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STUDY PROTOCOLS

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Clinical utility of diaphragmatic ultrasonography for mechanical ventilator weaning in adults: A study protocol for systematic review and meta-analysis

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Abstract

Background and Aims: Mechanical ventilation is associated with several risks, including barotrauma, ventilator-associated pneumonia, and ventilator-induced diaphragmatic dysfunction. A delay in weaning from mechanical ventilation increases these risks, and prolonged weaning has been shown to increase hospital mortality. Various tools have been used in clinical practice to predict successful weaning from mechanical ventilation; however, they have a low prognostic accuracy. The use of ultrasonography in intensive care units is an area of growing interest since it is a noninvasive, convenient, and safe modality. Since ultrasonography can provide real-time assessment of diaphragmatic morphology and function, it may have clinical utility in predicting successful mechanical ventilator weaning. This study aimed to describe a protocol to assess the effectiveness of diaphragmatic ultrasonography in the decision-making process for ventilator weaning in terms of its impact on clinical outcomes.

Methods: This systematic review of published analytical research will use an aggregative thematic approach according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines. We will perform a comprehensive search for studies on the MEDLINE, Embase, and Cochrane Central Register of Controlled Trials databases. Two authors will independently perform abstract and full-text screening and data extraction. Additionally, a meta-analysis and the risk of bias evaluation will be conducted, as appropriate.

Conclusion: Systematic reviews on the effectiveness of diaphragmatic ultrasonography in the decision-making process for ventilator weaning in terms of its impact on clinical outcomes are lacking. The results of this systematic review may serve as a basis for future clinical trials. Systematic review registration: This protocol was registered with the Open Science Framework: https://osf.io/cn8xf.

KEYWORDS

diaphragmatic dysfunction, ultrasound, ventilator weaning

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1 | INTRODUCTION

1.1 | Description of the condition

Mechanical ventilation is required for 33% of patients admitted to the intensive care unit (ICU).[1] Studies have reported a 28% increase in the rates of ventilator-related lung injury and ventilator-related complications and a 60%–80% increase in the rate of ventilator-induced diaphragmatic dysfunction during ventilatory management.[2,3] Furthermore, a delay in weaning from mechanical ventilation increases these risks, with a 2.5% increase in hospital mortality in cases of three or more failed weaning attempts and when the weaning period is longer than 7 days.[4] The weaning period may account for approximately 41% of the duration of ventilation.[5] Minute volume, maximal inspiratory pressure, and rapid shallow breathing index (RSBI: respiratory rate/tidal volume) have been used in clinical practice to predict successful weaning from the ventilator; however, these measures based on physical examination alone have proven inadequate in predicting weaning.[6] Even with the use of spontaneous breathing trial, which is now widely used for weaning patients from mechanical ventilation, 13%–26% of patients who were successfully weaned from mechanical ventilation needed re-intubation within 48 h, complicating the prediction of an appropriate time for weaning patients from mechanical ventilation.[1,7]

The difficulty in weaning patients from mechanical ventilation is attributed to various conditions that result in an imbalance between respiratory muscle strength and respiratory load. There is an increasing awareness that diaphragmatic dysfunction is common and frequently severe in mechanically ventilated patients and likely contributes to weaning failure.[3] The diaphragm is the major inspiratory muscle, and its proper functioning is critical for optimal breathing. Under resting conditions, the diaphragm carries out approximately 75% of the pulmonary ventilation process, with an excursion of 1–2 cm; in contrast, the amplitude ranges from 7 to 11 cm during forced breathing. The diaphragm can be damaged by hypotension, hypoxia, and sepsis, which are commonly observed in patients with critical illnesses. Additionally, ventilator-induced diaphragmatic dysfunction can occur under mechanical ventilation due to decreased force on the diaphragm. Numerous studies have indicated that diaphragmatic dysfunction can lead to weaning failure and prolonged mechanical ventilation, as well as pulmonary complications, such as atelectasis and pneumonia, which are risk factors for extubation failure. Accordingly, diagnosing diaphragmatic dysfunction early, before extubation, is critical for avoiding weaning failure. This study aimed to describe a protocol to assess the effectiveness of diaphragmatic ultrasonography in the decision-making process for ventilator weaning in terms of its impact on clinical outcomes.

1.2 | Description of the intervention

Owing to its noninvasive nature, ease of use, and patient safety, the use of ultrasonography in ICUs is an area of growing interest.

Key points

- **What is known**: Delayed weaning from mechanical ventilation is associated with ventilator-related lung injury and ventilator-related complications.
- **What is new**: Currently, predicting the success of ventilator weaning based on physical examination alone is complicated, and a predictive index for successful weaning has not yet been established. However, the findings of the systematic review are expected to serve as a foundation for future clinical trials.
- **Clinical implication**: Carrying out this systematic review on the effectiveness of diaphragmatic ultrasonography during ventilator weaning will help translate the evidence on the new ventilator weaning index into clinical practice.

Since ultrasonography can provide real-time assessment of diaphragmatic morphology and function, it may have clinical utility in predicting successful mechanical ventilator weaning. Furthermore, it has been suggested that diaphragm muscle thickness and maximal diaphragmatic excursion (DE) on ultrasonography at the time of weaning can be used to accurately predict successful weaning.[8,9]

The following three diaphragm sonographic predictors of successful ventilation weaning have been proposed: DE, diaphragm thickening fraction (DTF), and the diaphragmatic rapid shallow breathing index (DRSBI). Under the M-mode, the DE is defined as the distance between the highest and lowest diaphragm-movement positions. The DTF indicates the variation in diaphragm thickness during respiratory effort and is calculated as follows:

$$\mathrm{DTF} = \frac{\text{Thickness at end of inspiration} - \text{Thickness at end of expiration}}{\text{Thickness at the end of expiration}}$$

DRSBI is the ratio between respiratory rate (RR) and DE, and is calculated as follows:

$$\mathrm{DRSBI} = \frac{\mathrm{RR}}{\mathrm{DE}}$$

1.3 | How the intervention might work

Physicians can use ultrasonography during critical care to dynamically evaluate pulmonary and extrapulmonary factors that cause respiratory and weaning failure. Additionally, data on diaphragmatic movement parameters (e.g., amplitude, force, and contraction velocity), specific motion patterns, and changes in diaphragmatic thickness during inspiration are readily

available as bedside assessments. As diaphragmatic and skeletal muscle parameters are related to muscle strength and function, ultrasonography is an effective method for the early detection and assessment of acquired weaknesses.

Additionally, ultrasonographic assessment of the diaphragm enables noninvasive determination of the timing of ventilator weaning, leading to successful weaning. Past randomized control trials (RCTs) have defined successful weaning from a ventilator as maintenance of 48 h of spontaneous breathing.[8,10] Alansary and Hakim[8] reported significantly improved weaning rates when ventilation weaning was based on protocols using ultrasonography to evaluate DTF and DE compared to ventilation weaning without ultrasonography guidance. Mowafy and Abdelgalel[10] reported no significant differences in rates of successful weaning when ventilation weaning was based on protocols using ultrasonography to evaluate DRSBI compared to ventilation weaning without ultrasonography guidance, but found that DRSBI had better diagnostic accuracy compared to using the rapid shallow breathing index without ultrasonography guidance when predicting successful ventilation weaning.

1.4 | Significance of this review

There are several systematic reviews and meta-analyses on the prognostic accuracy of diaphragmatic dysfunction during ventilator weaning.[11,12] However, to our knowledge, the effectiveness of using ultrasonography in making decisions about ventilator weaning in terms of its impact on clinical outcomes has not been reported previously. Several RCTs assessing the effectiveness of clinical decision-making based on the ultrasonographic assessment of diaphragm function in ventilated patients have been reported recently, highlighting the importance of this systematic review. Considering this background, the aim of our study was to describe a protocol for conducting a systematic review of available RCTs to assess the effectiveness of diaphragmatic ultrasonography in the decision-making process for ventilator weaning in terms of its impact on clinical outcomes.

2 | MATERIALS AND METHODS

2.1 | Protocol development

This protocol is compliant with the standards of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols Statement[13] and is registered on the Open Science Framework Registries (OSF) website: https://osf.io/cn8xf.

The systematic review will be conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions.

3 | CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

3.1 | Studies

We decided to include clinical trials with parallel-group RCTs and crossover trials.

3.2 | Participants

All adult ICU patients who had been intubated and were managed by mechanical ventilation will be included.

3.3 | Interventions

All studies employing the use of ultrasonographic assessment of the diaphragm to guide clinical decision-making regarding extubation will be included.

3.4 | Outcome measures

A table of findings based on the following primary and secondary outcomes will be created. We will use the mean difference or standardized mean difference for continuous outcomes and the risk difference or risk ratio with a 95% confidence interval for dichotomous outcomes, as appropriate. Where quantitative integration is impossible, the results will be narratively summarized and evaluated in individual tests.

3.5 | Primary outcome

Successful weaning from mechanical ventilation without reintubation within 48 h.

3.6 | Secondary outcomes

- Total duration of mechanical ventilation (time in hours, from mechanical ventilation initiation to discontinuation).
- Re-intubation after 48 h.
- Total ICU length of stay.
- Adverse event: infections arising from cross-contamination during ultrasonography procedures.

3.7 | Search methods for identification of studies

To identify the studies for inclusion in this review, the following electronic databases will be searched: MEDLINE, Embase, and

CENTRAL. This systematic search will be limited to human studies published in English. We designed the search strategy based on an advice from a librarian with experience in conducting systematic reviews. The search terms will include the following MeSH and keyword terms: respiration, ventilator weaning, diaphragm, and ultrasonography.

4 | DATA COLLECTION

4.1 | Selection of studies

The citations will be stored using the Endnote software, and removed if duplicated. Using the EndNote software, two review authors (NT and TI) will screen the titles and abstracts to identify articles that meet the inclusion criteria. Disagreements will be resolved by discussion; if necessary, a third author (TH) will be included in the discussion.

4.2 | Data extraction and management

Data extraction for eligible studies will be performed by two authors (NT and TI), who will independently extract data from articles that meet the inclusion criteria. The two authors will independently perform data extraction for the following outcomes: basic study characteristics (publication year, title, authors, and main aim), study methods (study design, exposures, primary outcome, secondary outcomes, and confounders used in analyses), and participant characteristics (age, sex, antecedents, and comorbidities). Additionally, for each study outcome, we will extract information on its definition, type, and assessment, as well as the amount of and reasons for missing data.

4.3 | Assessment of risk of bias in included studies

The risk of bias evaluation of all included papers will be performed by two authors (NT and HN) individually, using the Cochrane risk of bias tools described in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions Version 6.3.[14] A third author (TH) will resolve any discrepancies between the two reviewers (NT and HN). If necessary, differences in the bias risk assessment will be resolved by a fourth reviewer (EO). We will assess the following seven bias risk domains: sequence generation for randomization, allocation concealment, blinding of participants and personnel, blinding of outcome assessments, incomplete outcome data, selective outcome reporting, and other biases.

4.4 | Strategy for data synthesis

We will perform data synthesis analyses using the DerSimonian-Laird-type random-effects model. Bewteen-studies heterogeneity will be assessed using Cochrane's Q test and Higgins' I^2-statistic. Possible heterogeneity will be analyzed through meta-regression and subgroup analyses. Publication bias will be assessed using forest plots and the Egger test. Review Manager (RevMan) software, version 5.4 (Cochrane Collaboration), will be used for data analyses.

We intend to use the Grading of Evaluation, Development, and Evaluation Recommendation Rating pro (GRADEpro) tool to assess the overall strength of the evidence. In RCTs, the GRADE system evaluates the limitations of the study, inconsistencies, indirect evidence, inaccuracies, and publication bias, classifying the evidence as high, moderate, low, or very low.[15]

5 | STATUS OF THE STUDY

The study is in the data collection and analysis phase. The initial deadline for its completion is March 31, 2024.

6 | DISCUSSION

Currently, predicting the success of ventilator weaning based on physical examination alone is complicated, and a predictive index for successful weaning has not yet been established. Since diaphragmatic ultrasonographic evaluation is a noninvasive, simple, rapid, and detailed assessment of diaphragm morphology and function, it is expected to improve the success rate of ventilator weaning and shorten the weaning period when included as part of conventional weaning indices. Recently, several RCTs that have focused on the effectiveness of diaphragm ultrasonographic evaluation during ventilator weaning have reported it to be more accurate than conventional physical assessments, with improved weaning success rates and short weaning periods. However, no systematic review has summarized these RCTs or evaluated their quality to date. Therefore, this study aimed to describe a protocol for a systematic review of RCTs on the effectiveness of diaphragmatic ultrasonography during ventilator weaning to translate the evidence on the new ventilator weaning index into clinical practice.

AUTHOR CONTRIBUTIONS

Naonori Tashiro: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; validation; visualization; writing—original draft; writing—review and editing. **Takeshi Hasegawa**: Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing—original draft; writing—review and editing. **Hiroki Nishiwaki**: Formal analysis; investigation; methodology; validation; visualization; writing—original draft; writing—review and editing. **Takashi Ikeda**: Data curation; investigation; methodology. **Hisashi Noma**: Formal analysis; validation; writing—review and editing. **William Levack**: Supervision; writing—original draft; writing—review and editing. **Erika Ota**: Investigation; methodology; resources; software; supervision; validation; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data Availability Statement is not available.

TRANSPARENCY STATEMENT

The lead author Naonori Tashiro affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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