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# Emergency medicine updates: The physiologically difficult airway

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ABSTRACT

*Introduction:* Airway management is an integral skill for emergency clinicians. While most of the focus is often on anatomic challenges, clinicians must also consider the unique physiologic challenges that risk decompensation during airway management, often termed the physiologically difficult airway.
*Objective:* This paper evaluates key evidence-based updates concerning management of the physiologically difficult airway for the emergency clinician.
*Discussion:* Peri-intubation complications in the emergency department are often driven by physiologic instability rather than anatomic difficulty. Key phenotypes of the physiologically difficult airway include hypotension, hypoxemia, metabolic acidemia, and right ventricular dysfunction, and are associated with high rates of physiologic collapse with otherwise appropriate airway technique. Each phenotype requires targeted, physiology-driven strategies for risk mitigation. Hypotension is a strong predictor of peri-intubation cardiac arrest, with recent data emphasizing the role of pre-intubation risk stratification and targeted resuscitation with fluids, blood products, or vasopressors based on clinical scenario. For hypoxemic patients, noninvasive ventilation and high-flow nasal oxygen have demonstrated benefit in reducing peri-intubation desaturation. In metabolic acidemia, maintaining minute ventilation and minimizing apnea time are critical. Patients with right ventricular dysfunction require optimization of preload, afterload, and ventilatory strategy. Intracranial hypertension has recently received focus as a physiologically difficult phenotype, with avoidance of hypoxia, hypotension, and minimizing sympathetic surges key priorities to limit secondary brain injury. Across all phenotypes maximizing first-attempt success, preparing for rapid deterioration, and individualizing management are crucial.
*Conclusions:* Recent evidence has advanced the understanding of how to improve care of patients with a physiologically difficult airway.
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## 1. Introduction

Airway management, including tracheal intubation, is a complex but core skill for emergency clinicians [1]. There are over 13 million emergent intubations performed in critically ill adult patients annually worldwide [2,3]. In emergency departments (ED) across the United States, there are over 410,000 TIs performed annually [4-6]. However, intubation is associated with significant risk, with one study finding 32.3% of patients experienced a major adverse event, and the overall 28-day mortality was 45.1% [7].

Patients requiring intubation in the ED often present with one or more significant issues that increase the difficulty faced with airway management, including limited respiratory reserve, multiple comorbidities, and anatomical challenges (e.g., limited mouth opening or neck range of motion, large tongue excessive secretions) [8-16]. In 2015, the concept of the physiologically difficult airway was introduced to highlight specific physiologic derangements that create significant risk in airway management [17]. In the subsequent decade since this seminal publication, there have been significant advances in understanding the epidemiology, risks, and management of the physiologically difficult airway [18]. A prior article in this series evaluated evidence-based updates for ED patients undergoing intubation but did not specifically focus on the unique nuances of the physiologically difficult airway [19]. This paper will highlight key updates concerning the physiologically difficult airway from the last five years.

## 2. Discussion

### 2.1. What defines a physiologically difficult airway?

Historically, the term "difficult airway" has been used to describe anatomic challenges present in the patient (e.g., head and neck cancer,

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angioedema, airway trauma, cervical immobility, micrognathia, obesity) that decrease the chances of success viewing the vocal cords with a laryngoscope or passing an endotracheal tube (ETT). Much literature has focused on the anatomically difficult airway [20-25]. Given increased adoption of devices to overcome anatomical airway difficulties (e.g., video laryngoscope, flexible endoscopes, supraglottic airways), there has been a shift towards focus on the physiological difficulties present in certain patient populations undergoing tracheal intubation [18].

The "physiologically difficult airway" is an umbrella term to describe the patient with pathophysiologic alterations that increase their risk of an adverse event during intubation [26]. These risks include cardiovascular collapse or critical desaturation, which risks cardiac arrest. Pathophysiologic derangements that fall into the category of the physiologically difficult airway involve those where the patient is at higher risk of adverse events from the routine components of intubation including induction and the abrupt transition to positive pressure ventilation. These pathophysiologic derangements may also limit the effectiveness of mitigating strategies by the procedural team such as preoxygenation [17,18,27-29].

The major phenotypes initially described included hypotension, hypoxemia, metabolic acidemia, and right heart strain [17]. The literature since then has expanded to focus on these specific phenotypes, including several pathophysiologic alterations that could fall into these larger phenotypes but have received less attention, most notably critical valvular abnormalities, pericardial tamponade, and decreased functional residual capacity. Other proposed additions to the major phenotypes are increased intracranial pressure (ICP) and increased aspiration risk [27,29]. While the physiologically difficult airway is encountered anywhere that patients are intubated, patients intubated in the ED are more likely to represent a physiologically difficult airway than those undergoing airway management for elective surgical procedures [7,13,29].

### *2.2. What is the importance of first attempt success in patients with a physiologically difficult airway?*

Given the association between increased number of intubation attempts and adverse events, optimizing for first attempt success is critically important for all patients undergoing intubation [30-32]. In contrast to fully preoxygenated patients with normal physiology [33, 34], patients with a physiologically difficult airway are at higher risk of rapid decompensation such that first attempt success is not as protective against complications. Aggressive preoxygenation, discussed later, is critical in these patients to prolong the baseline minimal safe apnea time.

Strategies to maximize first attempt success include deliberate preparation and technique, using the most proficient operator, use of video laryngoscopy, appropriate use of adjuncts (e.g., endotracheal tube introducer), neuromuscular blockade co-administration with induction agents, optimized positioning, and team communication [9,35-40]. When success with oral tracheal intubation appears unlikely, clinicians should be prepared to promptly transition to a surgical airway [41,42].

Despite optimizing for first attempt success, cardiovascular collapse can occur in up to 20% of patients with physiologically difficult airways undergoing intubation [17,18]. To help mitigate this, beyond achieving first attempt success of the airway in a timely fashion, there are considerations based on the specific phenotypes of physiologic alterations the emergency clinician must be aware of, which are discussed in the following sections.

### *2.3. What should the emergency clinician consider when intubating a patient with hypotension?*

Hypotension among critically ill patients in the peri-intubation setting is common, occurring in 18-43% of patients [13,43,44]. Intubation-related factors that contribute to this include pharmacologic effects of induction agents on vascular tone and cardiac function, decreased venous return from positive pressure ventilation, and reduction in sympathetic drive from sedative hypnotic agents [45,46]. The presence of hypotension in the period prior to initiation of rapid sequence induction (RSI) is a strong predictor for hypotension in the post-intubation period [13], with one study showing an odds ratio (OR) of 32.43 [47]. Pre-intubation hypotension is also associated with a 3- to 6- fold increased risk of peri-intubation cardiac arrest [48-50]. The incidence of patients who are hypotensive prior to RSI is not well elucidated but estimated to be between 10-20% [47,51].

While the risk of cardiovascular collapse may be readily apparent in patients with hypotension, this is not always the case, and there are several means of assessing the degree of shock. One such tool is the shock index (SI), which can be used at bedside. It is calculated as heart rate (HR) divided by systolic blood pressure (SBP; SI = HR/SBP). A normal range of the SI is 0.5-0.7. The SI has been validated as a predictor of peri-intubation cardiovascular collapse, with an SI ≥ 0.8 - 1.0 a strong predictor of impending cardiovascular compromise (OR 3.2-55) [52-54]. In a sub-study of the KEEP PACE trial, authors found that with each 0.1 increase in SI, there was an OR of 1.16 (95% confidence interval [CI] 1.04-1.30) for hypotension [55]. The SI is also useful to identify patients who have either occult or compensated shock. The National Field Triage Guidelines recommend using HR > SBP (equivalent to a SI >1) as "Red Criteria" for high-risk patients, as this captures normotensive patients with an elevated SI that likely indicates compensated shock and subsequent significantly increased odds of requiring transfusion and hemodynamic support [56]. Taken as a whole, the SI can be useful into stratifying patients into low risk (normal SBP, normal SI), moderate risk (normal SBP, elevated SI), or high risk (low SBP, elevated SI) for development of peri-intubation hypotension or cardiac arrest [18].

Literature has evaluated the initiation of peri-intubation fluid administration and its impact on cardiovascular collapse. The PREPARE randomized control trial (RCT) evaluated 337 critically ill adults undergoing intubation across 9 intensive care units (ICUs) in the United States (US). Patients were randomized to initiate a 500 mL isotonic crystalloid bolus before induction versus no bolus. The primary outcome, a composite of cardiovascular collapse (SBP <65 mmHg, new or increased vasopressor support, cardiac arrest, or death <1 hour after intubation), was not different between the fluid bolus group versus no fluid bolus group (20% versus 18%, absolute difference 1.3%, 95% CI -7.1% to 9.7%). In-hospital mortality also was not different (29% versus 35%) [57]. However, there was a signal that a subgroup of patients who were undergoing positive pressure ventilation (PPV) did benefit from fluid bolus administration. To further investigate the potential subset of patients who did benefit from fluid bolus administration in PREPARE, a follow up study was undertaken. PREPARE II specifically looked at patients randomized to initiate a fluid bolus (500 mL) or not undergoing intubation who received PPV via bag-valve-mask (BVM) between induction and laryngoscopy. Using the same composite cardiovascular collapse definition, the authors enrolled 1,067 patients across 11 US ICUs and found no difference between the groups (21% versus 18%, 95% (CI -2 to 8%). There was no difference in any secondary outcome, including death [46]. Notably, in both trials patients were excluded if the treating clinicians felt a fluid bolus was required or contraindicated. Additionally, not all patients received the full 500 mL of fluids prior to induction or laryngoscopy. These RCTs suggest that for all comers, initiating a preemptive fluid infusion is unlikely to prevent cardiovascular collapse after intubation. Because they excluded patients for whom clinicians felt a fluid bolus was required, these results should not be interpreted to mean that pre-intubation volume resuscitation is not important, and in appropriate settings, volume resuscitation prior to intubation is critical. This includes patients who are hypovolemic with an abnormal SI. Volume resuscitation should be based on the suspected pathology. For example, pre-intubation resuscitation with blood products in hypotensive patients in hemorrhagic shock (i.e., a Circulation - Airway - Breathing

approach), a population minimally represented in PREPARE and PREPARE II, has been demonstrated to be protective against post-intubation cardiovascular collapse and reduce downstream mortality [58-61]. In contrast, crystalloid resuscitation of this same population has demonstrated higher downstream mortality [62].

In patients in whom volume resuscitation would not be tolerated, the emergency clinician should consider the use of vasoactive medications (e.g., norepinephrine). Of note, at this time, the evidence for or against both push dose and continuous vasoactive medication in the peri-intubation period is limited, with current societal guidelines making only conditional or no recommendations for use based on low quality and limited evidence [45,63]. While the administration of push-dose pressors during unexpected periods of hypotension has been found to be safe and effective [64], their protective effect on peri-intubation cardiovascular collapse was not demonstrated in a multicenter retrospective study and a 2025 meta-analysis of 24 RCTs [65,66]. The initiation of continuous vasopressors prior to intubation has also been evaluated without a clear demonstrated benefit. In the EPITUBE RCT, patients undergoing cardiac surgery were randomized to prophylactic norepinephrine versus as needed ephedrine. While the authors found a decrease in moderate hypotension (mean arterial pressure [MAP] < 65 mm Hg, 63.8% versus 78.1%, p = 0.02), there was no difference in rates of severe hypotension (MAP < 55 mm Hg) or intubation-related complications [67]. The INTUBE study, an observational cohort study of critically ill patients undergoing intubation, also found vasopressors initiated prior to induction were not associated with a reduction in risk of cardiovascular collapse (OR 1.33, 95% CI 0.84-2.11) [13]. Notably, the use of propofol in INTUBE cohort is a major confounder which may limit its applicability to EDs which rarely use it as part of RSI. However, vasopressors, notably push-dose vasopressors, are not without risk [63]. These studies highlight clinicians should not blindly initiate vasopressors on all patients undergoing induction, but must be thoughtful and selective of which specific patients may benefit. The role of other vasoactive medications, such as inhaled pulmonary vasodilators, can be considered on a pathology-specific basis and are discussed later.

Left-sided valvular dysfunction (mitral and aortic valves) can also lead to hemodynamic collapse during intubation secondary to the effects of induction agents and the transition to PPV [18,68]. The transition to PPV can lead to rapid pressure gradient changes across valves and subsequent changes in regurgitant flow [69]. Patients with valvular abnormalities require finesse during intubation to minimize abrupt flow changes secondary to sudden shifts in preload, afterload, and sympathetic tone. Invasive arterial monitoring can aid in real-time detection of hemodynamic changes [68,70]. Avoidance of tachy- or bradydysrhythmias is crucial [18,68]. Echocardiography can be used in the acute setting to evaluate for valvular pathology, if not already known [71]. There are specific considerations during intubation depending on the specific valvular abnormality present [68,70]. Patients with severe aortic stenosis are highly dependent on left ventricular preload to maintain cardiac output [68]. Reduction of systemic vascular resistance and preload during intubation can lead to decreased coronary perfusion pressure and subsequent myocardial ischemia with hemodynamic collapse. Phenylephrine and vasopressin can be used to help support systemic vascular resistance, and norepinephrine can be used if there is reduced left ventricular ejection fracture (LVEF). Fluid boluses can be used to address the need for adequate preload. Aortic regurgitation can be supported with a fluid bolus if the patient is hypovolemic, and vasopressors and inotropes can be added to support forward flow. If aortic regurgitation is present in a patient with hypertensive crisis, afterload should be reduced with vasodilators [18]. Mitral stenosis can lead to right ventricular volume overload and failure, and if present diuresis is recommended [18]. In patients with poor ejection fraction, milrinone can be used to decrease pulmonary vascular resistance and improve cardiac output [72]. Mitral regurgitation can be supported with dobutamine or norepinephrine. Noninvasive positive pressure ventilation (NIPPV) should be used for preoxygenation as the subsequent increase in intrathoracic pressure can reduce LV afterload, decreasing the regurgitant volume from the regurgitant mitral valve [18,68,69].

Pericardial tamponade has been suggested as an independent category of the physiologically difficult airway when symptomatic represents a form of obstructive shock leading to hypotension [27]. Tamponade creates a state where compensatory tachycardia and preload dependence make patients vulnerable to hemodynamic collapse during intubation [69]. If possible, intubation should be avoided until pericardial drainage is performed [69,73]. If unable to perform drainage prior to intubation, optimizing preload with fluid boluses and immediate availability of vasopressors are essential. Post-intubation the lowest possible positive end expiratory pressure (PEEP) (0-3 cmH2O) should be used until definitive drainage of tamponade can occur [69].

Lastly, the emergency clinician must consider the hemodynamic impact of induction agent choice for the patient who is hypotensive prior to intubation. The American College of Emergency Physicians (ACEP) recommend against the use of propofol, midazolam, and fentanyl as an induction or coinduction agent in this population given the association with hypotension in the peri-intubation setting [45]. Propofol is a direct myocardial depressant with vasodilatory properties, and its use is associated with cardiovascular collapse [13,63]. Midazolam is also a potent vasodilator when used at RSI doses and should be avoided unless specific clinical circumstances (e.g., status epilepticus) [63]. The co-administration of fentanyl during induction has also been associated with higher risk of post-intubation hypotension, but this association does not have a direct physiologic explanation [74]. However, given this association its use is not recommended at this time by ACEP [45,74].

The two most commonly used induction agents for intubation of the critically ill patient are etomidate and ketamine [75]. Etomidate is a GABA receptor agonist that is commonly used due to its favorable hemodynamic profile in the peri-intubation phase with minimal cardiovascular depression. However, past the peri-intubation stage, etomidate in some observational studies has been associated with worse long-term outcomes given its inhibition of 11β-hydroxylase, leading to a theoretical inhibition of adrenal corticosteroid synthesis [7,63]. In contrast, ketamine, a NMDA receptor agonist [76], has gained popularity as an induction agent choice for its purported indirect sympathomimetic properties. However, ketamine's sympathomimetic properties are dependent on indirect sympathomimetic effects of endogenous catecholamine release, which may be depleted in critically ill patients, leading to paroxysmal hypotension [51,77]. Additionally, ketamine is a direct myocardial depressant and potent sialagogue [78,79].

Evidence for or against each agent in prevention of peri-intubation cardiovascular collapse is mixed. One recent meta-analysis of 2,384 patients from 7 RCTs found ketamine was associated with more peri-intubation cardiovascular instability (as defined by original study authors) with ketamine (relative risk [RR] 1.29, 95% CI 1.07-1.57) [77]. The authors also concluded ketamine probably decreases the need for initiation of continuous infusion of vasopressors (RR 0.75, 95% CI 0.57-1.00, moderate certainty), and results in less adrenal suppression (RR 0.54, 95% CI 0.45-0.66, moderate certainty). Finally, they concluded that ketamine may have no effect on mortality (RR 1.00, 95% CI 0.83-1.21, low certainty) [77]. This is in contrast to another meta-analysis of 2,862 patients from 10 RCTs, which included all 7 RCTs from the above study. The authors concluded that etomidate and ketamine had comparable risk of peri-intubation cardiovascular collapse (OR 1.28, 95% CI 0.96-1.7). However, the authors also concluded that ketamine was associated with less adrenal insufficiency (OR 0.35, 95% CI: 0.15-0.86) and comparable all-cause mortality (OR 0.8, 95% CI 0.65-1.21) [80]. The RSI trial, which was not included in either of these meta-analyses, is the most recent RCT to evaluate ketamine versus etomidate [51]. Authors randomized 2,367 patients from 8 ICUs and 6 EDs in the US in a 1:1 fashion using permuted blocks of variable size stratified according to the trial site. Standardized doing was provided; for ketamine, full dose was 2.0 mg/kg, intermediate dose 1.5 mg/kg, and reduced dose

1.0 mg/kg. For etomidate full dosing was 0.3 mg/kg, intermediate 0.25 mg/kg, and reduced 0.2 mg/kg [81]. Induction agent dosing was based on clinician discretion. The primary outcome, 28-day-in-hospital all-cause mortality, was not different between ketamine and etomidate (28.1% versus 29.1%, risk difference adjusted for trial site -0.8%, 95% CI -4.5 to 2.9%). For secondary outcomes the authors evaluated a composite of cardiovascular collapse during intubation. This was defined by the presence of any of the following between induction and 2 minutes after intubation was confirmed: SBP < 65 mm Hg, new or increased vasopressor requirement, or cardiac arrest. The authors found ketamine was associated with higher risk of peri-intubation cardiovascular collapse compared to etomidate (30.6% versus 20.9%, absolute risk difference 9.7%, 95% CI 4.6 to 14.9%), mostly driven by new or increased vasopressor requirement, as there was no significant difference in instances of SBP <65 mm Hg or cardiac arrest [51]. This difference was more pronounced in patients with an Acute Physiology and Chronic Health Evaluation II (APACHE II) score ≥ 20. At this time, the RSI trial is the largest ever performed intubation related RCT, and the findings in this trial may hold more weight than other older meta-analyses or underpowered studies.

Reducing the dose of either agent does not appear to decrease hypotension risk based on the registry analysis of over 14,000 intubations or in comparison of dose groupings in the RSI trial [51,82]. Peri-intubation hypotension seems to be primarily driven by patient factors (e.g., increased age, SI, underlying diagnosis) rather than dose of the induction agent [83]. These conflicting studies highlight the complexities of evaluating patient centered outcomes undergoing intubation.

In conclusion, for hypotensive patients undergoing intubation it is important for clinicians to consider individual patient factors rather than using blanket strategies for volume resuscitation, vasopressor initiation, or induction agent selection and dosing. The SI can be used to stratify patients into low, moderate, and high risk. Those at moderate or high risk should undergo personalized resuscitation prior to intubation. Those who are volume responsive or tolerant should receive volume resuscitation (e.g., crystalloids or blood depending on clinical scenario), while those intolerant to additional volume should receive vasopressors (e.g., norepinephrine infusion). Scenarios and key clinician considerations for intubation of the hypotensive patient can be found in Table 1.

### *2.4. What should the emergency clinician consider when intubating a patient with hypoxemia?*

Tracheal intubation is most commonly required in acute hypoxemic respiratory failure [84]. Acute hypoxic respiratory failure occurs from any disruption of ventilation and perfusion matching in the lung leading to inadequate alveolar-capillary oxygen transfer (e.g., acute respiratory distress syndrome, pneumonia, pulmonary edema). Failure to correct hypoxemia can lead to hypoxic brain injury, hemodynamic instability, and cardiac arrest [84]. Patients with hypoxemic respiratory failure are at significant risk of rapid desaturation during intubation, which significantly increases the risk of cardiac arrest [85]. Other patients at risk of hypoxemia during intubation include pregnant and obese patients [10]. Both conditions lead to reduced functional residual capacity and in the case of pregnancy increased oxygen consumption, increasing the risk of critical hypoxia during the procedure [25,29].

The physiologic problems leading to hypoxemic respiratory failure (low functional residual capacity from volume loss and intrapulmonary shunting from ventilation:perfusion mismatch) make preoxygenation more difficult. Additionally, disruption of alveolar-capillary gas exchange may make preoxygenation less effective, making hypoxemic patients a physiologically difficult airway [86,87]. Recent studies have shown the utility of more aggressive non-invasive preoxygenation strategies, most notably high-flow nasal oxygen (HFNO) and NIPPV for preoxygenation of the critically ill patient [88].

HFNO systems deliver continuous heated and humidified oxygen at rates of 40-70 L/minute. Notably HFNO is more aggressive and a separate treatment modality than high-flow nasal cannula (HFNC). The terminology of HFNO is often mistakenly interchanged with HFNC, which describes large bore nasal cannula prongs used to oxygenate, often set at a "flush" (> 15 L/minute) rate. In those with mild to moderate hypoxemia prior to intubation, preoxygenation with HFNO has been shown to significantly reduce desaturation during the procedure [89-93]. A 2024 systematic review and meta-analysis of 3,914 patients from 52 studies found that preoxygenation with HFNO in the head-up position significantly prolonged safe apnea time when compared to facemask oxygen [89]. Overall, HFNO is a well-tolerated and effective preoxygenation modality that has the benefit that it can be left on the patient for apneic oxygenation during intubation, discussed later.

A point of vulnerability from an oxygenation standpoint during RSI is during apnea after induction and paralytic medications take effect before laryngoscopy begins. In the PreVent trial investigators studied whether performing NIV via bag-valve-mask ventilation (BVM) in between induction and laryngoscopy resulted in a higher lowest SpO2 compared to no ventilation [94]. Patients in the BVM group received ventilation at >15 L/minute $O_2$ flow with a PEEP valve (5-10 cm $H_2O$), an oropharyngeal airway, two-handed mask seal, and ventilation at 10 breaths/minute. Patients in the control group were allowed, but not mandated, apneic oxygenation. A total of 401 patients in 7 ICUs were randomized in a 1:1 fashion. The median lowest oxygen saturation in the BVM group was higher than the control group (96%; IQR 97-99% versus 93%; IQR 81-99%). Secondary outcomes showed severe hypoxia ($SpO_2$ <80%) was 10.9% in the BVM group versus 22.8% in the control group (RR 0.48; 95% CI 0.30 – 0.77), representing a number needed to treat of 9 to prevent one episode of severe hypoxemia.

Another noninvasive respiratory support modality for preoxygenation that is more aggressive than BVM during apnea only is NIPPV. A 2006 study in two-French ICUs randomized patients with acute hypoxic

**Table 1**
Scenarios and key clinician considerations for intubation of the hypotensive patient.

| Scenario | Key Considerations |
|---|---|
| Pre-intubation hypotension | — Strongly associated with peri-intubation hypotension and cardiac arrest<br>— Can risk stratify with the shock index |
| Hypovolemic shock | — Resuscitate with fluids or blood products based on etiology of hypovolemia |
| Distributive shock | — Consider vasopressors in the peri-intubation phase |
| Obstructive shock from pericardial tamponade | — Avoid intubation if possible<br>— Drain prior to intubation if possible<br>— Optimize preload<br>— Low positive end expiratory pressure after intubation |
| Valvular dysfunction | — Can use echocardiography to evaluate for valvular dysfunction<br>— Management is tailored to specific valve pathology present |
| Induction agent choice | — Most recent evidence supports the use of etomidate over ketamine in patients with shock or catecholamine depletion to prevent peri-intubation cardiovascular collapse<br>— Avoid primary or co-administration of propofol, midazolam, and fentanyl |

respiratory failure requiring intubation to either preoxygenation with BVM (n=26) or NIPPV (n=27) from the ventilator [95]. The authors found that the NIPPV group had higher SpO2 values at the end of preoxygenation (98 ± 2 versus 93 ± 6), during intubation (93 ± 8 versus 81 ± 15), and 5-minutes after intubation (98± 2 versus 94 ± 6) than the control group [95]. A 2018 multicenter follow up RCT by the same authors assessed for other endpoints, with the primary outcome maximum Sequential Organ Failure Assessment (SOFA) score within 7-days [96]. They found when comparing three minutes of preoxygenation with BVM (n= 99) to NIPPV (n=102), there was no difference in maximum SOFA score within 7-days (9 ± 6-12 vs 9 ± 6-12). However, authors found NIPPV resulted in less desaturation events during preoxygenation or intubation compared to BVM (16.6% versus 41.3%). A similar study done at a larger scale, the PREOXI trial, was completed and published in 2024 [97]. This was a RCT comparing NIPPV to non-rebreather (NRB) conducted in 24 EDs and ICUs across the US. This trial demonstrated that NIPPV (n=624) was associated with a 9.4% absolute risk reduction in hypoxemia during intubation compared to oxygen mask therapy (n=637) (9.1% versus 18.5%, 95% CI 5.6-13.2%). A subsequent meta-analysis of 3,420 patients from 15 RCTs comparing efficacy and safety of HFNO, NIPPV, and facemask oxygen during intubation of the critically ill found NIPPV likely reduces hypoxemia compared to HFNO (RR 0.73, 95% CI 0.55-0.98, moderate certainty) and facemask oxygen (RR 0.51, 95% CI 0.39-0.65, high certainty) [12]. In this study HFNO was also noted to reduce the incidence of hypoxia during intubation compared to facemask (RR 0.69, 95% CI 0.54-0.88, high certainty of evidence).

It is important to note that even with appropriate HFNO and NIPPV, patients can still desaturate, highlighting severe hypoxemia as a physiologically difficult airway. In the FLORALI-2 RCT, 313 patients from 28 French ICUs undergoing intubation for acute hypoxemic respiratory failure were randomized to either NIV or HFNO. Severe hypoxemia (defined as <80% SpO2 during intubation) occurred in 23% of patients randomized to NIV and 27% randomized to HFNO (absolute difference -4.2%, 95% CI -13.7 to 5.5) [98]. In FLORALI-2 patients were only enrolled if their indication for intubation was acute hypoxemic respiratory failure. The PREOXI trial enrolled patients with multiple indications for intubation but did perform a prespecified subgroup analysis of those intubated for acute hypoxemic respiratory failure. While they found a significant reduction in hypoxemia in the NIPPV group compared to facemask (9.8% vs 20.9%), nearly 1/10 patients became hypoxic during intubation [97].

An important secondary outcome of the PREOXI and PreVent trials for emergency clinicians was the overall low rate of aspiration. In PREOXI there no difference in the NIPPV and oxygen mask groups (0.9% versus 1.4%, absolute difference -0.4%, 95% CI -1.6% to 0.7%) [97]. In PreVent there was no difference in operator reported aspiration for those undergoing BVM versus not (2.5% versus 4.0%, p=0.41) or opacities on chest x-ray at 48 hours (16.4% versus 14.8% p=0.73) [94]. This adds to the growing body of evidence that, when appropriately monitored, NIPPV can be used in select patient populations with hypopnea without increased risk of aspiration [12,99]. NIPPV can also be employed for hypoxemic patients with a low functional residual capacity (e.g., obesity, late term pregnancy, airspace disease, effusions) [18]. In the absence of exclusion criteria for NIPPV (e.g., facial abnormalities, recurrent emesis, agitation), NIPPV should be used in the hypoxemic patient requiring intubation for preoxygenation. To help streamline the intubation process, patients can undergo NIPPV on the ventilator in a NIPPV mode, as opposed to requiring a separate NIPPV machine for preoxygenation. While not able to directly measure the level of denitrogenating during preoxygenation, the use of waveform end-tidal $CO_2$ can contribute to assessing preoxygenation adequacy by confirming a good mask seal when using NIV, and an end-tidal $CO_2$ measurement > 40 mmHg with a clear plateau can indicated effective ventilation [100,101].

One potential barrier to adequate preoxygenation, including NIPPV, (as well as other resuscitative measures), is the patient with significant agitation. In these cases, clinicians can consider delayed sequence intubation (DSI), also termed medication-assisted preoxygenation. In DSI ketamine is administered in dissociative dosing to facilitate preoxygenation. The prospective study which first described the technique in 2015 followed 62 agitated patients who received ketamine at a dose of 1mg/kg IV, with 0.5 mg/kg redosing as needed until dissociation was achieved, followed by preoxygenation with nonrebreather mask or NIPPV, then subsequently RSI [102]. Mean $SpO_2$ increased from 89.9% to 98.8% (95% confidence interval 6.4 – 10.9%). No complications were noted. This strategy has also been used successfully in the prehospital setting, again with no or minimal complications [103,104]. The 2023 Society of Critical Care Medicine Clinical Practice Guidelines for RSI acknowledge DSI, but note that data are sparse comparing medication-assisted preoxygenation to other methods and do not provide a strong recommendation for or against its use [63].

Given the risk for rapid desaturation, hypoxemic patients may theoretically benefit from apneic oxygenation during intubation but the literature evaluating apneic oxygenation during intubation is mixed. The method of delivering apneic oxygenation is a key factor in outcomes across various settings. A 2023 Cochrane systematic review of 23 RCTs (2 ED, 7 ICU, and 14 operating room-based studies) evaluated apneic oxygenation in 2,264 patients [100]. Delivery methods were divided into low-flow (15 L/minute or less) delivery (8 studies) and high-flow (>15 L/minute) delivery (15 studies). In predominantly critically ill patients, they found little to no difference in the incidence of severe hypoxemia ($SpO_2$ <80%) when using apneic oxygenation at any flow rate (RR 0.86, 95% 0.66-1.11). A prior meta-analysis found similar results, with 1,017 patients across 10 studies with similar rates of severe desaturation ($SpO_2$ <80%) between HFNO and conventional therapy (RR 0.98, 95% CI 0.68-1.42) [105]. However, prior to this a 2017 meta-analysis of emergency intubations found a pooled absolute reduction risk of hypoxia with apneic oxygenation compared to usual care by 30% (19.1% versus 27.6%, 95% CI 0.59-0.82) [106]. Notably, this meta-analysis defined hypoxia as $SpO_2$ <90-93% as this was felt to be clinically significant. A 2025 meta-analysis of 703 patients in six studies undergoing intubation for emergency surgery showed that HFNO significantly increased post-intubation $PaO_2$ (mean difference 62.02 mm Hg, 95% CI 8.99-117.05) and prolonged apnea time (mean difference 19.25 seconds, 95% CI 1.69-36.82) compared to face mask [107]. Another RCT randomized patients to either HFNO at 60 L/min for preoxygenation and apneic oxygenation (n=97) or NRB for preoxygenation with 15 L/min nasal cannula oxygen for apneic oxygenation (n=93) and found no difference in their primary outcome of lowest $SpO_2$ during intubation (15.5% versus 22.6% adjusted RR 0.68, 95% CI 0.37–1.25) [108]. Importantly, current evidence suggests that HFNO as a pre- and apneic oxygenation strategy is not associated with an increased risk of aspiration secondary to gastric insufflation [63,100,107].

Ultimately, there are mixed results in both high- and low-quality studies for apneic oxygenation. NIPPV has been shown to be superior to HFNO and facemask oxygenation for patients with acute hypoxemic respiratory failure, and thus NIPPV should be used in that population instead of relying solely on apneic oxygenation. Given that apneic oxygenation with HFNO is a relatively low risk intervention tolerated well by patients, it should be considered in all other populations undergoing intubation. Notably, it is possible to combine both NIPPV and HFNO for preoxygenation and then leave the HFNO on the patient during laryngoscopy to provide apneic oxygenation. The OPTINIV RCT was a small ICU based study in which patients were randomized to NIPPV preoxygenation with HFNO (n=23) with HFNO subsequently left in for apneic oxygenation versus NIPPV preoxygenation alone (n=24). They found no incidences of $SpO_2$ values < 80% in the intervention group, while 5 (21%) patients in the control group desaturated to <80% (p=0.05) [109].

Another alternative to RSI that preserves respiratory drive in critically hypoxemic patients is an awake intubation [28,110]. One small retrospective study found reduced complication rates in patients intubated

awake with topicalization on HFNC when compared to RSI [111]. Some airway management guidelines now recommend considering an awake intubation approach in patients at risk of rapid desaturation [20,22,70].

In select cases, an invasive procedure such as extracorporeal membrane oxygenation (ECMO) is needed to correct refractory hypoxemia. Several practice guidelines and societies have recently discussed ECMO as a rescue technique for anticipated, unanticipated, and rescue from emergency difficult airway management [20,112]. While unlikely to be feasible as a rescue attempt after initiation of laryngoscopy for the hypoxemic patient, ECMO has been discussed as an emerging preemptive measure for critically hypoxemic patients who would otherwise be intubated for hypoxemic respiratory failure [113,114]. However, unless standby ECMO is part of an experienced workflow and readily available in the ED, time to cannulation must be considered [115,116]. More study is necessary on the ideal candidate and feasibility of the use of ECMO compared to intubation for patients with hypoxemic respiratory failure. Scenarios and key clinician considerations for intubation of the hypoxemic patient can be found in Table 2.

### 2.5. What should the emergency clinician consider when intubating a patient with metabolic acidemia?

Patients with metabolic acidemia (arterial pH < 7.3) are at high risk of complications during intubation. One study found patients with an arterial pH < 7.3 develop post-intubation complications at a significantly higher rate compared to those without it (OR 4.06, 95% CI 2.31-7.11) [117] and are more likely to develop peri-intubation cardiac arrest (OR 2.58, 95% CI 1.04-6.39) [118]. Metabolic acidemia predisposes a patient to cardiovascular collapse through several mechanisms. Decreased intracellular pH inhibits calcium release from the sarcoplasmic reticulum, reduces calcium binding affinity to troponin-C, and directly interferes with contractile machinery, all leading to impaired cardiac contractility [119]. Catecholamines, which could be protective against cardiovascular collapse by stimulating the heart through beta-adrenergic mechanisms, have a blunted effect in an acidotic environment [120,121]. This leads to decreased effects of both endogenously released catecholamines and any exogenously administered vasopressors. Acidemia also causes vasodilation of large arteries through calcium sequestration and nitric oxide-dependent pathways, leading to systemic vasodilation and subsequent reduction in systemic vascular resistance [120,121]. Patients with metabolic acidemia will work to create a compensatory alkalosis through hyperventilation [120]. When a patient is induced for intubation, induction agents in combination with neuromuscular blockade leads to apnea, and respiratory compensation suddenly ceases which can lead to rapidly worsening acidemia. The transition to PPV and subsequent increase in intrathoracic pressure decreases venous return, which is magnified if the patient is acidotic, potentially leading to systematic vasodilation and decreased cardiac contractility [69,122,123].

All these mechanisms work synergistically to create an environment in which the patient with metabolic acidemia is highly susceptible to cardiovascular collapse [117]. The gradient of risk directly correlates with worsening levels of acidemia [124,125], and those with severe acidemia (pH < 7.1-7.2 based on definition) are at particularly high risk [126]. A base excess of > -4.1 mmol/L can be used to predict acidotic patients who are at the highest risk of peri-intubation cardiovascular collapse (sensitivity 71%, specificity 70%, area under the curve [AUC] 0.74) [117]. A lactic level ≥ 2 mmol/L is also an independent risk factor for post-intubation cardiac arrest (OR 4.24, 95% CI 1.46-12.27) [118].

Almost all recommendations surrounding management of metabolic acidosis during intubation are theoretical, with limited studies specific to this patient population. Sodium bicarbonate has long been used in patients with metabolic acidemia. Despite theoretical benefits, its use has not been shown to improve overall outcomes in all-comers with severe metabolic acidemia [127,128]. It may improve renal outcomes in patients with sepsis, as demonstrated in the BICAR-ICU and BICARICU-2 trials [127,128], but sodium bicarbonate has never been studied in the peri-intubation setting. A risk of empiric sodium bicarbonate administration in the peri-intubation period includes paradoxical intracellular acidosis. This occurs due to carbon dioxide ($CO_2$) generation from bicarbonate rapidly crossing the cellular membrane while bicarbonate ions cannot [129]. This effect is most pronounced with rapid bolus administration of sodium bicarbonate, highlighting potential risk of empiric administration in an attempt to correct acidemia in the peri-intubation period [129]. Currently the evidence does not support sodium bicarbonate administration to correct acidemia before intubation.

Induction agent selection for the patient with severe metabolic acidosis includes both ketamine and etomidate as the preferred agents, with avoidance of sole induction or coinduction use of propofol, midazolam, and fentanyl given their association with adverse events during the procedure [45].

While not independently studied in patients with metabolic acidemia, there is theoretical appeal to either preservation of respiratory drive or manually provided respiration between the period of induction and neuromuscular blockade for intubation [130]. This would potentially mitigate the risk of rapid accumulation of $CO_2$ and subsequent worsening acidemia. The bulk of the risk is likely in the few minutes after intubation as acidemia rapidly worsens. Unfortunately, while intuitive, hyperventilation of acidotic patients prior to intubation has not been shown affect post intubation pH levels, despite possible transient improvements in pH [131,132]. The PreVent trial, discussed above, did not perform a subgroup analysis of patients intubated with pre-existing metabolic acidosis and did not track whether ventilation between induction and laryngoscopy maintained $CO_2$ clearance or mitigated acidemia [94]. Thus, the most important component of airway management in these patients, based on available information, is to match post-intubation minute ventilation with pre-intubation minute ventilation where possible and limit apnea to the shortest duration possible. Given the significant risk associated

**Table 2**
Scenarios and key clinician considerations for intubation of the hypoxemic patient.

| Scenario | Key Considerations |
|---|---|
| Pre-intubation hypoxemia | — Strongly associated with peri-intubation hypoxia and cardiopulmonary compromise<br>— Patients with acute hypoxemic respiratory failure, pregnancy, and obesity are at highest risk |
| Preoxygenation with high-flow nasal oxygen | — Generally well tolerated.<br>— Can be used as primary preoxygenation when non-invasive positive pressure ventilation is not feasible or the patient is on high flow nasal oxygen before decision to intubate.<br>— Can be left on for apneic oxygenation during TI attempt |
| Preoxygenation with non-invasive positive pressure ventilation | — Use for hypoxemic patients prior to intubation, considering relative contraindications (e.g., emesis, hypopnea, agitation).<br>— Can use ventilator in non-invasive mode to streamline process |
| Apneic oxygenation | — High quality evidence suggested no benefit, but well tolerated and safe |
| Awake intubation | — Consider in patients at risk for rapid desaturation or need for preservation of respiratory drive |
| Extracorporeal membrane oxygenation | — Can consider pre-intubation cannulation for critically hypoxemic patients if time allows and team workflow for emergency department cannulation is in place |

with intubation in this patient population, avoiding intubation when possible is ideal. This includes optimized noninvasive respiratory support modalities to support work of breathing when mental status is amenable, aggressive resuscitation (for lactic acidosis related to shock), fluid resuscitation and insulin infusion (for diabetic ketoacidosis), and emergent dialysis (for metformin or salicylate toxicity). Scenarios and key clinician considerations for intubation of the patient with severe metabolic acidosis can be found in Table 3,

### *2.6. What should the emergency clinician consider when intubating a patient with right ventricular dysfunction?*

There are a variety of conditions associated with right ventricle (RV) dysfunction, including pulmonary hypertension, acute pulmonary embolism, acute respiratory distress syndrome (ARDS), cor pulmonale from chronic lung disease, RV myocardial infarction, and sepsis-induced RV dysfunction [133-135]. The RV poorly tolerates the hemodynamic changes associated with TI when it is already strained. This is mostly due to its sensitivity to the increased afterload that occurs during and immediately after intubation [133]. The normal pressure gradient between the venous circulation and RV is 4-8 mm Hg, making the RV particularly vulnerable to significant changes in pleural pressure [69]. Pre-existing moderate or severe RV dysfunction is independently associated with significantly higher rates of post-intubation hemodynamic instability and cardiac arrest [18,136]. In patients with severe RV dysfunction, 30-day mortality after intubation can reach 86% [137].

The pathophysiology of RV dysfunction leading to increased risk of complication during intubation is multifactorial. RV dysfunction occurs through direct cardiodepressant effects of pro-inflammatory cytokines, ischemia, arrhythmias, increases in afterload from endothelial dysfunction, hypoxic pulmonary vasoconstriction, and pulmonary microthrombi [133]. The transition from spontaneous negative pressure ventilation to positive pressure ventilation creates several adverse effects on RV function [138]. As described, ventilatory-induced positive pressure increases pleural and intrathoracic pressure, decreasing venous return and RV preload, while simultaneously increasing RV afterload through elevated transpulmonary pressure. The general effect of ventilatory-induced positive pressure also increases pulmonary vascular resistance (PVR). However, concurrent ventilatory assisted correction of atelectasis, hypoxia, or hypercapnia can lead to reduction in PVR. Additionally, the limited myocardial mass of the RV wall makes it more sensitive to changes in afterload than preload in contrast to the left ventricle [69].

Positive end-expiratory pressure (PEEP) has a U-shaped relationship with PVR. While moderate PEEP can relieve atelectasis and improve blood flow, PEEP that causes alveolar overdistension compresses extra-alveolar vessels and increases PVR [69]. RV afterload increases linearly with tidal volume and driving pressure [139]. The combination of decreased preload, increased afterload, and potential RV ischemia from reduced coronary perfusion pressure creates a physiologic condition conducive for cardiovascular collapse during intubation [140].

Given the associated risk, identification of RV dysfunction before intubation is crucial. Point-of-care ultrasound (POCUS) can be used by the emergency clinician to identify signs of acute or chronic RV dysfunction. Common methods of POCUS to assess for RV dysfunction include RV dilation (RV size ≥ LV size), tricuspid regurgitation, an akinetic RV free wall with preserved apical function (McConnell's sign) on the apical four-chamber view and bowing of the interventricular septum on parasternal short axis view [141,142]. Quantitative measures of RV function on POCUS that suggest RV dysfunction include a tricuspid annular plan systolic excursion (TAPSE) <17 mm [142,143]. POCUS should also evaluate the inferior vena cava (IVC) size and collapsibility as part of the assessment of RV dysfunction, which can help guide management [18,141,143].

When RV dysfunction is identified or suspected, optimization of RV hemodynamics is crucial to mitigate risk prior to induction and intubation. Given the narrow window of physiologic tolerance of the RV, invasive hemodynamic monitoring (e.g., arterial line) should be considered to help guide resuscitation and management [144]. Arrhythmias in patients with RV dysfunction increase risk of hemodynamic compromise during intubation, electrical restoration of sinus rhythm should strongly be considered prior to induction [144,145]. Preload must be optimized given the sensitivity of the RV to volume status. POCUS evaluation can help guide volume resuscitation or diuresis. If the IVC is flat or with high collapsibility (>50%) volume resuscitation should be considered, while a dilated IVC with low (<50%) or no collapsibility should prompt consideration of diuresis [18]. In line with volume resuscitation is careful evaluation and maintenance of MAP. To ensure RV coronary perfusion, which occurs during both systole and diastole, maintaining a MAP ≥60 mmHg is recommended [144,146]. To support MAP, vasopressors can be utilized. Comparative data on vasopressors in acute RV failure are limited, with expert consensus supporting norepinephrine as a first-line agent [144,147]. However, vasopressin should be considered if available, as it may reduce pulmonary artery pressure [148]. Phenylephrine should be avoided, as its pure alpha-1 agonism will increase pulmonary arterial pressure [144].

Inhaled pulmonary vasodilators, such as nitric oxide and epoprostenol, can also be considered. These agents selectively reduce pulmonary vascular resistance without causing systemic hypotension. The American Heart Association and American College of Cardiology suggest the use of inhaled pulmonary vasodilators in patients with pulmonary hypertension undergoing intubation for procedures to reduce elevated RV afterload and prevent acute RV decompensation [144,149]. If these agents are not available, nebulized nitroglycerin can be considered, as nitroglycerin is metabolized into nitric oxide. Several studies have demonstrated that nebulized nitroglycerin can safely result in pulmonary vascular vasodilation, reducing pulmonary artery pressures [150-155]. The dose is 5 mg nitroglycerin over 15 minutes, which can be repeated.

Emerging considerations for intubation of patients with RV dysfunction include consideration of awake intubation and early initiation of mechanical circulatory support. Small case series have shown successful outcomes with a primary awake intubation approach in patients with RV dysfunction [156-158], and the 2020 American Heart Association consensus statement discusses awake intubation to reduce complications in the cardiac ICU. However, there are limited data, and consideration of awake intubation depends on operator comfort, available equipment, and patient specific considerations. If timing and institutional protocols are established, one can consider preemptive ECMO or having an ECMO team on standby to support high-risk patients or rescue worsening or refractory hemodynamic derangements

**Table 3**
Scenarios and key clinician considerations for intubation of the patient with severe metabolic acidosis.

| Scenario | Key Considerations |
|---|---|
| Pre-intubation metabolic acidemia (arterial pH < 7.30) | — Strongly associated with peri-intubation cardiovascular collapse<br>— Gradient of risk correlates with level of acidemia |
| Use of sodium bicarbonate | — Current evidence does not support sodium bicarbonate administration to correct acidemia before intubation |
| Preservation of respiratory drive | — May consider awake intubation if feasible |
| Correction of acidosis | — Consider pathology specific treatments prior to intubation (e.g., dialysis for salicylate toxicity) |
| Post-intubation ventilation settings | — Match post-intubation minute ventilation with pre-intubation minute ventilation<br>— - Limit apnea to the shortest duration possible |

**Table 4**
Scenarios and key clinician considerations for intubation of the patient with right ventricular dysfunction.

| Scenario | Key Considerations |
|---|---|
| Pre-intubation right ventricular dysfunction | — Can be associated with a variety of clinical conditions, acute or chronic<br>— - Associated with peri-intubation cardiovascular collapse |
| Use of point-of-care ultrasound | — Identification of pre-intubation right ventricular dysfunction is crucial and can be completed with ultrasound<br>— Signs of right ventricular dysfunction on ultrasound: right ventricular dilation, akinetic right ventricular free wall, tricuspid regurgitation, intraventricular septum bowing, tricuspid annular plane systolic excursion < 17 mm |
| Optimization prior to tracheal intubation | — Consider invasive arterial monitoring, targeting mean arterial pressure > 60 mmHg<br>— Use vasopressors as needed, primarily norepinephrine or vasopressin<br>— Rapidly address and treat arrhythmias<br>— - Optimize preload, using ultrasound to guide volume resuscitation or diuresis |
| Use of pulmonary vasodilators | — Inhaled pulmonary vasodilators can be used in the peri-intubation phase (e.g., nitric oxide, epoprostenol)<br>— If inhaled nitric oxide or epoprostenol are not available, consider nebulized nitroglycerin |
| Advanced airway techniques | — Consider awake intubation<br>— Consider pre-intubation extracorporeal membrane oxygenation cannulation if time allows and team workflow for emergency department cannulation is in place |

[135,140,144,149,156]. Scenarios and key clinician considerations for intubation of the patient with right ventricular dysfunction can be found in Table 4.

*2.7. What other pathophysiologic derangements have been proposed as a physiologically difficult airway and what unique considerations are needed?*

Beyond the four main phenotypes of the physiologically difficult airway, pericardial tamponade, left-sided valvular dysfunction, obesity, pregnancy, high aspiration risk, and intracranial hypertension have been proposed as specific phenotypes of interest [11,25,27]. We have discussed pericardial tamponade and left-sided valvular dysfunction under the hypotension phenotype. The main concerns in pregnancy and obesity are related to increased risk of hypoxia, and thus we have included them under that phenotype. Aspiration can lead to hypoxia if it occurs, but this is a universal risk of RSI, not a distinct, measurable, physiologic state for patients requiring emergency airway management in the ED. The INTUBE study found aspiration of gastric contents occurred in 3.9% of all critically ill intubations, not just those identified as "high risk" [13]. A single center prospective observational study similarly found that 66 of 879 (8%) of patients intubated in the ED developed aspiration pneumonia, with no differences in intubation parameters or patient differences associated with its development [159].

Intracranial hypertension does not fit into the initially described phenotypes which warrants specific considerations, as laryngoscopy and intubation can lead to acute elevations in ICP, precipitating herniation or worsening secondary brain injury [160-162]. This occurs as laryngoscopy and tracheal intubation can provoke a sympathetic response. In head injured patients there is impairment of cerebral autoregulation, and the sympathetic response from laryngoscopy and intubation is transmitted to the cerebral vasculature, which can lead to sudden increases in ICP. One study of 97 head-injured patients undergoing orotracheal intubation found a hypertensive response occurred in 80% of patients, and this response was not attenuated by increasing head injury severity, highlighting that even deeply comatose head injury patients are at risk [161]. Placing the patient in the sniffing position can also increase ICP on average 5mmHg secondary to impedance of jugular venous outflow [160].

There are several considerations when performing intubation on patients with known or suspected intracranial hypertension. Elevation of the head of the bed to 30 degrees prior to and during intubation can reduce ICP by 5.6 mmHg compared to supine positioning [163]. Video laryngoscopy is suggested as the primary device technique, as it is associated with higher first attempt success, and prevention of repeated attempts at laryngoscopy reduces the chance for sympathetic surges [37]. It also generally requires less force than direct laryngoscopy, which has direct correlations with the amount of sympathetic response during the procedure [164,165]. Theoretically the use of hyperangulated video laryngoscopy (HAVL) would cause less sympathetic surge, as studies show its use compared to standard geometry video laryngoscopy (SGVL) result in significantly lower mean and peak forces on pharyngeal and laryngeal tissue [165]. However, a 2025 RCT found that HAVL was associated with a higher incidence of vagal responses compared to SGVL (OR 5.73) [166]. Notably, this was attributed to the technique of direct epiglottis lifting, which in this study was more common in the HAVL group, and not the recommended primary technique when using HAVL [40]. At this time there is no evidence to support HAVL or SGVL over one another and clinicians should use whichever device they are most facile with and the clinical situation dictates.

The concept of the "neuroprotective intubation" first emerged in the early 2000s, with studies examining the use of lidocaine and fentanyl as premedication to blunt the sympathetic surge from laryngoscopy [167]. More contemporary perspectives have shifted away from pretreatment and emphasize a goal of a hemodynamically neutral intubation, first-attempt success, and post-intubation optimization [168-170]. This includes emphasis on prevention of hypoxia and hypo and hypertension

**Table 5**
Scenarios and key clinician considerations for intubation of the patient with intracranial hypertension.

| Scenario | Key Considerations |
|---|---|
| Pre-intubation intracranial hypertension | — Laryngoscopy and intubation can cause sympathetic surge, increasing ICP, leading to herniation or secondary brain injury |
| Patient positioning | — If possible, elevate the head of bed to 30 degrees before and during laryngoscopy |
| Hemodynamic optimization | — Target a hemodynamically neutral intubation<br>— Consider pre-intubation placement of invasive arterial monitoring<br>— No current support for pre-medication with fentanyl to blunt the sympathetic surge of laryngoscopy |
| Laryngoscopy considerations | — Use video laryngoscopy; no current evidence to support hyperangulated or standard geometry blades over one another<br>— Do not use induction agent to control hemodynamics<br>— Use paralytic agent to prevent coughing/gagging, subsequent ICP increases |
| Post-intubation ventilation and sedation | — Target eucapnia<br>— Adequate sedation is essential to prevent ventilatory dyssynchrony and ICP increases |

ICP, intracranial pressure.

during the procedure, which was previously discussed in detail. Notably, the proceduralist should not plan to use the induction agent for RSI to help "control" the blood pressure. Patients should undergo full RSI with complete paralysis to prevent coughing or straining, which can lead to increased ICP [171]. Either succinylcholine or rocuronium can be used as the neuromuscular blocker to facilitate the procedure, as there is no evidence to support that fasciculation from succinylcholine increases ICP [172-175]. Post-intubation goals are to maintain $PaCO_2$ 35-40 mmHg, which prevents cerebral vasodilation [176]. Adequate sedation is essential to prevent ventilator dyssynchrony and subsequent ICP spikes [164]. Scenarios and key clinician considerations for intubation of the patient with intracranial hypertension can be found in Table 5.

## 3. Conclusions

The physiologically difficult airway is a high-risk scenario, and the first step in management is an understanding of the concept. Patients with a physiologically difficult airway have pathophysiologic alterations that increase their risk of an adverse event during intubation. The major phenotypes of the physiologically difficult airway include patients with hypotension, hypoxemia, metabolic acidemia, and right ventricular dysfunction. These patients do not lend themselves to a "one-size-fits-all" approach. Clinicians must understand how to identify, manage, and risk-mitigate based on the phenotype(s) and the underlying condition driving the pathophysiological alteration of the physiologically difficult airway present. These patients require early recognition and respect of the high-risk nature of the procedure. Patients with a physiologically difficult airway are complex and resource intensive (both time and interventions), with meticulous and precise pre-intubation evaluation, resuscitation, and procedural skills required. These steps leverage the skills of the emergency physician (e.g., POCUS, resuscitation decision making, awake intubation). With an appropriate understanding, vigilance, and focus there can be mitigation of some, but not all, of the risk of the physiologically difficult airway.

## CRediT authorship contribution statement

**Aaron J. Lacy:** Writing – review & editing, Writing – original draft, Conceptualization. **Brit Long:** Writing – review & editing, Writing – original draft, Conceptualization. **Michael Gottlieb:** Writing – review & editing, Writing – original draft, Conceptualization. **Jarrod M. Mosier:** Writing – review & editing, Writing – original draft, Conceptualization.

## Declaration of competing interest

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