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Optimizing Peep in ARDS: A Narrative Review of Personalized Strategies, Advancements, and Clinical Outcomes

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Abstract:
This document presents a comprehensive review of recent literature on positive end-expiratory pressure (PEEP) in acute respiratory distress syndrome (ARDS) patients, with a focus on personalized strategies, advancements, and clinical outcomes. The purpose of the study is to synthesize existing research, identify research gaps, and provide insights for clinical practice.

The methodology involves a systematic search of electronic databases for relevant studies published in recent years. Inclusion criteria encompass various study designs, such as randomized controlled trials and observational studies, involving adult and pediatric patients.

The main findings highlight the importance of personalized PEEP strategies in ARDS management. Patient-specific characteristics, such as lung mechanics, hemodynamics, and disease severity, influence the optimal PEEP level. The review explores different approaches and strategies for PEEP titration in mechanical ventilation and emphasizes the need for individualized PEEP based on patient-specific factors.

The results demonstrate that personalized PEEP strategies have the potential to improve clinical outcomes, including oxygenation, lung recruitment, and mortality. However, challenges and limitations in implementing personalized PEEP strategies in clinical practice are identified.

The study concludes that a one-size-fits-all approach to PEEP in ARDS is inadequate, given the heterogeneity of patient populations. Personalized PEEP strategies, considering individual characteristics, offer a promising avenue for optimizing patient outcomes. The findings of this review have implications for clinical practice, emphasizing the need for incorporating patient-specific characteristics into PEEP titration protocols.

Keywords: ARDS, PEEP, COVID19, PEEP optimization

Introduction:

a. Background:

Management of ARDS in critical care involves meticulous attention to ventilatory strategies, with PEEP playing a crucial role in improving oxygenation and reducing lung injury. PEEP maintains positive pressure in the lungs to keep alveoli open and improve gas exchange, with ongoing research focusing on personalized application due to the heterogeneity of ARDS patients. Recent advancements in PEEP research include personalized strategies, understanding pathophysiological mechanisms, and evaluating outcomes through various studies and trials (Carpio & Mora, 2023a; Chikhani et al., 2016; Cutuli et al., 2023a; Sklar & Munshi, 2022).

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b. Rationale:

This literature review justifies the need for evidence-based approaches in ventilatory management for ARDS, especially in light of the recent SARS-CoV-2 pandemic, aiming to optimize PEEP and improve patient outcomes.

The review focuses on recent studies exploring PEEP application in ARDS across various clinical settings, including observational studies, personalized strategies, pathophysiological explorations, and randomized controlled trials(Coleman & Aldrich, 2021; Mart & Ely, 2020; Schmidt et al., 2020; Yamamoto et al., 2022a).

c. Objectives:

The main objectives of this narrative review are to:

1. Synthesize the current literature on PEEP titration strategies in mechanical ventilation.
2. Evaluate the effectiveness of personalized PEEP strategies based on patient-specific characteristics and their impact on clinical outcomes.
3. Identify research gaps and implications for future clinical practice and research directions.

d. Research questions:

Research questions focus on current PEEP titration approaches, patient-specific characteristics in PEEP strategies, impact on clinical outcomes, limitations in implementation, efficacy in specific patient subgroups, gaps in literature, and implications for clinical practice.

These questions aim to address knowledge gaps and explore the link between patient-specific traits and personalized PEEP strategies in mechanical ventilation.

1. What are the current approaches and strategies for PEEP titration in mechanical ventilation?
2. What patient-specific characteristics have been taken into account in the formulation of individualized PEEP strategies?
3. How have patient-specific characteristics influenced the choice and optimization of PEEP levels in various patient cohorts, including adults and pediatric patients?
4. What is the impact of personalized PEEP strategies on clinical outcomes, such as oxygenation, lung recruitment, and mortality?
5. What are the limitations and challenges associated with implementing personalized PEEP strategies in clinical practice?
6. Are there specific patient subgroups or clinical conditions where personalized PEEP strategies have shown greater efficacy or benefit?
7. What gaps exist in the current literature regarding the development and validation of personalized PEEP strategies based on patient-specific characteristics?
8. What are the implications of the findings for clinical practice, and what recommendations can be made for incorporating patient-specific characteristics into PEEP titration protocols?

These research questions will guide the narrative review by addressing the current knowledge gaps and exploring the relationship between patient-specific characteristics and the development of personalized PEEP strategies.

Methodology:

a. Inclusion Criteria: we will select relevant studies based on the publication date range, study designs (e.g., randomized controlled trials, observational studies), and populations (e.g., adult patients, pediatric patients).
b. Databases: the electronic databases to be searched will include PubMed, Semantic scholar, and Google scholar.
c. Search Terms: Provide a comprehensive list of keywords and Medical Subject Headings (MeSH) terms to be used during the literature search.
d. Study Selection: studies discussing PEEP titration strategies and ventilatory protocols

Data Extraction

a. Data Items: Define the variables to be extracted from each included study, such as patient demographics, PEEP titration methods, outcomes, and any patient-specific characteristics considered in the PEEP strategy.
b. Data Extraction Process.

The conceptual variables and their inter-relationships:

1. Independent Variables:

1.1. Patient-specific characteristics:

These characteristics can impact the optimal PEEP level by influencing lung mechanics, hemodynamics, and disease severity. For instance, individuals with higher lung compliance might be able to withstand higher PEEP levels, whereas those with severe pulmonary hypertension may necessitate lower PEEP levels to prevent hemodynamic compromise (Ranieri et al., 2012; See, Sahagun, & Taculod, 2021).

1.2. Optimal PEEP level:

This is the PEEP level that optimizes lung mechanics, hemodynamics, and gas exchange for a given patient. The optimal PEEP level may vary depending on the patient's individual characteristics(Ranieri et al., 2012; van den Boom et al., 2020; Walkey et al., 2017).

2. Dependent Variable:

2.1 Optimal PEEP level:

Optimal PEEP can be considered as a dependent variable, as the optimal PEEP level may vary depending on the individual characteristics of the patient(Ranieri et al., 2012).

2.2 Outcome Variables:

Mortality
Ventilator-free days
ICU length of stay

3. Control Variables:

3.1 Ventilator settings (other than PEEP):

These settings may affect lung mechanics and gas exchange and, therefore, need to be controlled for when determining the optimal PEEP level(van den Boom et al., 2020; Walkey et al., 2017).

3.2 Sedation and analgesia:

These medications may affect respiratory drive and lung mechanics and, therefore, need to be controlled for when determining the optimal PEEP level(Zersen, 2023a).

3.3 Fluid management:

Fluid overload can exacerbate pulmonary edema and elevate the likelihood of ventilator-induced lung injury, underscoring the importance of its management in establishing the optimal PEEP level (Keddissi, Youness, Jones, & Kinasewitz, 2019).

3.4 Other medical interventions:

Other medical interventions, such as prone positioning and neuromuscular blockade, may impact lung mechanics and gas exchange, and thus should be taken into account when determining the optimal PEEP level(Fielding-Singh, Matthay, & Calfee, 2018).

4. Mediator Variables:

4.1 Lung mechanics:

PEEP can influence lung mechanics by augmenting lung volume and diminishing airway resistance. These alterations in lung mechanics have the potential to enhance gas exchange and mitigate the likelihood of ventilator-induced lung injury(Zeng et al., 2023).

4.2 Hemodynamics:

PEEP can influence hemodynamics by elevating intrathoracic pressure and diminishing venous return. These alterations in hemodynamics may result in hypotension and compromised organ perfusion, particularly in patients with underlying cardiovascular conditions(L. Zhou et al., 2019).

4.3 Gas exchange:

PEEP can enhance gas exchange by augmenting lung volume and diminishing airway resistance. These alterations in lung mechanics have the potential to optimize the matching of ventilation and perfusion, consequently improving oxygenation and decreasing carbon dioxide retention(Carpio & Mora, 2023b).

5. Moderator Variables:

5.1 Patient age:

Age may impact lung mechanics, hemodynamics, and disease severity, thus potentially moderating the relationship between patient-specific characteristics and the optimal PEEP level(J. Zhou et al., 2021).

5.2 Disease severity:

Disease severity may impact lung mechanics, hemodynamics, and gas exchange, potentially moderating the relationship between patient-specific characteristics and the optimal PEEP level(Krebs, Pelosi, Tsagogiorgas, Alb, & Luecke, 2009).

6. Outcome Variables:

6.1 Mortality:

Optimal PEEP levels can impact mortality by decreasing the likelihood of ventilator-induced lung injury and enhancing gas exchange(Zersen, 2023b).

6.2 Ventilator-free days:

PEEP may increase ventilator-free days by reducing the duration of mechanical ventilation(Algera et al., 2020).

6.3 ICU length of stay:

PEEP may decrease ICU length of stay by enhancing clinical outcomes and mitigating the risk of complications (K. T. Kim et al., 2020).

Conceptual Framework:

The conceptual framework of the study is based on the hypothesis that patient-specific characteristics influence the optimal PEEP level in ARDS patients. We will investigate this hypothesis by examining the relationships between the independent variables, dependent variables, and outcome variables. The results of the study will be used to develop a personalized PEEP strategy that takes into account patient-specific characteristics(Griffiths et al., 2019; Umbrello, Formenti, Bolgiaghi, & Chiumello, 2017).

Relationships between variables:

1. **Direct Effect (Independent Variable → Dependent Variable):**
   - Increasing PEEP levels may lead to improved oxygenation (dependent variable) in patients.

2. **Mediation (Independent Variable → Mediator → Dependent Variable):**
   - Higher PEEP levels improve lung compliance (mediator), which subsequently enhances oxygenation (dependent variable).

3. **Moderation (Independent Variable × Moderator → Dependent Variable)**:
   - The impact of PEEP on outcomes (dependent variable) may vary depending on the patient's BMI (moderator).

Table 1: Conceptual Variables[9-25]

Variable Type	Description	Role	Relationship
Independent Variable	The factor that is manipulated or controlled by the researcher. In the context of PEEP strategies, this could be the level of PEEP applied during mechanical ventilation.	Determines the treatment or intervention.	Influences the outcome variable (e.g., patient outcomes, lung function).
Dependent Variable	The outcome or response that is measured. In this case, it could be patient outcomes such as oxygenation, lung compliance, or mortality.	Represents the effect of the independent variable.	Affected by the level of PEEP.
Control Variable	A variable that is held constant to minimize its impact on the relationship between the independent and dependent variables. For example, patient age,	Ensures that other factors do not confound the relationship.	Helps isolate the effect of PEEP on patient outcomes.

Variable Type	Description	Role	Relationship
	comorbidities, and baseline lung function could be controlled.		
Mediator Variable	A variable that explains the process through which the independent variable affects the dependent variable. In the context of PEEP strategies, a potential mediator could be lung compliance or oxygenation.	Part of the causal pathway.	Helps understand why PEEP influences patient outcomes.
Moderator Variable	A variable that affects the strength or direction of the relationship between the independent and dependent variables. For instance, patient body mass index (BMI) might moderate the impact of PEEP on outcomes.	Influences the relationship.	Determines whether the effect of PEEP varies across different BMI levels.

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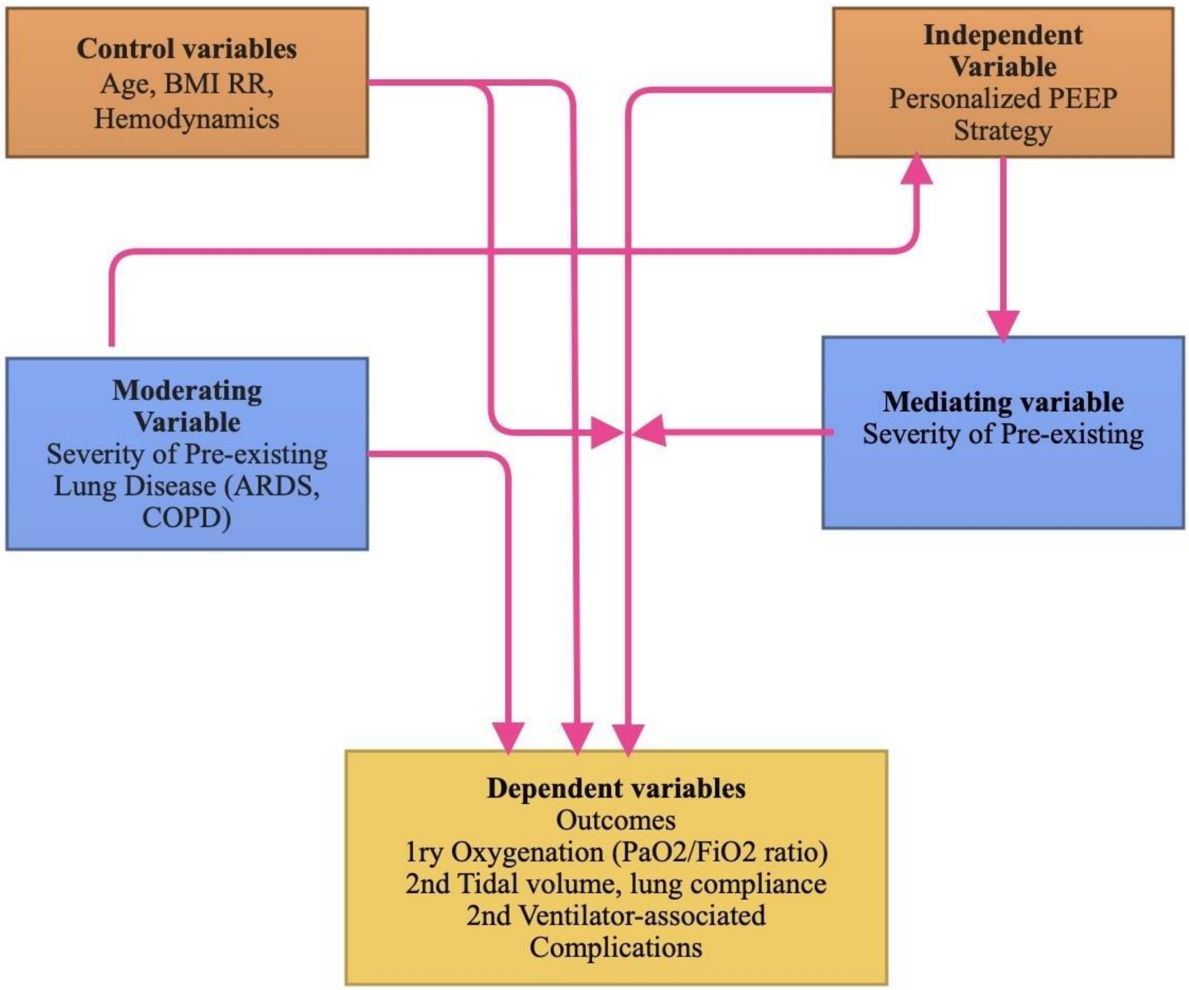

Figure1.PEEP Conceptual Variables Interrelationships

(BMI) body mass index,(RR) respiratory rate, (PEEP) positive end expiratory pressure, (ARDS) Acute distress respiratory syndrome, (COPD) chronic obstructive pulmonary disease, (PaO2) oxygen partial pressure, (FIO2) fraction of inspired oxygen

Figure 1. PEEP Conceptual Variables Interrelationships [9-25]

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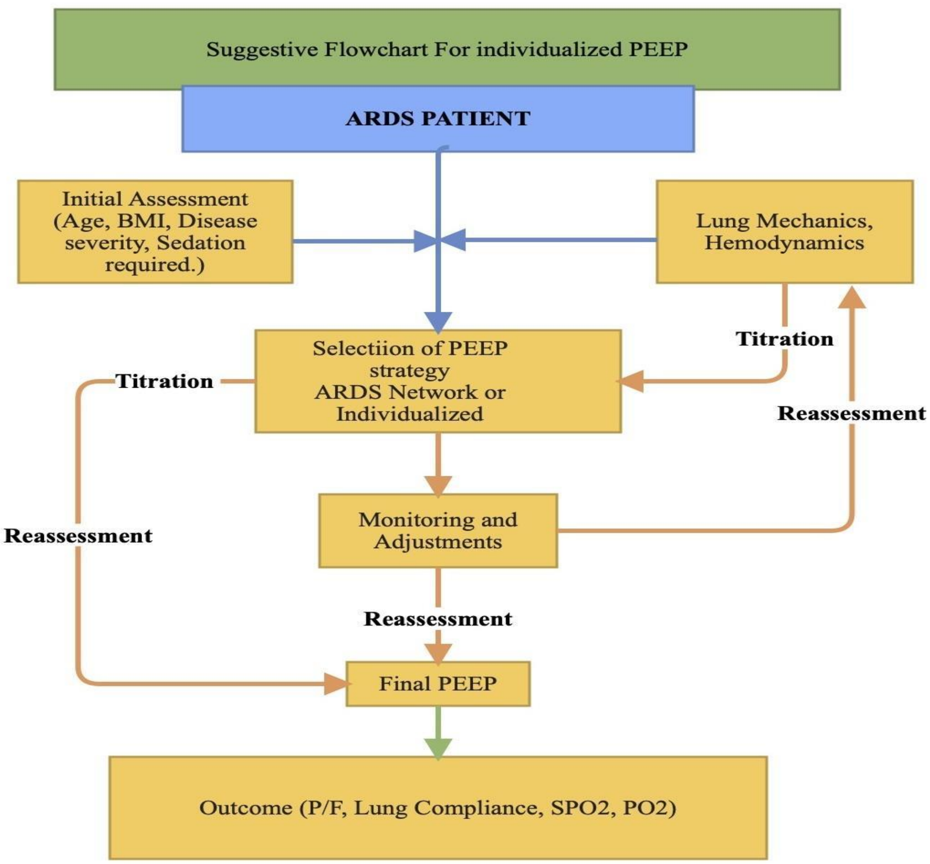

Explanation:

1. The process starts with an **Initial Assessment** gathering patient data like age, BMI, underlying conditions, ARDS severity, and sedation level. Hemodynamic status is also considered.
2. Based on the assessment, a **PEEP Selection Strategy** is chosen. This might involve using the ARDS Network PEEP/FiO2 Table as a starting point, with potential adjustments for specific patient characteristics (high/low BMI, older age with heart issues, sedation level).
3. If using the PEEP/FiO2 table, a **PEEP Titration** phase follows. Here, PEEP is gradually increased while monitoring oxygenation, lung mechanics, and hemodynamics. The goal is to find the lowest PEEP that achieves adequate oxygenation, acceptable lung function, and stable blood pressure.
4. Throughout the process, **Monitoring & Adjustments** are crucial. Oxygenation, lung mechanics, and hemodynamics are continuously monitored, and PEEP is adjusted as needed based on patient response.
5. **Reassessment** is performed regularly to adapt the PEEP strategy as the patient's condition evolves throughout their ICU stay.
6. The process ends with a **Final PEEP** setting chosen based on the ongoing monitoring and adjustments.

Figure 2.Flowchart For individualized PEEP

Figure 2. Flowchart For individualized PEEP (modified from (Mauri, 2021a; Nijbroek et al., 2023; Q. Y. Wang, Ji, An, Cao, & Xue, 2021)

Literature reviews:

1. Observational studies on PEEP in ARDS patients

1.1 Findings

In recent literature, there is a growing emphasis on the importance of personalized ventilatory support strategies in managing ARDS patients. Studies highlight the necessity of tailoring PEEP settings to optimize patient outcomes. Radhi et al. (2023) discuss the significance of personalized PEEP in ARDS management, noting the lack of a definitive superior strategy between high and low PEEP levels. They explore the physiological impacts of PEEP and different approaches to determining the ideal PEEP, offering guidance to clinicians and paving the way for further research. Additionally, discussions on personalized ventilatory support, particularly in the context of SARS-CoV-2 pneumonia, underscore the need for adaptable strategies across various respiratory conditions. Protective ventilation strategies, as demonstrated in gynecological surgeries by another study, show benefits beyond ARDS, indicating the broader applicability of such approaches(Radhi, Freebairn, Chiew, Chase, & Cove, 2023).

The current literature highlights the increasing importance of personalized ventilatory support strategies in managing patients with Acute Respiratory Distress Syndrome (ARDS). Studies emphasize the need for tailored positive end-expiratory pressure (PEEP) settings to optimize patient outcomes. Despite numerous large studies, no definitive superior strategy between high or low PEEP has been established, suggesting that the optimal PEEP level may vary for each patient. Authors discuss the physiological impacts of PEEP, different approaches to determining ideal PEEP levels, and the development of personalized ventilation concepts in response to complex respiratory support needs, such as in the context of the SARS-CoV-2 pandemic(Pelosi et al., 2021; Radhi et al., 2023).

Additionally, evidence supports the use of protective ventilation strategies, including PEEP, in various clinical contexts beyond ARDS, such as during surgical procedures. Protective lung strategies, like intraoperative PEEP combined with low tidal volume and recruitment maneuvers, have shown benefits in enhancing postoperative oxygenation and reducing atelectasis occurrence(Pelosi et al., 2021; Radhi et al., 2023).

Overall, there is a consensus among studies that personalized ventilation strategies, including individualized PEEP settings, can lead to improved patient outcomes. The literature advocates for moving away from a one-size-fits-all approach to PEEP in ARDS and stresses the importance of tailoring PEEP levels based on patient response. While the application of protective ventilation strategies with PEEP has shown benefits in non-ARDS scenarios, further research is needed to establish definitive guidance on determining the optimal PEEP for each patient, highlighting the need for continued investigation in this area.

1.2 Research Gaps

The existing literature highlights the benefits of individualized and protective ventilation strategies, yet several research gaps and discrepancies persist, necessitating further investigation. Key areas for exploration include:

1. Optimal PEEP Determination: The absence of a definitive superior strategy for determining the optimal positive end-expiratory pressure (PEEP) in ARDS patients underscores the need for standardized, evidence-based protocols considering variables like lung mechanics and patient response.
2. Personalized Ventilation Beyond ARDS: Studies focusing on different respiratory conditions, such as SARS-CoV-2 pneumonia and ARDS, suggest the need to adapt personalized ventilation strategies for various diseases through comparative studies.
3. Protective Ventilation in Surgery: While beneficial effects of protective ventilation in prolonged gynecological surgeries have been shown, further research is needed to assess the generalizability of these results to diverse surgical procedures and specialties.
4. Methodological Differences: Variations in methodologies across studies may impact the generalizability and replicability of findings, highlighting the importance of harmonizing methodologies or conducting multicenter trials.
5. Synthesis of Evidence: There is a gap in synthesizing evidence from different studies and contexts. Systematic reviews and meta-analyses could integrate data to provide more robust conclusions on personalized and protective ventilation strategies.

In conclusion, while there is a promising shift towards personalized ventilation strategies for improved patient outcomes, addressing these research gaps through collaborative efforts could lead to significant advancements in respiratory condition management and the development of innovative strategies in clinical and non-clinical settings(Pelosi et al., 2021; Radhi et al., 2023).

1.3 Implications

Theoretical Implications:

o The research enhances the theoretical understanding of ventilation strategies in medical and public health contexts, challenging traditional one-size-fits-all theories of ventilatory support.

o Concepts like individualized positive end-expiratory pressure (PEEP) emphasize the complexities of human respiratory physiology and advocate for precision medicine tailored to each patient's unique attributes.

o Findings contribute to the theoretical basis for perioperative care, supporting lung-protective strategies to reduce postoperative complications and potentially prompting a reexamination of current management theories for intubated patients(Andrews et al., 2022; Sklar, Patel, Beitler, Piraino, & Goligher, 2019).

Practical Implications:

- o Transitioning towards personalized PEEP strategies in ARDS management could lead to the development of new protocols and tools to optimize mechanical ventilation settings for individual patients, potentially improving outcomes and reducing ventilator-associated complications.
- o Evidence presented may influence modifications in intraoperative and postoperative care protocols in surgical practice, potentially enhancing recovery quality and shortening hospital stays for surgical patients.
- o Identified research gaps suggest the need for future directions, such as multicenter trials to validate protective ventilation strategies across diverse patient populations and clinical settings(Andrews et al., 2022; Sklar et al., 2019).

Overall, the recent research supports a shift towards more nuanced and patient-centered ventilation approaches, with significant implications for clinical practice, public health policy, and the broader healthcare system.

2. Personalized PEEP strategies

2.1 Findings

The articles discussed the application of personalized Positive End-Expiratory Pressure (PEEP) strategies in managing patients with Acute Respiratory Distress Syndrome (ARDS). ARDS is a complex condition with high mortality and limited therapeutic options where PEEP plays a crucial role in optimizing respiratory system compliance and oxygenation. Traditional clinical trials comparing low and high PEEP levels have not shown a superior strategy, leading to the proposal of personalized PEEP strategies tailored to individual patient factors such as lung compliance and oxygenation status. The concept of individualized PEEP aims to optimize patient outcomes by adjusting PEEP levels based on patient-specific responses(Bellani et al., 2016; Cutuli et al., 2023b).

Studies have explored the efficacy of personalized PEEP strategies in conjunction with prone positioning for ARDS management. The research highlighted the importance of understanding the interaction between PEEP strategies and prone positioning, optimal PEEP titration methods, long-term clinical outcomes, patient selection, and comparative effectiveness. While personalized PEEP strategies show promise in improving patient outcomes, further research is needed to address these research gaps and optimize ventilatory support in ARDS patients(Bellani et al., 2016; Cutuli et al., 2023b).

The articles emphasize the significance of personalized PEEP strategies in optimizing lung-protective ventilation, preventing alveolar collapse, improving compliance, and reducing ventilation heterogeneity. They advocate for individualized approaches to PEEP management based on physiological considerations and patient responses. Tools like esophageal manometry and bedside electrical impedance tomography are proposed to aid in PEEP titration and optimize lung mechanics and oxygenation. Overall, the articles support the use of personalized PEEP strategies to enhance clinical outcomes in ARDS patients by tailoring ventilation to individual patient needs(Cutuli et al., 2023b).

2.2 Research Gaps

The research on personalized Positive End-Expiratory Pressure (PEEP) strategies in managing patients with Acute Respiratory Distress Syndrome (ARDS) highlights several key gaps and implications for further investigation:

1. Interaction Between PEEP Strategies and Prone Positioning: While there is potential for optimizing lung-protective ventilation in ARDS patients through personalized PEEP strategies and prone positioning, further research is needed to understand the precise mechanisms and long-term outcomes of these strategies.
2. Optimal PEEP Titration: Despite advancements in individualized PEEP titration, controversy remains regarding the optimal strategy. Additional research is required to validate the impact of different PEEP titration approaches across diverse patient populations.
3. Long-term Clinical Outcomes: Studies evaluating immediate physiological responses to personalized PEEP strategies and prone positioning lack assessment of long-term outcomes such as ventilator-free days, mortality rates, and quality of life measures. Future research should focus on evaluating the efficacy and safety of these interventions on patient-centered outcomes.
4. Patient Selection and Generalizability: The specific cohort of patients with moderate to severe ARDS in current studies raises questions about the generalizability of findings. Further exploration is needed to assess the applicability of personalized PEEP strategies and prone positioning across different ARDS severity levels and etiologies.
5. Comparative Effectiveness: While different PEEP titration strategies are compared, there is a lack of direct comparison with other interventions or standard care protocols. Future research should investigate the comparative effectiveness of personalized PEEP strategies against alternative ventilation approaches in ARDS management(Battaglini et al., 2023; Mauri, 2021b).

In conclusion, while personalized PEEP strategies show promise in optimizing ventilator management for ARDS patients, further research is essential to validate their efficacy, compare them with alternative approaches, determine optimal PEEP levels, assess long-term outcomes, and consider the influence of ARDS subphenotypes. Collaboration between clinicians, researchers, and industry partners is crucial to advance personalized medicine in critical care settings.

3. Reviews and meta-analyses of PEEP trials

The findings from various papers on Positive End-Expiratory Pressure (PEEP) in mechanical ventilation strategies across different clinical settings highlight the following key points:

1. Optimized Ventilation Strategies for Specific Patient Populations:
- Studies focus on tailoring mechanical ventilation strategies for specific patient groups like those with obesity and Acute Respiratory Distress Syndrome (ARDS).
- A network meta-analysis(J. Wang et al., 2022a) suggests that volume-controlled ventilation with individualized PEEP and recruitment maneuvers is effective for improving oxygenation and reducing pulmonary atelectasis in obese patients.
- Conversely, a systematic review (Yamamoto et al., 2022b) evaluating higher PEEP in ARDS patients did not show a significant decrease in 28-day mortality compared to lower PEEP, indicating that the benefits of higher PEEP may not universally apply to all ARDS patients.
2. Driving Pressure-Guided Ventilation Strategy:
- Papers by(Yang, Hu, & Sun, 2022) and (LI et al., 2022) explore a ventilation strategy guided by driving pressure (DP).
- The driving pressure-guided ventilation strategy is proposed to be more effective in reducing postoperative pulmonary complications and is associated with decreased mortality and improved oxygenation index in mechanically ventilated patients.
- While there is consensus on the importance of individualized approaches and recruitment maneuvers in patients with obesity, the benefits of higher PEEP in ARDS patients are less agreed upon. Emerging evidence suggests that driving pressure-guided ventilation strategies may offer advantages over traditional parameters like PEEP levels(LI et al., 2022; Yang et al., 2022).

Overall, these findings enhance our understanding of the role of PEEP and mechanical ventilation strategies in diverse clinical settings, emphasizing the importance of individualized approaches and highlighting the potential benefits of driving pressure-guided ventilation strategies.

3.2 Research Gaps

The research gaps and discrepancies identified in the studies on mechanical ventilation strategies include:(Villar et al., 2021)

1. Lack of Consensus on PEEP Optimization in ARDS:

- Variability in the effectiveness of PEEP optimization strategies for different patient populations, with individualized PEEP showing benefits in obesity but not significantly reducing mortality in ARDS patients.
- Highlighting the need for further research to explore patient-specific factors or disease severity influencing responses to varying PEEP levels in ARDS.

2. Variability in Quality of Evidence:

- o Studies reporting varying qualities of evidence, ranging from very low to moderate, due to differences in study design, sample sizes, and patient populations.
- o Emphasizing the necessity for large-scale, high-quality randomized controlled trials with standardized protocols to enhance the quality of evidence and provide clearer guidance on mechanical ventilation strategies.

3. Challenges in Driving Pressure-Guided Ventilation Strategy Efficacy:

- o The concept of driving pressure as a ventilation guide is relatively new, requiring further validation through large-scale RCTs to determine its optimal integration into current mechanical ventilation protocols.

4. Need for Individualized Ventilation Approaches:

- o Significance of personalized ventilation strategies, particularly in obesity, but a lack of specific guidelines on customizing parameters like PEEP and driving pressure.
- o Urging further research to develop and validate algorithms or decision-support tools for adjusting ventilation settings based on individual patient physiology in real-time.

5. Long-Term Outcomes and Integration with Other Therapies:

- o Limited information on the long-term effects of various ventilation strategies on pulmonary function, quality of life, and rehabilitation outcomes.
- o Insufficient data on optimizing the interaction between mechanical ventilation strategies and other therapeutic interventions like prone positioning, sedation, and neuromuscular blockade to enhance patient outcomes(Villar et al., 2021).

In conclusion, addressing these research gaps and discrepancies through ongoing efforts can lead to more personalized, effective, and evidence-based mechanical ventilation practices that improve patient outcomes across diverse clinical settings.

3.3 Implications

The implications of recent research on mechanical ventilation strategies are profound and multifaceted, impacting clinical practice, policy formulation, and future research directions in respiratory care and critical medicine.

From a clinical perspective, the identification of VCV+PEEPind+RM as an optimal strategy for obese patients undergoing surgery provides clear guidance for enhancing perioperative lung protection and oxygenation in this high-risk group. This may lead to the implementation of more personalized ventilation protocols considering patient-specific factors like body mass index, lung mechanics, and intraoperative positioning(J. Wang et al., 2022b).

In the context of ARDS, the lack of consensus on the benefits of higher PEEP suggests the need for a nuanced approach in managing these patients, considering factors like lung recruitability and individual patient response for more personalized treatment plans.

The implications for policy are significant, with emerging evidence on the efficacy of driving pressure-guided ventilation strategies potentially influencing updates to healthcare guidelines to incorporate this parameter into lung-protective ventilation protocols(J. Wang et al., 2022b).

Future research directions highlight the necessity for large-scale, multicenter randomized controlled trials to establish more definitive evidence for specific mechanical ventilation strategies. Additionally, exploring predictive tools using machine learning and artificial intelligence for real-time adjustment of ventilation parameters for individual patients is recommended(Pinto et al., 2023; Stivi et al., 2024).

On a theoretical level, the findings challenge and refine existing theories on the pathophysiology of mechanically ventilated patients, emphasizing the importance of driving pressure and shifting theoretical emphasis towards a holistic view of lung mechanics during ventilation. This may lead to the development of new theoretical frameworks explaining the complex interactions between ventilation parameters and patient outcomes(Pinto et al., 2023; Stivi et al., 2024).

In conclusion, the insights from recent research underscore the importance of individualized care, the potential shift towards driving pressure-guided ventilation, and the reaffirmed significance of effective ventilation systems in public health, shaping the dynamic landscape of respiratory care and its foundational theories.

4. Randomized controlled trials of PEEP strategies

4.1 Findings

Findings from various randomized controlled trials on Positive End-Expiratory Pressure (PEEP) strategies in mechanical ventilation cover different patient populations and contexts:

1. Pediatric Cardiac Surgery: Studies in pediatric cardiac surgery focused on ventilation strategies during cardiopulmonary bypass (CPB) to improve oxygenation and reduce pulmonary complications. Research compared different ventilation approaches during CPB, such as no mechanical ventilation, continuous positive airway pressure (CPAP), and low tidal volume (LTV) pressure-controlled ventilation. While maintaining ventilation during CPB, particularly with the LTV strategy, improved post-bypass oxygenation, there was no significant reduction in postoperative pulmonary complications (PPCs) among the strategies. Another study on a 'protective' low-tidal/low-frequency ventilation strategy during CPB in children with congenital heart disease found it safe but did not provide substantial benefits in postoperative ventilation time(Elhaddad, Youssef, Ebad, Abdelsalam, & Kamel, 2022).

2. Mechanical Ventilation in Various Patient Populations: Studies in this group assessed PEEP strategies in adult patients undergoing mechanical ventilation and animal models of acute respiratory distress syndrome (ARDS). A meta-analysis focused on a driving pressure-guided ventilation strategy in adults compared to a lung protective ventilation (LPV) strategy, aiming to optimize mechanical ventilation strategies. Another study in piglet models of ARDS induced by paraquat showed that a lung-protective ventilation approach with lower tidal volumes reduced extravascular lung water and improved oxygenation(Güldner et al., 2015).

3. Premature Infants with Respiratory Distress Syndrome: In neonatal care, particularly for premature infants with respiratory distress syndrome (RDS), different ventilation strategies can impact long-term respiratory outcomes. A study implementing high-frequency oscillatory ventilation (HFOV) with volume guarantee (VG) as early rescue therapy for severe RDS reported improved respiratory outcomes at two years in preterm infants, including higher survival without bronchopulmonary dysplasia (BPD) and reduced respiratory treatments and hospital admissions(Cools, Askie, Offringa, & Collaboration), 2009).

Overall, while there is a general consensus on the potential benefits of tailored ventilation strategies, further research is needed to establish best practices and guidelines that can be universally applied.

4.2 Research Gaps

The research highlighted several critical research gaps in the field of mechanical ventilation strategies across various patient populations(Bignami et al., 2017):

1. Optimal Ventilation Strategies during CPB in Pediatric Cardiac Surgery: Studies evaluating ventilation strategies during cardiopulmonary bypass (CPB) in pediatric cardiac surgery lack a consensus on the optimal approach. Discrepancies in findings regarding the effectiveness of different ventilation strategies, such as low tidal volume (LTV) versus low-tidal/low-frequency ventilation, underscore the need for further research focusing on larger sample sizes, long-term outcomes, and the interaction with specific congenital heart defects(Elhaddad et al., 2022).
2. Driving Pressure-Guided Ventilation Strategy in Adults: Research gaps exist in the area of driving pressure-guided ventilation strategies in adults, with a lack of detailed outcomes hindering comparisons with traditional lung-protective strategies. Standardized definitions, protocols, and direct comparisons with existing strategies are needed to clarify patient-centered outcomes like mortality, ICU length of stay, and long-term pulmonary function.
3. Lung Protective Strategies in Models of ARDS: While studies in piglet models of acute respiratory distress syndrome (ARDS) support lung protective strategies using lower tidal volumes, challenges remain in translating these findings to human patients with different types of ARDS. Understanding the trade-off between reducing ventilator-induced lung injury and maintaining gas exchange requires further investigation.
4. Long-term Outcomes in Neonatal Care: Research on lung protection strategies with high-frequency oscillatory ventilation with volume guarantee (HFOV-VG) in preterm infants

shows enhanced long-term respiratory outcomes. However, gaps exist in understanding the underlying mechanisms of improved outcomes, their generalizability, and the neurodevelopmental consequences of HFOV-VG, necessitating longitudinal studies on cognitive and motor outcomes(Cools et al., 2009).

5. Methodological Considerations and Standardization: There is a need for greater standardization of ventilation strategies, definitions of pulmonary complications, and outcome measures across studies to enhance comparability and develop evidence-based guidelines. Methodological differences in ventilation protocols, patient selection criteria, and follow-up duration may contribute to discrepancies in findings(Blackwood et al., 2019).

Future research directions should focus on conducting multicenter trials, exploring individualized ventilation strategies, investigating long-term pulmonary and neurodevelopmental effects, developing predictive models, and integrating advanced monitoring techniques to optimize ventilator settings in real-time. Addressing these research gaps can lead to more personalized and effective mechanical ventilation strategies that optimize outcomes for patients with diverse respiratory needs.

4.3 Implications

The implications of the findings from the studies on mechanical ventilation are both theoretical and practical, offering valuable insights that may shape future research, clinical practice, and policy in the field. The theoretical implications contribute to the evolving understanding of lung mechanics and ventilator-induced lung injury (VILI). The exploration of different PEEP strategies highlights the complexity of pulmonary responses to mechanical ventilation, supporting a more individualized approach to ventilatory support tailored to the patient's condition and phase of illness or surgery(de Prost, Ricard, Saumon, & Dreyfuss, 2011; Grune, Tabuchi, & Kuebler, 2019).

Practically, the studies have significant implications for clinical practice. For example, the use of low-tidal volume ventilation during pediatric cardiac surgery and high-frequency oscillatory ventilation in neonatal care could influence guidelines and improve outcomes. In adult patients with ARDS, lung protective strategies and driving pressure-guided ventilation may enhance critical care protocols and patient outcomes. These findings may prompt healthcare systems to adopt evidence-based ventilation strategies, especially in pediatric and neonatal intensive care(Al-Ayed et al., 2023; Miller, Tan, Smith, Rotta, & Lee, 2022).

Future research directions should focus on conducting extensive studies with standardized protocols, exploring long-term outcomes in neonatal care, and utilizing advanced monitoring techniques to refine ventilation strategies and personalize care. Developing predictive models using artificial intelligence could assist clinicians in optimizing ventilator settings in real-time. Overall, the shift towards personalized mechanical ventilation strategies based on patient-specific characteristics and responses to therapy has the potential to improve patient outcomes, reduce complications associated with mechanical ventilation, and advance our theoretical understanding of respiratory physiology and artificial ventilation(Y. Kim et al., 2023).

Discussion:

This narrative review highlights several limitations and challenges encountered in the implementation of personalized PEEP strategies, including:

1. Lack of Consensus: The absence of agreement on the optimal method for personalizing PEEP strategies based on patient-specific characteristics hinders the establishment of standardized guidelines.
2. Difficulty in Identifying Relevant Patient-Specific Characteristics: Determining which patient-specific factors should guide PEEP titration is complex, as the relative importance and optimal thresholds of factors like lung compliance and severity of lung injury remain uncertain.
3. Variability in Measurement Techniques: Challenges in accurately measuring patient-specific characteristics, such as lung compliance, can impact the reliability of personalized PEEP strategies.
4. Limited Availability of Monitoring Tools: Some patient-specific characteristics necessary for PEEP titration may require specialized monitoring tools not universally accessible, hindering widespread implementation.
5. Time and Resource Constraints: Implementing personalized PEEP strategies may demand additional time and resources, posing challenges in busy clinical settings.
6. Lack of Robust Evidence: Despite growing interest, evidence supporting the effectiveness of personalized PEEP strategies remains limited, necessitating well-designed clinical trials for validation.
7. Potential for Harm: Individualizing PEEP levels based on patient-specific characteristics carries the risk of harm if not accurately determined.
8. Training and Education: Adequate training and education are crucial for healthcare professionals to safely and effectively implement personalized PEEP strategies.

Addressing these limitations is crucial to enhance the feasibility and clinical utility of personalized PEEP strategies in routine clinical practice. To tackle the lack of consensus, potential solutions include:

1. Conducting Well-Designed Clinical Trials
2. Collaboration and Consensus-Building Efforts
3. Systematic Reviews and Meta-Analyses
4. Development of Clinical Decision Support Tools
5. Education and Training Programs
6. Multidisciplinary Approach
7. Continuous Quality Improvement Initiatives
8. Knowledge Translation and Dissemination

A collaborative, evidence-based approach involving research, education, and multidisciplinary efforts is essential to establish standardized guidelines and improve the clinical implementation of personalized PEEP strategies.

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Conclusion:

The studies reviewed offer valuable insights into mechanical ventilation strategies in various clinical contexts, showing progress in developing personalized, lung-protective protocols. However, research gaps persist that could be addressed to enhance outcomes. Large, multicenter studies are necessary to validate findings and establish best practices with robust evidence. Future research should explore personalization approaches using advanced monitoring, consider long-term impacts, and integrate theoretical frameworks that account for physiological complexity. Collaborative, interdisciplinary efforts are essential to fully leverage mechanical ventilation for precise respiratory support and improved patient experiences globally. The review emphasizes the importance of incorporating patient-specific characteristics in personalized PEEP strategies to enhance patient outcomes. Further research is crucial to advance the understanding and implementation of tailored ventilation approaches, ultimately benefiting respiratory health and patient experiences.

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