CHAPTER 3

The Physiologically Difficult Airway

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DEFINITION OF THE PHYSIOLOGICALLY DIFFICULT AIRWAY

Critically ill patients present a unique danger during airway management. The risk with intubation-related complications was traditionally thought to be largely a result of anatomic challenges that confound attempts at intubation and leave a patient without an unsecured airway or effective respiration for a prolonged period. Reducing that risk was intimately tied to laryngoscopy device and skill and if, for example, a patient with refractory hypoxemia needed intubation, the mindset was to "do what you are best at" and do it quickly before the patient arrests. The fact that the risk of complications increases after a single missed attempt only reinforces the urge to fall back on laryngoscopy skills to race the impending cardiac arrest. Thankfully, over the last 15 years, video laryngoscopy, second-generation supraglottic airway devices, and disposable flexible endoscopes have largely overcome the challenges posed by anatomic obstacles to laryngoscopy and rescue ventilation. Yet, despite all the technological devices available to us resulting in higher success rates, there are still unsettlingly high rates of desaturation, hypotension, and cardiac arrest during emergency airway management. Although difficult intubations dramatically increase the risks of these complications, a recent study showed half of all critically ill patients had complications despite only a 5% difficult intubation incidence (see "Evidence" section). This risk is caused by cardiopulmonary decompensation during intubation from physiologic disturbances despite the presence or absence of anatomic challenges to intubation—*the physiologically difficult airway*.

PREDICTING THE PHYSIOLOGICALLY DIFFICULT AIRWAY

There are myriad reasons why a patient may decompensate from physiologic derangement during intubation. Abnormalities in isolation, or in combination, are exacerbated by intubation drugs, apnea, and the transition to positive pressure ventilation (PPV) and together affect the patient's cardiopulmonary status. The most seen preintubation abnormalities that should be considered are summarized by the CRASH mnemonic (**Box 3.1**).

*C*onsumption: Pediatric patients, sepsis, acute respiratory distress syndrome (ARDS), or other high-demand states such as excited delirium, thyrotoxicosis, and pregnancy all increase the consumption of oxygen. Although there is redundancy in oxygen delivery to meet this demand (thus why normal Svo_2 is 75% and not 0%), patients at or near their anaerobic threshold with a critical illness that increases oxygen consumption and

BOX 3.1 The CRASH Mnemonic

	Physiologic Abnormality	Response
C	Increased oxygen **C**onsumption	Optimize preoxygenation, apneic oxygenation
R	**R**ight ventricular failure	Optimize preoxygenation, inhaled pulmonary vasodilators, choice of induction agents, early use of vasopressors
A	**A**cidosis (Metabolic)	Correct underlying issues, avoid mechanical ventilation if possible, minimize apnea time, consider awake intubation, maintain increased minute ventilation
S	Risk of de**S**aturation	Optimize preoxygenation
H	**H**ypotension	Volume resuscitation, vasopressors

decreases oxygen delivery are at risk of rapid desaturation despite normal or near normal oxygen saturation during preoxygenation.

Right Ventricular Dysfunction/Failure: Patients with right ventricular (RV) dysfunction or failure are at very high risk of decompensation during intubation. The right ventricle has very little reserve to overcome increased afterload. Early on, the right ventricle can increase contractility through interventricular dependence with the left ventricle, but as dilation and regurgitant flow across the tricuspid valve worsens, contractility worsens, and further dilation eventually impairs left ventricular diastolic filling. Cardiac output is only maintained by tachycardia at this point, and any further increase in RV afterload, or further volume loading of the right ventricle, can push the right ventricle too far and result in cardiac arrest. Hypercapnia, atelectasis, hypoxemia all independently increase pulmonary vascular resistance, and positive pressure can increase RV afterload as well—often to the point of cardiovascular collapse.

Acidosis: Severe metabolic acidemia increases risk by further decreasing the pH with any interruption of compensatory ventilation during intubation or unmatched alveolar ventilation requirement after intubation. Although many patients can increase their $Paco_2$ during intubation, those trying to compensate for a severe metabolic acidosis can be tipped over the edge during this brief period. Profound acidosis can have negative inotropic effects on the heart, worsen shock states, and instigate malignant ventricular dysrhythmias.

Saturation: Critically ill patients with airspace diseases such as ARDS have limitations in the ability to preoxygenate to provide an adequate safe apnea duration. Preoxygenation should address the three components required for a safe apneic interval: denitrogenation, improving functional residual capacity (FRC), and reducing ventilation/perfusion mismatch. Monitoring end-tidal oxygen (ETO_2) can assist in ensuring optimal denitrogenation, which is best performed with a tight-fitting mask and 100% flush-flow rate oxygen, or heated high-flow nasal oxygen (HFNO; see Chapter 8). In patients where safe apnea is limited or not possible, the strategy should be changed to accommodate the potential for rapid desaturation.

Hypotension/volume: Critically ill patients are at significant risk of peri-intubation hypotension from many factors. Volume depletion, vasoplegia, and cardiomyopathy are all relatively easily identified and steps can be taken to address them prior to intubation. The response to induction agents and positive pressure are more difficult to predict and when combined with any of the former increase the risk of precipitating a decompensated state. An elevated shock index (SI) is helpful to predict those patients at high risk, but a low SI should not necessarily be reassuring.

PREPARATION FOR THE PHYSIOLOGICALLY DIFFICULT AIRWAY

After assessing for anatomic difficulty (eg, "LEMON," "ROMAN," "RODS," and "SMART" mnemonics, see Chapter 2), one generally has an idea who is eligible for rapid sequence intubation (RSI) based on the predicted success with laryngoscopy, intubation, bag-mask ventilation, and

rescue strategies or who is forced to be intubated with RSI despite anatomic challenges (ie, "forced to act," see Chapter 5). After the airway anatomy has been assessed, the patient's physiologic vulnerability is evaluated for potential decompensation (eg, "CRASH") during intubation. After assessing the physiology, the following questions should be addressed?

- ***What can I do to augment the physiology and proceed with my strategy (ie, RSI)?*** For example, intubation drug choice, positioning, preoxygenation maneuvers, etc.
- ***Do I need to change my strategy because of physiology that is refractory to intervention?*** For example, intubate awake because of refractory hypoxemia?

After the general strategy is determined, specific plans within the strategy are developed.

MANAGING THE PHYSIOLOGICALLY DIFFICULT AIRWAY

Oxygenation

The goal of preoxygenation is to build an oxygen reservoir for the patient to draw upon during apnea and maintain oxygen saturation. Successful preoxygenation is dependent on three components: (i) a volume of gas to work with (FRC), (ii) replacement of that gas with oxygen (denitrogenation), and (iii) availability of that volume to the pulmonary circulation (minimized ventilation/perfusion [V/Q] mismatch and shunt). One or a combination of abnormalities of those necessary requirements limits the goal of achieving time for laryngoscopy, intubation, and initiation of mechanical ventilation. For example, patients with severe ARDS can be easily denitrogenated, but a small volume FRC and low V/Q (high shunt) dramatically reduces the time available for intubation. High oxygen consumption also increases the rate at which that reservoir of oxygen is consumed. This is primarily driven by the patient's illness and is difficult to manipulate in the peri-intubation period. Preventing desaturation is a critical step for the safety of emergency airway management. "Racing" hypoxemia by attempting a fast intubation as a "forced to act," while tempting in a stressful situation, is fraught with danger for many patients such as refractory hypoxemia and ARDS. Although you may get lucky and the oxygen saturation would not have dropped critically during the attempt, it could plummet even before intubating conditions are creating by the RSI drugs. The oxygen saturation inevitably drops after the attempt as the desaturated blood passing through the pulmonary circulation makes it to the oxygen saturation sensor on the finger. If any unexpected delay occurs (eg, challenging and prolonged laryngoscopy), this may be the tipping point into a bradycardic arrest. The safest option is to optimize the three necessary variables for preoxygenation.

Functional Residual Capacity

As there is no tidal breathing during apnea, by definition, the reservoir of gas available is that which is present in the lungs at the end of end-expiration and is called the FRC. The FRC is dependent on height and age. In a healthy adult, the FRC is roughly 25 to 30 mL/kg, resulting in around 2 L in a 70-kg adult. Anything that compresses or fills the alveoli will reduce the FRC. Thoracic or abdominal fat, ascites, or late-term gravid uteri all compress the alveoli externally, whereas hemorrhage, pneumonia, edema, and ARDS all obliterate airspace internally. In patients intubated for pneumonia or other causes of hypoxemia, or in patients with ascites, late-term pregnancy, pleural effusions, and obesity, the FRC is often the limiting factor in preoxygenation. In these cases, consider interventions in **Box 3.2** to increase the FRC.

Denitrogenation

Denitrogenating the FRC and replacing it with oxygen will maximize the potential amount of oxygen available during apnea. Denitrogenation can be accomplished with 3 minutes of tidal breathing or eight vital capacity breaths if the patient is breathing on a closed circuit and 100% F_{IO_2} (assuming a normal respiratory rate and tidal volume). In emergency airway management, closed circuits are rarely available and most oxygen sources available using conventional oxygen therapy involve loosely fitting reservoir-based nonrebreather masks. Although the oxygen flowing into the reservoir is constant, which increases the F_{IO_2} and volume available during inspiration, the inspiratory flow rate generated by the patient leads to room air entrainment around the nonrebreather mask,

BOX 3.2 Variables for Preoxygenation

Limiting Factor	Intervention
Reduced functional residual capacity	1. Position the patient upright. 2. Recruit any recruitable alveoli (ie, Bi-PAP).
Denitrogenation	1. Use flush rate oxygen via nonrebreathing mask or high-flow nasal cannula. 2. Monitor with ETO_2, if available. 3. Keep the source of oxygen in place until the patient is apneic. 4. Controlled bag-mask ventilation between induction and laryngoscopy in patients at low risk for aspiration. 5. Apneic oxygenation with standard nasal tubing at 5-15 L/min.
V/Q mismatch (shunt)	1. Reduce work of breathing and recruit alveoli with high-flow nasal oxygen or NIPPV. 2. Diurese patients with significant pulmonary edema.

Bi-PAP, bi-level positive airway pressure; ETO_2, end-tidal oxygen; NIPPV, noninvasive positive pressure ventilation.

contaminating the inspired volume with ambient air. As the inspiratory flow generated by the patient often increases with the severity of respiratory failure, ambient air entrainment worsens as respiratory effort increases. The result is that ambient room air dilutes the FRC, and the severity of this dilution increases in patients that need to increase F_{IO_2} the most.

The best way to compensate for the entrainment of ambient room air in the absence of a closed circuit is to use "flush-flow rate" flow through a wide-open valve (see Chapters 8 and 20). The more pressurized the hospital's oxygen system, the higher the flow will be achieved at flush rate. Flush rate can be as high as 90 L/min or more, which provides enough flow to more closely approximate the inspiratory flow rate of the critically ill patient with a high respiratory demand breathing supplemental oxygen with an open circuit. One important consideration is that any spontaneous breaths after removing the source of oxygen can result in rapid renitrogenation, thus the patient should be fully apneic before removing the oxygen source.

The effect of denitrogenation can be prolonged, theoretically indefinitely, with the application of oxygen continuously to the nasopharynx during apnea. The ability to maintain alveolar oxygenation during apnea, or apneic oxygenation, is contingent upon the pressure gradient between the nasopharynx and the alveoli, which is a function of the amount of flow applied and the rate of peripheral oxygen consumption. This passive flow of oxygen from the glottic inlet to the gas-exchanging portions of the lungs is known as "aventilatory mass flow" and is discussed in more detail in Chapter 8. Thus, apneic oxygenation performed using HFNO systems, such as Vapotherm or Optiflow, is expected to perform better than apneic oxygenation using 10 to 15 L/min from a standard nasal cannula. Apneic oxygenation has been shown to lengthen the period of safe apnea and increase first-attempt success (secondary to more laryngoscopy time) although it does not perform as well in patients with significant V/Q mismatch. Interventions for denitrogenation are found in Box 3.2.

V/Q Mismatch

A fully denitrogenated patient with an FRC of 2 L and an oxygen consumption of 250 mL/min should have several minutes of safe apnea. This, however, requires that this reservoir of oxygen is fully available to the pulmonary circulation. There are normal V/Q differences in the lung because of gravity, such that the apices have more ventilation than perfusion (dead space) and the bases are the opposite (shunt). However, the global V/Q mismatch is minimal, with a normal shunt fraction of roughly 2%, meaning that a fully denitrogenated FRC is widely available to resaturate hemoglobin as it passes through the pulmonary circulation.

As airspace or interstitial disease worsens, however, the alveolar-arterial gradient increases and V/Q mismatch moves toward the shunt end of the spectrum, which means that even though

maximal alveolar oxygenation can still be achieved, oxygen is less available at the alveolar-capillary interface to resaturate hemoglobin. In emergency department (ED) patients, the V/Q mismatch can be improved by recruiting atelectatic regions of the lung with positive end-expiratory pressure (PEEP), reducing interstitial edema with diuresis, or improving myocardial performance in the case of cardiogenic pulmonary edema. Inhaled pulmonary vasodilators, often used in the intensive care unit (ICU), can be helpful in some cases. Occasionally, decreased lung compliance and the airspace disease is refractory to any effort at improving V/Q mismatch. This results in a small available FRC despite being fully denitrogenated.

Who Should Be Intubated Awake?

In the most refractory cases, preoxygenation fails to provide an adequately available reservoir of oxygen and an acceptable safe apnea time is not possible. In these patients, an awake intubation with continuous high-flow oxygen may be the safest path to securing the airway to initiate invasive mechanical ventilation. The risk of critical desaturation and cardiac arrest is significantly high enough in these patients that one should strongly consider an awake approach. The decision is more difficult in patients that have improved with noninvasive respiratory support. At the end of the preoxygenation process in these patients with hypoxemic respiratory failure, where any recruitable alveoli have been recruited, the FRC is maximized as much as possible and fully denitrogenated, the partial pressure of arterial oxygen (Pao_2) from an arterial blood gas (ABG) can provide a good assessment of the degree of shunt. Although the Pao_2 does not contribute substantively to oxygen delivery, in this instance it is a good indicator of oxygen availability in the alveoli to the pulmonary circulation, and thus safe apnea time. Consider two patients with ARDS that are preoxygenated using identical methods, both with an oxygen saturation of 95%. The first patient's Pao_2 is 220 mmH_2O and the second patient's Pao_2 is 79 mmH_2O. Despite the same oxygen saturation, the second patient's oxygen reservoir is far less available to resaturate hemoglobin and very likely to desaturate rapidly upon induction.

How Do I Stratify Preoxygenation?

During an emergency intubation, preoxygenation is the most important preinduction step as safe apnea is paramount for patient safety during RSI. Although denitrogenation can easily be quantified by measuring ETO_2, the patient's total oxygen reserve (FRC) is hard to measure and the oxygen saturation only tells part of the story, as mentioned above. Although a strategy involving ABG sampling is often undertaken in the ICU, it can be impractical and logistically challenging to accomplish in the context of a deteriorating hypoxemic emergency department patient. In practice, it can be helpful to place patients into one of three categories based on their ease of preoxygenation. The default approach is to place the patient upright or in reverse Trendelenburg position and apply standard nasal cannula along with a nonrebreather mask using flush rate oxygen. If the saturation is below 94%, then there is significant intrapulmonary shunt, and the patient should be transitioned to HFNO or bi-level positive airway pressure (Bi-PAP) to reduce the shunt fraction and improve the Sao_2. In these patients, even if the saturation improves, the total oxygen reserves and, therefore, duration of safe apnea is not known. If temporarily stabilized while preoxygenating on HFNO or Bi-PAP *and* an ABG is easily obtained, then a Pao_2:Fio_2 ratio can inform the clinician as to who is at highest risk of dangerous desaturation with RSI despite the improved saturation. A Pao_2:Fio_2 ratio <100 indicates a very high-risk situation and an awake approach is preferred. If, despite noninvasive positive pressure ventilation (NIPPV) or HFNO, the patient remains $<94\%$, critical hypoxemia will occur during RSI and may be evident even before sedative and neuromuscular blocking agents have taken effect. Similarly, these patients are best intubated using awake techniques (see Chapter 24).

Hemodynamics

Hemodynamic challenges have risen as the pinnacle source of danger to patients requiring intubation in the ED or ICU. In a recent worldwide study across 29 countries, less than 10% of patients were intubated for hemodynamic instability but almost half developed hemodynamic instability as a result of the intubation. Thus, preintubation management of patients' hemodynamics are as important as preoxygenation for emergency airway management. Unfortunately, hemodynamic

disturbances are as, or more, complex than hypoxemia. The overarching goal is to safely transition a patient, often with limited or no reserve, through apnea and laryngoscopy to PPV. To accomplish that, we most commonly use medications that blunt the survival (sympathetic) drive and often have hemodynamic consequences of their own. With 1 in 3 patients suffering cardiovascular collapse and nearly 1 in 30 a cardiac arrest, emergency airway management must include peri-intubation management of hemodynamics.

The evidence for optimizing hemodynamics is challenged by a lack of standardized definitions regarding vital sign thresholds or the peri-intubation period. Despite these limitations, observational data show that preintubation shock index (SI, heart rate/systolic blood pressure), older age, hypotension, shock, intubation for respiratory failure and a higher severity of illness (APACHE) score are all factors associated with a higher likelihood of postintubation cardiovascular collapse. Various methods to reduce hypotension rates have been attempted or debated as long as critically ill patients have required intubation. Early on, patient positioning was altered to overcome hypotension associated with thiopental. Etomidate and ketamine have been debated for 20 years. Bolus-dose vasopressors and fluid resuscitation strategies have been proposed, and debated, without definitive evidence for either of these interventions. Resuscitation, when used as a part of a bundle in the perioperative period has been shown to reduce complications. Blood products prior to intubation in trauma patients has also been shown to improve outcomes. Unfortunately, none of these findings have been reproducible, illustrating the complex pathophysiologic disturbances that require personalization for each patient.

Consider the following example to demonstrate this complex milieu: a patient with severe ARDS. There is significant airspace disease resulting in the loss of FRC as described in the "Oxygenation" section. That worsens ventilation/perfusion ratios to make preoxygenation more difficult, but also increases the pulmonary vascular resistance and increases the strain on the right ventricle. Any hypercapnia or hypoxemia that occurs during apnea can further increase the pulmonary vascular resistance, and when added to any induction agent-induced venodilation or myocardial depression, or positive pressure induced reduction in preload, can lead to a precipitous cardiovascular collapse. The same phenomenon can occur with patients with massive pulmonary embolism, decompensated pulmonary hypertension, or cardiac tamponade. Septic patients lie on a spectrum from vasodilation and high cardiac output to high systemic vascular resistance and myocardial depression. Patients with heart failure with preserved ejection fraction have high left ventricular filling pressures and high pulmonary venous pressures leading to pulmonary edema, whereas patients with heart failure with reduced ejection fraction have poor contractility leading to high pulmonary venous pressures and pulmonary edema. Although all of these patients may present with hypoxemia, respiratory failure, and hypotension, the management for each of them needs to be tailored to attenuate the physiologic weakness (**Figure 3.1**). Vasoplegia is a major factor contributing to the negative hemodynamic effects seen in the peri-intubation period and may not be easily measured or adequately addressed. Additionally, the choice of induction agents and vasoactive medications further adds to these myriad factors. Any of these factors may be responsible for cardiovascular collapse in a fragile, critically ill patient. As such, these dynamic cardiopulmonary changes are challenging to predict, understand, and optimize. We offer a stepwise hemodynamic approach.

Stepwise Hemodynamic Strategy

There are many factors that can collude to cause postintubation cardiovascular collapse. Thus, there is no one-size-fits-all approach to hemodynamic assessment or resuscitation prior to intubation. There is no single induction agent that can eliminate concern of the underlying pathophysiology and no vasopressor that can eliminate peri-intubation deterioration. Volume depletion, vasoplegia, ventricular performance, hemodynamic effects of induction agents, and PPV are all important factors that need to be carefully considered. There are several concepts that can lead to a stepwise hemodynamic strategy with emergency airway management.

1. **Replete volume loss:** Most critically ill patients are volume depleted, either through fluid or blood loss, insensible losses, or fluid shifts. Thus, most patients require some form of fluid resuscitation. Methods for assessing volume responsiveness, or volume tolerance, are beyond the scope of this chapter—but there are many easily available and easy to

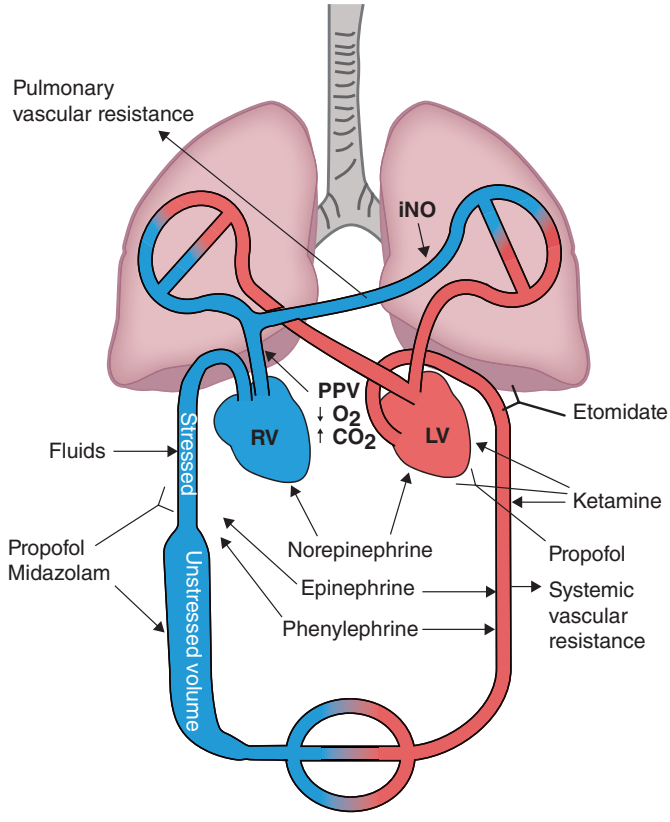

Figure 3.1: Factors affecting hemodynamics during intubation. Respiratory factors include the effects of positive pressure ventilation (PPV), desaturation, or hypercapnia which all increase pulmonary vascular resistance and right ventricular (RV) afterload, whereas inhaled nitric oxide (iNO) vasodilates the pulmonary circulation and decreases RV afterload. Fluids can often increase stressed volume, whereas sedatives have varying effects. Propofol and midazolam can decrease the stressed volume, thereby increasing the unstressed volume and decreasing the preload. Etomidate can decrease arterial elastance causing hypotension. Propofol can cause arterial dilation and depression of left ventricular (LV) contractility, whereas ketamine can cause arterial constriction and increased LV contractility through its indirect sympathomimetic effect, or LV suppression though its myocardial depressant effect. Vasopressors affect the cardiovascular system dependent on their potency and receptor profile.

perform methods to assess both. In patients who are likely to be volume responsive, fluid resuscitation should be performed. The type and volume of fluid will be dependent on the underlying pathophysiology and severity. The goal is to increase the circulating stressed volume. The stressed volume is the circulating volume that exerts a pressure against the vascular walls, and thus contributes to blood pressure, cardiac output, and oxygen delivery. Fluid resuscitation that does not lead to an increase in cardiac output or blood pressure is contributing to unstressed volume, which is volume that is stored in the high capacitance venous system.

2. **Reduce unstressed volume and vasoplegia:** Any fluid bolus that does not contribute to increased cardiac output is fluid stored as unstressed volume. Additionally, venodilating induction agents convert stressed volume into unstressed volume. Thus, patients not responsive to fluid resuscitation should be started on vasopressor infusions to reduce unstressed volume with vasoconstriction—particularly venoconstriction.

   Patients with a SI ≥0.8 are at high risk of developing postintubation hypotension. Individual vital signs that are not alarming in isolation, such as a heart rate of 100 and

systolic blood pressure of 100 mm Hg, when evaluated together with the SI, can be very concerning. This patient has a SI of 1 and at very high risk of decompensation in the peri-intubation period. These patients are at risk from any myocardial depression or vasodilation and should be started on in-line continuous vasopressors before intubation rather than relying on a bolus-dose vasopressor for rescue *after* decompensation.

3. **Augment ventricular performance:** After fluid resuscitation and vasopressors, the next principle is to determine whether there is any left ventricular or RV dysfunction that will decompensate with induction and PPV. Ventricular contractility that remains poor despite a vasopressor such as norepinephrine may require augmentation with an inotrope such as dobutamine or milrinone. In some instances (eg, restrictive physiology), the left ventricle may need afterload reduction and inotropic support rather than vasopressors.
4. **Mitigate effect of the induction agent:** All induction agents used for RSI have unfavorable hemodynamic consequences. These need to be balanced with optimizing intubating conditions for the patient to maximize the chances of first-pass success. At the doses required for RSI, propofol and midazolam result in venodilation, reducing both preload and blood pressure. Etomidate is considered a hemodynamically neutral drug, but recent evidence shows that etomidate reduces arterial elastance, which can cause hypotension. Ketamine has indirect sympathomimetic effects, however, is a direct myocardial depressant. Where one patient may respond to the sympathomimetic effect, another may get predominantly myocardial depression. Recent observational data have shown that ketamine was associated with more postintubation hypotension than etomidate, even when controlling for confounders and propensity matching. Induction agent choice will influence the choices made in steps 2 and 3 above, and vice versa. Regardless of the induction agent used, a reduced dose should be used in patients with hemodynamic instability.
5. **Protect the right ventricle:** Patients with RV failure should have an RV-focused resuscitation and intubation. The "RV spiral of death" involves decreased RV systolic function leading to RV pressure/volume overload that decreases left ventricular filling, reducing cardiac output and worsening hypotension, which may then reduce RV function further. Intubation is often the final insult that tips the RV over the edge because of the increase in pulmonary vascular resistance that results from any atelectasis, ventilation/perfusion mismatch, hypoxemia, and hypercapnia that comes with apnea. Additionally, the increase in RV afterload from PPV can be very deleterious and result in postintubation hypotension or even cardiac arrest. Patients with RV failure may ultimately need pulmonary vasodilators to reduce RV afterload. In the ED, the key step is to recognize at-risk patients (eg, obstructive shock from a large pulmonary embolus) and initiate norepinephrine to increase mean arterial pressure, maintain coronary perfusion pressure, and RV contractility.

Complicating Factor of Acidosis

Metabolic derangements have widespread, varying, and complex effects on the respiratory and cardiovascular systems. Metabolic acidosis is the most troublesome of these derangements. Although mild metabolic acidosis can increase cardiac output modestly, it does so at the cost of increased myocardial oxygen demand and higher propensity for dysrhythmias. Severe metabolic acidosis results in myocardial depression. Blunting of myocardial response to circulating catecholamines is also an important factor. Catecholamine release in response to metabolic acidosis results in arterioconstriction, which again can lead to tachycardia, shortened filling time, and dysrhythmias.

When patients with severe metabolic acidosis have maximized their alveolar ventilation to maintain a pH barely compatible with life, the RSI-induced apnea can often be the tipping point into cardiac arrest as the $Paco_2$ can rise rapidly and result in a plummeting pH. Before RSI is performed in these patients, one must treat the underlying etiology for the metabolic acidosis as best as possible, feel confident that the patient can tolerate a drop in pH, and ensure that the patient's current alveolar ventilation can be matched with mechanical ventilation.

Who Should Be Intubated Awake?

Just as with hypoxemia, some patients have hemodynamics or acidemia that are so fragile and cannot be adequately attenuated that the only safe path to intubation for them is an awake intubation approach. This avoids the hemodynamic effects and alveolar ventilation effects associated with induction and neuromuscular blockade. Additionally, awake intubation permits a more gradual transition to PPV. In these cases, one must sacrifice the safety of first-attempt success with laryngoscopy for the cardiopulmonary safety associated with spontaneous ventilation.

TIPS AND PEARLS

- Patients should be assessed for the physiologically difficult airway during the preintubation evaluation, and mitigation strategies must be incorporated into the preintubation planning.
- The physiologically difficult airway can be thought about in two large buckets, the dangers of rapid desaturation and dangers of cardiovascular collapse, as well as factors that make the previous two more likely such as RV failure or severe metabolic acidosis.
- Factors associated with rapid desaturation include those that reduce the size of the FRC, limit denitrogenation, increase right-to-left shunt physiology, or increase peripheral oxygen consumption.
- Preoxygenation should be meticulously performed with the intent of complete denitrogenation, recruiting any available airspace, and reducing ventilation/perfusion mismatch. In patients that are refractory to preoxygenation, an awake approach should be strongly considered to maintain spontaneous ventilation.
- Cardiovascular collapse is often difficult to predict and prevent, and factors associated with cardiovascular collapse include those that increase vasodilation and those that reduce cardiac output. A stepwise progression involving fluid resuscitation, vasopressor and inotrope support, and RV function support is required to minimize the risk of cardiovascular collapse in critically ill patients.

EVIDENCE

What is the evidence for the physiologically difficult airway?

Most studies on emergency airway management in the ED and ICU have shown a peri-intubation cardiac arrest rate between 1% and 4%.[1-3] When patients are hypoxemic or hypotensive prior to intubation (ie, the physiologically difficult airway), they have an adjusted odds of cardiac arrest almost 6 times that of patients that are neither hypoxemic nor hypotensive. When critically ill patients have a difficult airway, half have life-threatening complications.[3,4] However, the major increase in the risk to critically ill patients occurs with a second attempt.[3,5,6] What is most concerning is that despite increased first-attempt success rates in the published literature, complication rates remain alarmingly high. Sakles et al, Hypes et al, and De Jong et al all reported complication rates, mostly hypoxemia and hypotension, in patients with first-attempt success between 14% and 30%.[5-8] Russotto et al recently published the results of an observational study of intubations performed in critically ill patients across 29 countries and found that despite 95% of patients being successfully intubated in one or two attempts, half of the patients still experienced life-threatening complications.[4] Pacheco et al found that the presence of either anatomically or physiologically difficult airway characteristics decreased the first-attempt success *without* a complication by 10% (92% to 82%), and an additional 12% (82% to 70%) when both were present.[9] The adjusted odds ratio for first-attempt success without a complication was nearly the same when either was present (0.37 with anatomically difficult airway characteristics present, 0.36 with physiologically difficult airway characteristics present), and was only 0.19 when both were present. Overall, the data in the

published literature support the physiologically difficult airway as a distinct source of danger to patients that requires careful assessment and planning to the same degree as anticipated difficult laryngoscopy.

What are the risk factors for desaturation?

McKown et al evaluated patients enrolled in randomized clinical trials to determine independent risk factors for desaturation.[10] They identified the following independent risk factors: hypoxemic respiratory failure as the indication for intubation (OR 2.70), lower oxygen saturation at induction (OR 0.92 per 1% increase [above 95%]), younger age (OR 0.97 per 1 year increase), higher body mass index (OR 1.03 per 1 kg/m^2 [above 23 kg]), race (OR 4.58 for white vs black), and operator experience (OR 2.83 if <100 intubations).

What are the risk factors for hypotension?

Elevated SI has been shown consistently as a specific, yet insensitive, indicator of postintubation hypotension.[10-16] Three recent studies have shown that independent predictors of cardiovascular collapse include older age, hypotension or shock prior to intubation, intubation for respiratory failure, and higher APACHE scores prior to intubation.[15,17-19] In other words, sick patients with respiratory failure requiring intubation are at very high risk of *both* desaturation and cardiovascular collapse.

What is the evidence for advanced methods of preoxygenation?

Interpreting the evidence for preoxygenation is challenging. First, the PreVent trial showed that mask ventilation after induction but before laryngoscopy reduces severe hypoxemia rates from 23% to 11%. The INTUBE study that demonstrated a nearly 50% complication rate showed that 63% of patients were preoxygenated with bag-valve-mask ventilation. Compared to bag-valve-mask, preoxygenation with NIPPV in hypoxemic patients resulted in fewer desaturation events.[20] Vourc'h et al studied HFNO and reported that the rate of difficult intubation was 1.6% in the HFNO group and 7.1% in the facemask group, although it did not reach statistical significance.[22] Studies commonly do not evaluate apnea duration, but rather success rates as the surrogate, and are plagued with significant heterogeneity in definition and patient population. Yet, HFNO appears to be generally at least as good as facemask preoxygenation[22-25] for success rates, but has the added benefit of remaining in place to provide apneic oxygenation and has shown that compared to facemask, it prevents desaturation, prolongs safe apnea time, and limits the depth of desaturation.[21-23,25-31] Miguel-Montanes et al found that HFNO is an independent predictor of preventing desaturation <80% (adjusted odds ratio [aOR] 0.14).[27] In the patients with the most severe hypoxemia undergoing RSI, NIPPV may provide the best preoxygenation.[24,25,31] However, HFNO can remain in place for apneic oxygenation and may provide some benefit. In a recent study, NIPPV had fewer desaturations, but none of the HFNO patients desaturated to <70% although 13% of patients preoxygenated with NIPPV desaturated to <70%.[22]

What is the evidence for resuscitation?

Jaber et al found that resuscitation, when included in an intubation bundle, significantly decreased complications in the ICU.[32] However, replication has proved elusive. A randomized controlled trial of patients without hypotension that required intubation, a 500-mL crystalloid bolus did not decrease the chances of hemodynamic collapse.[33] A randomized controlled trial of fluid *optimization* prior to induction in an operating room did not show a difference in outcomes either, and one-third of the patients were on vasopressors within 15 minutes of induction regardless of goal-directed optimization.[34] In trauma patients however, a preintubation blood product-based resuscitation reduced the incidence of hypotension, cardiac arrest, and mortality in injured combat troops.[35]

What is the evidence for induction agents?

A recent study showed that hypotension from etomidate may be mediated through a reduced arterial elastance, causing arterial dilation after induction.[36] Recent observational studies using the National Emergency Airway Registry (NEAR) database showed that ketamine was associated with a

higher incidence of hypotension compared to etomidate, even after propensity matching and correcting for confounders,[37,38] a finding that was the opposite of a similar study in Japan.[39] A recent study in the ICU showed that etomidate and ketamine had similar outcomes, and both appeared to be worse than propofol as the sedative.[40,41]

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