REVIEW

The physiologically difficult airway: an emerging concept

Sheila Nainan Myatra[a], *Jigeeshu Vasishtha Divatia*[a], *and David J. Brewster*[b]

Purpose of review
The physiologically difficult airway is one in which physiologic alterations in the patient increase the risk for cardiorespiratory and other complications during tracheal intubation and transition to positive pressure ventilation. This review will summarize the recent literature around the emerging concept of the physiologically difficult airway, describe its relevance and various patient types in which this entity is observed, and suggest strategies to mitigate the risks of airway management in patients with a physiologically difficult airway.

Recent findings
Physiologic derangements during airway management occur due acute illness, pre-existing disease, effects of anesthetic agents, and positive pressure ventilation. These derangements are especially recognized in critically ill patients, but can also occur in otherwise healthy patients including obese, pregnant and pediatric patients who have certain physiological alterations. Critically ill patients may have a physiologically difficult airway due to the presence of acute respiratory failure, hypoxemia, hypotension, severe metabolic acidosis, right ventricular failure, intracranial hypertension, and risk of aspiration of gastric contents during tracheal intubation.

Summary
Understanding the physiological alterations and the risks involved in patients with a physiologically difficult airway is necessary to optimize the physiology and adopt strategies to avoid complications during tracheal intubation. Further research will help us better understand the optimal strategies to improve outcomes in these patients.

Keywords
airway in the obese, airway management in ICU, airway management in the critically ill, difficult airway, obstetric airway, pediatric airway

INTRODUCTION

The 'difficult airway' has been defined by the 2022 American Society of Anesthesiologists (ASA) guidelines on management of the difficult airway as the clinical situation in which anticipated or unanticipated difficulty or failure is experienced by a physician trained in anesthesia care, including but not limited to one or more of the following: facemask ventilation, laryngoscopy, ventilation using a supraglottic airway, tracheal intubation, extubation, or invasive airway [1▪]. The focus of airway evaluation and management has traditionally been on anatomical factors that may make mask ventilation, laryngoscopy, or tracheal intubation difficult [2]. Modern strategies, including devices, such as videolaryngoscopes and flexible bronchoscopes, improved peri-intubation oxygenation techniques, and availability of guidelines [1▪,3,4], have overcome several of the challenges posed by the anatomically difficult airway.

Even in patients whose airways are not 'anatomically difficult', physiologic derangements due to acute illness, pre-existing disease, the effects of anesthetic agents and positive pressure ventilation can result in severe cardiopulmonary complications during tracheal intubation. This risk is especially recognized in critically ill patients but can also occur in otherwise healthy patients with physiological

[a]Department of Anesthesiology, Critical Care and Pain, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India and [b]Intensive Care Unit, Cabrini Hospital, Malvern, Victoria, Australia. Central Clinical School, Faculty of Medicine, Monash University, Melbourne, Victoria, Australia

Correspondence to Sheila Nainan Myatra, Department of Anesthesiology, Critical Care and Pain, Tata Memorial Hospital, Dr Ernest Borges Road, Parel, Mumbai, Maharashtra, India. Tel: +91 9820156070; e-mail: sheila150@hotmail.com

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KEY POINTS

- The physiologically difficult airway is characterized by physiologic alterations that place the patient at an increased risk for cardiovascular collapse and other complications during tracheal intubation and transition to positive pressure ventilation.
- Physiologic derangements occur due to acute illness, pre-existing disease, effects of anesthetic agents, and positive pressure ventilation.
- These derangements are especially recognized in critically ill patients but can also occur in otherwise healthy patients with physiological alterations, including obese, pregnant, and pediatric patients.
- It is important to understand the physiological alterations and the risks involved to optimize the physiology and adopt strategies to avoid complications during tracheal intubation in patients with a physiologically difficult airway.

alterations that may increase the risk of complications during tracheal intubation. These include obese, pregnant, and pediatric patients. It is therefore important to understand the concept of the physiologically difficult airway as one in which physiologic alterations place the patient at an increased risk for cardiovascular collapse and death during tracheal intubation and transition to positive pressure ventilation [5]. Figure 1 depicts differences in the time to desaturation in different types of patients, after the administration of a neuromuscular blocking agent.

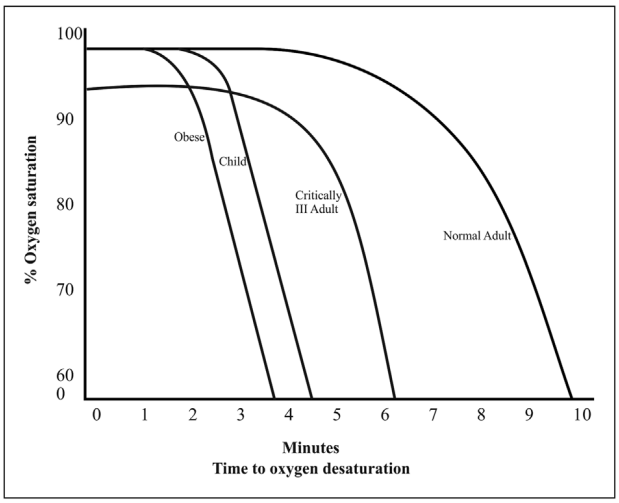

FIGURE 1. Graph showing differences in the time to critical oxygen desaturation in a normal healthy adult, a critically ill adult, a child, and an obese patient after administration of neuromuscular blockade.

In the National Audit Project Four (NAP4) report, complications that resulted in death or brain injury occurred in 61% of airway management episodes in the intensive care unit (ICU) compared to 14% of airway management episodes during anesthetic care [6]. The International Observational Study to Understand the Impact and Best Practices of Airway Management in Critically Ill Patients (INTUBE) involving 2964 critically ill patients undergoing tracheal intubation from 29 countries, found at least one major adverse peri-intubation event in 45.2% of patients. The predominant complication was cardiovascular instability, (42.6% of patients), followed by severe hypoxemia (9.3%) and cardiac arrest (3.1%). Risk factors for major adverse events included lower systolic arterial pressure, administration of a fluid bolus before intubation, higher heart rate and cardiovascular instability as a reason for tracheal intubation. First-pass intubation success was associated with a reduced likelihood of peri-intubation complications [7▪▪]. A multicenter study in which the incidence of cardiac arrest during intubation in the ICU was 2.7%, identified preintubation hypotension, preintubation hypoxemia, obesity, nonperformance of preoxygenation, and age more than 75 years as predictors for cardiac arrest [8▪▪]. During failed tracheal intubation, significantly more obstetric patients had SpO2 < 90% compared to nonobstetric patients (70 vs. 2%), and the lowest SpO2 observed was 40% and 84% in obstetric and nonobstetric patient, respectively [9]. Kinsella *et al.* reviewed the literature on obstetric failed tracheal intubation and found 1 death per 90 failed intubations for cesarean section. Maternal deaths occurred due to aspiration or hypoxemia after airway obstruction or esophageal intubation [10,11].

These studies suggest that physiological derangements are associated with increased post-intubation complications. It is therefore essential to evaluate patients for a physiologically difficult airway and to have strategies to prevent cardiovascular decompensation and other complications arising from a physiologically difficult airway. These strategies include improving preoxygenation and peri-intubation oxygenation, improving first-attempt intubation success rate, and preventing hemodynamic decompensation during and after intubation [3,12,13▪,14▪,15▪▪,16]. Further, patients with both an anatomically and physiologically difficult airway are at grave risk and alternative strategies including awake intubation may be required [17]. This review will focus on the recent literature regarding the emerging concept of physiologically difficult airway, its relevance and various patient types in which this entity is observed.

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TYPES OF PHYSIOLOGICALLY DIFFCULT AIRWAY

The presence of a physiologically difficult airway increases the risk of complications during tracheal intubation [18]. This risk is especially recognized in critically ill patients but can also occur in otherwise healthy patients with physiological alterations, including obese, pregnant, and pediatric patients [19▪].

Critically ill patients

Critically ill patients may have a physiologically difficult airway due to the presence of acute respiratory failure, hypoxemia, hypotension, severe metabolic acidosis, right ventricular failure, intracranial hypertension, and risk of aspiration of gastric contents during tracheal intubation.

Hypoxemia

Patients with pre-existing hypoxemia are at increased risk of complications, such as desaturation, hypoxic brain injury, cardiac dysrhythmias, and cardiac arrest during tracheal intubation [18]. The common causes of acute hypoxemic respiratory failure include pneumonia, acute respiratory distress syndrome, pulmonary edema, and asthma. The mechanism of hypoxia is due to a shunt and ventilation-perfusion (V/Q) mismatch. In normal healthy mechanically ventilated patients under anesthesia, there may be a V/Q mismatch; however, this mismatch can be easily overcome by recruiting the lungs and increasing the fraction of inspired oxygen (FIO_2). In critically ill patients, there is a significant shunt where alveoli in the affected area are unable to participate in gas exchange. In these cases, increasing the FIO_2 alone would not help, as the oxygen delivered is not able to reach the capillaries. Hence, these patients are at an increased risk of rapid desaturation during tracheal intubation. In such patients, the use of measures to prolong the safe apnea time (time until significant desaturation after inducing apnea) and optimize peri-intubation oxygenation using various strategies is paramount [20▪▪].

Hypotension

The most predominant complication in critically ill patients during tracheal intubation is cardiovascular instability [7▪▪]. Peri-intubation hypotension is associated with adverse events, such as bradycardia, cardiovascular collapse, and death. Common causes of hypotension among critically ill patients are hypovolemia, capillary leak, decreased peripheral vascular resistance, and positive pressure ventilation following tracheal intubation. Pre-existing hypotension and shock index, *i.e.,* heart rate/systolic blood pressure more than 0.8 both increase the risk of postintubation hypotension and cardiac arrest [21]. Not all patients will be in shock due to reflex compensatory mechanisms. Therefore, an elevated shock index represents an early sign of shock despite otherwise normal vitals.

In a spontaneously breathing person, negative intra-thoracic pressure helps improve the venous return. When the pressure in the right atrium increases due to positive pressure ventilation, this increase in pressure decreases the venous return thereby decreases the cardiac output. While normal healthy patients can easily compensate for this reduction in cardiac output, critically ill patients, who may already be hypotensive and have exhausted their compensatory mechanisms, may worsen. The high incidence of cardiovascular instability following tracheal intubation in the critically ill makes it imperative to prevent hypotension with the early use of fluids or vasopressors, and identify and treat the hypotension early, if it occurs.

Right ventricular failure

The right ventricle, a highly compliant, low-pressure chamber is often a neglected entity. Its unique structure allows it to accommodate greater volume, *i.e.,* preload. However, it does not tolerate increases in afterload as readily as the left ventricle. Conditions that increase right ventricle afterload are chronic pulmonary hypertension secondary to lung or left heart disease, pulmonary embolism, and left ventricular failure. The right ventricle responds to this increase in afterload by increasing its contractility, preload, and eventually undergoing hypertrophy. Patients with pulmonary hypertension thus need evaluation of right ventricular dysfunction and right ventricle failure (RVF). Consequences of RVF include right ventricular dilatation, tricuspid insufficiency, decreased right coronary artery perfusion, hypotension, and cardiovascular collapse. In patients with RVF, mechanical ventilation has deleterious effects. Positive pressure ventilation can lead to an increase in airway pressure which in turn gets transmitted to pulmonary vasculature, resulting in increase in afterload in addition to reduction in preload. This results in a high risk of cardiovascular collapse in patients with RVF who transition to positive pressure ventilation. Other conditions that increase the pulmonary pressures and subsequently worsen RVF are hypoxia and hypercarbia, which can occur during a brief duration of apnea during airway management [22].

Echocardiography can be used to evaluate the right ventricular function. In patients with right ventricle dysfunction, judicious fluid loading may

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be beneficial. However in patients with RVF, this may be deleterious as it may worsen left ventricular filling and stroke volume. Vasopressors can be used prior to intubation with the goal of increasing the mean arterial pressure without increasing pulmonary artery pressures. Hypoxia and hypercarbia should be avoided during the peri-intubation period along with maintenance of a low mean airway pressure.

Metabolic acidosis

Critically ill patients may have associated metabolic acidosis. Common causes are diabetic ketoacidosis, lactic acidosis, and salicylate poisoning. The presence of organic acids increases in proportion to the nonorganic ions when there is metabolic acidosis. This acidosis leads to a compensatory increase in alveolar ventilation to maintain acid base balance. Patients with severe metabolic acidosis are at increased risk of complications during intubation as brief periods of apnea can cause a sharp rise in CO_2 that can derange acid-base balance. Following tracheal intubation, the increased ventilation requirements may not be met with the limitations due to lung protective strategies used which can lead to a drop in arterial pH and precipitate cardiac arrest. A trial of noninvasive ventilation may be given to reduce work of breathing during which correction of the underlying acidosis may be undertaken. Ventilator modes should be chosen that allow the patient to maintain their respiratory compensation. However, these patients with high minute ventilation are at risk of developing relative hypoventilation, flow starvation, patient-ventilator asynchrony, and worsened acidosis [5].

Neurological injury

In brain injured patients such as those with traumatic brain injury, it is important to maintain cerebral perfusion pressure and avoid secondary injuries due to hypoxia and hypercapnia. These patients often need tracheal intubation due to an altered sensorium or to facilitate surgery. Induction of anesthesia can lead to hypotension which may compromise cerebral perfusion pressure. Laryngoscopy can lead to sympathetic stimulation which may increase the intracranial pressure. Hypoxia or hypercarbia during tracheal intubation can further worsen neurological injury [23].

During tracheal intubation in these patients, induction agents with the least hemodynamic effects, such as etomidate and ketamine, should be used. Ketamine may be safely used as it does not increase the intracranial pressure, as was previously believed. Pharmacological agents to reduce the sympathetic surge due to tracheal intubation may be used. The duration from laryngoscopy should be as minimized and hypoxia and hypercarbia should be avoided [24].

Obese patients

Difficult intubation and related complications are twice as common in obese patients in the ICU as the odds ratio of severe complications related to intubation occurred 20 times more often in the ICU [25]. Obese patients are at higher risk for anatomical factors associated with increased difficulty in tracheal intubation [25,26]. In addition, these patients have a physiologically difficult airway due to the higher resting metabolic demand, higher oxygen consumption, and a higher cardiac output. This hypermetabolic state is also an independent risk factor for heart failure due to changes in the heart resulting from volume and pressure overload and the vascular stiffness. The resulting left ventricular hypertrophy and decrease in left ventricular compliance may cause left ventricular failure. Delayed gastric emptying in obese patients also increases the risk of aspiration [27].

Obese patients have a diminished total lung capacity and vital capacity. This, along with the decreased chest wall compliance and increased intra-abdominal pressure, significantly reduces the functional residual capacity (FRC) and the closing capacity to the extent that many a times the closing capacity is higher than the FRC thereby closing the smaller airways even during normal tidal volume breathing. Oxygen desaturation often occurs early after induction, secondary to the FRC and atelectasis worsened by the supine position [26]. Obese patients may have obstructive sleep apnea causing intermittent and repeated upper airway collapse, leading to partial or total airway occlusion for short periods during sleep. This condition results in an irregular breathing pattern, episodic sleep-associated oxygen desaturation, and hypercarbia, along with cardiovascular dysfunction and excessive daytime sleepiness. Frequent episodes of hypoxia and hypercarbia may also lead to an increase in pulmonary arterial pressures with subsequent right ventricular dysfunction.

These factors result in an increased risk of hypoxemia in obese patients due to the short safe apnea time, making tracheal intubation challenging and increasing the risk of complication compared to other patients [27]. During tracheal intubation, preoxygenation with ramped position is widely recommended. The use of videolaryngoscopy and apneic oxygenation has been recommended during tracheal intubation in this high-risk group. After tracheal intubation, application of positive end expiratory pressure is recommended [26].

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Pediatric patients

The pediatric airway differs from the adult both anatomically (larger occiput, larger, or more pronounced epiglottis and/or tongue, anterior larynx, and a tendency for airway obstruction from flexion of the cervical spine) and physiologically. The most dreaded complication during tracheal intubation in a child is hypoxemia. The average oxygen consumption is double that in the adult. When combined with a lower FRC and a higher closing capacity, this elevated oxygen consumption makes children vulnerable to rapid desaturation and hypoxia during tracheal intubation [28]. The muscle tone is further reduced following anesthesia and sedation and can lead to collapse of the small airways [29,30]. A higher carbon dioxide (CO_2) production also results in a need for greater respiratory rate to achieve adequate CO_2 clearance [31]. Furthermore, gastric distension may occur because of prolonged bag-mask ventilation. The major physiological differences in children are most pronounced before the age of two years. These factors make children vulnerable to rapid desaturation during tracheal intubation. Peri-intubation oxygenation and other strategies to avoid complications are vital in this vulnerable group [32].

Pregnant patients

Pregnancy increases the risk of hypoxemia, aspiration, cardiopulmonary arrest, and mortality following attempted intubation. The obstetric airway is usually handled only when a need arises to give general anesthesia during an obstetric emergency related to the fetus or mother, such as an emergency cesarean delivery or critical illness of the mother. The incidence of failed intubation in obstetrics was 1 in 224 patients as per a 2013 UK study [9]. The reason is due to both anatomical changes and physiological alterations in the parturient.

Hormonal changes and fluid retention in late pregnancy led to a variety of physiological changes that include an increase in oxygen consumption, upward displacement of the diaphragm, reduced FRC, and increased minute ventilation which further increases during active labour. Anemia related to pregnancy may contribute to decreased oxygen reserves. These factors reduce the safe apnea time while securing the airway and increase the risk of hypoxemia. In addition, the decrease in the tone of the lower esophageal sphincter due to delayed gastric emptying and the action of progesterone makes them vulnerable for gastric reflux and pulmonary aspiration [33].

A potential for cardiovascular instability also arises in pregnant patients due to the occurrence of massive bleeding from ante-partum or postpartum hemorrhage. Pre-eclampsia is a specific complication of pregnancy that further increases the physiological difficulty of airway management. Pre-eclampsia may cause narrowing of the upper airway or enlargement of the tongue, and/or increase the risk of airway bleeding following multiple attempts at laryngoscopy, secondary to coagulopathy of thrombocytopenia [33,34].

Intubation in the pregnant patient is more often performed out of hours or in an emergent situation. As a result, human factors play a significant role in the potential for error and a failed intubation [35]. Recent guidelines have been proposed for airway management of the pregnant patient. They include a need for a thorough airway assessment, limiting intubation attempts, early insertion of a supraglottic airway after failed intubation, and regular discussion and teaching of airway management of this patient group [36,37].

At risk for aspiration

The NAP4 study estimated fatal aspiration to occur in 1 in 350,000 episodes of anesthesia, making it the most significant cause of airway-related mortality and responsible for 50% of anesthetic deaths [6]. Patient factors increasing the risk of peri-intubation aspiration include a full stomach, delayed gastric emptying (pregnant patients, trauma patients and gastroparesis of critical illness, diabetes), incompetent lower esophageal sphincter, esophageal diseases, and intestinal obstruction. Surgical factors include gastrointestinal surgery, lithotomy, or head down position and laparoscopy [38]. These patients are at an increased risk for regurgitation and pulmonary aspiration during induction and tracheal intubation. Pulmonary aspiration can lead to hypoxia, pneumonitis, pneumonia, acute respiratory distress syndrome, and even cardiovascular collapse and death. Recommendations to reduce aspiration have included reducing gastric pressure and pH, having an experienced airway operator for all cases, rapid sequence intubation, and extubation awake and/or in the lateral position [3,4].

CONCLUSION

Patients with physiologic derangements due to acute illness, pre-existing disease, and the effects of anesthetic agents and positive pressure ventilation can have severe complications during tracheal intubation, even without an having anatomically difficult airway. This risk is especially recognized in critically ill patients but can also occur in otherwise healthy patients with physiological alterations

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which include obese, pregnant, and pediatric patients. The physiologic alterations in these patients put them at an increased risk for hypoxemia or cardiovascular collapse during tracheal intubation. A thorough understanding of the physiological alterations and the risks involved is essential to adopt strategies to avoid complications during tracheal intubation in patients with a physiologically difficult airway.

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Conflicts of interest

None.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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This prospective observational study that included 2964 patients from 197 sites across 29 countries showed that among an international sample of critically ill patients undergoing tracheal intubation, major cardiopulmonary events occurred frequently. At least one major clinical event occurred after intubation in 45.2% of patients, including cardiovascular instability in 42.6%, severe hypoxemia in 9.3%, and cardiac arrest in 3.1%.

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This review highlights the high risk of complications associated with tracheal intubation in patients with a physiologically difficult airway. This includes those who are critically ill and those who are not. Strategies to prevent complications associated with a physiologically difficult airway including measures to improve the chance of first-pass intubation success are included in this review.

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