Invasive and Noninvasive Pediatric Mechanical Ventilation

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Both invasive and noninvasive mechanical ventilation techniques are inherent to the care of most patients admitted to intensive care units. Despite the everyday use of mechanical ventilation for thousands of patients and the availability of thousands of reports in the medical literature, there are no clear and consistent guidelines for the use of mechanical ventilation for pediatric patients. In many areas data are lacking, and in other areas data are extrapolated from studies performed with adult subjects. Despite the variability in views about mechanical ventilation, 2 themes are consistent. First, modern pediatric respiratory care requires a substantial institutional commitment for state-of-the-art management of the mechanically ventilated patient. Second, a team approach involving physicians, nurses, and respiratory therapists is essential. This review highlights some of the major issues affecting the pediatric patient who requires invasive or noninvasive mechanical ventilation. These issues are pertinent to critical care clinicians because one of the most common reasons for admission to an intensive care unit is the need for mechanical ventilation. Furthermore, the duration of mechanical ventilation is one of the major determinants of the duration and cost of an intensive care unit stay. 

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Introduction

Artificial ventilation for respiratory failure is not a new concept. Galen was the first scientist to describe ventilation of an animal.1 As early as the 16th century the concept of artificial ventilation for humans was presented. Vesalius believed that people could be artificially ventilated with air blown through a tube passed from the mouth into the trachea.2 The use of mechanical devices to assist ventilation became a clinical reality in the late 19th century. Most of these early ventilators functioned through the use of negative pressure and not positive pressure. At the beginning of the 20th century, Emerson first used artificial positive-pressure mechanical ventilation in the operating room with anesthesia.3 Subsequently, the use of prolonged mechanical ventilation to maintain life became widely accepted during the polio epidemic of the 1950s.4–5 Today mechanical ventilation plays an important role in most intensive care units (ICUs) on a daily basis.

Artificial ventilation techniques are among the most important clinical skills for any pediatric intensivist. Artificial mechanical ventilation has substantially improved outcomes of children suffering respiratory failure, by maintaining adequate oxygenation and ventilation until the underlying pathologic process resolves. It must be appreciated that (1) mechanical ventilation is supportive (not therapeutic) and (2) positive-pressure mechanical ventilation inherently causes secondary lung injury of various degrees, depending on the ventilatory strategies employed and the clinical condition of the patient.

Mechanical ventilation can be delivered via positive-pressure breaths or negative-pressure breaths. Additionally, the positive-pressure breaths may be delivered noninvasively or invasively. This review will focus on positive-pressure ventilation, both noninvasive and invasive.

Although artificial ventilation techniques have dramatically improved over recent years, many questions remain unanswered, especially in relationship to the appropriate strategy for weaning and extubating patients from mechanical ventilation. Considering the wide range of disease entities encountered daily in clinical practice, it is important to note that the medical literature does not provide a consensus concerning which ventilatory modes or strategies are best applied to pediatric patients.

Indications for Mechanical Ventilation

Mechanical ventilation refers to the use of life-support technology to perform the work of breathing for patients who are unable to do so on their own. One of the most common reasons for ICU admission is the need for mechanical ventilation. Patients most commonly require mechanical ventilation for respiratory failure or impending respiratory failure. Respiratory failure occurs during conditions of inadequate gas exchange of oxygen and/or carbon dioxide. This failure of adequate oxygenation or ventilation can occur as a result of lung disease, cardiac dysfunction, neurologic abnormalities, multi-organ system dysfunction/failure, and/or secondary to the effects of surgery or cardiopulmonary bypass. Primary lung injury can occur from a multitude of causes, including pneumonia, inhalation injury, chest trauma, near-drowning, hemorrhage, and aspiration. Patients with cardiovascular dysfunction may require mechanical ventilation to minimize the work of breathing, which, if excessive, could cause lactic acidosis by increasing oxygen consumption at a time when oxygen delivery may be limited.6 Patients with neurologic injury may require mechanical ventilation for airway protection and/or for hyperventilation to improve intracranial hypertension. Thus, the overall goals of mechanical ventilation are to optimize gas exchange, patient work of breathing, and patient comfort while minimizing ventilator-induced lung injury.

Noninvasive Mechanical Ventilation

Noninvasive ventilation (NIV) is defined as the use of a mask or nasal prongs to provide ventilatory support through a patient’s nose and/or mouth. By definition this technique is distinguished from those ventilatory techniques that bypass the patient’s upper airway with an artificial airway (endotracheal tube [ETT], laryngeal mask airway, or tracheostomy tube). NIV was first introduced in the late 1980s, for patients with nocturnal hypoventilation.7–8 Subsequently, NIV has seen increasing popularity for pediatric patients with both chronic and acute respiratory failure of numerous etiologies.9–12

The primary advantage of NIV is the avoidance of endotracheal intubation or tracheostomy. The secondary advantages of not requiring an invasive airway include: decreased risk of nosocomial pneumonia; ability to manage many of these patients outside of the ICU (which may decrease hospital costs); decreased sedation requirement (including many patients who require no pharmacologic sedation); improved ability to tolerate enteral feeds (including a regular diet for some patients); and NIV allows the patient to ambulate more easily. The ability to care for patients who require NIV outside of the ICU setting differs from one hospital to the next. When patients requiring NIV are managed outside the ICU setting, close monitoring is required, and protocols should be in place to help the clinician determine when transfer to an ICU is warranted.

Noninvasive ventilation may be provided by either bi-level pressure support or continuous positive airway pressure. Bi-level support provides an inspiratory positive airway pressure for ventilatory assistance and lung recruit-
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Invasive Mechanical Ventilation

Although it is reasonable to attempt NIV in certain patient populations, the vast majority of patients who require ventilatory support need invasive, positive-pressure mechanical ventilation, either conventional or high-frequency. In 1997 an estimated 100,000 positive-pressure ventilators were utilized around the world, and approximately half were in use in North America. Approximately 1.5 million patients in the United States receive mechanical ventilation outside of operating rooms and recovery rooms every year.

Mortality among patients who require mechanical ventilation is widely variable and dependent on the underlying clinical condition that necessitated the ventilatory support. For pediatric patients with rapidly reversing conditions and who are otherwise healthy, mortality rates approach 0%. Patients with severe acute respiratory distress syndrome (ARDS) suffer 30–60% mortality. Ventilated patients with severe multi-organ system failure and/or severe immunodeficiency suffer 90–100% mortality.

Conventional Mechanical Ventilation

Multiple mechanical ventilation modes are currently used in clinical practice to provide respiratory support for a wide spectrum of patients, ranging from no lung disease to acute lung injury (ALI) to ARDS. To date no data exist to determine the ventilatory mode that provides the greatest benefit with the least risk to an individual pediatric patient.

Each new generation of conventional mechanical ventilators brings new ventilation modes and new features. However, despite a multitude of new modes, no study has shown that any mode is better than another in improving survival rates for ALI patients. It should be noted that in reality it might not be possible to demonstrate a significant change in mortality based only on changes in ventilator mode, because of the extremely low baseline mortality rate for intubated infants and children in pediatric ICUs.

Inspiratory Flow Pattern

Various inspiratory gas flow patterns are available on conventional ventilators. Regardless of the inspiratory flow pattern chosen, gas flow will always follow the path of least resistance. Variations in the inspiratory flow pattern will affect the distribution of inspired gas flow based on...
Optimal Patient-Ventilator Interaction

Optimizing patient-ventilator interaction is essential to providing the best possible care for any intubated patient. Optimal patient-ventilator interaction will improve patient comfort while potentially decreasing the requirement for pharmacologic sedation and thereby may help to minimize the duration of mechanical ventilation. Graphic analysis of ventilation and respiratory mechanics monitoring has become an integral part of conventional ventilator management and is an important tool in assessing and changing ventilation strategy. This technology incorporates monitoring the patient, the ventilator, and patient-ventilator interaction. Effective respiratory monitoring of a conventionally ventilated patient should assist the clinician in assessing adverse patient-ventilator interactions and provide important information to help clinicians intervene prospectively. If ventilated infants and children are to be comfortable, ventilated for the shortest possible time, and optimally use the nutritional support provided, the patient and ventilator system must interact synchronously. Recent advances in ventilator technology allow the clinician to customize the patient-ventilator interface, resulting in a more optimal interaction. Rosen et al demonstrated a reduction in ventilator-induced lung injury when respiratory mechanics measurements (at the ETT) were used in the care of neonates.

Thus, with the numerous ventilator modes, inspiratory flow patterns, and patient-triggering options available for the patient’s underlying clinical pathophysiology. Accelerating-flow patterns deliver the highest gas flow at end inspiration, when the effects of resistance and elastance are increased. Thus, accelerating-flow patterns typically produce higher peak inspiratory pressure (PIP) than other flow patterns and are rarely used in current clinical practice. In contrast, decelerating-flow patterns deliver maximum flow at the initiation of inspiration, when resistance and elastance are decreased. Inspiratory flow then decreases during inspiration as delivered gas volume increases. Peak airway pressures are lower but mean airway pressures are higher with a decelerating-flow pattern than with a constant-flow pattern. In general, as the maximum inspiratory flow changes from the start to the end of the inspiratory cycle, mean airway pressure will decrease and PIP will increase, for the same positive end-expiratory pressure (PEEP), inspiratory time, and delivered \( V_T \). Thus, decelerating-flow patterns have a theoretical advantage over accelerating-flow patterns, especially with ALI patients. A square wave, constant inspiratory flow pattern will typically have peak and mean airway pressures somewhere between the values seen with accelerating and decelerating patterns (Fig. 1).

Variable-flow ventilation (ie, pressure-controlled, or pressure-regulated volume-controlled) uses a decelerating-flow pattern. The rapid increase in inspiratory flow that occurs with variable, decelerating-flow ventilation leads to early filling of alveoli and sustains alveolar pressure longer than in a constant-flow pattern. Thus, variable, decelerating-flow ventilation potentially provides better alveolar recruitment and should improve gas distribution throughout the lungs. By improving gas distribution the desired \( V_T \) can be delivered at a lower PIP than with a constant inspiratory flow, corresponding to improved lung compliance.

The rapid increase in airway pressure in decelerating-flow ventilation can also lead to an increase in the overall mean airway pressure, and, thus, better arterial oxygenation and oxygen delivery. In adults the increase in mean airway pressure associated with decelerating-flow ventilation is not associated with hemodynamic abnormalities. Thus, respiratory pathology characterized by low pulmonary compliance (ie, ALI and ARDS) may benefit from a decelerating-flow inspiratory pattern, in which PIP is reduced but the mean airway pressure is increased.

The clinician should attempt to match the inspiratory flow pattern to the patient’s clinical condition. In contrast to the case of ALI, in diseases that cause high airway resistance (asthma, bronchiolitis, airway obstruction) peak airway pressure may, theoretically, be reduced by avoiding flow patterns that have high peak inspiratory flows. In high-airway-resistance patients a square-wave constant-flow pattern may generate a lower PIP than a decelerating-flow pattern, as a result of the lower peak inspiratory flow. However, conclusive data are lacking in support of this speculation.

In summary, the single most important aspect of the ventilation mode chosen for an individual patient may be the inspiratory flow pattern associated with the mode. Beyond the issue of inspiratory flow patterns, the optimal mode of ventilation for infants and children remains unclear.
neonatal and pediatric ventilation, graphic analysis of ventilation has become an important tool for determining the most beneficial ventilatory strategy for each patient and for identifying the presence of adverse patient-ventilator interactions.

An integrated graphic display that reflects patient response and ventilator performance. This information may improve detection and identification of critical events, enabling the practitioner to rapidly determine the presence of respiratory pathophysiology by evaluating $V_T$, airway pressures, gas flow, and pressure/volume and flow/volume relationships. The primary adverse patient-ventilator interactions that can impact the medical management of patients include pulmonary overdistention, intrinsic PEEP, and patient-ventilator asynchrony (Figs. 2-4).25

Pulmonary overdistention can cause volutrauma and ventilator-induced lung injury. Clinically important intrinsic PEEP may cause gas trapping, impaired gas exchange, pulmonary overdistention, and elevated mean intrathoracic pressure. Patient-ventilator asynchrony can cause the patient to become uncomfortable with the ventilator. If patient-ventilator asynchrony is not appreciated by the clinician, unnecessary pharmacologic sedation may be administered, prolonging the mechanical ventilation. Patient-ventilator asynchrony most commonly results from
an inappropriately set inspiratory trigger or inadequate inspiratory flow.

Inadequate trigger sensitivity is the most common cause of patient-ventilator asynchrony with infants. The frequency of this type of asynchrony has decreased as more ventilators have provided flow-triggering, regardless of the ventilation mode. A spontaneously breathing patient who is unable to trigger a mechanical breath will appear agitated and will “fight the ventilator.” If this patient is treated with increased pharmacologic sedation, the patient will appear more comfortable as the spontaneous respiratory drive is suppressed, but the patient will probably require a more prolonged mechanical ventilation. The ideal therapeutic option is to improve the trigger sensitivity to allow the patient to freely interact with the ventilator.

Flow asynchrony results when a patient does not receive the inspiratory flow he or she desires at any point during inspiration. Flow asynchrony is most commonly seen in modes that have a square wave, constant inspiratory flow pattern. Although the synchrony may be improved by increasing the set inspiratory flow in a constant-flow mode, this most commonly results in increased PIP. A better option to treat flow asynchrony is to change to a mode that uses a variable, decelerating inspiratory flow pattern. With a variable flow pattern the inspiratory flow is better matched with the patient’s demand throughout the breath.

In summary, it is important to optimize the patient-ventilator interaction by optimizing the ventilator settings before resorting to sedation. Sedative use in the first 24 hours of weaning from mechanical ventilation influences the duration of mechanical ventilation and extubation failure in infants and children.27

Low Tidal Volume Ventilation

The ARDS Network reported in 2000 that with ALI/ARDS patients, mechanical ventilation with a VT of approximately 6 mL/kg resulted in lower mortality and fewer ventilator days than a more traditional VT of 12 mL/kg.28 The mortality rate was 31.0% in the low-VT group and 39.8% in the high-VT group (p = 0.007). Additionally, the plateau pressure was significantly lower in the low-VT group on days 1, 3, and 7. This study was limited to adult patients (average age approximately 51 years). However, the results are very likely to be applicable to pediatric ALI patients. Until a similar large-scale, prospective, randomized trial is performed with infants and children, it seems reasonable to follow the low-VT guidelines. It should be emphasized that the low-VT data were obtained from ALI patients, and it remains uncertain whether larger VT can be safely used in patients with normal lung function (ie, those intubated for nonpulmonary reasons).

Tidal Volume Determination

To successfully accomplish low-VT ventilation it is essential to know the exact VT that is delivered to the lungs. Conventional ventilator displays of exhaled VT are clinically used to indicate the delivered VT. Some ventilators use a pneumotachometer to measure expired VT at the ETT, whereas others measure VT at the ventilator’s expiratory valve. VT measurements at the ventilator’s expiratory valve might not be able to compensate for the compliance of the ventilator circuit nor for uncontrolled clinical variables, including secretions, changes in humidification, changes in temperature, condensation, in-line suction devices, and end-tidal carbon dioxide monitor adapters. Theoretically, a VT measured with a pneumotachometer positioned at the ETT is a more accurate and reliable measurement of the VT actually delivered to the patient’s lungs than is a VT measured at the ventilator expiratory valve. This issue may not be clinically important for large pediatric patients and adult patients, but may be very important for infants and small children.

An alternative to placing a pneumotachometer at the ETT is to use a mathematical model to estimate the volume of gas delivered to the ETT (calculated effective VT). Theoretically, the effect of the circuit compliance on the accuracy of the VT measurement made at the ventilator expiratory valve can be mathematically eliminated without requiring a pneumotachometer. Effective VT is calculated by subtracting the VT “lost” to the ventilator circuit from the VT displayed by the ventilator.29 The effective VT has traditionally been defined as the ventilator-measured VT minus the volume “lost” because of the distensibility of the ventilator circuit. That is:

$$\text{Effective } VT = \text{ventilator expired } VT \quad - (\text{circuit compliance } \times (\text{PIP} - \text{PEEP}))$$

The compliance of a ventilator circuit can be obtained from the manufacturer or calculated from pressure and VT measurements at both ends of the circuit. However, more elaborate equations are required to estimate the effects of the other variables in the ventilator circuit (eg, temperature, condensation, secretions, in-line suction devices).

The difference between the ventilator-determined VT, the pneumotachometer-determined VT, and the calculated effective VT may be clinically important. The ventilator circuit compliance is particularly relevant in determining the actual volume that enters the lungs of neonates, infants, and small children, given the overall small VT. Knowing the exact delivered VT is essential when ventilating
infants, because the volume “lost” to the distensibility of the circuit can be equal to the desired $V_T$.

Cannon et al reported that with infants ventilated using a neonatal ventilator circuit the expiratory $V_T$ measured at the ETT is on average only 56% of that measured at the ventilator.30 Somewhat better correlation was seen in pediatric patients ventilated with a pediatric circuit: the average $V_T$ measured at the ETT was 73% of that measured at the ventilator expiratory valve.

Additionally, Cannon et al demonstrated that the basic correction equation listed above is not sufficient.30 The study found a poor correlation between the calculated effective $V_T$ and the exhaled $V_T$ measured by the pneumotachometer at the ETT. All of the ventilator circuit variables listed above can compromise the accuracy of the calculation by adding uncontrolled and variable dead space to the circuit. However, it must be noted that some new-generation ventilators include more advanced calculations that might calculate $V_T$ delivery more accurately and obviate the pneumotachometer at the ETT. The accuracy of these advanced software calculations has not yet been fully tested in the clinical setting.

Especially with infants and small children, inaccuracies in $V_T$ measurement may have important adverse clinical consequences. The young patient may be at high risk for ventilator-induced lung injury, hypoxia, and hypercapnia if the actual volume entering the lungs is not accurately measured.31–36 If the $V_T$ is inappropriately small, atelectasis and ventilation-perfusion mismatching may occur.34 If atelectasis develops, increased mean and/or peak airway pressures may be required to recruit the collapsed lung regions, potentially leading to increased shear injury and barotrauma.34–35 Although atelectasis can be overcome by “simply” increasing the $V_T$ and/or the PEEP, the $V_T$ that must be set on the ventilator to deliver the appropriate volume remains unknown.

Additionally, even before atelectasis develops, the clinician may attempt to compensate for the discrepancy in the $V_T$ measured in the ventilator by increasing the set limit for each breath ($V_T$ or PIP), as determined by chest auscultation. However, overcompensation may occur, causing excessive delivered $V_T$ and ventilator-induced, iatrogenic lung injury.31,32,34,36,37 Ventilation with excessive $V_T$ results in disruption of the pulmonary architecture.35,38

A pneumotachometer placed at the ETT (either connected to the ventilator or a stand-alone respiratory mechanics monitor) offers a reliable measurement of the delivered $V_T$ and may help to minimize iatrogenic lung injury in infants and small children.39,40 Additionally, optimizing the actual delivered $V_T$ may help to limit intrathoracic pressure and potentially minimize secondary cardiovascular and neurologic adverse sequelae.26,39–41

### High-Frequency Ventilation

High-frequency ventilation is defined as ventilation that delivers a $V_T$ that is less than the dead space volume. Additionally, the respiratory rate in pediatric HFV is defined as $> 150$ breaths/min. The concept of HFV is not new. In 1915 Henderson and Chillingworth described the theoretical effects of a rapid ventilatory rate on gas exchange.42 In 1952 Emerson patented the first high-frequency device for clinical use,42 and in 1972 the first high-frequency oscillator was described by Lunkenheimer.43 The theoretical advantage of HFV is that it maintains an open lung with the use of relatively high mean airway pressure but low phasic volume and pressure changes. This concept was well demonstrated over a decade ago by Kinsella et al, who reported that optimizing functional residual capacity in a manner that promotes lung inflation and minimizes cyclical stretch of the lungs attenuates ventilator-induced lung injury.44

Although most ALI patients are adequately oxygenated and ventilated with conventional mechanical ventilation, there is a subset of ALI patients who require “excessive” PIPs with conventional ventilation to maintain lung recruitment. With these patients HFV may prevent or minimize ventilator-induced lung injury.45,46 Arnold et al demonstrated in a multicenter, prospective, randomized study that despite the higher mean airway pressure, high-frequency oscillatory ventilation (HFOV) was associated with less chronic lung disease, as indicated by less need for supplemental oxygen at 30 days and better outcome than with conventional ventilation.45 This study additionally demonstrated that among patients who were ventilated with HFOV and survived, the risk of chronic lung disease was associated with the duration of conventional ventilation before initiation of HFOV. However, although this important study demonstrates the potential benefit of HFOV for pediatric ALI and ARDS, it should be noted that the study analyzed a limited number of patients ($n = 58$).

The pressure-volume curve in Figure 5 illustrates the potential lung-protective advantage of HFV.47 Below the lower inflection point, low lung volumes, derecruitment, and atelectasis result in ventilator-induced lung injury with every breath, as the lung is opened by the delivered $V_T$ and then allowed to collapse (atelectrauma). Above the upper inflection point, ventilator-induced lung injury occurs as alveoli become overdistended (volutrauma). HFV allows gas exchange to occur between the upper and lower inflection points and, theoretically, minimizes ventilator-induced lung injury.

Although various high-frequency devices are used with neonates, the most frequently used device for pediatric ALI and ARDS is the SensorMedics 3100A oscillator, which was the first such device approved (1995) by the United States Food and Drug Administration (FDA) for
early intervention in pediatric respiratory failure. For pediatric ALI and ARDS patients who weigh >35 kg, the SensorMedics 3100B oscillator (which received FDA approval in 2001) can generate a greater power output and can function at a higher bias flow to allow for more efficient ventilation in these larger patients.

One of the more difficult clinical decisions concerning HFOV is when to initiate it. Although there are no clear guidelines, a recent publication reviewed the use of HFOV in 290 pediatric patients over 18 months at 10 tertiary care pediatric ICUs.48 On average, HFOV was initiated in patients who did not have prior lung disease when the PIP on conventional ventilation was $34.2 \pm 7.9$ cm H$_2$O, and the oxygenation index (OI) was $27.5 \pm 14.1$. The OI was calculated as:

$$OI = \frac{P_{aw} \times F_{I02} \times 100}{P_{aO2}}$$

in which $P_{aw}$ is mean airway pressure and $F_{I02}$ is fraction of inspired oxygen. For patients who had prior lung disease PIP was $34.2 \pm 7.5$ cm H$_2$O, and OI was $28.7 \pm 16.1$. These relatively high oxygenation indices for initiation of HFOV are in contrast to the FDA approval of the oscillator as an early intervention device. Based on the previous study by Arnold et al, earlier use of HFOV may improve outcome for pediatric ALI patients by minimizing ventilator-induced lung injury.45 However, it must be noted that no study has been done with pediatric patients to compare HFOV to conventional ventilation with an “open lung strategy” and low $V_T$.

The most recent HFOV study by Arnold et al represents the largest series of pediatric patients receiving HFOV, and, thus, the results help to define the current utilization patterns of HFOV and to predict outcome for subgroups of patients.48 In this study immunocompromise was associated with a significantly higher mortality risk. Patients with sepsis and ALI had a higher risk of chronic lung disease than nonseptic ALI patients. Overall, patients who demonstrated a minimal therapeutic response within the first 24 hours of HFOV had an extremely high mortality risk.

With the growing use of HFV the term “nonconventional ventilation” is becoming a misnomer. There is no longer anything nonconventional about HFV. HFOV has been an FDA-approved mode of ventilation for more than a decade and thus should now be considered another conventional ventilation mode.

**Weaning from Mechanical Ventilation**

A major difficulty involving definitions continues to exist with regard to weaning from mechanical ventilation. Some clinicians define weaning as the decrease of ventilatory support in preparation for imminent extubation; other clinicians state that weaning should be initiated as soon as a patient is intubated. The current, generally accepted philosophy is that it is necessary to gradually wean the patient from mechanical ventilation implemented because of respiratory failure, to retrain their respiratory muscles. Whether this philosophy is actually supported by scientific data remains controversial. In 1987 Hall and Wood disagreed with the traditional view and suggested the term “liberation from mechanical ventilation.”49 It is becoming more evident that many patients who have been traditionally weaned over the course of days can be rapidly extubated without complication.50 Thus, the traditional view of a gradual weaning process is being questioned.

Regardless of whether a patient is “weaned” or “liberated” from mechanical ventilation, the goal should be to minimize the duration of ventilation for every patient. Prolonged mechanical ventilation is associated with prolonged ICU stay, prolonged hospital stay, higher costs, higher risk of nosocomial pneumonia, progressive ventilator-induced lung injury, airway injury, excessive pharmacologic sedation, and possibly higher mortality.51–54 Thus, minimizing the duration of ventilation is clinically important. On the other hand, discontinuing ventilation prematurely can necessitate reintubation, which is associated with similar complications.

The optimal weaning process can be a clinically difficult balance between minimizing the duration of mechanical ventilation and decreasing the risk of reintubation. This clinical balance plays a very important role in the management of critically ill infants and children in ICUs every day.

**Protocol Versus No Protocol**

Despite the use of mechanical ventilators in ICUs every day, the ideal method to wean infants and children from...
respiratory support has only recently been studied.\textsuperscript{27,55} Traditionally, weaning methods for children have been extrapolated from studies with adults and premature neonates. The unique aspects of pulmonary physiology, respiratory mechanics, and the epidemiology of ALI in infants and children make it unlikely that strategies extrapolated from other populations will be effective.\textsuperscript{56} The duration of weaning is usually shorter with infants and children because they have healthier baseline lung function than adults, so recovery from a pulmonary insult is usually more rapid.

Studies with adult patients have demonstrated that when protocols are used to guide ventilator weaning, the duration of ventilation is significantly less than when care is guided by individual clinician practice.\textsuperscript{57,58} However, currently there are no generally accepted weaning protocols for children, and the lack of evidence on optimal use of weaning techniques results in great variability in the way they are clinically utilized.

A recent randomized, prospective study by the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network was designed to study protocol weaning versus nonprotocol weaning in a population of children with ALI.\textsuperscript{27} The use of weaning protocols in the population of infants and children studied had no impact on the duration of mechanical ventilation. This is in direct contrast to the available data from the adult population.\textsuperscript{57,58} An important difference between adult and pediatric patients is the shorter duration of weaning with infants and children. In the PALISI study the mean duration of weaning was only 2.9 days (median 1.7 d) in the protocol groups and 3.2 days (median 2.0 d) in the control group.

### Extubation

Similar to the situation with weaning, the ideal extubation timing for the ALI patient has been elusive, and the techniques used have traditionally been more art than science. As with weaning, extubation involves substantial risks; failed extubation increases the risk of pneumonia, prolongs ICU stay, increases the risk of death, and increases costs.\textsuperscript{59–65} Over the last several years increased interest in this issue has led to important scientific results.

Predicting successful extubation of infants and children presents unique challenges to pediatric intensive care clinicians. Currently there are no widely accepted methods for predicting successful extubation in pediatric patients. Methods used to predict extubation in adults, such as the ratio of respiratory frequency to VT, the CROP (compliance, rate, oxygenation, and pressure) index, T-piece trial, and negative inspiratory effort measurements are either unreliable or not easily performed with children.\textsuperscript{66–68}

As discussed above, it is often difficult to obtain the ideal balance between minimizing the duration of ventilation and minimizing the risk of reintubation. Although the appropriate balance is often discussed with various answers, the largest series of pediatric patients studied to determine an expected failure rate for planned extubation was by Edmunds et al.\textsuperscript{69} The study was a retrospective chart review of 632 patients. The overall failure rate of planned extubations in that pediatric population was 4.9%. As expected, younger patients who underwent longer duration of ventilation were at higher risk for extubation failure.\textsuperscript{59}

A pediatric clinical study by Khan et al characterized multiple predictors of extubation failure.\textsuperscript{70} Unfortunately, these authors were unable to identify a single variable or formula for predicting the success of extubation with children and concluded that a combination of factors should influence any extubation decision.

Hubble et al evaluated the usefulness of pulmonary dead space measurements in predicting pediatric extubation outcomes.\textsuperscript{71} Dead space represents the portion of the pulmonary system that is not involved in gas exchange, including both airway dead space and alveolar dead space. Dead space is often expressed as the ratio of dead space to VT ($V_d/VT$), also known as the physiologic dead space ratio.

During the past 2 decades intensivists have identified several clinical applications for $V_d/VT$. In adult patients $V_d/VT$ has been used to reliably and quickly identify pulmonary embolism, monitor the effects of fluid infusion in intubated asthmatic patients, and measure the effects of bronchodilators in patients with chronic obstructive pulmonary disease.\textsuperscript{72–76} $V_d/VT$ has been identified as a predictor of mortality among neonates suffering congenital diaphragmatic hernia,\textsuperscript{77} and it has been used to detect pulmonary shunt in congenital heart patients\textsuperscript{78} and to determine pulmonary improvement in patients supported with extracorporeal membrane oxygenation.\textsuperscript{79} Since $V_d/VT$ has proven reliable in assessing the progression of lung disease, it would also be expected to correlate with the regression of lung disease.

Traditionally, $V_d/VT$ was measured by collecting expired gas. Recent advances in computer and capnography technology simplified the calculation of $V_d/VT$ from single-breath carbon dioxide waveforms. Hubble et al\textsuperscript{71} successfully identified $V_d/VT$ values predictive of extubation success and failure for infants and children, using single-breath carbon dioxide measurements. $V_d/VT$ values $\leq 0.50$ at the time of extubation were associated with extubation success, and $V_d/VT$ values $> 0.65$ were associated with the need for additional respiratory support following extubation.

A recent multicenter pediatric ALI trial used objective criteria to determine extubation readiness by protocol ver-
sus by physician judgment in the no-protocol arm of the study. Objective criteria did no better than physician judgment in determining which patients could be successfully extubated. The average extubation failure rate was 19% using an extubation readiness test and 17% using physician judgment. These failure rates are consistent with some previously reported rates in the literature. However, other reports quote reintubation rates as low as 5%. Differences between inclusion and exclusion criteria in these clinical studies, specifically the issues of upper airway obstruction and minimal duration of ventilation, make comparison of these reports difficult. Additional difficulties are the somewhat subjective nature of the decision as to whether a patient has failed extubation, the variable use of NIV to help avoid reintubation, and the variable time frame that patients are followed after extubation. Published extubation failure rates in adult studies range from 1.8 to 18.6%. It should be noted that all of the extubation readiness tests presented above for the pediatric and adult population test only the patient’s pulmonary status. The patient’s overall clinical status must be considered before a patient is extubated. Neurologic considerations include the patient’s sedation status, ability to protect the airway, and acceptable intracranial pressure. Cardiovascular considerations include the degree of inotropic support, the presence of hemodynamic stability, and the anticipated effects of increased respiratory effort on cardiac function. Additional considerations include the presence of an air leak around the ETT and the resolution of the underlying process that necessitated intubation.

Summary

The field of pediatric mechanical ventilation has advanced dramatically over the last decade. During this period many changes have occurred and continue to occur. Noninvasive ventilation is being used at an increasing rate to obviate invasive ventilation in a subgroup of patients with impending respiratory failure. More data are needed to help define which acute respiratory failure patients are most likely to benefit from noninvasive ventilation.

The importance of monitoring the patient-ventilator interface is more fully appreciated today than ever before. Optimizing patient-ventilator interaction is essential to minimizing adverse effects. The use of HFOV for pediatric ALI is now commonplace. However, HFOV is still often started late in the course of pediatric ALI, and earlier initiation of HFOV may help minimize ventilator-induced lung injury and improve outcomes. As the use of HFV continues to increase, this mode of ventilation should be considered another form of conventional ventilation, as its use is no longer “nonconventional.”

Many pediatric patients can be “liberated” from mechanical ventilation without a long weaning process. Although protocol-guided weaning has been successful with adults, this has not been demonstrated to be true for pediatric ALI patients. Recent data support the view that there may be objective extubation predictors and criteria for pediatric patients.

The most important issue affecting the field of pediatric mechanical ventilation is the need for multicenter, randomized, prospective studies. In the past decade the field of pediatric mechanical ventilation has progressed dramatically. With increasing research efforts this progress should be anticipated to continue.

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Discussion

Donn: Very nice presentation, Ira. I would mirror your comments about weaning and extubation as they apply to neonatal and mechanical ventilation. I think if you look in the index of either of the 2 leading textbooks on neonatal/perinatal medicine, you don’t find the word “weaning” appearing at all. Maybe part of the issue with the big trial that you presented is that it was a trial.

What I have found is a parallel with what we were all taught as pediatric residents—if you think about a spinal tap, you ought to do it. Weaning is the same way. You have to think about it. What we try to convey to our pediatric trainees is that weaning begins immediately after intubation. The idea is to get the patient off the ventilator as rapidly as possible, but, obviously, without jeopardizing well-being in the postextubation phase.

We’ve seen a very dramatic change in our very-low-birth-weight babies; in the past there was enormous reluctance to extubate a baby who was < 1,000 g, for reasons that totally baffle me. But now we’re seeing 600–800 g babies extubated very early in the course of the disease and maintained on continuous positive airway pressure or nasal cannula oxygen, with surprisingly good success, so I think it’s still our last frontier. But the take-home message is, you’ve got to think about it to do it.

Cheifetz: I fully agree with you. In the weaning study by Randolph et al1 no difference was found between protocol weaning and non-protocol weaning. Your point is excellent. There were a substantial number of inclusion and exclusion criteria, and the subgroup of patients studied might be
a relatively small subset of the total group of patients. Additionally, upon entry into the study the patients already had resolution of the acute phase of the illness. So, I agree, the results of any study really depend on the details of the specific population you are investigating, how you are studying the question, and how you extrapolate data from one study to all of pediatrics.

REFERENCE


Kercsmar: You mentioned the importance of using NIV, or at least trying it, and that one advantage is the possibility of using NIV outside of the ICU; it might be less expensive, more comfortable for the patient, and offer more options. One difficulty we’ve had is that that’s often easier said than done. At our institution the rules require that patients who might need various forms of noninvasive mechanical ventilation must go to the ICU unless they are at the chronic and stable stage. Would you expand a bit about NIV criteria and what you mean by “sites outside of the ICU” that would permit safe and effective use of NIV?

Cheifetz: It is difficult to set exact criteria of what can be done in the various clinical care locations within a hospital. Early in our NIV program we did all of our NIV in the ICUs. Now we also use NIV in our step-down unit, our pediatric wards, and in our bone marrow transplant ward. So we’ve expanded NIV out of the ICU to more effectively utilize our resources.

And we do have objective criteria for the use of NIV in these various settings. Patients outside the ICU must be clinically stable. They cannot be requiring increasing noninvasive support. Any increase in support beyond minimal titrations warrants a trip to the ICU. We also have FiO2 requirements. Any patient who has an escalating FiO2 requirement or an FiO2 > 50% must be moved into the ICU. Beyond the ICU, noninvasive ventilation must be used as a respiratory assistance device and not as a life support device. Or stated differently, the non-ICU patient receiving NIV must be able to tolerate disconnection from the ventilator for a reasonable period of time. The use of NIV outside the ICU requires protocols and guidelines to provide safe and effective care.

Black: Regarding weaning criteria, the rapid shallow breathing index that’s commonly used with adults seems to work very well with all different situations where intubation and mechanical ventilation are required, including lung disease, trauma, closed head injury, and other conditions. The majority of intubated patients in our pediatric ICU have closed head injuries from motor vehicle accidents. Do you think Vd/Vt will work with those patients?

Cheifetz: With adult patients the rapid shallow breathing index works extremely well for predicting successful extubation. In pediatrics it fails miserably because there are so many additional variables that affect respiratory rate, including the patient’s fear when awakening in a strange setting. So I don’t think the rapid shallow breathing index is useful in pediatrics.

In terms of the Vd/Vt, one of the key points concerning predicting the success of extubation is that it only considers the pulmonary process. However, in a patient with a closed head injury, in which the primary issue is neurologic, the Vd/Vt will not be useful at all.

REFERENCE


Myers: Referring to the measurement of pressure, volume, and flow, in some of the studies that we’ve done, pumping gas from a calibrated syringe through a pneumotachograph, adult pneumotachographs seem to be fairly accurate and have good precision. The smaller, infant pneumotachographs, while they’re very precise, they all seem to have a built-in inaccuracy to them, which scares me about using volume-targeted ventilation in the neonatal ICU.

The second issue is that in the majority of our patients we’re using uncuffed ETTs, so there is an air leak between the ETT and trachea. Where is the cutoff point at which we should stop believing all the pulmonary mechanics measurements (compliance and resistance) with which we’re trying to make treatment decisions? We often have patients who look much better from the perspective of pulmonary mechanics, but if the system has a 35% leak, then the pulmonary mechanics monitor is practically a random number generator!

Cheifetz: Those are important clinical issues. The clinician must consider the detailed specifications and accuracy of the monitoring device. Most of the pneumotachometers that we use in the pediatric ICU have accuracy and precision well within clinical acceptability. With neonates and small premature infants I don’t have enough experience to comment on whether the devices are accurate or precise enough. In terms of air leak it is a difficult question, a huge ques-
tion. The data I presented about $V_T$ measurements specifically represented exhaled volumes, to avoid the issue of air leak. The underlying question is, what is an acceptable air leak? I think if we ask everyone in this room, “what is an acceptable air leak?” we would probably have 20 different answers concerning (1) clinical management and (2) respiratory mechanics measurements.

A question you did not mention is, when do you monitor respiratory mechanics in small neonates? When you consider some of the variables in this population, it becomes apparent that the compliance of the ventilator circuit can be greater than the compliance of the patient’s lungs, so it becomes a difficult question. There are huge number of questions and research projects that need to be answered before we can come to any kind of conclusion.

**Hansell:** With HFOV, especially with larger patients, when we get into high distending pressures, we increase the potential to damage the lungs, which releases many mediators that actually increase the negative effect of being septic. In septic patients we may actually be increasing the morbidity and mortality if we use HFOV improperly. I think that is another reason we ought to consider implementing HFOV very early in the course of disease.

The other factor is that $\Delta P$ (the change in pressure) is less attenuated as we get into larger ETTs. The larger the ETT, the more like conventional ventilation HFOV becomes. Whether that is important and whether we should put them on HFOV, I don’t know. Nevertheless, I think we need to be aware that when we use large $\Delta P$ and high mean airway pressure we may actually be closer to ventilating them as we would if they were on a conventional ventilator at a high respiration rate.

**Cheifetz:** That is an important point. You can’t really compare a large adult patient who’s using a large ETT to a small infant who’s using a small ETT, because the changes in pressure can be attenuated much more dramatically in a smaller patient. I would say, and we have investigated this in bench studies, that even with large ETTs and large amplitudes on HFOV, pressure amplitude is still dramatically attenuated. Although $\Delta P$ is larger than in very small patients, the $\Delta P$ that is delivered to the adult ARDS patient is still going to be dramatically less than the $\Delta P$ on a conventional ventilator, any way you look at it. So I still think HFOV is a lung-protective strategy in all patient populations—all sizes and all ages.

**Salyer:** I think there is compelling evidence from animal tests and growing evidence from tests with humans that what causes ventilator-induced lung injury, at least the mechanical injury, as opposed to biochemical injury, is overdistention of the lung, which is a volume-related phenomenon. If you give the same $V_T$ with 2 different flow patterns, at the end of inspiration you have the same volume in the lung, and the differences in airway pressure between the 2 flow patterns are just a result of the resistance to flow during the breath. So it’s unclear to me why such a reduction in peak pressure would offer any benefit to the patient.

**Cheifetz:** There are a couple of issues here. Yes, I agree that if you overdistend the lungs, you can cause volutrauma. But if you are attempting to compare 2 different flow patterns at the same $V_T$, and that $V_T$ is within acceptable limits (ie, the lungs are not overdistended), then the issue is probably different. If you can deliver the same 6 mL/kg $V_T$ at a lower peak inspiratory pressure, I think you are less likely to cause barotrauma and secondary lung injury. I must admit, though, that I don’t have convincing data to support this theoretical point, and I do not know if there are data in the literature that address the issue. It begs further study.

**Rotta:** I second your enthusiasm for HFOV for pediatric ARDS patients. HFOV is not a fad and it is not a nonconventional strategy. Centers that have used HFOV for a while are comfortable with it and are using it earlier and earlier in the course of disease, and are seeing good results, as you see in your service at Duke and as I see in Buffalo. I think the problem we are seeing now in gaining more acceptance of HFOV is that centers that are just beginning to use it are going through the problems of learning and mastering the new technology—technology that when not used properly can give results that are interpreted as bad outcomes, such as hypoxemia. In addition, centers that are reluctant to start HFOV until the patient is moribund will continue to see bad results because HFOV will not resurrect someone who is near death.

Now, addressing the previous comment on whether you still have lung protection during HFOV with the bigger patient, who has lower respiratory rate and a larger ETT, there are now good data suggesting that lung protection persists in adult ARDS patients ventilated with the SensorMedics 3100B ventilator. These adult patients are being ventilated using the same principles that have been applied to neonatal and pediatric patients for years.

**REFERENCE**

Cheifetz: I agree. The important point, as you mentioned, is education. The SensorMedics 3100B is not a new device: it was originally FDA-approved in 1991. However, with any device new to a specific institution there will be a learning curve. I would say again that I think HFOV is today a conventional ventilation mode, but centers that don’t have substantial experience with HFOV will have to learn to apply it most efficiently.

Wagener: I totally agree that high-frequency should be considered conventional ventilation now; about the terminology we could argue one way or another. But I’d point out that it’s not appropriate to extrapolate from a limited-size study in a limited number of centers and with a select population and make the statement that no further randomized, controlled study needs to be done, especially knowing that in the adult studies of HFOV there has not been the success that we’ve seen with babies. And in pediatrics we’re covering the whole spectrum of patients in between. It may be that we have certain situations that were selected for in that reasonably planned study in which HFOV was effective, and we also have other situations that were not included in that study for which it’s not going to be proven as effective. So HFOV, whether you call it conventional or something else, it’s one standard form of ventilation.

Cheifetz: I need to clarify something I said. I do believe it is important to have another larger, multicenter, randomized, prospective, controlled trial investigating HFOV for pediatric ARDS. I think such a study would be important, especially if both the intervention and control groups used alveolar recruitment maneuvers. My point is that I don’t believe that will ever occur. I do not think that there will be enough centers with expertise in HFOV that would agree to participate in a randomized, controlled trial, without crossover. I am not sure if a crossover trial would fully address your concerns. Some centers might raise ethical concerns with randomizing patients away from a technique (ie, HFOV) that is in clinical practice and in the medical literature is an approved, established therapy. Whether that is right or wrong I do not know.

Wiswell: The other side of the ethical issue is that if we don’t do that trial, many centers are not going to start using HFOV, because they will not believe there is adequate evidence that it works, and so their patients will not receive the benefit of our knowledge that HFOV does work and ought to be the standard of care. Though I’m a firm believer in HFOV, I’m not sure the existing data are going to convince a lot of people that HFOV works. Steve Donn and I are long-time New York Yankee fans and remember the saying of Yogi Berra, “It’s déjà vu all over again.” I say that because embracing new treatment technologies, such as high frequency oscillation, without validation by randomized, controlled trials has happened all too frequently in neonatology.

Cheifetz: This is a hard issue. How do you perform a study with a technique that has become an accepted standard clinical practice? I am not saying it is correct that it is an accepted, standard clinical practice. But once a technique is widely accepted, it is hard to convince enough centers to go back and study it.

Wagener: Maybe at your center that is true, but remember that there are other centers at which it’s not standard practice and a study could be performed.

Donn: Aren’t we lucky that Alexander Fleming’s first patient didn’t develop anaphylaxis to penicillin?

Rotta: I think this is going to be one of those cases when we pediatricians are going to follow the results of adult studies that learned from techniques that were applied in pediatrics first.

Cheifetz: Let me go out on a limb here and ask a question of everyone in the room. If there were a proposed randomized, controlled, prospective trial of HFOV versus conventional ventilation in pediatric ALI/ARDS without crossover (which is what the study design probably would need), who here would enroll patients, knowing that your patient might be randomized to the control group (ie, could not use HFOV)? Who here would do that?

Wiswell: If I were a pulmonologist and not a neonatologist, I would.

Cheifetz: Who would like to answer my question? One hand. Two? Just a couple. It is a small minority of the people in the room.

Wiswell: I’ve been involved in a lot of large randomized, controlled trials that have examined therapies that my colleagues and I truly believed in, but—damn!—the randomized, controlled trial showed there was no difference between the “magical” new therapy and controls! The marvelous thing about a large, randomized, controlled trial is that if there is a difference, you’re going to see it. But if there’s not, you’re going to see that there’s not. Equally important is that potential complications are going to rear their ugly heads too. I was in Texas in 1984, in the baboon lab helping develop the first-generation high-frequency oscillator, and I’m a firm believer in it as an effective therapy. But you’ve got to prove it is effective, and you’ve got to prove it on a large scale.
Cheifetz: Fine. But for HFOV there are randomized, controlled, prospective studies. There are studies in the neonatal population. In John Arnold’s study, admittedly, the number of patients was relatively small, but it is a good, randomized, controlled trial.1,2 And recently published adult studies support the use of HFOV in adults.3–6 It’s not as if oscillation is being used without any randomized, controlled studies. There just has not been a large pediatric study. The published pediatric investigation was smaller, and we may have to extrapolate data for pediatrics from the neonatal and adult populations, as Dr Rotta mentioned earlier.

REFERENCES

Rotta: Once you start studying the effect of more than one lung-protective strategy in a clinical trial, it is even harder to show that one strategy is better than another. That’s why, for instance, liquid ventilation is not approved and probably will not be approved, since it has been studied in the era of lung-protective conventional ventilation. It is very hard to show separation between 2 groups in clinical trials when both are subjected to some form of lung protection.

Just for illustration, in the successful ARDS Network trial,1 although the entry V\textsubscript{T} was approximately 10 mL/kg, the low-V\textsubscript{T} group received 6 mL/kg, whereas the V\textsubscript{T} in the conventional treatment group was increased to 12 mL/kg. This was not done by chance, but to provide separation between the 2 groups,1 which had not occurred in a previous trial.2

In the laboratory HFOV does not appear to be superior (purely from a lung-injury standpoint3–4) to a conventional ventilation strategy using the open-lung approach used by Dr Amato in Brazil,5 although animals treated with HFOV have more stable hemodynamics.3,4 Throw these 2 strategies into a clinical trial and your differences get even more dilute. Compare HFOV with the conventional ventilation (control) group of the Amato trial5 and HFOV would probably look really good. But no one would do that study now. It is all a matter of timing.

REFERENCES

Wagener: But you can’t say that there’s one approach that has a clear advantage over another until you have tested your hypothesis.

Cheifetz: That’s correct, but what I’m saying is that HFOV should be considered as another mode of mechanical ventilation. I think everyone in the room would agree that there has not been any published study that demonstrates that a particular mode of ventilation, whether it be volume-control, pressure-support, pressure-regulated volume-controlled, or pressure-control, significantly affects outcome for a given patient population. My point is that the oscillator should be viewed as another mode of standard ventilation, not a nonconventional “rescue” or “heroic” therapy. It should be viewed as a conventional ventilation therapy. You are correct, Dr Rotta: if we performed a head-to-head comparison of HFOV and the open-lung conventional strategy, no one knows what the results would reveal. But from the available published studies and clinical experience, I do not believe there are any important adverse effects associated with HFOV. There is obviously a fair amount of debate and controversy in this room, and I would then go out on another limb and challenge someone in this room to coordinate the study. I am a little skeptical about how many centers would participate and how many patients would be enrolled.
Donn: Maybe what we need to do is just expunge the word “conventional.” In the past it was used to talk about things that were done conventionally. What we need to do is just talk about tidal ventilation versus nontidal ventilation, and then we get away from what’s conventional and what isn’t.

Cheifetz: I guess the biggest problem I have with the whole discussion is the use of that term “nonconventional.” The take-home message I want to send is that HFOV is no longer nonconventional ventilation. It is conventional ventilation.

Black: I don’t think you’re ever going to get away from the use of the term “nonconventional” because, let’s face it, when you use what we call “conventional” ventilation, we do everything we can to make that conventional ventilation mimic our own natural spontaneous ventilation. And there is nothing about HFOV (unless you want to talk about panting dogs) that mimics normal spontaneous ventilation. But that’s not to say that it isn’t a superior therapeutic technique in certain clinical situations. I’m a very strong believer in early use of HFV.

Cheifetz: Let me comment on that point before you continue. My comment is, if you think about spontaneous normal breathing, everyone in this room is breathing using what? Negative-pressure ventilation! So, to use your definition, positive-pressure “conventional” ventilation is really nonconventional!

Black: Well, you’re right—absolutely correct! But it’s closer to conventional ventilation than HFV. I think a clinical trial of that nature, without the potential for crossover, may border on unethical today. The study that you showed, even with the crossovers, showed very clear statistically significant results. My point is that with sophisticated statistical techniques, things like crossovers, which obviously do muddy the waters, can be gotten around. There are also statistical techniques that allow you to continuously analyze the data as they are being gathered, and when you reach the point of significance, you can stop the study. These techniques were widely used by the pharmaceutical industry, but they haven’t really made their way into testing of ventilators.