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Tracheal intubation in critically ill adults with a physiologically difficult airway. An international Delphi study



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Abstract

Purpose: Our study aimed to provide consensus and expert clinical practice statements related to airway management in critically ill adults with a physiologically difficult airway (PDA).

Methods: An international Steering Committee involving seven intensivists and one Delphi methodology expert was convened by the Society of Critical Care Anaesthesiologists (SOCCA) Physiologically Difficult Airway Task Force. The committee selected an international panel of 35 expert clinician–researchers with expertise in airway management in critically ill adults. A Delphi process based on an iterative approach was used to obtain the final consensus statements.

Results: The Delphi process included seven survey rounds. A stable consensus was achieved for 53 (87%) out of 61 statements. The experts agreed that in addition to pathophysiological conditions, physiological alterations associated with pregnancy and obesity also constitute a physiologically difficult airway. They suggested having an intubation team consisting of at least three healthcare providers including two airway operators, implementing an appropriately designed checklist, and optimizing hemodynamics prior to tracheal intubation. Similarly, the experts agreed on the head elevated laryngoscopic position, routine use of videolaryngoscopy during the first attempt, preoxygenation

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with non-invasive ventilation, careful mask ventilation during the apneic phase, and attention to cardiorespiratory status for post-intubation care.

Conclusion: Using a Delphi method, agreement among a panel of international experts was reached for 53 statements providing guidance to clinicians worldwide on safe tracheal intubation practices in patients with a physiologically difficult airway to help improve patient outcomes. Well-designed studies are needed to assess the effects of these practice statements and address the remaining uncertainties.

Keywords: Tracheal intubation, Delphi, Physiologically difficult airway, Airway management, Intubation, Intratracheal/adverse effects, Guidelines, Intratracheal/methods

Introduction

Tracheal intubation is frequently performed in critically ill adults. In a prospective study evaluating airway management practice in critically ill adults across 29 countries, at least one major peri-intubation adverse event occurred in 45% of patients [1], including cardiovascular collapse, severe hypoxemia, and cardiac arrest. The occurrence of these events was associated with an increased risk of both intensive care unit (ICU) and 28-day mortality. The observed adverse events have led critically ill adults to be described as having a physiologically difficult airway (PDA), wherein pathophysiologic alterations increase the risk of cardiovascular, respiratory and other complications during tracheal intubation [2, 3]. Such alterations may limit the effectiveness of preoxygenation [4], exaggerate the hemodynamic effects of anesthetic induction agents, or reduce the tolerance of transitioning to positive pressure ventilation. Complications during tracheal intubation in critically ill adults are more likely than in patients undergoing airway management for elective surgical procedures [5], and may occur even when tracheal intubation is successfully completed at the first attempt [6].

The "difficult airway" has traditionally been described in the context of anatomic difficulties that make tracheal intubation challenging [7, 8]. Hence, most guidelines have focused on overcoming these anatomical difficulties using advanced airway management devices (e.g., video laryngoscope [VL] and flexible bronchoscope) [9, 10], and only a few guidelines provided recommendations on addressing physiologic challenges associated with tracheal intubation [3, 11]. Identification of patients undergoing tracheal intubation who are at risk for a physiologically difficult airway allows clinicians to develop strategies to mitigate risks, such as advanced preoxygenation techniques, emphasis on first-pass intubation success, and prevention of hemodynamic collapse [12-14]. Despite increasing recognition, and research around techniques to mitigate peri-intubation complications, robust evidence to guide practice is lacking [11, 13]. We aimed to address these evidence gaps by generating consensus among experts on the definition and management of a physiologically difficult airway in critically ill adults using a Delphi process. The results of the Delphi process were presented at the Society of Critical Care Medicine Annual Congress 2024, at Phoenix, AZ, USA [15].

Methods

Delphi process

An international Steering Committee (KK, PN, MJ, DB, CSJ, ADJ, SNM) involving seven intensivists and one Delphi methodology expert was convened by the Society of Critical Care Anaesthesiologists (SOCCA; https://socca.org) Physiologically Difficult Airway Task Force. The Steering Committee prepared the statements for the first Delphi round, recruited an international panel of experts, coordinated the Delphi process, and drafted the expert clinical practice statements. The Steering Committee did not participate in the Delphi surveys. The study protocol was registered with ClinicalTrials.gov (NCT05762068). This study was unfunded, and the members of the Steering Committee reported no financial conflicts of interest.

The Steering Committee convened an international panel of physician experts through a purposive sampling after reviewing recent publications in the field of airway management in critically ill adults. A concerted effort was taken to constitute a diverse expert panel meeting the predefined selection criteria. Forty experts were invited to participate via email, and each expert met predefined inclusion criteria: (1) clinical expertise in the airway management of critically ill adults, (2) teaching experience in airway management, and (3) research projects or publications in airway management. Upon acceptance, experts were included in the Delphi process. Neither patients nor the public were included in this study because of the complexities involved in integrating their perspective into the highly technical aspects of tracheal intubation in a physiologically difficult airway. The experts remained anonymous until the end of the Delphi process to avoid bias or group pressure. Participation in the Delphi process was voluntary and implied consent.

The Steering Committee performed a focused literature search of articles published between January 1, 2000, and February 1, 2023, using PubMed headings: "Airway Management" OR "Intubation" OR "Intratracheal" AND "Critical Illness" OR "Risk Factors" OR "Hypoxia" OR "Hypotension". Results informed initial draft statements for the Delphi process. A list of interventions related to the physiologically difficult airway with absence and/or paucity of clear evidence was used to draft statements for the first round of the Delphi process. The ACcurate COnsensus Reporting Document (ACCORD) checklist is enclosed in the electronic supplementary material (ESM).

Statements were drafted in English and organized into five domains: definition and risk of physiologically difficult airway, preparing the team, preparing the patient, performing the procedure, and post-intubation care. The survey for each Delphi round was distributed using Google Forms. Responses were constructed in a sevenpoint Likert scale or multiple-choice format. The survey was piloted among the Steering Committee for clarity of the statements and technical aspect of the survey. Multiple reminders were sent to experts during each round to encourage completion of the survey. In addition, the experts were prompted for feedback during each round. Based on the feedback, questions were modified or deleted in the subsequent rounds. The results of each round were consolidated, summarized, and anonymized by the Steering Committee, and then sent to the experts along with the subsequent round questionnaire as documented in the ESM. Notably, members of the Steering Committee did not participate in voting.

Consensus and stability

For statements with seven-point Likert scale responses, consensus was defined as \geq 70% agreement (scores 5–7) or disagreement (scores 1–3) with a statement. Medians (interquartile range, IQR) were used to describe the central tendency and dispersion of responses. For statements with multiple-choice responses, consensus was defined as \geq 80% agreement for a given choice. Stability of responses between rounds was assessed using a non-parametric chi-square (χ^2) test or the Kruskal–Wallis test from round two onwards. A *p* value <0.05 was considered a significant variation, or unstable [16, 17]. Microsoft Excel (MS Office 2019, Microsoft Corp, WA, USA) was used for statistical analysis. Statements were included in the Delphi rounds until the criteria for stability were reached.

Expert clinical practice statements

The Steering Committee drafted expert clinical practice statements from the survey statements that achieved consensus. The results of the Delphi process, clinical practice statements, and the manuscript were circulated among the experts for feedback and approval before submission for publication.

Results

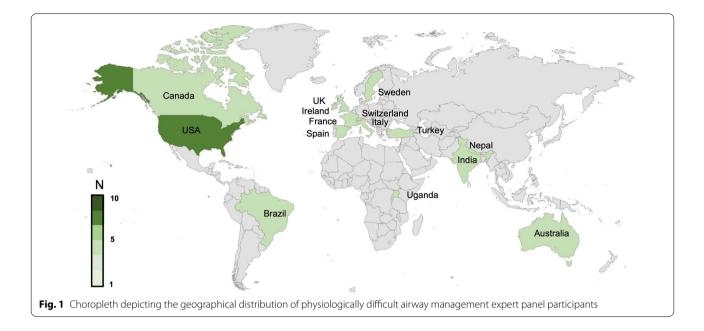
Out of 40 experts invited, 35 (90%) from 15 countries across six continents participated (Fig. 1). The remaining five experts did not respond to multiple email reminders for participation. The median age of the participating experts was 49 (44–57) years, and six (17%) were women. Of 35 experts, 26 (74%) were affiliated with university hospitals. The primary training specialty of the experts included anesthesiology (66%), critical care medicine (11%), pulmonary medicine (11%), and emergency medicine (11%).

Seven Delphi rounds evaluating 61 statements in five domains were conducted between March 19, and June 18, 2023, and 33 (94%) experts completed all rounds of the Delphi process (ESM Fig. S1). At completion, 54 (88%) statements reached consensus and stability (ESM Table S1). From these, 38 expert clinical practice statements were drafted (ESM Tables S2 and S3). During review of the clinical practice statements, concern arose that a statement about the application of cricoid pressure was ambiguous and could jeopardize patient safety. The Steering Committee made the decision to allow for an additional post hoc round of anonymous voting to address this issue. Experts were asked to vote on excluding or retaining the statement. The statement was dropped in response to a majority (88%) anonymous vote, leaving 53 of 61 (87%) statements that reached consensus and stability. Figures 2 and 3 outline the expert clinical practice statements, while Fig. 4 summarizes the most clinically relevant statements (not those with the highest consensus) related to the physiologically difficult airway. The full results of the individual Delphi rounds are available in the ESM.

Definition and constituents

- A physiologically difficult airway is defined as one in which the patient's physiological and pathophysiological alterations increase the risk for complications during tracheal intubation and transition to positive pressure ventilation.
- Pathophysiological alterations, such as hypoxemia, cardiovascular instability, right ventricular dysfunction, and increased intracranial pressure, as well as physiological alterations that occur in obesity and pregnancy constitute a physiologically difficult airway.

Critically ill adults may have a physiologically difficult airway due to various pathophysiological conditions. The



initial description of a physiologically difficult airway [2] and the consensus statement from the Society for Airway Management [11] identified four clinically relevant conditions associated with a physiologically difficult airway: hypoxemia, hypotension, severe metabolic acidosis, and right ventricular failure. In addition, intracranial hypertension, risk of aspiration of gastric contents during tracheal intubation, and physiological alterations that occur in obesity and pregnancy have also been described as causes of a physiologically difficult airway [2, 3].

In this Delphi process, the experts did not feel that severe metabolic acidosis or risk of aspiration of gastric contents constitute a physiologically difficult airway. While the presence of severe metabolic acidosis may present challenges associated with post-tracheal intubation mechanical ventilation, it may not predispose patients to a physiologically difficult airway. Similarly, it was felt that aspiration risk might be considered an anatomical problem, with the potential to become a physiologic problem due to the development of hypoxemia and/or shock state after an aspiration event. Thus, while both conditions certainly have the potential to incur morbidity during airway management, they were not further considered in this process.

The presence of intracranial hypertension was thought to constitute a physiologically difficult airway by the experts. Tracheal intubation may increase intracranial pressure, which may lead to complications during the procedure in brain-injured patients. The experts concluded that the physiologic alterations associated with pregnancy and obesity also constitute a physiologically difficult airway, predominantly due to the reduction in functional residual capacity (FRC), which increases the risk of hypoxemia during tracheal intubation.

Location and factors increasing the risk of complications

- Environmental and human factors (including experience of the airway operator), in addition to the patient's physiologic derangements, contribute to an increased risk of complications during the management of a physiologically difficult airway.
- The likelihood of encountering patients with a physiologically difficult airway is higher in the intensive care unit and the emergency department, as compared to other locations in the hospital.

Although patients with a physiologically difficult airway may be encountered in any location within the hospital, it was agreed that patients with significant physiologic derangements requiring tracheal intubation are most likely to be encountered in the intensive care unit (ICU) and in the emergency department (ED). The experts believed that logistical and organizational challenges, as well as human factors, contribute to a higher risk of complications in patients with a physiologically difficult airway. Logistic challenges are common, especially in unfamiliar locations. Gaining access to the head of the bed and optimal positioning for larvngoscopy may often be challenging, as is the access to advanced airway management tools and availability of a comprehensive selection of intubation drugs. Relevant human factors, including the culture and regulations of an organization

Definition and Risk Factors		Patient Preparation and Optimization	
Definition	A PDA is defined as one in which the patient's physiological and pathophysiological alterations increase the risk for complications during tracheal intubation and transition to positive pressure ventilation.	Assessment and Counseling	Critically ill adults requiring tracheal intubation should routinely undergo pre-procedural airway assessment (whenever feasible) to screen for potential anatomic/technical airway difficulty. Screening tools that assess factors beyond predicted anatomic
Contributory Factors	Pathophysiological alterations, such as hypoxemia, cardiovascular instability, right ventricular dysfunction, and increased intracranial pressure, as well as physiological alterations that occur in obesity and pregnancy constitute a PDA.	Hemodynamic Monitoring and Optimization	difficulty, such as MACOCHA and HYPS scores, may be used to identify patients at risk of a PDA.
			Patients with a PDA should be counseled about airway management prior to tracheal intubation, if feasible.
	Environmental and human factors (including experience of the airway operator), in addition to the patient's physiologic derangements, contribute to an increased risk of complications during the management of a PDA.		The minimum mandatory monitoring in patients with a PDA undergoing tracheal intubation should include non-invasive blood pressure, continuous electrocardiogram, and pulse oximetry.
	The likelihood of encountering patients with a PDA is higher in the intensive care unit and the emergency department, as compared to other locations in the hospital.		Hemodynamics should be optimized prior to tracheal intubation in patients with a PDA. Interventions such as vasopressor and/or inotrope infusion administration can help prevent and/or minimize peri-intubation cardiovascular collapse.
	eam Preparation and Human Factor Considerations		Use of peri-procedural point-of-care ultrasound, when feasible,
Checklist	An appropriately designed intubation checklist that addresses equipment, drugs, team roles/composition, patient optimization, and both primary and backup plans for airway management can reduce errors of omission and may improve patient outcomes		can improve the safety of the tracheal intubation by aiding the assessment and management of cardio-respiratory compromise.
\Box	during the management of a PDA.		Preoxygenation with NIV (pressure support with positive end-
Team	The intubation team should consist of at least three healthcare providers during the management of a PDA. This should ideally include two airway operators, at least one of whom should be	Optimization	expiratory pressure, if available) is the preferred method to minimize the risk of oxygen desaturation during tracheal intubation in patients with a PDA.
	experienced.		Apneic oxygenation (i.e., oxygen delivery during apnea) using high flow nasal oxygenation is an acceptable technique to minimize oxygen desaturation during tracheal intubation in patients with a PDA.
	Assigning roles and responsibilities of team members, ensuring a shared mental model amongstteam members, discussion of		
	primary and rescue plans, gathering and interpreting information, as well as anticipating problems can improve team performance during the management of a PDA.		Careful mask ventilation may be performed during the apneic phase of rapid sequence intubation (RSI) to minimize desaturation.
	Post-procedural team debriefings can help improve team performance for the future management of a PDA.		In patients with a PDA who are difficult to pre-oxygenate due to lack of cooperation, the benefits of a sub-anesthetic dose of sedative-hypnotic while preserving spontaneous ventilation (i.e., delayed sequence intubation) may outweigh the risks.
Training	Training requirements for providers performing airway management in patients with a PDA should be well-defined.		
	Simulation-based training should be a part of the curriculum for providers performing airway management in patients with a PDA.	Position	Head Elevated Laryngoscopic Position (HELP), also known as the semi-Fowler position, with the head of the bed elevated to 30 degrees, should be used for TI in patients with a PDA.

Fig. 2 Physiologically difficulty airway expert clinical practice statements: definition and risk factors, team preparation and human factors, and patient preparation. This figure is intended to summarize expert clinical practice statements related to the definition of a physiologically difficult airway and relevant risk factors, team preparation and human factors considerations, and patient preparation. *NIV* noninvasive ventilation, *PDA* physiologically difficult airway, *TI* tracheal intubation

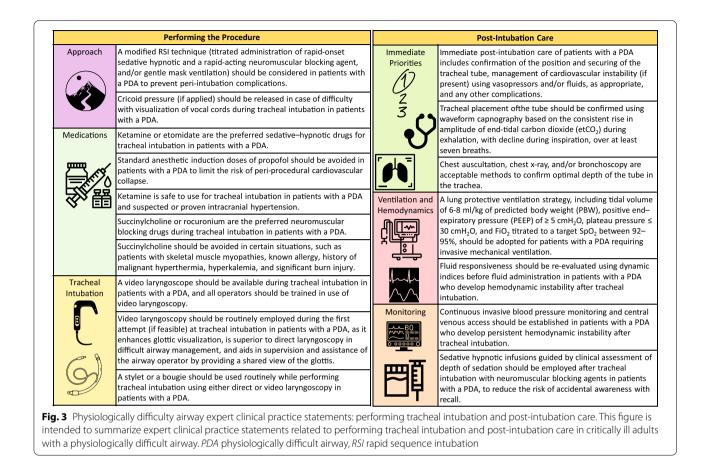
that may influence individuals' relationships and performance within complex healthcare systems, are also contributory [18]. Recommendations to optimize human factors have only recently been incorporated into airway guidelines [10]. The experts concurred that experience of the airway operator is a critical human factor that can contribute to peri-intubation complications.

Team preparation and human factor considerations

- An appropriately designed intubation checklist that addresses equipment, drugs, team roles/ composition, patient optimization, and both primary and backup plans for airway management can reduce errors of omission and may improve patient outcomes during the management of a physiologically difficult airway.
- The intubation team should consist of at least three healthcare providers during the management of a physiologically difficult airway. This

should ideally include two airway operators, at least one of whom should be experienced.

- Assigning roles and responsibilities of team members, ensuring a shared mental model among team members, discussion of primary and rescue plans, gathering and interpreting information, as well as anticipating problems can improve team performance during the management of a physiologically difficult airway.
- Post-procedural team debriefings can help improve team performance for the future management of a physiologically difficult airway.
- Training requirements for providers performing airway management in patients with a physiolog-ically difficult airway should be well defined.
- Simulation-based training should be a part of the curriculum for providers performing airway management in patients with a physiologically difficult airway.



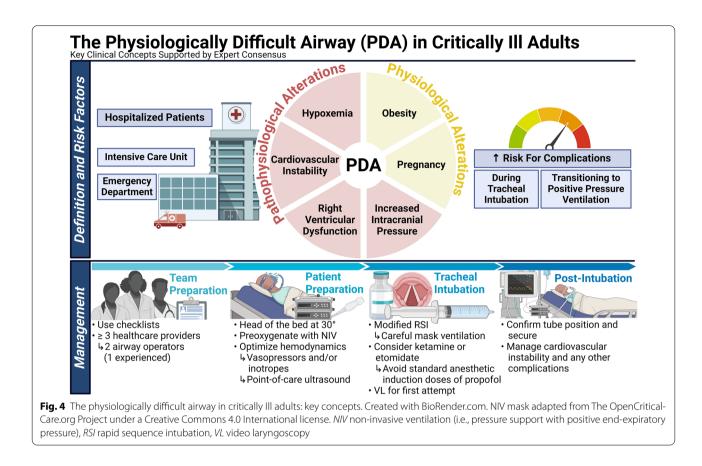
The use of airway management checklists has been increasing [19, 20], allowing teams to mitigate risks of tracheal intubation in stressful situations [21, 22]. Data on the effectiveness of such checklists in reducing adverse outcomes associated with tracheal intubation in critically ill adults have yielded conflicting results, likely due to variation in components of checklists between study protocols [23–25]. Specifically, pre-intubation checklists may be more effective when interventions for physiological optimization are included and when they are used by less experienced teams, as demonstrated in a before and after multi-center study [23].

The composition of the team required for managing a physiologically difficult airway depends on various factors, such as clinical urgency, availability and skill set of team members, and local practices. There was consensus among the experts that a minimum of three team members should be present. The Difficult Airway Society guidelines recommend a minimum of four and up to six staff for performing tracheal intubation in critically ill adults [12]. Jaber et al. found complication rates to be lower when tracheal intubation was performed by a team including two airway operators, one of whom was experienced [26]. This was also endorsed by the All India

Difficult Airway Society guidelines [27]. The experts agreed that an intubation team should consist of at least three healthcare providers, including two airway operators, at least one of whom should be experienced.

The experts did not reach agreement on the definition of an experienced operator. Some experts prioritized years of experience with tracheal intubation or number of procedures performed, while others considered dedicated training in critical care medicine more important when defining an experienced airway operator. This discrepancy of opinion may reflect the multitude of definitions in the literature and the wide variation in the training curricula of ICU practitioners internationally.

The process of role allocation and discussion of primary and back up plans prior to tracheal intubation has become a cornerstone of human factor considerations in guidelines from international airway societies [18]. Assigning dedicated roles within the team allows an experienced airway operator to focus on the task of successful tracheal intubation while being adequately supported by the team. Debriefing in the ICU has demonstrated positive effects on clinician learning (e.g., improved knowledge and skill acquisition) after management of emergencies [28]. Real-time feedback and post-procedural debriefing



allows clinicians the opportunity to cement positive behaviors and identify any barriers to team performance that can be improved [29]. The experts agreed that these approaches can improve team performance.

Cross-sectional studies have demonstrated variations in training on tracheal intubation, especially outside the operating room [30–32]. The training requirements should include locally available infrastructure, including equipment, checklists, and treatment algorithms, and should involve all stakeholders with a focus on skill development and retention [12, 33]. Furthermore, the training should assess competence; however, defined criteria for this are lacking. In particular, optimal training to manage the physiologically difficult airway requires further exploration. The experts agreed that training requirements for tracheal intubation in patients with physiologically difficult airway should be well defined.

Although not studied in the context of managing patients with a physiologically difficult airway, simulation has proven effective at enhancing skill acquisition and has been adapted in several ICUs [33, 34]. Virtual reality based simulation for airway management has been explored recently but needs further evaluation [35]. Simulation-based team training in the ICU is well received by staff, with perception of benefit, and some evidence

of improved staff behaviors [36, 37]. Following the coronavirus disease 2019 (COVID-19) pandemic, simulation has been widely adopted as a modality of airway training. The experts agreed that simulation should be a part of the curriculum for airway providers managing patients with a physiologically difficult airway.

Patient preparation and optimization

1. Airway assessment

- Critically ill adults requiring tracheal intubation should routinely undergo pre-procedural airway assessment (whenever feasible) to screen for potential anatomic/technical airway difficulty.
- Screening tools that assess factors beyond predicted anatomic difficulty, such as MACO-CHA and HYPS scores, may be used to identify patients at risk of a physiologically difficult airway.
- Patients with a physiologically difficult airway should be counseled about airway management prior to tracheal intubation, if feasible.

Airway assessment in the critically ill patient is often limited by a lack of patient cooperation, altered

consciousness, and the emergency nature of the procedure [14]. Early identification of risk factors for difficult intubation can help clinicians anticipate complications and better prepare for anatomical and physiological difficulty. The MACOCHA score [38], which considers not only anatomical difficulty but also physiological alterations and the experience of the operator, has demonstrated that difficult intubation is significantly associated with moderate and severe life-threatening complications, highlighting the importance of airway assessment in these patients, if feasible [38]. The HYPS score is another tool that was recently proposed for prediction of periintubation hypotension in the critically ill [39].

2. Hemodynamic monitoring and optimization

- The minimum mandatory monitoring in patients with a physiologically difficult airway undergoing tracheal intubation should include non-invasive blood pressure, continuous electrocardiogram, and pulse oximetry.
- Hemodynamics should be optimized prior to tracheal intubation in patients with a physiologically difficult airway. Interventions such as vasopressor and/or inotrope infusion administration can help prevent and/or minimize periintubation cardiovascular collapse.
- Use of peri-procedural point-of-care ultrasound, when feasible, can improve the safety of the tracheal intubation by aiding the assessment and management of cardiorespiratory compromise.

Cardiovascular collapse and hypoxemia are the most common complications associated with tracheal intubation in critically ill adults [1]. The experts reached consensus on the value of related monitoring modalities, emphasizing the need for continuous electrocardiogram, continuous pulse oximetry, and non-invasive blood pressure monitoring as standard practice during tracheal intubation of a patient with a physiologically difficult airway, especially when performing tracheal intubation in more remote areas of the hospital, where such monitoring is not normally utilized. However, the experts did not reach consensus on the role of continuous end-tidal capnography apart from confirmation of tracheal tube position. Fluid loading and early use of vasopressors have been recommended to decrease the incidence of cardiovascular collapse during tracheal intubation [23, 40, 41]. Two trials in critically ill adults suggest a lack of efficacy with empirical administration of a 500 ml intravenous fluid bolus prior to tracheal intubation to prevent cardiovascular collapse among an unselected ICU population and those receiving positive pressure ventilation between induction and laryngoscopy [42, 43]. Nonetheless, the administration of fluids during these situations may be considered on a caseby-case basis, possibly after assessing fluid responsiveness, if feasible.

Future research should explore whether specific subgroups benefit from a fluid bolus, the effectiveness of preintubation vasopressors, and the interaction between the two [44]. Two ongoing international trials (the FLUVA Trial [NCT05318066] and the PREVENTION trial [NCT05014581]) are investigating the effectiveness of pre-emptively administering vasopressors in preventing cardiovascular collapse in critically ill adults undergoing tracheal intubation. Bedside point-of-care ultrasound (POCUS) can help identify at-risk patients and provide real-time hemodynamic and respiratory assessment, and may aid in physiological optimization in these patients, warranting further research [45].

3. Peri-intubation oxygenation and respiratory optimization

- Preoxygenation with noninvasive ventilation (NIV) (pressure support with positive endexpiratory pressure, if available) is the preferred method to minimize the risk of oxygen desaturation during tracheal intubation in patients with a physiologically difficult airway.
- Apneic oxygenation (i.e., oxygen delivery during apnea) using high flow nasal oxygenation is an acceptable technique to minimize oxygen desaturation during tracheal intubation in patients with a physiologically difficult airway.
- Careful mask ventilation may be performed during the apneic phase of rapid sequence intubation (RSI) to minimize desaturation.
- In patients with a physiologically difficult airway who are difficult to pre-oxygenate due to lack of cooperation, the benefits of a sub-anesthetic dose of sedative hypnotic while preserving spontaneous ventilation (i.e., delayed sequence intubation) may outweigh the risks.

After cardiovascular instability, hypoxemia is the second most frequent complication observed in critically ill adults undergoing tracheal intubation [1]. The PRO-TRACH study showed no difference in the primary outcome of lowest oxygen saturation during tracheal intubation in critically ill adults undergoing preoxygenation with high-flow nasal oxygen (HFNO) (continued during laryngoscopy) or by standard bag-valve-mask oxygen SMO for standard bag-valve mask ventilation. While the median lowest pulse oximetry values were 99% in the SMO group and 100% in the HFNO group, desaturations below 95% were significantly more frequent with SMO (23%) than with HFNO (12%) (risk ratio [RR] 0.51, 95% confidence interval [CI] 0.26–0.99, p=0.045) [46]. The FLORALI 2 study, which randomized hypoxemic, critically ill adults undergoing tracheal intubation to preoxygenation with NIV and/or HFNO (continued during laryngoscopy) showed no difference in the incidence of severe hypoxemia [47]. However, the subgroup analyses suggested a potential benefit for NIV among patients with a PaO₂/FiO₂ ratio < 200 mmHg. Prior studies comparing preoxygenation using NIV versus bag-valve mask (BVM) or conventional facemask also found less oxygen desaturation with the use of NIV [48, 49]. In the PREOXI study, preoxygenation with NIV resulted in a lower incidence of hypoxemia (i.e., oxygen saturation of less than 85% during the interval between induction of anesthesia and 2 min after tracheal intubation) than preoxygenation with an oxygen mask (9% vs. 18%, 95% CI, -13.2 to -5.6; p < 0.001) [50]. Taken together, these trials suggest that in critically ill adults preoxygenation with NIV or HFNO (continued during laryngoscopy) are superior to conventional preoxygenation. In addition, NIV may be superior to HFNO for preoxygenation in patients with moderate to severe hypoxemia. While the exact settings for NIV and HFNO were not included in the statements, 100% FiO₂ should be provided prior to and during the procedure. In patients with high minute ventilation, flows > 30 L/min on HFNO may be needed to avoid entrainment of room air. Similarly, high positive end-expiratory pressure may be needed in patients with low P/F ratio. These settings would need to be adjusted on a case-by-case basis.

A recent randomized controlled trial (RCT) [51] found that delayed sequence intubation (DSI) using a dissociative dose of ketamine to facilitate preoxygenation significantly decreases peri-intubation hypoxia compared to standard RSI, justifying the use of DSI in patients who are difficult to pre-oxygenate due to compromised mental status.

4. Patient positioning

 Head elevated laryngoscopic position (HELP), also known as the semi-Fowler position, with the head of the bed elevated to 30 degrees, should be used for tracheal intubation in patients with a physiologically difficult airway.

The superiority of 'sniffing' or the semi-upright, 'ramped' position (keeping the external auditory meatus leveled with the sternal notch) in facilitating glottic visualization and tracheal intubation is debatable [52]. A randomized study in the critically ill showed that ramped position was associated with increased tracheal intubation difficulty compared with the sniffing position, although the

use of suboptimal ramped positioning was an important limitation in this trial [53]. The upright position improves preoxygenation, prevents reduction in the FRC, and may reduce the risk of pulmonary aspiration [54]. A prospective observational study and a large retrospective study showed improved first-pass intubation success and reduced complication rates, respectively, with upright positioning compared to supine position during emergency tracheal intubation [55, 56]. Though RCTs are lacking, recent guidelines have recommended HELP, especially in patients at a high risk of aspiration or desaturation [12, 27]. However, the hemodynamic status of the patient should be taken into consideration before placing the patient in the HELP position.

Performing the procedure

1. RSI and drugs for tracheal intubation

- A modified RSI technique (titrated administration of rapid-onset sedative hypnotic and a rapidacting neuromuscular blocking agent, and/or gentle mask ventilation) should be considered in patients with a physiologically difficult airway to prevent peri-intubation complications.
- Cricoid pressure (if applied) should be released in case of difficulty with visualization of vocal cords during tracheal intubation in patients with a physiologically difficult airway.
- Ketamine or etomidate is the preferred sedative– hypnotic drugs for tracheal intubation in patients with a physiologically difficult airway.
- Standard anesthetic induction doses of propofol should be avoided in patients with a physiologically difficult airway to limit the risk of peri-procedural cardiovascular collapse.
- Ketamine is safe to use for tracheal intubation in patients with a physiologically difficult airway and suspected or proven intracranial hypertension.
- Succinylcholine or rocuronium are the preferred neuromuscular blocking drugs during tracheal intubation in patients with a physiologically difficult airway.
- Succinylcholine should be avoided in certain situations, such as patients with skeletal muscle myopathies, known allergy, history of malignant hyperthermia, hyperkalemia, and significant burn injury.

Discussion

There is no agreed definition of RSI or modified RSI in the literature. The choice of sedative-hypnotic agents for induction of anesthesia is especially important when considering hemodynamic complications. A post hoc

analysis of the INTUBE study showed that the use of propofol for induction was significantly associated with cardiovascular collapse, irrespective of the blood pressure before tracheal intubation [57]. Importantly, these hemodynamic complications are associated with an increased risk of death. Propofol, when used as a hypnotic agent, is likely detrimental and may reduce survival in perioperative and critically ill adults, as reported in a recent meta-analysis of RCTs [58]. Induction drugs with a more stable hemodynamic profile, such as ketamine and etomidate, have been shown to be safe for tracheal intubation in critically ill adults and are commonly used [59]. Trials comparing ketamine and etomidate for tracheal intubation in critically ill adults have not conclusively established the superiority of either agent [59–61]. However, a recent Bayesian meta-analysis comparing the two drugs for tracheal intubation in critically ill adults showed a moderate probability that induction with ketamine is associated with a reduced risk of mortality [62]. Similarly, a recent meta-analysis of RCTs found a high probability that etomidate increases mortality when used as an induction agent in critically ill adults. Since this meta-analysis was only published after the completion of the Delphi, it is unclear if the expert opinion regarding the use of etomidate in these situations would have changed. Additionally, previous meta-analyses of etomidate have yielded both similar and contradictory findings pertaining to patient mortality [63], indicating a possible role for selecting etomidate on an individual patient basis. Drug admixtures such as propofol combined with ketamine (i.e., ketofol), may have a favorable hemodynamic profile [64], but the ratio is neither well defined, standardized, nor approved. The experts failed to achieve consensus on avoidance of opioid co-administration with induction agents to prevent cardiovascular instability. While some suggested dosing opioids judiciously and titrating as needed to preserve hemodynamics, others were in favor of avoiding their use entirely.

A 2019 RCT found that, among adults undergoing tracheal intubation in an out-of-hospital emergency setting, rocuronium was non-inferior to succinylcholine with regard to successful first-pass intubation without major complications [65]. Interestingly, the trial showed better first-pass success with succinylcholine but fewer complications with rocuronium. The experts agreed on the use of either drug for tracheal intubation in patients with a physiologically difficult airway, with caution advised when using succinylcholine in certain situations.

Applying cricoid pressure during RSI has been long debated, and, although it may be effective for the occlusion of the upper esophagus, its clinical benefits are unproven [66, 67]. The experts agreed that cricoid pressure should be released when it impairs visualization

of the vocal cords. Notably, the experts felt that a statement concerning the management of cricoid pressure in response to regurgitation of gastric contents was ambiguous, and it was ultimately dropped in response to a majority vote. Further work will be needed to clarify if and when cricoid pressure should be released in other circumstances, namely if its application results in active vomiting in an awake patient, as has been previously suggested [68].

2. Devices and tools to aid tracheal intubation

- A video laryngoscope should be available during tracheal intubation in patients with a physiologically difficult airway, and all operators should be trained in use of video laryngoscopy.
- Video laryngoscopy should be routinely employed during the first attempt (if feasible) at tracheal intubation in patients with a physiologically difficult airway, as it enhances glottic visualization, is superior to direct laryngoscopy in difficult airway management, and aids in supervision and assistance of the airway operator by providing a shared view of the glottis.
- A stylet or a bougie should be used routinely while performing tracheal intubation using either direct or video laryngoscopy in patients with a physiologically difficult airway.

Successful first-pass (i.e., first-attempt) intubation is an established endpoint in tracheal intubation trials [65], with multiple attempts at intubation being associated with peri-procedural complications and death [69]. Tools and strategies that can improve first-pass intubation success may, therefore, help to avoid complications, and use of VL may be one of those. A recent Cochrane systematic review and meta-analysis of trials including adults undergoing tracheal intubation in all locations demonstrated that VL was associated with reduced rates of failed tracheal intubation and complications with improved glottic visualization irrespective of the VL design used [70]. The INTUBE study showed VL use in only 17% of tracheal intubations in critically ill adults [1], and this could be because previous studies in the critically ill have failed to demonstrate a clear benefit of VL over direct laryngoscopy (DL) [71, 72]. However, a sub-analysis of the INTUBE study data demonstrated that VL was associated with higher first-pass intubation success rates despite a higher prevalence of difficult anatomic predictors in the VL group [73]. Recently, Prekker et al. found that the use of VL resulted in a higher incidence of successful intubation at the first attempt than the use of DL among critically ill adults undergoing tracheal intubation, with no effect on severe complications

[74]. The incidence of first-pass success by operators that had performed > 100 prior intubations was 89% with VL versus 83% with DL in a subgroup including 213 patients of 1417 in the trial. This difference did not reach significance and suggested some degree of effect moderation relative to operator experience. Despite this evidence, the experts failed to reach consensus on the proportion of patients for whom they would consider using VL. Also, the experts could not reach a consensus on the type of VL blade design they would advise, reflecting a lack of certainty of evidence in these areas. While most evidence on VL use comes from resource-rich settings, we realize that VL may not be routinely available in resource-limited settings. Furthermore, in view of limited evidence favoring VL with experienced providers, the use of DL may be equally acceptable.

The use of a stylet to facilitate tracheal intubation varies in clinical practice. In the Stylet for Orotracheal intubation (STYLETO) trial [75], using a stylet during tracheal intubation with DL resulted in a significantly higher first-pass success rate. Another recent study comparing the use of a bougie vs. stylet among critically ill adults undergoing tracheal intubation reported that the use of a bougie did not significantly increase the incidence of first-pass success when compared to use of a tracheal tube with stylet [76]. It is worth noting that this study included both DL and VL, without showing differences in the primary outcome between the groups. Despite certain methodological limitations, taken together these studies highlight the importance of using a stylet or a bougie during the first attempt at tracheal intubation, rather than as a rescue, to improve first-pass success.

Post-intubation care

- Immediate post-intubation care of patients with a physiologically difficult airway includes confirmation of the position and securing of the tracheal tube, management of cardiovascular instability (if present) using vasopressors and/or fluids, as appropriate, and any other complications.
- Tracheal placement of the tube should be confirmed using waveform capnography based on the consistent rise in amplitude of end-tidal carbon dioxide (etCO₂) during exhalation, with decline during inspiration, over at least seven breaths.
- Chest auscultation, chest X-ray, and/or bronchoscopy are acceptable methods to confirm optimal depth of the tube in the trachea.
- A lung protective ventilation strategy, including tidal volume of 6–8 ml/kg of predicted body weight (PBW), positive end-expiratory pres-

sure (PEEP) of \geq 5 cmH₂O, plateau pressure \leq 30 cmH₂O, and FiO₂ titrated to a target SpO₂ between 92 and 95%, should be adopted for patients with a physiologically difficult airway requiring invasive mechanical ventilation.

- Fluid responsiveness should be re-evaluated using dynamic indices before fluid administration in patients with a physiologically difficult airway who develop hemodynamic instability after tracheal intubation.
- Continuous invasive blood pressure monitoring and central venous access should be established in patients with a physiologically difficult airway who develop persistent hemodynamic instability after tracheal intubation.
- Sedative hypnotic infusions guided by clinical assessment of depth of sedation should be employed after tracheal intubation with neuromuscular blocking agents in patients with a physiologically difficult airway, to reduce the risk of accidental awareness with recall.

The Fourth National Audit Project (NAP4) report highlighted substantial morbidity and mortality after airway management in the ICU [77]. Similarly, the INTUBE study demonstrated high rates of major adverse periintubation events, underscoring the need to identify and manage physiologic compromise in the post-intubation period [1].

Esophageal intubation remains a source of avoidable morbidity and mortality associated with tracheal intubation in critically ill adults, with recent data suggesting an incidence of 5% [1]. Unrecognized esophageal intubation was more commonly seen in the ICU and the ED when compared with tracheal intubation performed in the operating room [78]. The Project for Universal Management of Airways (PUMA) guidelines recommend using detection of sustained exhaled carbon dioxide to confirm alveolar ventilation following passage of a tracheal tube [79]. The guidelines emphasize the availability of exhaled carbon dioxide monitoring for all episodes of tracheal intubation, with recommendations to use continuous waveform capnography, if available. Waveform capnography is also recommended as the gold standard for confirming tracheal intubation by the NAP4 report, by the American Heart Association for use in emergency airway management, and by multiple international guidelines for airway management in critical illness [78, 80]. The experts agreed with the need for waveform capnography to confirm tracheal intubation and the importance of ensuring at least seven breaths of consistent or increasing exhaled carbon dioxide. Continuous waveform capnography can help to gauge the adequacy of ventilation via a

facemask or supraglottic airway; however, the experts did not reach consensus on its necessity for these purposes.

Following confirmation of tracheal tube placement by waveform capnography, assessment of tube positioning is necessary to recognize malposition, including endobronchial intubation. While the experts agreed that chest auscultation, chest X-ray, and/or bronchoscopy were acceptable methods to confirm optimal insertion depth of the tracheal tube, they did not agree on the utility of ultrasound for confirmation. Although the use of ultrasound for this purpose is an emerging modality, further evaluation is warranted [81].

Lung protective ventilation with low to intermediate tidal volumes (6–8 ml/kg PBW) minimizes the adverse outcomes associated with barotrauma and volutrauma in all patients and can reduce morbidity and mortality in the setting of acute respiratory distress syndrome (ARDS) [82]. Tidal volumes less than 6 ml/kg PBW may be needed to keep the plateau pressure \leq 30 cmH₂O in patients with poor lung compliance. Although the experts supported lung protective ventilation, they did not agree that targeting a driving pressure less than 15 cmH₂O was important. This may reflect the lack of prospective evidence supporting driving pressure as a modifiable target for ventilation [83–85].

Although cardiovascular collapse is common following intubation of a physiologically difficult airway [1], evidence is lacking for empirical fluid bolus administration prior to tracheal intubation [86, 87]. The experts agreed that administration of IV fluids following tracheal intubation should be supported by the presence of fluid responsiveness using dynamic indices. This may represent a shift in clinical practice towards individualized fluid use throughout critical illness [88], with cumulative positive fluid balance being associated with adverse outcomes [89].

Although the literature examining clinical outcomes associated with invasive venous and arterial vascular access has not uniformly demonstrated clinical benefits in at-risk patients, these modalities are often necessary in patients with persistent shock [90–92]. Such patients typically require continuous blood pressure monitoring to titrate vasoactive medications, dynamic evaluation of fluid responsiveness, and reliable access for intravenous medication delivery. These goals are facilitated through arterial and central venous vascular access. In addition, arterial blood pressure monitoring is more accurate compared to traditional, oscillometric non-invasive modalities in patients with shock [93, 94].

Accidental awareness is a feared complication following administration of neuromuscular blocking agents (NMBAs) for tracheal intubation, with a reported frequency of 4% [95]. The experts agreed that patients who receive NMBAs during tracheal intubation should receive a sedative-hypnotic infusion to prevent awareness during neuromuscular blockade. Notably, they agreed on the use of clinical assessment of depth of sedation, rather than processed electroencephalogram (EEG). Processed EEG has been used to minimize awareness during total intravenous anesthesia, but its utility to guard against awareness in critically ill adults has yet to be demonstrated [96–98]. It is important to note that 89% of the experts voted against the routine reversal of neuromuscular blockade following tracheal intubation in critically ill adults.

Strengths and limitations

Our study has several strengths. First, this study used a robust Delphi process to achieve consensus among an international group of experts and develop clinical practice statements regarding management of the physiologically difficult airway where evidence remains limited. Second, we included experts with clinical, teaching, and research experience in airway management in critically ill adults across various medical specialties (i.e., anesthesiology, emergency medicine, and pulmonology) and from diverse geographical regions, representing both resource-rich and resource-limited settings. Third, to avoid bias from dominance and group pressure, the anonymity of the experts and their individual responses was preserved until the completion of the Delphi rounds. Fourth, we were able to complete the seven Delphi rounds within 3 months, maintaining a tight timeline, with an attrition rate of only 6%. Finally, we were able to reach consensus in 87% of our clinical statements. We believe that this review provides important guidance for the management of patients who present with a physiologically difficult airway, including viewpoints from global experts who are also frontline clinicians dealing with this entity on a regular basis.

The study has some limitations. Although the intention was to recruit a diverse panel with representation from experts of different sex and from different income group countries, we were able to include only 17% female and 11% of participating experts from low- to middle-income countries, meeting the desired criteria. We elected to focus on recruiting only physician experts and acknowledge this as a limitation considering the irreplaceable role that nurses, respiratory therapists, and other professionals (e.g., advanced practice providers, pharmacists, and physiotherapists) play in intensive care. In addition, we did not solicit specific representatives from professional societies other than SOCCA. Some statements included multiple components, and it cannot be determined whether consensus or disagreement was driven by the full statement or specific components. However, feedback from the experts (allowed in all rounds) and the stability of the responses should have ensured fidelity

Table 1 Future research priorities for physiologically difficult airway (PDA) management

Evaluating the reciprocal relationship between elevated intracranial pressure and airway management, including the impact of respiratory derangements and relevant pharmacologic agents

Defining what constitutes an "experienced airway operator", in the context of PDA management while assessing the relationship between training background, practical experience, and/or competencies and relevant clinical outcomes

Further comparing non-invasive ventilation paired with nasal oxygenation versus other approaches to pre-oxygenation

Critically appraising interventions to prevent cardiovascular collapse in patients with a PDA, for example the role of co-administration of opioids with anesthetic induction drugs and awake tracheal intubation

Understanding the value, if any, of cricoid pressure application in patients with a PDA

Identifying barriers to the universal availability and application of video laryngoscopy to support safe airway management

Evaluating the impact video laryngoscope profile (i.e., hyperangulated, conventional, channeled, etc.) on first-pass intubation success

Developing and evaluating optimal approaches to the use of point-of-care ultrasound in the evaluation and management of patients with a PDA

Developing and evaluating approaches to the reduce the risk of accidental awareness with recall in patients that receive neuromuscular blocking drugs during PDA management

Identifying means by which to optimize PDA management in resource-limited settings, including understanding and overcoming barriers to best practice adoption and implementation

Delineating thresholds for risk factors, such as pre-intubation hypoxemia and cardiovascular instability, at which critically ill adults are at heightened risk for adverse outcomes during and after tracheal intubation

of the responses and minimized individual bias. Factors such as non-availability of certain modalities and variation in local or national practices might have affected experts' opinions. Although acceptable methodologically, we believe that a higher (>70%) threshold for agreement would have been better considering the high risks associated with performing tracheal intubation in critically ill patients. Lastly, evidence is still emerging in this area, and best practices may change as evidence evolves. Based on the feedback received from the experts, statements that failed to reach consensus, and from peer review, further areas of research in the field have been outlined (Table 1).

Conclusion

Using a Delphi method, consensus among experts was reached for 53 statements from which 38 expert clinical practice statements were derived for the management of a physiologically difficult airway, addressing important decisions for patient management in areas where evidence is lacking. These clinical practice statements provide guidance to clinicians worldwide for safe tracheal intubation practice in patients with physiologically difficult airway to improve patient outcomes. Well-designed studies are needed to assess the effects of these practice statements and to address the remaining uncertainties.

Supplementary Information

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Declarations

Conflicts of interest

ADJ: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events: Medtronic, Sanofi, Viatris; Section chair APM ESICM, Section editor ICM. JL: Consulting fees: Cellenkos. LB: Royalties: UpToDate: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events: Teleflex Medical; Member, Teleflex Medical Advisory Board, and Masimo Scientific Advisory Board; Past President Society For Airway Management. AT: Receives salary support for editor duties with Anesthesia & Analgesia. JM: Partner, Course director for The Difficult Airway Course: Critical Care; Patent holder for US Patent #: 11727828 (Virtual reality environment adapted to model the mammalian airway for intubation and airway management training). JAL: Royalties from Wolters-Kluwer for UpToDaite chapter on Video laryngoscopy; honoraria for teaching The Difficult Airway Course (USA) and the AIME airway course (Canada). MS: Consulting fees: MSD Italia, Medtronic USA, DEAS Italia, Verathon Medical; Patent co-owner DEAS Italia, no royalties. NDA Flexicare, Al Endoscopic. SJ: Consulting fees: Fisher-Paykel, Mindray, Medtronic, Baxter. AH: Executive of Project for the Universal Management of the Airway. RG: European Resuscitation Council Board Director of Guidelines and ILCOR, ILCOR Task Force Chair Education, Implementation, Team; Editor in Chief Trends in Anaesthesia and Critical Care. OR: Grants from Hamilton Medical AG, Fisher & Paykel Ltd; Honoraria from Hamilton Medical AG. Fisher & Paykel Ltd. and Aerogen Ltd: Stock options, Tesai Care SL; Non-funded research support from Timpel. DP: Honoraria from Fisher & Paykel. GK: Honoraria for teaching Airway Interventions and Management in Emergencies (AIME) Program. JD: Lecture fees from Edwards India paid to my institution. AK: Grants from the Wellcome Trust; NIHR; Fisher & Paykel Ltd; Gradian Health Systems; Vygon Ltd; Speaker support from the ESICM; Makerere university Research and Innovation Fund. CAB III: Partner, Airway Management Education Center. Royalties—UpToDate and Wolters Kluwer. Honoraria for teaching at The Difficult Airway Course: Emergency. BE: Advisory Board for Breas, Consultant for Fisher & Paykel.

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