REVIEW ARTICLE

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Promoting Evidence-Based Practice in Acute Respiratory Distress Syndrome: A Systematic Review

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OBJECTIVE: Low tidal volume ventilation and prone positioning are recommended therapies yet underused in acute respiratory distress syndrome. We aimed to assess the role of interventions focused on implementation of low tidal volume ventilation and prone positioning in mechanically ventilated adult patients with acute respiratory distress syndrome.

DATA SOURCES: PubMed, Excerpta Medica Database, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Central Register of Controlled Trials.

STUDY SELECTION: We searched the four databases from January 1, 2001, to January 28, 2021, for studies that met the predefined search criteria. Selected studies focused on interventions to improve implementation of low tidal volume ventilation and prone positioning in mechanically ventilated patients with acute respiratory distress syndrome.

DATA EXTRACTION: Two authors independently performed study selection and data extraction using a standardized form.

DATA SYNTHESIS: Due to methodological heterogeneity of included studies, meta-analysis was not feasible; thus, we provided a narrative summary and assessment of the literature. Eight nonrandomized studies met our eligibility criteria. Most studies looked at interventions to improve adherence to low tidal volume ventilation. Most interventions focused on education for providers. Studies were primarily conducted in the ICU and involved trainees, intensivists, respiratory therapists, and critical care nurses. Although overall quality of the studies was very low, the primary outcomes of interest suggest that interventions could improve adherence to or implementation of low tidal volume ventilation and prone positioning in acute respiratory distress syndrome.

MEASUREMENTS AND MAIN RESULTS: Two authors independently performed study selection and data extraction using a standardized form. Due to methodologic heterogeneity of included studies, meta-analysis was not feasible; thus, we provided a narrative summary and assessment of the literature. Eight nonrandomized studies met our eligibility criteria. Most studies looked at interventions to improve adherence to low tidal volume ventilation. Most interventions focused on education for providers. Studies were primarily conducted in the ICU and involved trainees, intensivists, respiratory therapists, and critical care nurses. Although overall quality of the studies was very low, the primary outcomes of interest suggest that interventions could improve adherence to or implementation of low tidal volume ventilation and prone positioning in acute respiratory distress syndrome.

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CONCLUSIONS: There is a dearth of literature addressing interventions to improve implementation of evidence-based practices in acute respiratory distress syndrome. Existing interventions to improve clinician knowledge and facilitate application of low tidal volume ventilation and prone positioning may be effective, but supporting studies have significant limitations.

KEY WORDS: acute respiratory distress syndrome; adherence; implementation; prone position; systematic review; tidal volume

Acute respiratory distress syndrome (ARDS) is a common form of respiratory failure with substantial global impact and high mortality (1, 2). Landmark studies have demonstrated a significant reduction in mortality with the use of low tidal volume ventilation (LTVV), defined as tidal volume (TV) of less than or equal to 6 mL/kg of predicted body weight (PBW), and the use of early prone positioning in mechanically ventilated patients with ARDS (3, 4). Based on these findings, multisociety guidelines strongly recommend LTVV with TV of 4–8 mL/kg PBW for mechanical ventilation in all patients with ARDS as well as prone positioning in patients with severe ARDS (5).

Despite convincing evidence of the benefits of these interventions, the adoption of LTVV and prone positioning for ARDS has been suboptimal (6–10) with recent studies estimating only 65% of patients with ARDS receive LTVV, and only 10–33% of patients with moderate-to-severe ARDS receive prone positioning (2, 11, 12). Key barriers to successful implementation include failure to recognize ARDS, inaccurate measurement of patient height for calculation of PBW, and concerns about patient discomfort (2, 10). It is unclear what strategies are currently being employed to overcome these barriers.

To develop a better understanding of existing approaches to implementation of LTVV and prone positioning, we conducted a systematic review of the literature to identify interventions designed to improve implementation of, or adherence to LTVV and prone positioning in mechanically ventilated patients with ARDS. The objective was to determine whether the presence of practice guides such as protocols, policies, aids, checklists, or educational interventions increases the use of evidence-based practices in ARDS.

MATERIALS AND METHODS

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist to report the methods of this review (13). Our review was registered with the international prospective register of systematic reviews (The International Prospective Register of Systematic Reviews [PROSPERO] ID: CRD42019123131).

Clinical Questions and Outcomes

This systematic review addressed the following questions in population, intervention, comparator, outcome (PICO) format: 1) Does the presence of practice guides (e.g., protocols, policies, aids, checklists and/or props) compared with no practice guides increase the adherence to or implementation of LTVV in mechanically ventilated patients with ARDS? and 2) Does the presence of practice guides (e.g., protocols, policies, aids, checklists and/or props) compared with no practice guides increase the adherence to or implementation of prone position in mechanically ventilated patients with ARDS? Although our initial PROSPERO application included a PICO related to the use of neuromuscular blockade as an adjunctive therapy in ARDS (14), a randomized controlled trial (Reevaluation of Systemic Early Neuromuscular Blockade trial) was published after our protocol was created, finding no significant difference in 90-day mortality with the use of early neuromuscular blockade in patients with moderate-to-severe ARDS (11). In light of these results, we removed this PICO from our review.

Primary outcomes were the proportion of eligible patients who receive LTVV or prone positioning. Secondary outcomes of interest included the following: in-hospital mortality, 30- and 90-day mortality, cost, hospital and ICU length of stay, duration of mechanical ventilation, adverse events to patients or staff (such as physical injuries) directly related to implementing the intervention, and staff comfort with the intervention as reported by study-specific survey or scale.

Data Sources and Search Strategy

With the help of a professional medical librarian at the University of Washington Health Sciences Library, we developed search strategies specific to the PICO

questions. We then searched PubMed, Excerpta Medica Database, Cochrane Central Register of Controlled Trials, and Cumulative Index to Nursing and Allied Health Literature from January 1, 2001 until January 28, 2021. Our search strategy included subject and text-word terms to identify articles on protocols, policies, aids, checklists, and/or props to enhance implementation and adherence to LTVV and prone positioning in patients greater than or equal to 18 years (**e-Appendix 1**, http://links.lww.com/CCX/A579).

Eligible studies detailed interventions intended to increase implementation of or adherence to LTVV and prone positioning in adults with ARDS. We did not include studies focused solely on the efficacy or effectiveness of adjunctive therapies for ARDS (i.e., studies designed to assess the benefits and harms of LTVV).

The inclusion criteria were specified as studies published in English that reported on detailed interventions intended to increase implementation or adherence to LTVV or prone positioning in mechanically ventilated adult patients (≥ 18 yr) with ARDS. We limited the search to studies published in English and limited to those published after 2001, to account for the impact of a landmark study showing a significant reduction in in-hospital mortality when using lower TVs in patients with ARDS (3).

We excluded studies in subjects younger than 18 years old, those evaluating nonmechanically ventilated subjects, studies focused solely on the efficacy or effectiveness of therapies for ARDS (e.g., a study designed to assess the benefits and harms of LTVV), studies lacking outcome measures, non-English language publications, conference abstracts, unpublished trial data, and dissertations/theses.

Study Selection, Extraction, and Analysis

Results were exported to RefWorks (ProQuest). Two authors (S.P.G., S.L.) simultaneously and independently screened all titles/abstracts for relevance to our PICO questions, obtained full-text articles that were potentially eligible for inclusion, and selected the relevant studies for the review. We also screened the reference lists of included articles for additional potentially relevant articles.

Two reviewers (S.P.G., T.L.S.) then independently and simultaneously reviewed the relevant studies and abstracted data on study characteristics and results using standardized forms, which were then reviewed for accuracy and completeness by a third reviewer (A.L.J). Finally, two authors (S.P.G., A.L.J) independently assessed the quality of the retrieved evidence using the "Grade of Recommendations, Assessment, Development and Evaluation" (GRADE) approach (15). An objective of this review was to perform a meta-analysis of the data identified in our review; however, heterogeneity in study design and reporting of outcomes precluded this type of quantitative analysis. Therefore, studies were summarized using a narrative format.

RESULTS

Study Characteristics

Our search identified a total of 8,015 citations; 2,693 duplicates were excluded, leaving 5,322 titles and abstracts to be screened. Title and abstract screening led to the exclusion of 5,244 articles. Full-text articles were retrieved for 78 articles. Of these 78 articles, nine met our eligibility criteria (16–24) (**Fig. 1**). No additional studies were identified from screening reference lists.

Of the nine studies, seven were prepost studies (16–21, 23), one was an interrupted time series (22), and one was a retrospective, observational study (24). Additional study characteristics are highlighted in **e-Table 1** (http://links.lww.com/CCX/A580). Seven of the included studies focused on the use of LTVV with definitions of LTVV varying by study (16–18, 20, 22–24). Two studies assessed the effect of an intervention on the use of prone positioning (19, 20). Although all patients were mechanically ventilated, patient populations varied across studies as defined by the study authors including patients with primarily ARDS (18, 19, 21) or acute lung injury (ALI) (22), patients with ALI and ARDS (16, 23, 24), and patients with primary lung disease or complications of lung disease (including ARDS) (17) (e-Table 1, http://links.lww.com/CCX/A580). With the exception of one study which included ICU and emergency department (ED) settings (18), all others were conducted in an ICU setting. Based on GRADE assessment, the overall quality of evidence was very low (**e-Appendix 2**, http://links.lww.com/CCX/A579) (15).

Interventions

A variety of interventions at the patient, provider, or system level were evaluated with outcomes measured at the patient level (**Table 1**). Five studies in this

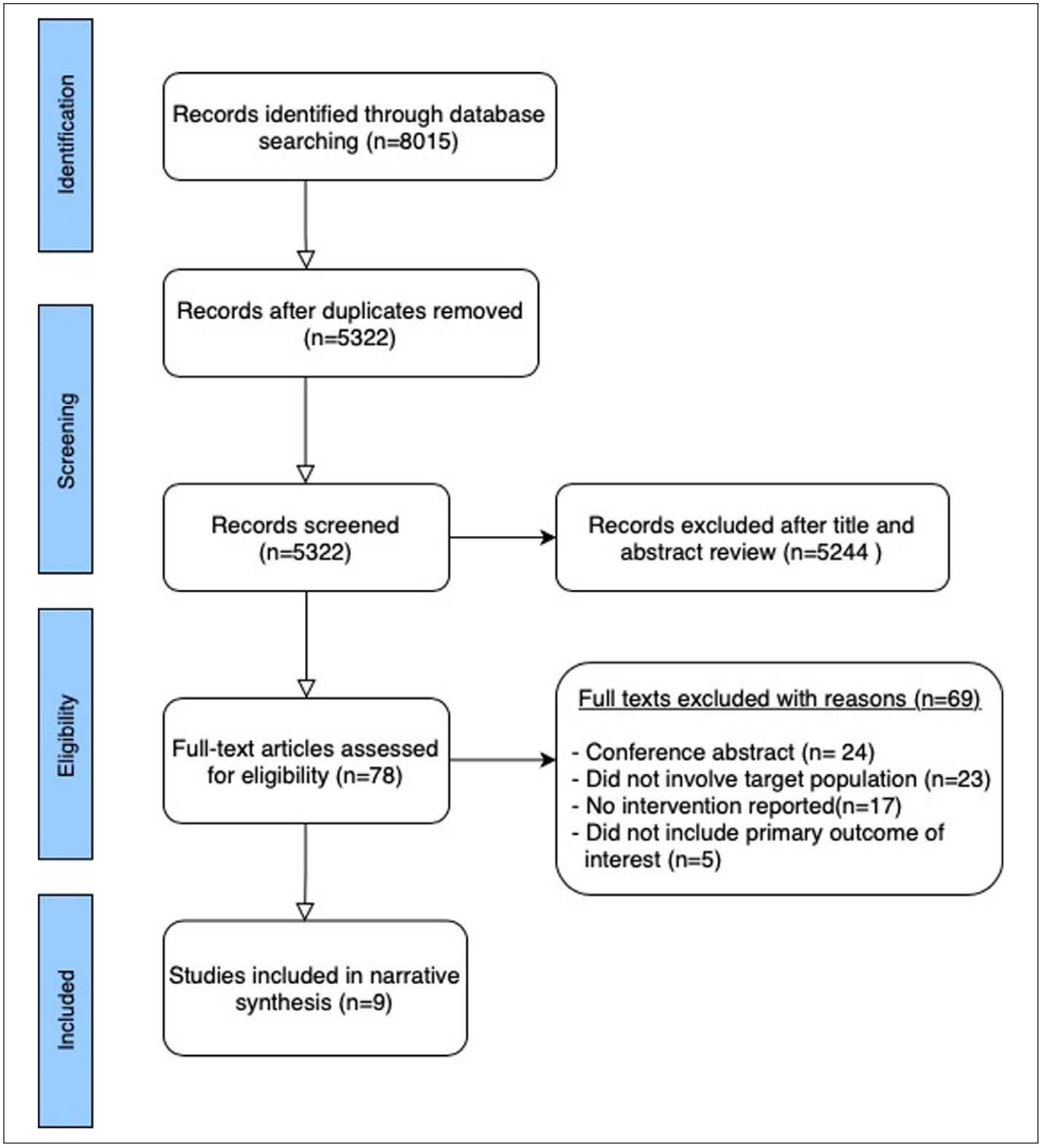

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses inclusion diagram.

review used some type of educational intervention, including a combination of lectures (18, 23, 24), journal club discussions (18), or bedside tutorials (17, 18, 22). These interventions were directed at interdisciplinary teams in the ICU or ED and focused on the evidence and merits of LTVV and guidelines for the use of LTVV (17, 18, 22–24). Examples included distribution of tables with ulnar length and TV for each room to assist in documentation of PBW and application of LTVV (17) or providing links to resources containing

TABLE 1.
Description of Interventions

References	Interventions
Belda et al (16)	"Online education tool about ARDS management": An initial survey appraising experience caring for patients with ARDS, querying various management options in ARDS, and other critical care topics was administered to all critical care, internal medicine, and anesthesiology physicians as well as critical care nurses and RTs to test baseline understanding of evidence-based practice. Respondents who agreed to take a repeat survey of the same questions were provided with hypertext links to details from a summary of primary articles regarding ARDS management. A repeat survey was administered after the respondents reviewed the links.
Birkhoelzer et al (17)	"Doctors in training were appointed in each ICU to initiate change and promote LTVV": Audits of LTVV were conducted a year apart with the intervention between audits. Standardized teaching to the multidisciplinary team was provided by each local lead, and ulnar length and TV tables were distributed to all bed spaces to assist documentation of IBW and TV for mandatory ventilated patients.
Fuller et al (18)	"Journal club, meetings, lectures and bedside education on merit and implementation of early LTTV": Preintervention consisted of a 6 mo period where LTVV was implemented as the default ventilator strategy in the ED, complimented by education through journal club review on merits of early LTVV, meetings, lectures, and bedside education. This was followed by the intervention period which targeted the ED, with a protocol distributed on TV recommendations. The ED RT obtained height to measure predicted body weight for TV, and ventilator settings were established per protocol
Gallo de Moraes (19)	"Integration of an ARDS diagnostics and management guideline in the ICU": A multidisciplinary team composed of key stakeholders (critical care physicians, RTs, nurses) developed an evidence-based best practice guideline for identifying and managing ARDS and when to implement adjunctive therapies. The protocol was introduced into routine care across different critical care units with support from ICU leadership.
Kalb et al (20)	"Multidisciplinary ventilator rounds with tele-ICU intensivists, respiratory therapy and nursing": Meetings were held between tele-ICU medical directors, nursing, and respiratory therapy to introduce the concept and purpose of ventilator rounds and to welcome input. The intensivist then conducted tele-rounds with nursing and respiratory therapy at the bedside of each intubated patient to discuss ventilator setting changes, including adjustment of TV. Each member used a template ventilator round checklist to input observations on ventilator settings, imaging, and laboratory work. Intensivists were provided guidelines regarding how to conduct rounds.
Luedike et al (21)	"Integration of an ARDS SOP into daily routine": The SOP was a one-page protocol described as a "hands-on-sheet" which included both diagnostic and therapeutic approached to ARDS. It was implemented in the ICU to support decision-making for the physician team.
Nota et al (22)	"Written guidelines, trainee teaching and impromptu bedside ventilator tutorials": Ventilation guidelines recommending TV of ≤ 6 mL/kg IBW were distributed on the hospital intranet and disseminated at nursing leadership meetings. Senior nursing staff educated fellow nurses, medicine trainees received formal education at weekly education sessions, and nursing/trainees received impromptu ventilator rounds and tutorials designed to ensure adherence to LTVV.
Wolthuis et al (24)	"Feedback and education on LTVV, protocol recommending LTVV": ICU physicians and nurses received feedback on current practice related to LTVV use in their ICU, and a presentation of clinical and animal studies on benefits of LTVV in ARDS. This was followed by discussion of barriers and hesitations to using LTVV, and ultimately a new mechanical ventilation protocol recommending the use of 6–8 mL/kg TV.
Wolthuis et al (23)	"Feedback and education on LTVV, EMR tool to facilitate application of LTVV": ICU physicians and nurses received feedback on current practices related to LTVV in their ICU, a presentation of clinical and animal studies on benefits of LTVV in ARDS. This was followed by discussed of barriers and hesitations to using LTVV. The process of feedback, education, and discussion was repeated 3 times. A tool was programmed into the EMR that automatically calculated ideal TV and was easily visible for clinical providers in the system.

ARDS= acute respiratory distress syndrome, ED = emergency department, EMR = electronic medical record; IBW= ideal body weight, LTVV= lung-protective ventilation, RT = respiratory therapist, SOP = standard operating procedure, TV = tidal volume.

evidence-based articles and guideline recommendations on treatment modalities in ARDS (16).

Interventions involved trainees (residents and fellows) (17, 23, 24), intensivists, (16–18, 20, 23, 24), respiratory therapists (RTs) (16–18, 20, 24), and critical care nurses (16–18, 20, 22–24) (Table 1). Several studies (17, 18) proposed multicomponent interventions which combined targeted education on the merits of LTVV for physicians and nurses and protocol implementation (i.e., obtaining height to measure PBW and setting ventilation settings) by respiratory therapy. Efforts to involve the interdisciplinary team included appointing trainees as leads to promote standardized teaching sessions on LTVV (17) and telemedicine ICU rounds including RTs, nurses, and intensivists to address interventions related to critical care medicine and ARDS (20). One intervention primarily focused on education for critical care nurses, including bedside tutorials and guideline discussion on LTVV (22).

Two studies presented clinical providers with data on current ventilator practice in their ICU prior to education on evidence-based recommendations for LTVV (23, 24). One study implemented a tool that automatically calculated TV based on PBW in the electronic health record, which was highlighted for providers in the electronic health record (23). Two studies addressed implementation of prone positioning, where the interventions included a one-page standard of operations protocol and a guideline on diagnostic and therapeutic approaches for management of ARDS in the ICU (19, 21).

Outcomes

Although the outcomes reported were heterogenous, all studies reported at least one outcome improvement after intervention (e-Table 1, http://links.lww.com/CCX/A580). For studies assessing LTVV, primary outcomes included mean patient TV at day 1 and day 3 of mechanical ventilation during the 6 months before and 6 months after the intervention (16), mean ICU TV at 6 months and 1 year to determine long-term effects of the intervention (24), compliance with LTVV measured as a percentage of total time ventilated less than 8 mL/kg PBW (17), or adherence to a goal TV (20, 22) (e.g., TV < 6.5 mL/kg). One study reported a 12% increase in time ventilated less than 8 mL/kg PBW (17), and two other studies reported an increase in adherence to TV less than 6.5 mL/kg PBW of 13.7% (19) and 29.4% from baseline (22). Studies measured mean TV with one study reporting a decrease in mean patient TV at day 3 from 10.3 to 8.9 mL/kg PBW (16) in 45 patients with ARDS during the 6 months before and 6 months after the intervention and another study reporting a reduction in mean ICU TV at 6 months after the intervention from 9.9 to 8.2 mL/kg PBW (24) in patients with ARDS. Studies assessing prone positioning reported improvements in utilization and timing of prone positioning. One study reported an increase in prone positioning from 7% to 73% following the intervention (21), and another reported decreased time to initiation of prone positioning from onset of severe ARDS (defined as either a $Pao_2/Fio_2 < 100$ or $Pao_2 < 60$ mm hg and $Fio_2 > 70\%$ for 1 hr with positive end-expiratory pressure ≥ 15) from 42.2 hours before to 16.3 hours after intervention ($p = 0.007$) (19).

Secondary outcomes measured included hospital mortality (16–19), 28-day mortality (21), ICU mortality (19), 180-day mortality (21), ICU length of stay (19), hospital length of stay (19), and ventilator-, ICU-, and hospital-free days (18) (e-Table 1, http://links.lww.com/CCX/A580). Reports on hospital mortality were varied, with studies reporting an increase from 43% to 50% ($p = 0.77$) (16), significant reduction from 54.8% to 39.5% after intervention (odds ratio, 0.36; 95% CI, 0.16–0.82; $p = 0.02$) or no significant reduction in 28- and 180-day mortality (21) or ICU and hospital mortality (19). One study reported ventilator-free days were significantly higher in the intervention group (7.7 ± 9.9 before vs 11.6 ± 10.8 after, $p = 0.03$); however, hospital-free days (7.2 ± 9.4 before vs 9.1± 9.2 after; $p = 0.23$) and ICU-free days (4 ± 6.3 before vs 5.7 ± 7.7 after; $p = 0.20$) were not significantly different (18). In a final study, ICU (14.3 d before vs 6 d after; $p = 0.04$) and hospital length of stay (21.9 d before vs 7.5 d after; $p = 0.08$) were both reduced after the intervention was implemented (19).

DISCUSSION

Our systematic review included nine nonrandomized controlled trials. The study designs and outcomes measured were varied, with heterogeneous populations and diverse interventions. This variability limited our ability to conduct a quantitative analysis. The PICO questions guiding this review could not be answered definitively by studies published to date. Despite this, two important observations emerged that

warrant further investigation: 1) there are few studies focusing on improving implementation of LTVV and prone positioning and 2) educational interventions that champion the potential benefits of LTVV and prone positioning may be effective approaches to improve adherence to evidence-based practices in the ICU.

Overall, the quality of evidence for the included studies was very low. Interventions primarily targeted providers and focused on the dissemination of educational materials through a variety of tools (e.g., lectures, bedside teaching, rounds and journal clubs, standardized tables on measurement of patient height and equivalent TVs, electronic tools in the electronic health record, ARDS protocols integrated into daily routine). This focus on promoting knowledge and practical implementation of LTVV or prone positioning is reasonable given findings from prior studies that barriers to successful implementation of these therapies include the failure to recognize ARDS or lingering concern about patient comfort (2, 10). Dissemination of information using lectures and journal clubs may provide opportunities to address concerns or reservations about LTVV or prone positioning while identifying important knowledge gaps. Teaching at the bedside or during rounds can facilitate the immediate application of knowledge, whereas integration of checklists into ICU rounds may prompt real-time discussion of these therapies and empower team members to implement a recommended practice (25).

Electronic tools (i.e., interactive prompts, alerts, and reminders in the electronic health record) may increase adherence to evidence-based practice and guideline recommendations (26–29) and implementation of clinical algorithms in medicine (30, 31). However, the utility of such tools could be limited by provider override or disregard of prompts (32) and alert fatigue (33). A well-designed electronic support tool with a clear and concise message that is easily accessible may potentially facilitate clinical decision-making, promote interprofessional communication, and improve knowledge on guidelines and protocols. However, definitive data on the optimal electronic tool in the electronic health record to prompt the use of evidence-based practice and the long-term impact on provider behavior are lacking and highly warranted.

The existing literature suggests the application of these approaches to improve adoption of evidence-based practices may be beneficial but is not sufficient to identify which of these strategies may be most effective. There is limited although increasing evidence suggesting less benefit with passive dissemination of knowledge (e.g., mailed knowledge pamphlets) (34, 35) and increased efficacy with interactive educational meetings and patient- or encounter-specific reminders (e.g., verbally, on paper or via Electronic Medical Record) (36, 37). On the other hand, it is uncertain whether use of multifaceted (two or more components) or single-component interventions is more effective in changing behavior (34, 35). Studies specifically focused on knowledge transfer in critical care suggest benefit in using a combination of protocols, guidelines, or bundles with or without education to implement best practices in the ICU (38). Although the question of the most effective implementation strategy has no clear answer, strategies that target specific barriers/facilitators and hypothesized causal mechanisms have been proposed for greatest success in knowledge and practice uptake (39–41). Additionally, there is a lack of literature on appropriate timing for implementation of a new therapy. Further studies are required to better understand the drivers of organizational decisions and how much individual and structural factors influence enthusiasm for evidence-based uptake.

In addition to determining which content may be most effective at promoting the use of LTVV or prone positioning, it is important to consider which members of the ICU team should be involved in these interventions. Most of the identified studies targeted a combination of clinicians, RTs, and nurses. This is likely due to the fact that the care of mechanically ventilated patients with ARDS requires multidisciplinary care. Ensuring a baseline fund of knowledge about the benefits and application of these therapies among these important stakeholders is imperative to guarantee successful buy-in for the use of LTVV and prone positioning. It is particularly important to have collaboration among the interprofessional team in the ICU as demonstrated in a study by Cook et al (42), where semirecumbent positioning for prevention of ventilator associated pneumonia was underused due to insufficient awareness of benefits, deterrents, lack of agreement about implementation responsibility, and lack of reinforcing strategies among interprofessional critical care providers.

Notably, the role of nursing and respiratory therapy varies between LTVV and prone positioning. Initiation

of LTVV requires significant RT-physician interaction, and introduced protocols, tools, or guidelines require joint buy-in and participation prior to design and implementation. Meanwhile, prone positioning is a physical maneuver that requires an interprofessional team—nurses, RTs, clinicians, and patient care technicians. Ideally, the person in charge of the prone maneuver should be the patient's primary ICU nurse. Hence, to improve implementation, interventions should be tailored and adapted to consider these distinctions, with stakeholder engagement that is relevant to the design and uptake of the intervention.

Finally, there is a need for uniformity in the inclusion criteria and the reporting of outcomes for studies addressing utilization of or adherence to evidence-based practices in ARDS. The existing literature includes patients without ARDS, which is interesting given that guideline recommendations for LTVV are specific to the management of ARDS, and data in patients without ARDS are mixed, with no study demonstrating a clear mortality benefit with use of LTVV in this population (43–46). Inclusion of patients without ARDS may influence clinician willingness to apply these therapies, which may contribute to a bias against the intervention. Another significant issue affecting the ability to appraise the existing literature is heterogeneity in reported outcomes. Outcomes assessing success of the evaluated interventions were difficult to compare and included day 1 and day 3 mean patient TV (16), compliance with LTVV measured as a percent of total time ventilated less than 8 mL/kg of ideal body weight (17), adherence to LTVV defined as TV less than 6.5 mL/kg PBW for patients with ARDS (20, 22), and mean ICU TV at 6 months and 1 year after intervention (23, 24). These variations make it difficult to provide precise estimates of the effect an intervention may have on improving use of LTVV.

There is still a significant gap in our understanding of how best to translate knowledge to practice in medicine, and we lack an effective framework for implementing clinical practice. Identified barriers to integration of evidence in the ICU include knowledge gaps, limited interdisciplinary collaboration, and complexity of care (47). Particularly in ARDS, the initial identification of ARDS is an important diagnostic step prior to initiating possible therapies (10). Future implementation strategies could focus on improving baseline knowledge of ARDS diagnostics and therapies, engaging interdisciplinary teams in the ICU, involving a robust collaborative leadership team, and using existing implementation conceptual frameworks such as the consolidated framework for implementation research (48) to identify and classify barriers to evidence uptake into major domains and themes.

Our study has several limitations. First, we acknowledge that institutions may have existing protocols in place to improve the use of LTVV and prone positioning but have not studied or publicly reported data about these protocols. This could lead to erroneous conclusions about the quality and quantity of existing implementation tools. However, the failure to generate data about institutional protocols prevents an assessment of their effectiveness. As previously noted, existing studies describe inadequate application of LTVV and prone positioning (2, 11, 12). Even if some institutional protocols are effective, their use cannot be extended to other locations if no one else is aware of them. Second, we only reviewed literature published in English, which may have limited identification of pertinent studies. Although it is always possible to miss relevant literature while performing a systematic review, our review was performed using a rigorous approach, which involved experts in the field of ARDS, adherence to PRISMA guidelines, and the application of GRADE methodology.

It is also important to note that ICU structure, availability of equipment, infrastructure, and human resources such as the presence of RTs, adequate training among critical care providers, and ICU staffing models naturally vary between institutions and could be critically limited or absent in resource limited countries. These variations may limit the generalizability of our findings given the dependency of certain interventions on these resources (e.g., availability and experience of RTs for a primarily RT–driven intervention). It would be beneficial for future research in this area to consider variations in working environment as this may aid in analysis of relevant barriers when designing implementation interventions.

Additionally, it is unclear how short-term changes in knowledge and organizational structure across institutions during the coronavirus disease 2019 (COVID-19) pandemic will affect the use of LTVV and prone positioning. However, there was a significant uptake in observational studies from April 2020 to February 2021 on various structural adoptions such as dedicated prone teams (49, 50) to facilitate prone positioning when hospital systems were facing a surge of critically ill patients

with COVID-19–related ARDS. Similar studies after the pandemic may serve to inform future intervention strategies to increase prone positioning uptake.

IMPLICATIONS AND FUTURE DIRECTIONS

Despite these limitations, this study is of vital importance for future research directions. These findings highlight the critical need to address the existing gaps in implementation of evidence-based therapies in ARDS. The heterogeneity of the studies in published literature thus far suggests that future research could benefit from focusing on processes of care associated with patient-centered outcomes. Targeting populations with ARDS as opposed to all mechanically ventilated patients or mixed populations with ARDS/ALI would also reduce heterogeneity. Finally, identifying the specific components of interventions that render them effective, sustainable, and/or generalizable would improve their utility. Formation of interdisciplinary groups with important stakeholders (e.g., clinicians, administrators, policy makers and researchers) and using an implementation science framework to identify important context factors prior to designing interventions could further improve the design of future implementation studies.

CONCLUSIONS

In conclusion, there is limited evidence supporting interventions designed to enhance the use of LTVV or prone positioning in patients with ARDS. Existing studies describe interventions that are mainly education based, targeting the multidisciplinary team. Although these interventions suggest potential improvements in adherence to recommended practices, the overall quality of evidence supporting their implementation is very low. There is an urgent need to employ high-quality implementation science in this area. Key areas for future research include development of novel interventions that involve the multidisciplinary team, an uniform approach to outcomes, and a focus on patients most likely to benefit from LTVV and prone positioning.

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Dr. Giovanni is responsible for the integrity of the work as a whole. Dr. Giovanni served as primary author, designed the study protocol, developed the search strategy, reviewed all studies, performed data abstraction, analyzed the data, wrote the article and its revisions, and approved the final version of the article. Dr. Jennerich designed the study protocol, refined the search strategy, reviewed all studies, analyzed the data, edited drafts of the article, and approved the final version of the article. Dr. Steel performed data abstraction, edited drafts of the article, and approved the final version of the article. Dr. Lokhandwala reviewed all studies, performed data abstraction, edited drafts of the article, and approved the final version of the article. Drs. Alhazzani and Weiss edited the study protocol, drafts of the article, and approved the final version of the article. Dr. Hough designed the study protocol, refined the search strategy, edited drafts of the article, and approved the final version of the article.

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