [54]. PES can be associated with a failure of extubation requiring reintubation with mechanical ventilation within 24 to 72 hours after planned extubation [55,56]. Failure of extubation increases the in-hospital length of stay, morbidity, and mortality [54,57]. It is difficult to predict the risk of PES and subsequent reintubation prior to a planned extubation. It is also difficult to determine the presence of upper airway edema by direct examination of the vocal cords in intubated patients.

The CLT is used to indirectly assess laryngeal edema [58,59]. It is a quantitative method that measures the difference between the amount of expired air when a balloon cuff is inflated and deflated. Normally, air leaks around the endotracheal tube when the balloon cuff is deflated, and that leakage is reduced in the presence of laryngeal edema.

Summary of Evidence

No RCTs have evaluated the effect of the CLT. We identified 16 relevant observational cohort studies that used different methods for the CLT, generally auscultation of airflow as a qualitative test or measurement of cuff leak volume as a quantitative test [55,56,60-66]. The threshold for a failed CLT in quantitative testing was a cuff leak volume between 50 and 283 ml (median, 110 ml) and a proportion of cuff leak volume between 10% and 57% (median, 15.1%). Six studies assessed the rate of PES in patients undergoing CLT, and three studies assessed the incidence of reintubation in patients undergoing CLT. In our meta-analysis, patients with a failed CLT had an increased incidence of PES (pass 15.9% vs. failure 44.8%; odds ratio, 4.01; 95% CI, 2.31–6.96; P=0.02), but a failed CLT was not

associated with an increased reintubation rate (pass 13.1% vs. failure 14.5%; odds ratio, 1.38; 95% CI, 0.50–3.82; P=0.54). Our meta-analysis showed that a failed CLT had low sensitivity but high specificity as a predictor of PES, with a pooled sensitivity and specificity of 0.52 (95% CI, 0.44–0.59) and 0.8 (95% CI, 0.87–0.90), respectively. The pooled positive and negative likelihood ratios of CLT for the prediction of PES were 4.06 (95% CI, 2.99–5.50) and 0.51 (95% CI, 0.36–0.72), respectively, and the pooled diagnostic odds ratio was 9.68 (95% CI, 4.92–19.04). The area under the summary receiver operating characteristics curve of CLT for the prediction of PES was 0.88. Four studies evaluated the rate of reintubation in patients who developed PES, and six studies examined the duration of mechanical ventilation in patients with and without PES. Our meta-analysis shows that patients with PES had an increased rate of intubation (PES positive 50% vs. PES negative 5.7%; RR, 14.59; 95% CI, 9.11–23.37; P<0.001) and prolonged duration of mechanical ventilation (RR, 2.63; 95% CI, 1.17–4.09; P<0.001).

In summary, the present meta-analysis shows that patients who failed the CLT were associated with an increased incidence of PES, and patients with PES were likely to have increased reintubation rates. The CLT is simple, inexpensive, safe, and easy to perform according to a protocol at the bedside, and it can be useful in making the decision to extubate if the patient passes it. However, despite its high specificity, the CLT has low sensitivity for predicting PES, so passing the CLT does not exclude upper airway obstruction or reduce the likelihood of reintubation, as our meta-analysis shows. Several studies have reported that administering steroids to patients who failed a CLT can significantly reduce PES and reintubation rates [67-70]. Given the high specificity of the CLT, clinicians should consider administering systemic steroids to patients with a failed test to reduce PES and reintubation. This meta-analysis shows that patients who undergo reintubation for PES require a longer duration of mechanical ventilation. High risk factors for PES include being female, duration of intubation >6 days, large endotracheal tube and high cuff pressure, traumatic intubation, and reintubation after unplanned extubation [71-76]. We recommend performing a CLT prior to extubation in adult patients who are at high risk of developing PES, at the discretion of the clinician.

KQ 4. Steroids for Patients with a Failed CLT

Question 4: Are steroids recommended before extubation in mechanically ventilated patients with a failed CLT?

Recommendation

To prevent PES and reintubation, we recommend the administration of steroids before extubation of adult patients who have failed a CLT (recommendation B, conditional recommendation, moderate level of evidence).

Remarks: Steroids were administered at least 4 hours before extubation in patients intubated for 24 to 48 hours, but no standard method or dosage for prophylactic steroids has been established.

Values and Preference

This recommendation places a high value on minimizing the incidence of PES and reintubation in patients with a failed CLT and a lower value on the burden associated with the side effects of steroid use.

Background

Laryngeal edema typically occurs in patients with endotracheal intubation for more than 36 hours. Inflammation and edema of the laryngeal mucosa after extubation can cause upper respiratory tract obstruction, PES, and respiratory failure. Extubation failure occurs when reintubation and mechanical ventilation support are required within 24–72 hours after planned extubation, and patients with such a failure have a poor prognosis and increased in-hospital lengths of stay and mortality.

Steroids are known to prevent PES by reducing the deposition of inflammatory cells in the larynx caused by long-term intubation [77,78]. Although a recent guideline recommended the administration of systemic steroids prior to extubation, the literature supporting this recommendation was sparse, and the included studies used different regimens, which led to inconsistent results [14].

Summary of Evidence

Among the 548 studies returned in the literature search, 440 were reviewed, and eight were included in the meta-analyses. Of those, we analyzed four RCTs involving patients ready to be liberated from mechanical ventilation who failed a CLT [67]. A study by Cheng et al. [67] compared outcomes between methylprednisolone (MPD; 40 mg every 6 hours for 24 hours), MPD (40 mg once for 24 hours), and no treatment [68,69]. The studies by Lee et al. [68] and Baloch et al. [69] compared the results of dexamethasone (5 mg every 6 hours for 24 hours) with the results of no treatment [58,59]. Another study by Cheng et al. [70] compared the outcomes of MPD (40 mg administered 4

hours prior to extubation) with those of no treatment. In our meta-analysis, patients with a failed CLT who received systemic steroids had a significantly lower incidence of PES and reintubation than those with a failed CLT who did not receive steroid treatment (RR, 0.37; 95% CI, 0.24– 0.57; P<0.0001 and RR, 0.29; 95% CI, 0.15–0.56; P=0.0003). However, the duration of intubation did not differ significantly between patients receiving systemic steroids and those not receiving systemic steroids (MD, 0.91 days; 95% CI, –3.47 to 5.29; P=0.68).

In summary, the present meta-analysis shows that the administration of systemic corticosteroids is associated with a reduced incidence of PES and reintubation in patients who fail the CLT. The 2017 American Thoracic Society/American College of Chest Physician guideline on weaning from mechanical ventilation recommends that steroids be administered for at least 4 hours before extubation of adult patients who have failed a CLT but are nonetheless ready for be weaned from mechanical ventilation [14]. However, no protocol has been standardized for the dosage, timing, or methods of administering prophylactic steroids to patients with a failed CLT. Further research is needed on the use of steroids to prevent airway complications and reintubation after extubation in patients with absolute contraindications to steroids, such as a history of hypersensitivity reactions, live vaccine injections, systemic fungal infections, osteoporosis, or uncontrolled hyperglycemia. A barrier to steroid application is the lack of clarity and variation in high-risk-group screening methods, types of steroids used, dosages, usage, and administration duration, which all differ depending on the country or institution. Multinational, multicenter studies are needed to remove this barrier. In conclusion, we recommend the administration of steroids at least 4 hours before extubation to prevent PES and reintubation in adult patients who have failed a CLT.

KQ 5. Rapid shallow breathing index

Question 5: Is it recommended to compute the RSBI before extubating mechanically ventilated adult patients?

Recommendation

The RSBI of adult patients being liberated from mechanical ventilation can be computed at the discretion of the clinician (recommendation B, conditional recommendation, low certainty in the evidence).

Values and Preference

Evidence is insufficient to recommend routine measurement of the RSBI before extubation to predict the successful liberation of mechanically ventilated adult patients.

Background

The RSBI is calculated as the ratio of respiratory frequency to tidal volume (f/VT), and it is used during unassisted spontaneous respiration to assess readiness to wean from mechanical ventilation [79]. The RSBI can predict the success or failure of weaning from mechanical ventilation [80]. An RSBI of less than 105 f/VT is associated with an increased likelihood of successful weaning. Patients on a ventilator who cannot tolerate unassisted spontaneous breathing tend to have a high RSBI, with rapid breathing and low tidal volumes. However, the RSBI is affected by several factors, including agitation, anxiety, fever, endotracheal tube size, and suctioning. The literature for the utility of the RSBI is limited, and what studies exist used different measurement methods, timing of measurement, settings at the time of measurement, and cut-off values.

Summary of Evidence

No RCTs have evaluated the utility of the RSBI. Among the 110 studies returned by our literature search, 22 were reviewed, and 8 were included in the meta-analyses, of which 7 were prospective and 1 was retrospective [79-88]. A prospective study conducted in 1995 by Epstain et al. reported that using an RSBI cut-off of 100, successful extubation could be predicted with a high positive predictive rate, low false negative rate, and high sensitivity [89]. In the largest multicenter study to date, by Frutos-Vivar et al. [81], 121 (13.4%) of 900 patients who passed the SBT had extubation failure; they showed that a 1-unit increase in the RSBI increased the risk of extubation failure by 0.9%. However, the reference value of the RSBI has varied in different studies, and several studies have suggested values (57–80 breaths/min/L) much lower than the previously recommended value of 105 breaths/min/L [81,83,85,87]. In four studies evaluating the predictive power of the RSBI for extubation failure, the area under the receiver operating characteristic curve ranged from 0.63 to 0.92, indicating good to excellent predictive power [82,83,85,87]. Segal et al. [84] compared the risk of extubation failure according to changes in the variation of RSBI values measured continuously for 2 hours and reported that an increase in the RSBI of 20% or more was associated with extubation risk. Thus, observed RSBI values have appeared to correlate with successful extu-

bation in several studies. However, the different measurement methods, measurement timings, settings at the time of measurement, and cut-off values used in the various studies make it difficult to present a standard protocol. Recent research has proposed a new measure to replace the RSBI, though it did not deny the clinical predictive value of the RSBI [87]. Another method attempted to improve the predictive ability of the RSBI without increasing the difficulty or complexity of the measurement. In conclusion, although results for a definitive RSBI value have been inconsistent among studies, the RSBI has been identified as a predictor of successful weaning from mechanical ventilation.

Panel Judgments

The evaluated studies show consistency in the usefulness of the RSBI, but there are not many high-quality systematic reviews and meta-analyses, and the level of evidence was judged to be low. The presented studies agree that the RSBI is an excellent predictor of successful extubation and report consistent results, but additional research is needed on the following two topics. First, it is necessary to demonstrate whether the previously suggested values of RSBI 100 or 105 breaths/min/L can be widely applied. Most of the literature referenced in this recommendation suggests lower values. Second, because the RSBI is known to have higher sensitivity than specificity, a reference value that can correct that deficiency is needed. An indicator that could be referenced together with the aforementioned optimal value of the RSBI would be very useful.

Because the RSBI is not a medical tool that provides additional tests, drugs, or treatments to the patient, it can cause no long-term harm to the patient, unlike other tests, if it is accurately measured and interpreted. However, it is difficult for inexperienced medical personnel to perform immediately, and the reliability of the results is lowered when it is measured without training. In addition, if the measurement results are distorted, the patient's mechanical ventilation period could be increased unnecessarily, or reintubation could be required due to premature extubation, either of which could cause harm to the patient. Therefore, careful attention is required when measuring the RSBI and applying the result to clinical practice.

The RSBI does not require expensive equipment or incur costs due to additional drug administration, but it does require trained personnel. Particularly in secondary hospitals that do not have a dedicated ICU doctor or do not work 24 hours a day, additional costs for education and personnel could be required. Therefore, because no standard value is available, it will be possible to apply the RSBI in 1st and 2nd level medical institutions in Korea only after the insurance system is overhauled.

KQ 6. Inspiratory muscle training

Question 6: Is IMT recommended for critically ill adult patients on mechanical ventilation?

Recommendation

For critically ill adult patients on mechanical ventilation, we recommend the use of IMT to increase the success rate of weaning from mechanical ventilation (recommendation B, conditional recommendation, low certainty in the evidence). Remarks: IMT can be performed when the patient is hemodynamically stable, maintains adequate oxygen saturation (PaO_2 ≥60 mm Hg, FiO_2 <0.4, PEEP 5–8 cm H_2O), and has an alert mental status, although results differ across studies.

Values and Preference

This recommendation places a high value on minimizing weaning failure rates and increasing maximal inspiratory pressure.

Background

IMT, which is a form of pulmonary rehabilitation, is a technique to improve inspiratory muscle strength and respiratory muscle function. Respiratory muscle training results in structural adaptations, including changes in muscle fiber, hypertrophy, and muscle thickness, and functional adaptations, including enhancements in strength, power, endurance, peak inspiratory flow, and maximal inspiratory and expiratory pressures [88]. IMT can help reduce dyspnea by improving the maximal inspiratory pressure in patients with severe COPD [89].

Prolonged mechanical ventilation is known to impair respiratory muscle function, particularly the diaphragm, and such weakening of the respiratory muscles is one of the important causes of failure to wean from mechanical ventilation [90]. The maximal inspiratory pressure is reported to predict the success of mechanical ventilation weaning [91,92].

Summary of Evidence

We found 288 studies, after excluding duplicates, through our literature search strategy. Of them, 288 studies were screened,

and 57 articles were reviewed. We then selected five RCTs and one retrospective cohort study [93-98]. In our meta-analysis, patients who received IMT showed a significantly lower unsuccessful weaning rate than those who did not receive IMT (RR, 0.61; 95% CI, 0.45–0.85; P=0.17). Patients receiving IMT had a trend toward a lower duration of mechanical ventilation and weaning time, but those differences were not statistically significant (MD, –16.07 days; 95% CI, –46.65 to 14.52; P=0.30 and MD, –9.65 hours; 95% CI, –25.42 to 6.13; P=0.23, respectively). Peak inspiratory pressure was significantly higher in patients receiving IMT than in those not receiving IMT (MD, –12.12 cm H_2O; 95% CI, –19.11 to –5.13; P<0.001).

In summary, the present meta-analysis shows that receiving IMT is associated with decreased weaning failure and increased peak inspiratory pressure, although the duration of mechanical ventilation and weaning time did not differ between patients receiving IMT and those not receiving IMT. IMT in mechanically ventilated patients could help maintain respiratory muscle function, potentially facilitating a smoother transition away from mechanical ventilation. A few studies have reported that a shorter duration of mechanical ventilation in patients receiving IMT was associated with an increased likelihood of being able to walk independently upon discharge from the hospital [7]. Therefore, IMT contributes to a rapid return to independent daily activities and improved quality of life after ICU discharge, as well as reduced medical costs [99]. Implementing IMT in clinical practice will require a respiratory rehabilitation protocol suitable for the Korean medical environment and an adequate number of ICU nurses or respiratory therapists. However, there is currently no standardized protocol regarding the devices and methods of IMT, so further research is needed. In conclusion, we recommend IMT to increase the success rate of weaning from mechanical ventilation in critically ill adult patients.

KQ 7. Early rehabilitation

Question 7: Is early physical rehabilitation recommended for critically ill patients on mechanical ventilation?

Recommendation

We recommend early rehabilitation to increase the success rate of weaning critically ill adult patients from mechanical ventilation (recommendation B, conditional recommendation, low level of evidence).

Remarks: There are different types of early rehabilitation protocols, and they should be applied according to the patient's condition, eligibility, and goals.

Values and Preference

This recommendation places a high value on reducing the ICU length of stay and the duration of mechanical ventilation.

Background

Prolonged mechanical ventilation can lead to ventilator-induced diaphragmatic dysfunction due to diaphragm weakness and muscle wasting and overall weakness due to a lack of physical activity or immobility, and both of those conditions can cause failure to wean from mechanical ventilation [100]. Prolonged mechanical ventilation and weaning failure are the main risk factors for death in the ICU, and they also increase the burden of medical costs [101]. Early rehabilitation during critical care is beneficial in reducing the incidence of ICU-acquired weakness, accelerating patients' functional recovery and increasing the likelihood of weaning from mechanical ventilation. Many clinicians have concerns and anxiety about the possibility that a patient's condition could deteriorate during rehabilitation because of the hemodynamic instability common in critically ill patients. However, comprehensive early rehabilitation is known to be safe and effective in reducing the occurrence of complications and the duration of hospitalization and mechanical ventilation in ICU patients [102]. Several guidelines recommend early rehabilitation in critically ill patients [103,104]. In those guidelines, "early rehabilitation" includes any early mobilization program administered by a nurse, physical therapist, or intensivist.

Summary of Evidence

We found 416 studies, excluding duplicates, through our literature search strategy, of which 288 studies were screened, and 57 articles were reviewed. We identified five RCTs and two retrospective cohort studies that evaluated the effects of early rehabilitation [105-111]. In our meta-analysis, patients in the RCTs who received early rehabilitation had a significantly shorter duration of mechanical ventilation than those who did not receive early rehabilitation (MD, –3.04 days; 95% CI, –4.98 to –1.10; P=0.002). A sensitivity analysis conducted with three RCTs showed the same result (MD, –2.07 days; 95% CI, –2.92 to –1.22; P<0.001), and the retrospective cohort studies also showed the same results (MD, –2.29 days; 95% CI, –3.94 to – 0.63). In addition, the RCTs showed a significantly shorter ICU length of stay in patients who received early rehabilita-

tion (MD, –3.42 days; 95% CI, –6.31 to –0.53; P=0.02), and the sensitivity analysis conducted with three RCTs confirmed that result (MD, –2.18 days; 95% CI, –3.69 to –0.67; P<0.001). However, there was no significant difference between the groups in the retrospective cohort studies (MD, 0.16 days; 95% CI, –6.49 to 6.81; P=0.96). No RCT reported results about unsuccessful weaning, but the retrospective cohort studies reported significant differences between the groups (RR, 0.69; 95% CI, 0.48 to 0.99; P=0.04).

In summary, the present meta-analysis shows that early rehabilitation is associated with a decreased duration of mechanical ventilation (2.29 days) and length of ICU stay (3.42 days). Past ICU treatment has focused on treating acute critical illness while sedating and restraining ICU patients. Several studies have reported that rehabilitation in the ICU strengthens muscles of the limbs and respiration, encourages the recovery of physical and mental function, reduces the incidence of ICU-acquired weakness, and improves quality of life after discharge [102]. Rehabilitation can be safely performed in the ICU, even in critically ill patients receiving extracorporeal membrane oxygenation (ECMO) or continuous renal replacement therapy (CRRT) [112,113]. Safe implementation of early rehabilitation in patients with a variety of devices, including a ventilator, central catheter, CRRT, and ECMO, requires a comprehensive and multidisciplinary approach, and efficiency can be maximized and safety secured only through cooperation among physicians, nurses, and physical therapists. It requires a collaborative effort from a multidisciplinary team to tailor interventions to each individual patient's needs and conditions. Therefore, implementing early rehabilitation for critically ill patients could be difficult, depending on the size of the hospital, the composition of the medical staff, and the severity of the patient's condition. In conclusion, we recommend early rehabilitation in critically ill adult patients on mechanical ventilation.

KQ 8. HFNC vs. NIV vs. COT

Question 8-1: Is HFNC recommended over COT for adult patients undergoing planned extubation?

Question 8-2: Is NIV recommended over COT for adult patients undergoing planned extubation?

Question 8-3: Is HFNC recommended over NIV for adult patients undergoing planned extubation?

Recommendations

(1) For successful weaning from mechanical ventilation, we recommend HFNC over COT in adult patients undergoing planned extubation (recommendation B, conditional recommendation, moderate certainty in the evidence). Remarks: Patients at high risk of post-extubation respiratory failure include those with chronic respiratory failure, hypercapnia ($PaCO_2$ >45 mm Hg) after successful SBT, failed first SBT, and chronic respiratory disorders.

(2) For successful weaning from mechanical ventilation, we recommend NIV over COT in adult patients undergoing planned extubation who are at high risk for weaning failure (recommendation B, conditional recommendation, moderate certainty in the evidence).

Remarks: Factors that increase the risk of weaning failure include a failed first SBT, old age (>65 years), body mass index (BMI) >30 kg/m^2, ejection fraction <40%, history of extubation failure, mechanical ventilation for heart failure, presence of COPD, Acute Physiology and Chronic Health Evaluation (APACHE) II score >12, airway disorder (e.g., high risk for laryngeal edema), impaired expectoration, comorbidities ≥2, delayed or failed weaning from mechanical ventilation, and duration of mechanical ventilation ≥7 days.

(3) Either HFNC or NIV can be applied in adult patients undergoing planned extubation, at the discretion of the clinician (recommendation E, expert consensus recommendation, very low certainty in the evidence).

Clinical considerations: Healthcare professionals in South Korea are more experienced with HFNC than NIV, which is different from those in Europe and China, and HFNC might be the better choice for high-risk patients in terms of patient comfort and potential skin damage. However, NIV might be more useful for patients with respiratory failure and hypercapnia caused by acute exacerbation of COPD or patients with pulmonary edema. Particularly for high-risk patients, the method of oxygen therapy following ventilator weaning should be chosen according to the healthcare provider's experience level, experiences in the ICU, the patient's adaptation, and patient-specific considerations (e.g., claustrophobia).

Remarks: Given the side effects of NIV, such as facial skin damage, abdominal discomfort, mask-related discomfort, eye irritation, mouth dryness, nasal congestion, and NIV intolerance, the purpose, benefits, and discomfort associated with NIV should be explained to the patient before NIV application, and treatment decisions should be made accordingly.

Values and Preference

These recommendations place a high value on minimizing respiratory failure after extubation and reintubation through the application of HFNC. NIV might produce the same results as HFNC, but only in high-risk patients, not all patients. Evidence is insufficient to recommend HFNC or NIV after extubation to reduce hospital mortality, ICU mortality, or ICU and hospital lengths of stay. HFNC and NIV do not differ in ICU or 28-day mortality and reintubation. However, HFNC is preferred over NIV in terms of patient comfort, the need for bronchoscopy for sputum removal, and the side effects of NIV.

Background

The final step of weaning from mechanical ventilation is extubation, and this critical step determines the success or failure of weaning. The functional residual capacity maintained using PEEP during invasive ventilation can drop rapidly and lead to hypoxemia and extubation failure, defined as the need for reintubation within 24–72 hours after planned extubation. Extubation failure occurs relatively frequently, at a rate of 10%–20%, and is associated with a longer overall duration of mechanical ventilation, higher risk for tracheostomy, increased healthcare costs, and higher mortality rate [114-118].

One of the most important factors in the prevention of reintubation is the choice of oxygen delivery system. COT uses a nasal cannula and oxygen mask. At a flow rate of 15 L/min, conventional oxygen delivery systems might be inappropriate for patients requiring rapid respiration and a high inspiratory flow rate. HFNC is a device that provides a high flow of warm and humidified oxygen, with a flow rate of up to 60 L/min, through a nasal cannula. It can generate PEEP, reduce CO_2 through a dead space washout, reduce the work of breathing, improve oxygenation, and comfort patients with respiratory failure [119]. The effects of HFNC in patients undergoing planned extubation remain unknown. Few studies have demonstrated that HFNC after extubation reduces the requirement for respiratory support escalation, improves oxygenation, or is associated with better comfort and a lower reintubation rate than COT [120,121]. Corley et al. [122] found no improvement in respiratory function in patients with BMI ≥30 kg/m^2 who underwent HFNC after planned extubation. NIV is a type of respiratory support delivered through a mask or helmet but without an invasive artificial airway such as intubation or tracheostomy. NIV has two primary types: continuous positive airway pressure and bilevel positive airway pressure (also called pressure support ventilation). It can improve oxygenation and comfort for patients with respiratory failure and decrease the need for invasive ventilation and its complications. Thus, NIV is recommended for patients with respiratory failure, particularly patients with hypercapnia and COPD exacerbation and patients with acute cardiogenic pulmonary edema [123]. Although NIV is more effective than COT in patients at high risk for extubation failure, there is a lack of consensus regarding the superiority of high-flow oxygen therapy or NIV for successful weaning and extubation. Therefore, we performed a systematic review and meta-analysis to compare the benefits of COT, HFNC, and NIV as prophylactic treatments intended to promote successful weaning from mechanical ventilation in patients undergoing planned extubation.

Summary of Evidence

Among the 1,559 studies returned by the literature search, 144 were reviewed, and 28 were included in the meta-analyses. Of those, 11 were RCTs comparing the effects of HFNC and COT in patients undergoing planned extubation [124-136], 12 were RCTs comparing outcomes between NIV and COT in patients undergoing planned extubation [137-141], and 5 were RCTs comparing the outcomes and adverse effects of HFNC and NIV in patients undergoing planned extubation [133-137].

HFNC vs. COT: In our meta-analysis, patients who received HFNC had a significantly lower incidence of weaning failure and reintubation after planned extubation than those who received COT (RR, 0.49; 95% CI, 0.39–0.61; P<0.001 and RR, 0.47; 95% CI, 0.29–0.76; P=0.002, respectively). The subgroup analyses of patients at high risk for post-extubation respiratory failure, i.e., those with chronic respiratory failure; hypercapnia ($PaCO_2$ >45 mm Hg) after successful SBT; a failed first SBT; and COPD, chronic bronchitis with dyspnea, smoking history, bronchiectasis, tuberculosis sequelae, chest wall deformity, or restrictive ventilatory defect, returned similar results for weaning failure (RR, 0.45; 95% CI, 0.34–0.61; P<0.001), but HFNC and COT did not differ in reintubation (RR, 0.76; 95% CI, 0.28–2.07; P=0.60). Hospital and ICU mortality did not differ significantly between the groups either (RR, 0.90; 95% CI, 0.52–1.54; P=0.70 and RR, 1.14; 95% CI, 0.31–4.17; P=0.84, respectively). Ventilator-associated pneumonia showed similar results (RR, 0.53; 95% CI, 0.23–1.25; P=0.15). No significant differences in ICU and hospital lengths of stay were observed between the groups, regardless of patients' risk status (MD, 0.10 days; 95% CI, –0.03 to 0.23; P=0.13 and MD, –0.29 days; 95% CI, –1.03 to 0.45; P=0.44, respectively).

NIV vs. COT: The high-risk factors for post-extubation respi-

ratory failure identified in these studies were: (1) chronic respiratory failure, (2) hypercapnia after successful SBT ($PaCO_2$ >45 mm Hg), (3) failed first SBT, (4) chronic respiratory disorders (e.g., COPD, chronic bronchitis with dyspnea, smoking history, bronchiectasis, tuberculosis sequelae, chest wall deformity, and restrictive ventilatory defect), (5) excessive phlegm and diminished coughing, (6) upper airway stridor after extubation, (7) age ≥65 years, (8) heart failure as the reason for mechanical ventilation, and (9) APACHE II score >12 on the day of extubation. In this meta-analysis, NIV was not significantly more effective in the total patient population in terms of weaning failure and reintubation (RR, 0.26; 95% CI, 0.04–1.76; P=0.17 and RR, 0.47; 95% CI, 0.14–1.60; P=0.23, respectively). Only high-risk patients who received NIV had a significantly lower incidence of weaning failure and reintubation after planned extubation, compared with those who received COT (RR, 0.30; 95% CI, 0.18–0.51; P<0.001 and RR, 0.63; 95% CI, 0.44–0.90; P=0.01, respectively). ICU and in-hospital mortality did not differ significantly between the groups, regardless of the level of risk (RR, 0.66; 95% CI, 0.35–1.25; P=0.67 and RR, 0.77; 95% CI, 0.43–1.39; P=0.37, respectively). Patients who received NIV showed a trend toward lower ICU mortality, but the difference was not statistically significant (MD, –2.17 days; 95% CI, –4.86 to 0.52; P=0.06). No significant differences in hospital length of stay or hospital length of stay after extubation were observed between the groups (MD, –1.03 days; 95% CI, –3.45 to 1.39; P=1.00 and MD, –3.04 days; 95% CI, –9.51 to 3.43; P=0.11, respectively).

HFNC vs. NIV: None of these studies included only adult patients who received mechanical ventilation, and all five studies included patients with underlying diseases or conditions that could pose a risk of weaning failure. HFNC and NIV did not differ in 28-day or ICU mortality (RR, 0.94; 95% CI, 0.42–2.09; P=0.33 and RR, 1.19; 95% CI, 0.79–1.78; P=0.40, respectively). In addition, reintubation and treatment failure (switch to another treatment or premature discontinuation) did not differ significantly between HFNC and NIV (RR, 0.98; 95% CI, 0.79–1.23; P=0.89 and RR, 1.04; 95% CI, 0.86–1.25; P=0.72, respectively). Patients who received HFNC had a significantly lower incidence of skin damage within 24 to 48 hours (RR, 0.50; 95% CI, 0.30–0.81; P=0.005).

In summary, the present meta-analysis shows that among all patients, not just high-risk patients, receiving HFNC is associated with a lower incidence of weaning failure and reintubation after planned extubation, compared with COT. NIV shows a significant reduction in weaning failure and reintubation after planned extubation, compared with COT, only in high-risk patients. However, the outcomes did not differ significantly between HFNC and NIV, except for skin damage.

HFNC has become essential equipment in the ICU and has been covered by health insurance in Korea since its designation as a new health technology in 2015. Compared with COT, HFOT has a significant advantage not only in successful ventilator weaning and prevention of reintubation, but also in reducing patient discomfort, such as dry airways and nasal pain, by providing humidification through the HFNC. Three studies reported cases of nasal pain, dry airways, and consequent patient discomfort due to low humidity; however, the prevalence of such cases was significantly lower in the HFNC group than in the COT group in all studies [106,107,117].

NIV is not effective in reducing weaning failure and reintubation among all patients, but it showed significantly better outcomes than COT in high-risk patients. NIV has various adverse effects, including facial skin damage, abdominal discomfort, mask-related discomfort, eye irritation, and NIV intolerance. Regarding skin damage, three studies reported skin redness or abrasion in 14 out of 48 (29%), 5 out of 79 (6%), and 2 out of 20 (10%) patients on NIV, respectively [121,122,131]. Two studies reported abdominal distention in 1 out of 79 patients (1%) and 5 out of 69 patients (7%), respectively [121,123]. Other symptoms, including eye irritation, oral dryness, and nasal congestion and mask intolerance, were reported in 7% of patients [121,124]. No study has investigated subjective preferences between NIV and COT among patients with respiratory failure undergoing planned ventilator weaning. Given the outcomes and side effects of NIV, it is not an ideal treatment for all patients; nonetheless, NIV can be considered an appropriate method for patients undergoing planned extubation who are at high risk of weaning failure. The purpose, benefits, and discomfort associated with NIV should be explained to the patient prior to NIV application, and treatment decisions should be made accordingly.

Except for the skin damage associated with NIV, the outcomes of mortality, reintubation, and treatment failure did not differ between HFNC and NIV in patients undergoing planned extubation. To date, no study has investigated patients' values or preferences between HFNC and NIV, but the dyspnea score did not differ between the two methods in the included studies [142,143]. However, the comfort score increased over time with HFNC, unlike with NIV, and the need for bronchoscopy for sputum removal after extubation was significantly lower with HFNC than NIV [144]. In addition, HFNC is associated

with less frequent abdominal distension and higher treatment tolerance [143,145]. Notably, HFNC can be perceived as a form of oxygen therapy, whereas NIV can be perceived as a form of mechanical ventilation. Because some patients or families have reservations about mechanical ventilation, it is important to adequately explain the effectiveness, purpose, type, and expected outcomes of each treatment, and obtaining informed consent from patients and their families is important.

The recent European Respiratory Society clinical guidelines on respiratory failure suggest using either HFNC or NIV in postoperative patients who are at high risk of respiratory complications, but they suggest using NIV rather than HFNC in non-surgical patients at high risk for weaning failure, so long as there are no absolute or relative contraindications [146]. Although the European Respiratory Society guidelines, which considered HFNC to have a higher reintubation rate than NIV, were based more on preventing reintubation than on patient discomfort, our meta-analysis suggests that either HFNC or NIV can be applied at the discretion of the clinician in adult patients undergoing planned extubation.

KQ 9. Early tracheostomy

Question 9: Should an early tracheostomy be performed to successfully wean adult patients from mechanical ventilation?

Recommendation

For patients expected to require prolonged mechanical ventilation, it is recommended that early tracheostomy not be performed for successful weaning from mechanical ventilation (recommendation I, conditional deferred, low certainty in the evidence).

Remarks: Early tracheostomy is defined as a surgical procedure performed no more than 7 days after endotracheal intubation in a patient requiring prolonged mechanical ventilation.

Values and Preference

This recommendation about the value of early tracheostomy, which has been considered to be associated with improved survival and reduced ventilator and ICU-related complications, remains controversial.

Background

Tracheostomy is a surgical procedure frequently performed in ICU patients requiring airway protection or prolonged ventilatory support due to airway narrowing or obstruction, difficulty removing excess sputum or saliva, altered of level of consciousness, or persistent respiratory failure [147]. Tracheostomy has been performed in a variety of clinical situations, with percutaneous techniques becoming increasingly popular in recent years. Early tracheostomy in patients requiring prolonged mechanical ventilation might have benefits such as reducing the work of breathing, reducing sedation requirements, and decreasing the risk of pneumonia [148-150]. However, early tracheostomy carries its own risks, including bleeding, infection, tube dislodgement, and laryngeal injury [151]. No optimal timing for the transition to tracheostomy has been established, and practice varies among clinicians, with most transitioning between 1 and 3 weeks after intubation [152]. No benefits for early tracheostomy (i.e., before 10 days after intubation) have been demonstrated, and it carries the potential of unnecessary surgery in patients who could be extubated.

Summary of Evidence

We found 941 studies, excluding duplicates, through our literature search strategy, of which 291 studies were screened, and 106 articles were reviewed. We identified 7 RCTs evaluating the effects of early tracheostomy in mechanically ventilated adults admitted to an ICU [153-159]. In the study of Rumbak et al. [153], tracheostomy was performed within 48 hours, whereas in studies by Bösel et al. [157] and Zheng et al. [158], tracheostomy was performed within 1–3 days and at 3 days, respectively. In studies by Blot et al. [155], Trouillet et al. [156], and Young et al. [159], tracheostomy was performed at 4 days. In the study by Barquist et al. [154], tracheostomy was performed at 8 days. In our meta-analysis, the duration of mechanical ventilation and the length of ICU stay in the early tracheostomy group (tracheostomy performed within 7 days) were 3.2 days and 5.8 days shorter, respectively, than with usual care. However, those differences were not statistically significant (MD, –3.16 days; 95% CI, –11.47 to 5.15; P=0.10 and MD, –5.80 days; 95% CI, –12.80 to 1.20; P=0.10, respectively). Patients who received an early tracheostomy had 14% less in-hospital mortality than those who received usual care, but that difference was not statistically significant (RR, 0.86; 95% CI, 0.74–1.01; P=0.07).

In summary, the present meta-analysis shows no statistically significant differences between early tracheostomy and usual care in terms of the duration of mechanical ventilation, ICU length of stay, or in-hospital mortality. Seven selected articles had limitations in that they varied in study design, target

disease, and when and how tracheostomy was performed (especially whether percutaneous tracheostomy was performed). In addition, we were unable to identify enough information about serious adverse events for analysis, so we had to reserve the assessment of safety issues. Guidelines for tracheostomy from the Korean Bronchoesophagological Society, published in Korea in 2020, recommend early (7–14 days) tracheostomy in patients who are predicted to need a ventilator for a long period of time (weak recommendation, low evidence), but they note that judgment based on the patient's condition is important [160]. The 2017 Guideline on Tracheostomy in Critically Ill Patients does not recommend early tracheostomy because, although it could reduce ventilator duration, it does not reduce the incidence of pneumonia or ICU length of stay or mortality [161]. Future large RCTs in specific disease groups or with percutaneous tracheostomy are needed, and we look forward to a further analysis of studies conducted in those conditions.

SUMMARY

We have conditionally recommended the following in these guidelines. Apply a weaning protocol to increase the success rate of liberation from mechanical ventilation, and allow both PSV and T-piece trials during spontaneous breathing attempts in adult patients undergoing mechanical ventilation, including high-risk patients. For patients at high risk of PES, perform a CLT (if appropriate under clinical judgment) before extubation. In patients who fail the CLT, administer steroids before extubation to prevent PES and the need for reintubation. When planning liberation from mechanical ventilation for adult patients, clinical judgment should be used in deciding whether to implement the RSBI, IMT, and early rehabilitation. Additionally, we suggest that using HFNC or NIV as post-extubation oxygen therapy is more advantageous than COT for preventing reintubation. When choosing between HFNC and NIV post-extubation, the expert consensus is that the choice can be made based on the clinician's judgment of patient condition and preferences. As for the effects of early tracheostomy (within 7 days) on the success of liberation from mechanical ventilation, we conditionally recommend that it not be performed. Much work remains to be done to improve the process of liberation from mechanical ventilation, and our guidelines will undergo revision based on future research findings.

CONFLICT OF INTEREST

All panel nominees were reviewed and vetted by a joint conflict of interest review committee composed of members from Korean Society of Critical Care Medicine. After review, nominees who were found to have no substantial conflict of interest were approved to conduct this work.

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SUPPLEMENTARY MATERIALS

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