Review

Invasive Mechanical Ventilation: When and to whom?

Indications and complications of Invasive Mechanical Ventilation

Danai Theodoulou[1], Emmanouil Alevrakis[2], Marianthi Iliopoulou[3], Theodoros Karampitsakos[4], Matthaios Katsaras[5], Stamatios Tsipilis[1], Konstantinos Tzimopoulos[6], Antonia Koutsoukou[1], Nikoletta Rovina[1]

[1]ICU, 1st Department of Respiratory Medicine, Medical School, National and Kapodistrian University of Athens and "Sotiria" Hospital for Diseases of the Chest, Athens, Greece
[2]4th Department of Respiratory Medicine
[3]7th Department of Respiratory Medicine
[4]5th Department of Respiratory Medicine
[5]6th Department of Respiratory Medicine
[6]2th Department of Respiratory Medicine, "Sotiria" Hospital for Diseases of the Chest, Athens, Greece

ABSTRACT

Although emergency endotracheal intubation and mechanical ventilation (MV) are undoubtedly a life-saving intervention, deciding when and whom to support remains challenging. Common indications include respiratory failure, shock, coma and operative procedures that require analgesia and sedation. Endotracheal intubation is well known for its potential difficulty and mechanical ventilation is associated with complications that may aggravate the critically ill patient. Although MV is used in intensive care units in order to maintain adequate gas exchange and decrease the work of breathing, these goals may be difficult to achieve if there is no proper interaction between patient and ventilator (patient-ventilator asynchrony). Therefore, it is important that clinicians suspect, recognize and resolve appropriately any adverse consequence associated with this intervention. Finally, with the widespread use of mechanical ventilation, ethical challenges arise; patients with terminal illnesses can be kept alive, with little to no prospect of having their underlying condition cured or improved. Of paramount importance is for chronically ill patients to partake in the decision to institute or withhold MV after being appropriately informed for its indications and limitations.

Pneumon 2020, 33(1):13-24.

Key words:
- Invasive mechanical ventilation
- indications
- complications

Correspondence to:
Danai Theodoulou
ICU, 1st Department of Respiratory Medicine, Medical School, National and Kapodistrian University of Athens and "Sotiria" Hospital for Diseases of the Chest, 11527 Athens, Greece
E-mail: danai.theodoulou@gmail.com

INTRODUCTION

The decision to intubate and apply mechanical ventilation to a patient is often challenging. Questions such as ''who and when'' remains a matter of ongoing debate. It is generally suggested that the patient should have a reversible underlying problem that can be resolved with the support of mechanical ventilation[1]. However, the decision to initiate MV should be based upon clinical judgment, that considers the entire clinical situation.

Summarizing the main objectives of invasive ventilation these aim in:

- Improving gas exchange, reversing hypoxemia, preventing acute respiratory acidosis and increasing lung volume.
- Decreasing oxygen consumption by reversing fatigue of respiratory muscles.
- Improving ventilation-perfusion ratio with prevention and reversal of atelectasis and improvement of lung compliance.
- Prevent further Ventilation Induced Lung Injury (VILI) damage.

INDICATIONS FOR MECHANICAL VENTILATION

Respiratory failure

Generally, arterial partial pressure of oxygen (PaO2) of less than 55mmHg, despite the delivery of the maximal possible fraction of inspired oxygen (FIO2) is an absolute indication for intubation[1,2]. According to ERS/ATS guidelines bilevel Non-Invasive Mechanical Ventilation (NIV) is recommended for patients with acute exacerbation of COPD with respiratory acidosis (pH ≤7.35), and bilevel NIV or CPAP for patients with acute respiratory failure due to cardiogenic pulmonary oedema because it reduces the need for endotracheal intubation and mortality (strong recommendation)[3,4]. However, increased partial pressure of carbon dioxide (PaCO2) with arterial pH less than 7.25 despite optimum pharmaceutical support, controlled oxygen therapy and application of NIV is another indication for intubation[5]. Other respiratory signs strongly suggestive of intubation are signs of respiratory muscle fatigue, tachypnea, bradypnea or apnea with respiratory arrest and alveolar-arterial gradient of oxygen tension (A-a DO2) with 100% oxygenation of greater than 450 mm Hg. Over the last decade, high flow nasal oxygenation (HFNO) has been widely adopted by intensivists for hypoxemic acute respiratory failure and its physiological benefits have been demonstrated. According to multicenter RCT FloRALI study[6] that compared NIV, HFO and Oxygen mask for patients with non-hypercapnic acute respiratory failure, HFNO does not reduce intubation rate, but in post hoc analysis it shows significantly lower intubation rate for those patients with PaO2/FiO2<200. Moreover, high-flow oxygen therapy, as compared with standard oxygen therapy or noninvasive ventilation, resulted in reduced mortality in the ICU and at 90 days. Since guidelines regarding HFO for ARF do not exist, application of HFO should only be made in a controlled ICU environment in order to avoid late intubation and increased mortality.

Common diseases leading to inefficient gas exchange and need of intubation include Acute Respiratory Distress Syndrome (ARDS), COPD, Pneumonia, Asthma, Pulmonary Edema. In such cases, the effort required to maintain the elevated work of breathing may result in respiratory muscle fatigue and respiratory failure[7,8] Mechanical ventilation can take over some or all of the increased work of breathing, allowing the respiratory muscles to recover from their fatigue. Moreover, neuromuscular disorders, central nervous system (CNS) diseases, chest wall deformities, and drug overdose may result in alveolar hypoventilation due to reduced respiratory drive or respiratory muscle weakness.

Several lines of evidence highlight that timing of intubation is crucial and thus, if a patient is worsening despite optimal care, intubation should be considered early and not be delayed until the need becomes emergent[9]. The criteria for initiating mechanical ventilation are summarized in Table 1.

Shock

Patients with shock refractory to fluid resuscitation could benefit from mechanical ventilation. In particular, mechanical ventilation unloads the diaphragm, saving about 15% of the cardiac output, reduces oxygen consumption (VO_2), increases brain and renal perfusion and prevents respiratory arrest[10,11].

TABLE 1. Criteria for the initiation of invasive mechanical ventilation

	Criteria for MV	Normal values
Breathing rate (/min)	>35	12-20
Vt (ml/Kg)	<5	5-7
PiMax (cm H_2O)	weaker than -25	-75 to -120
VC (ml/Kg)	<10	
VE (L/min)	<10	
Gas Exchange		
PaO_2 mmHg	<60 (FiO_2≥0.6)	80-100 (21%)
PCO_2 mmHg	>60	35-45
A-a DO_2 mmHg	>350 (FiO_2=1.0)	25-65
Vd/Vt	>0.6	0.3-0.4

Vt=Tidal volume, Pimax=Maximal inspiratory pressure, VC= Vital capacity, VE=Ventilation

A-a DO_2=Alveolo-arterial oxygen difference, (Vd/Vt)=Dead space (Vd)/Tidal volume (Vt)

Coma

Every patient with Glasgow Coma Scale <8 should be intubated to protect the airway and avoid detrimental complications such as gastric fluid aspiration. The only exception is cases considered immediately reversible including hypoglycemia, opiate or benzodiazepine poisoning, thiamine deficiency, and acute alcohol intoxication[12].

Scheduled operative procedures

Operative procedures often require high doses of analgesia and sedation. Thus, patients need to be intubated for a short period[13].

Endotracheal Intubation: Advantages and contraindications

Mechanical ventilation in emergencies is usually applied through endotracheal intubation. The endotracheal tube bypasses and isolates the upper airways (up to the first third of the trachea). As a result, it protects the lungs from aspiration, releases airways from obstruction, reduces dead space and protects airways and stomach from positive pressures. Also, it enables aspiration of secretion and bronchoscopy. Finally, it ensures stable and secure patient-to-ventilation communication.

There are only relative contraindications to endotracheal intubation. These can be summarized into the following categories[14,15]:

- increased risk of cervical spine injury or known spine injury or neck immobility (e.g. arthritis)
- supraglottic or glottic pathology that prevents the placement of an endotracheal tube device e.g. blunt trauma of the larynx, anaphylaxia or burns
- trauma of the upper airway (e.g. hematoma) or possible difficulties due to patient's anatomic features
- Mallampati score classes III and IV which is the visual assessment of the distance from the tongue base to the roof of the mouth, and therefore the amount of space in which there is to work during direct laryngoscopy. A high Mallampati score is associated with more difficult intubation.

In all of the above cases, emergency cricothyrotomy is indicated. Other possible alternatives could be nasal intubation or surgical airway depending on the patient's needs.

Complications of Mechanical Ventilation

Mechanical ventilation is often a life-saving intervention but carries potential complications.

1. Complications associated with intubation and existence of the tracheal tube

Endotracheal intubation, although widely regarded as a life-saving intervention, is notorious for its potential complications, especially in critically ill patients. The state of critical illness suggests a priori overt physiological dysregulation. As a result, the patient is at increased risk of complete cardiovascular and respiratory collapse when exposed to agents for induction of anesthesia, the peri-intubation apnoeic period or subsequent positive pressure ventilation. Pre-oxygenation of the patient with a markedly disturbed PaO_2/FiO_2 can never be optimal and a patient already on a high dose of vasopressors to maintain an adequate mean arterial pressure will be subjected to further hemodynamic compromise during intubation. Up to 30% of intubations in the ICU result in failure of "first pass success", 25% experience severe hypoxemia (defined as SpO_2 <80%) during the intubation procedure and around 6% have a predicted difficult airway. Additionally, major airway events in the ICU result in a 60-fold higher incidence of death and brain damage than in the operative room[16]. Interestingly, the majority of complications associated with endotracheal intubation seem to be related to the period after intubation; 82% of the airway device incidents in intensive care in the UK, reported to the UK National Patient Safety Agency, were post-placement and included blockage or displacement of the tube[17]. The most common complications are summarized in Table 2[18-21].

2. Mechanical ventilation effect on cardiovascular system

Positive pressure ventilation (PPV) frequently decreases cardiac output, which may cause hypotension. Several mechanisms contribute to that.

Decreased venous return - Intrathoracic and right atrial pressure increase during positive pressure ventilation, thereby reducing the gradient for venous return. This effect is accentuated by applied positive end-expiratory pressure (PEEP), auto-PEEP, or intravascular hypovolemia[22].

Reduced right ventricular output –During PPV the pulmonary vascular bed is compressed and this increases pulmonary vascular resistance, thereby reducing right ventricular output. Applied PEEP artificially elevates central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) measurements[23].

Reduced left ventricular output – Increased pulmonary vascular resistance can shift the interventricular septum to the left, impair diastolic filling of the left ventricle, and reduce left ventricular output. In contrast to these adverse

TABLE 2. Complications during and after endotracheal tube placement

During Laryngoscopy	After Intubation
• Sore throat • Traumatic blunt injury to the structures of the mouth, nose, pharynx and larynx • Cervical Trauma • Intubation of a main stem bronchus (3-9%) • Intubation of the esophagus Aspiration of gastric content (8-19%) • Bronchospam • Prolonged hypoxia – Hypoxic brain injury • Tachycardia/Bradycardia • Hypertension/Hypotension • Cardiac arrest	• Laryngeal Injury including: Inflammation and oedema, laryngomalacia vocal cord paralysis, ulcerations, granulomas, stenosis • Tracheomalacia, tracheal granulomas, tracheal stenosis, tracheoesophageal fistula • Sinusitis • Displacement or unplanned extubation • Blockage of the endotracheal tube with secretions or blood • Persistent cuff leak

effects, PPV may be beneficial in patients with left ventricular failure because increased intrathoracic pressure decreases both venous return and left ventricular after load and so improve ventricular performance[24].

The extent to which hemodynamic effects occur varies according to the chest wall and lung compliance. The effect is greatest when there is low chest wall compliance (eg, fibrothorax) or high lung compliance (eg, emphysema); it is least when there is high chest wall compliance (eg, sternotomy) or low lung compliance (eg, ARDS, heart failure).

In general, fluid resuscitation seems to correct hypotension caused by PPV. On the other hand, pulmonary edema may occur after extubation because sudden removal of PEEP leads to a large venous return.

3. Ventilator Associated Lung Injury

Barotrauma

Barotrauma refers to alveolar rupture due to elevated transalveolar pressure. This can appear as pneumothorax, pneumoperitoneum, subcutaneous emphysema, pneumomediastinum and can sometimes progress to bronchopleural fistula or tension pneumothorax (Figures 1 and 2). High end inspiratory (plateau) pressures predispose to barotrauma. Patients with obstructive airway disease or diseases of the lung parenchyma with low compliance (like ARDS or interstitial lung diseases) are at greatest risk. To prevent barotrauma, it is recommended to maintain the end inspiratory (plateau) pressure below 30 cm H_2O. Most of the consequences of barotrauma need no intervention other than close monitoring. Pneumothorax needs closer observation because it can progress rapidly to tension pneumothorax and needs decompression with thoracostomy[25-27].

Volutrauma

Alveolar overdistension, atelectrauma, and biotrauma are the principal mechanisms of ventilator induced lung

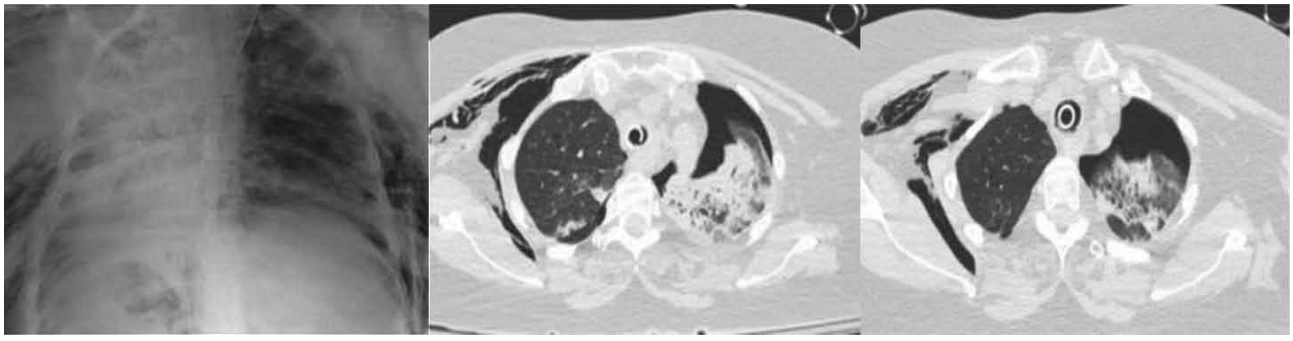

FIGURE 1. Barotrauma due to mechanical ventilation. CXR and CT demonstrated pneumothorax, and extensive subcutaneous emphysema.

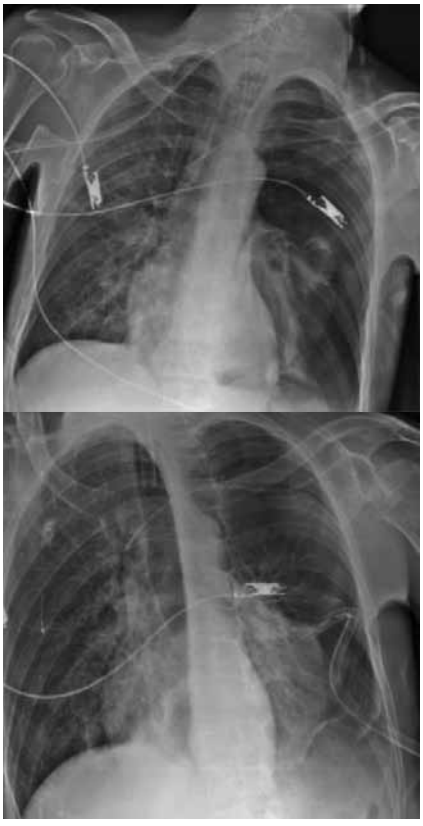

FIGURE 2. Left pneumothorax with collapsed lung. In ventilated patients a pneumothorax requires recognition and rapid decompression because tension pneumothorax may develop.

injury (VILI) during mechanical ventilation. Alveolar injury results in high alveolar permeability, interstitial and alveolar edema, alveolar hemorrhage, hyaline membranes, loss of functional surfactant, and alveolar collapse-findings similar to those observed in ARDS[27,28].

The alveolar injury caused by large tidal volumes is irrespective of airway pressures[29,30]. Randomized trials found that mechanical ventilation using tidal volumes of ≤6 mL/kg of predicted body weight improved mortality in patients with ARDS[32]. In patients intubated for reasons other than ARDS, overdistension from high tidal volumes has shown to increase the risk for VILI (odds ratio 1.3, 95% CI 1.12-1.51, for each mL above 6 mL per kg of ideal body weight)[31]. To investigate the potential effectiveness of low VT versus intermediate VT on patients without ARDS, the Protective Ventilation in Patients without ARDS (PReVENT) randomized control trial was conducted. A low-VT strategy was initiated in 475 subjects and defined as 6 mL/kg of predicted body weight. Comparatively, 480 individuals were assigned to a group with an "intermediate" VT of 10 mL/kg predicted body weight. Both groups had 21 (mean) ventilator free days with no significant differences in ICU length of stay or hospital length of stay. Other high-value outcomes of 28-d and 90-d mortality showed no significant differences between groups. However, by day 1, almost two-thirds of patients in the low tidal volume group received volumes >6 mL/kg PBW. Thus, insufficient differences between the achieved tidal volumes received by patients in both groups may have contributed to the lack of benefit[33].

Patients particularly prone to develop VILI are those receiving large tidal volumes, those with underlying restrictive lung diseases with ALI/ARDS, with acidemia (pH <7.35) and those who have received blood transfusions[31].

VILI can be prevented by applying two strategies. These strategies are based on studies on patients with ARDS (protective ventilation). The first is to prevent alveolar overdistension by applying low tidal volume ventilation and by limiting plateau pressure (Pplat) ≤30 cm H_2O. The general recommendation is to use tidal volumes of 4-8ml/kg of ideal body weight to get to the lowest tidal volume which the patient tolerates whilst providing acceptable oxygenation and ventilation. Mild acidosis and hypercapnia should be tolerated[34]. Finally, a recent observational study based on multiple RCTs demonstrated that low driving pressure (DP = plateau pressure – PEEP) is a better predictor of outcome in ARDS than either tidal volume or plateau pressure alone[35]. The second is to prevent collapse of alveoli during expiration and prevent cyclic atelectasis. The amount of PEEP needed to overcome cyclic atelectasis should be individualized[34].

Atelectrauma

Even physiologic or low tidal volumes can lead to VILI in some patients. This is because, in patients with atelectasis, air tends to flow towards more compliant alveoli (i.e. the ones that are already open) and overdistend them. The prolonged contact of alveolar surfaces has been associated with local inflammation. Furthermore, those parts of the lung which are atelectatic but are being opened with each breath (cyclic atelectasis) are also prone to lung injury. Animal models have demonstrated that cyclic alveolar expansion and collapse creates forces that cause injury to adjacent alveoli and airways[36,37].

This process is referred to as cyclic atelectasis or atelectrauma. Atelectrauma is generally managed using applied positive end-expiratory pressure (PEEP), although the optimal way to set the ideal level of PEEP is not clear.

Biotrauma -inflammation

Biotrauma is characterized by ventilator-induced release of inflammatory mediators from cells within the injured lung[38]. Both alveolar overdistension and atelectrauma in animals increase inflammatory cells including tumor necrosis factor (TNF)-alpha, interleukin (IL)-6, IL-8, matrix metalloproteinase-9, and transcription factor nuclear factor (NF)-kB[39,40].

In patients with ARDS ventilated with low volume strategies, randomized trials report a reduction in lavage and serum cytokines simultaneously with mortality benefit[41].

There is also evidence that injurious ventilatory strategies may lead to development of pulmonary fibrosis (in animals)[42] and the development of multi-organ failure (in humans)[43], although the precise mechanisms are unclear.

Ventilator induced diaphragmatic dysfunction (VIDD)

Mechanical ventilation causes diaphragmatic muscle atrophy, a phenomenon called ventilator induced diaphragmatic dysfunction (VIDD). Controlled mechanical ventilation may lead to diaphragmatic muscle fibers atrophy within the first day of mechanical ventilation. Long-term mechanical ventilation (defined as >24 hours) was associated with diaphragmatic muscle injury, atrophy, and proteolysis compared to short-term mechanical ventilation (defined as two to three hours)[44]. VIDD appears to be mediated by oxidative stress. VIDD may be associated with prolonged mechanical ventilation, difficulty weaning, prolonged ICU stay, and a higher risk of complications[45].

Diaphragm structure and function are very sensitive to high and low loading conditions. Goligher at al. studied invasively ventilated ICU patients and examined whether changes in the thickness of the diaphragm, as assessed by ultrasound, were associated with adverse outcomes, including prolonged ventilator dependence, re-intubation, and death. The results highlight that when diaphragm muscle thickness decreased by ≥10% this was associated with a lower probability of ventilator liberation, prolonged ICU admission, and respiratory complications (including reintubation and tracheostomy) compared with patients with a <10% change in diaphragm thickness. In 24% of the patients, diaphragm thickness increased by ≥10% in the first week of ventilation, and this was also associated with prolonged ventilation. The authors also demonstrated that the change in diaphragm thickness varied with diaphragm effort: low effort was associated with reduced thickness and high effort was associated with increased thickness[46].

4. Oxygen related complications

Oxygenation goals should be individualized and hyperoxia should be avoided. According to human and animal studies, high concentrations of inspired oxygen can cause a spectrum of lung injury, ranging from mild tracheobronchitis to diffuse alveolar damage (DAD). Hyperoxia appears to produce cellular injury through increased production of reactive oxygen intermediates (ROIs), such as the superoxide anion, the hydroxyl radical, and hydrogen peroxide resulting in inflammatory response and cell death[47,83]. Moreover, high FiO_2 results in washout of alveolar nitrogen and the absorption of oxygen in alveolus cause absorptive atelectasis.

A meta-analysis of 25 randomized trials that compared a conservative oxygen strategy (FiO_2 0.21; range 0.21-0.5) with a liberal oxygen strategy (median FiO_2 0.52; range 0.28 to 1.0 for a median duration eight hours) in over 16,000 critical ill patients showed that a liberal oxygen strategy was associated with a small but increased hospital mortality (relative risk [RR] 1.21, 95% CI 1.03-1.43) and mortality at 30 days (RR 1.14, 95% CI 1.01-1.29). Importantly, as SpO_2 increased in the liberal strategy group, mortality also increased, indicating a dose-response relationship[48]. For most critically ill patients, the lowest possible FiO_2 necessary to meet oxygenation goals should be used, ideally targeting a peripheral arterial saturation between 90 and 96 percent[49]. This will decrease the likelihood of adverse events such as absorption atelectasis, accentuation of hypercapnia, airway injury, and parenchymal injury.

5.Infection Related Complications (VAP)

Ventilator associated pneumonia (VAP) is defined as pneumonia which occurs after 48-hours of intubation and mechanical ventilation. The incidence is between 8–28% and it is associated with considerable mortality (up to 50%)[50,51]. The tracheal tube allows pathogens to enter the trachea, damages cough and mucus clearance and favors retention of secretions. The risk rises with the duration of ventilation. Oropharyngeal secretions and leakage of secretions around the cuff are the primary routes of infection. Efforts should be made to minimize the risk of aspiration. Elevating the head of the bed to 30°, minimizing sedation or paralysis, frequent suctioning of subglottic secretions and maintaining the cuff pressure at least 20cm H_2O are measures that may limit aspiration. In addition, there is evidence that decontaminating the oral cavity with chlorhexidine swabs has reduced the incidence of VAP. Early recognition and treatment are important.

New onset of fever, purulent sputum, leucocytosis, and desaturation should prompt further investigation. In addition to a new infiltrate on radiography, they are enough to initiate empiric treatment. Antibiotics can be de-escalated or modified later based on cultures or response[50].

6. AutoPEEP

AutoPEEP refers to hyperinflation of the lungs due to air trapping. It is caused by initiation of inspiration before expiration is complete. It can be caused by large tidal volumes, high respiratory rate (insufficient time for expiration), obstructive airway disease or narrow endotracheal tube. By looking at the flow versus time waveform, if inspiratory flow begins before expiratory flow has stopped, then autoPEEP will develop.

Unchecked autoPEEP can lead to barotrauma as well as worsening of the hemodynamic effects of positive pressure ventilation (PPV). Increased intrathoracic pressure leads to decreased venous return which in turn leads to decreased cardiac output and hypotension as mentioned above. This effect is further exacerbated in the hypovolemic patient. AutoPEEP can also worsen ventilation-perfusion (V/Q) mismatch by compressing capillaries in the healthy part of the lung and diverting blood to the diseased lung. Work of breathing may also be increased because in pressure support settings it makes it harder to trigger a breath[52].

In patients with high minute ventilation, lowering the tidal volume, respiratory rate or increasing the inspiratory flow rate may help. In patients with obstructive airway disease, if bronchodilators or steroids are not helpful and the above strategies have also failed, applying PEEP may be useful. Applying external PEEP of 50-100% of measured static auto-PEEP keeps the airways from collapsing during expiration and may improve ventilation perfusion matching and oxygenation without any effect on cardiac output[53].

7. Other

Gastrointestinal

Positive pressure ventilation for greater than 48 hours is a risk factor for gastrointestinal bleeding due to stress ulceration. Positive airway pressure (especially PEEP) is also associated with decreased splanchnic perfusion. Other gastrointestinal complications include vomiting, pharyngeal irritation, and hypomotility mostly due to drugs like opiates[54]. It is uncertain whether these complications are due to mechanical ventilation or critical illness.

Renal

Mechanical ventilation is associated with the development of acute renal failure. In a prospective cohort study of 29,269 critically ill patients, positive pressure ventilation was an independent risk factor for acute renal failure (odds ratio 2.11, 95% CI 1.58-2.82)[55]. The mechanism for renal injury is likely multifactorial. Hypotheses include renal injury through the release of inflammatory mediators (eg. interleukin-6) and impaired renal blood flow due to decreased cardiac output, increased sympathetic tone, or activation of humoral pathways[56].

Central nervous system

Positive pressure ventilation increases intracranial pressure (ICP). Positive pressure maintained in the chest may decrease venous return from the head, increasing intracranial pressure and this may cause deterioration of patients with brain injury and already elevated ICP.

Weakness

Systemic muscular weakness is common among patients who undergo mechanical_ventilation. Potential causes include immobilization, prolonged use of sedatives, use of neuromuscular blocking agents, and critical illness. Early mobilization and exercise may increase the likelihood that the patient will return to an independent functional status[57].

Sleep

Sleep disruption in the critically ill can be severe and is characterized by sleep fragmentation, abnormal circadian rhythms, increased light sleep and decreased slow-wave and rapid eye movement (REM) sleep[58]. Mechanical ventilation may disturb sleep by destabilizing the patient's breathing and dyssynchronization between the ventilatory efforts of the patient and the machine. Indirect negative effects on sleep include discomfort related to endotracheal intubation, noise from the ventilator alarms, and the use of sedation and analgesia[59]. Some modes and ventilator settings may be more beneficial regarding sleep than others. Guidelines from the Society of Critical Care Medicine endorse the use of assist-controlled ventilation rather than pressure support ventilation during the night in critically ill patients[60]. Although newer modes such as proportional assist ventilation (PAV) and neurally-adjusted ventilation (NAVA), may improve ventilator asynchrony, strategies to fully optimize sleep are not fully known[61].

VENTILATOR-PATIENT ASYNCHRONY

Patient-ventilatory asynchrony exists if the phases of breath delivered by the ventilator do not match that of the patient and it is common during mechanical ventilation (24% of mechanically ventilated patients)[62]. Patient-ventilator asynchrony exceeding 10% of the overall breath are considered clinically important and can cause dyspnea, may increase the work of breathing, prolong the duration of mechanical ventilation[63-65] including higher rate of tracheostomy and increase intensive care unit (ICU) and hospital mortality[62]. It is still unclear whether this relationship between asynchronies and poor outcome is causative, i.e. asynchronies are responsible for the worsened outcome, or asynchrony is a marker of severity of illness. However, identifying and correcting for asynchronies has been recognized as a crucial issue (Figure 3)[66].

Ineffective triggering, also known as wasted efforts, may occur in case of a weak respiratory drive and/or effort, a high intrinsic positive end-expiratory pressure (PEEPi), an excessively low ventilator trigger sensitivity, higher levels of pressure support and higher tidal volumes[62,67].

Auto-triggering takes place when the ventilator delivers assistance unrelated to patient's effort.

Double triggering, also named as breath stacking, occurs when a patient triggers a new breath before the completion of the prior ventilator-delivered breath because the ventilator inspiratory time is shorter than the patient's inspiratory time.

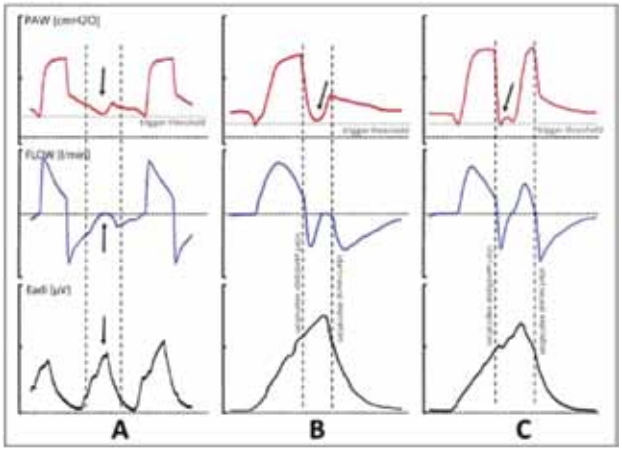

FIGURE 3. (A) Ineffective effort during pressure support ventilation (PSV). (B) Premature cycling during PSV. (C) Double triggering during PSV.
Note. Reprinted after permission from "Patient-ventilator asynchronies: types, outcomes and nursing detection skills", Acta Biomed for Health Professions 2018.[62]

A challenging approach to improve patient–ventilator synchrony is matching ventilator support to ventilator demand. For this purpose, two modes referred as proportional modes, are presently available for intubated patients: proportional assist ventilation (PAV) and neurally adjusted ventilatory assist (NAVA). PAV is a mode of ventilation that instantaneously delivers inspiratory support in proportion to patients' generated flow (flow assist) and volume (volume assist). Therefore, an increased patient's effort corresponds to increased support delivered by the ventilator[72]. NAVA has the unique feature of controlling ventilator functioning through a non-pneumatic signal, assessed by diaphragm electrical activity (EAdi)[68,69]. The airway pressure applied by the ventilator depends on the magnitude of EAdi. Those models are promising for weaning, reducing the duration of mechanical ventilation.

ETHICAL CHALLENGES OF MECHANICAL VENTILATION

With the widespread use of mechanical ventilation - a medical technology of the latter half of the previous century- patients with terminal illnesses can be kept alive, without having their underlying condition cured or improved[73]. When treating patients near the end of life, invasive mechanical ventilation and cardiopulmonary resuscitation (CPR) frequently pose questions regarding their appropriateness as forms of medical therapies. In the 1974 and 1980 CPR guidelines and standards, it is stated that "The purpose of CPR is the prevention of sudden, unexpected death. CPR is not indicated in certain situations, such as in cases of terminal irreversible illness where death is not unexpected" and "Resuscitation in some circumstances may represent a positive violation of an individual's right to die with dignity"[73,75]. Thus, clinicians, acting according to the principles of beneficence and non-maleficence, usually come across ethical decisions concerning the withholding of mechanical ventilation, in cases when it is considered to be futile.

A European survey in respiratory intermediate units, about end-of-life decision making, assessed the reasons for withholding and withdrawing treatment[76]. These include low probability of hospital survival, poor predicted functional status after hospital discharge, patient's preference and older age. There are cases where NIV is used as a ceiling of ventilatory care. However, this practice remains still controversial in patients with Do-Not-Resuscitation orders. On one hand, it can relieve dyspnoea, comfort the patient and provide him time to interact with his

loved ones, but on the other hand, it prolongs the dying process and is not as effective in dyspnoea relief as other palliative measures[77-79].

Interestingly, the attitude towards end-of-life practices in European ICUs was studied and data were compared during two different periods,1999-2000 and 2015-2016 with Ethicus 1 and 2 prospective observational studies. They demonstrate that treatment limitations (withholding or withdrawing life-sustaining treatment or active shortening of the dying process) occurred significantly more frequently (89.7% vs 68.3%) in the second period, whereas death without any limitations in life-prolonging therapies occurred significantly less frequently (10.3% vs 31.7%). These findings suggest that end-of-life care practices in European ICUs changed from 1999-2000 to 2015-2016 with more limitations in life-prolonging therapies and fewer deaths without treatment limitations[80].

Of paramount importance is for patients, especially the chronically ill, to partake in the decision to institute or withhold mechanical ventilation. As this process requires thought, it should be done timely, and preferably before respiratory failure demands an urgent answer[79,81].

It is also important to explore family perception about palliative care and ventilator withdrawal for the chronical ill and prolonged ventilated patient. Because the majority of those patients have poor consciousness level, decisions about their support often fall to their relatives. When family opinion was studied, the vast majority agreed to palliative care and half of the family members regretted having chosen prolonged mechanical ventilation[82]. Poor patient quality of life (QoL) and higher family member knowledge of palliative care were found to significantly increase the willingness to receive palliative care and withdraw life-sustaining treatments in the terminal stage of life. These findings imply that physicians should thoroughly discuss mechanical ventilation benefits and burdens and poor QoL should be more effectively communicated to families in order to have realistic expectations. Withholding futile interventions does not mean abandoning the patient; on the contrary, appropriate treatment aims to alleviate the patient's discomfort and not merely prolong suffering.

CONFLICTS OF INTEREST

Authors have no conflicts of interest

ΠΕΡΙΛΗΨΗ

Επεμβατικός μηχανικός αερισμός: Πότε και σε ποιόν; Ενδείξεις και επιπλοκές του επεμβατικού μηχανικού αερισμού

Δανάη Θεοδούλου[1], Εμμανουήλ Αλευράκης[2], Μαριάνθη Ηλιοπούλου[3], Θεόδωρος Καραμπιτσάκος[4], Ματθαίος Κατσαρας[5], Σταμάτιος Τσιπιλης[1], Κωνσταντίνος Τζιμόπουλος[6], Αντωνία Κουτσούκου[1], Νικολέττα Ροβίνα[1]

[1]Μονάδα Εντατικής Φροντίδας, Α΄ Πνευμονολογικό Τμήμα, Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, ΓΝΝΘΑ "Η Σωτηρία", Αθήνα, [2]4ο Πνευμονολογικό Τμήμα, [3]7ο Πνευμονολογικό Τμήμα, [4]5ο Πνευμονολογικό Τμήμα, [5]6ο Πνευμονολογικό Τμήμα, [6]2ο Πνευμονολογικό Τμήμα, ΓΝΝΘΑ "Η Σωτηρία", Αθήνα

Η επείγουσα διασωλήνωση και ο επεμβατικός μηχανικός αερισμός είναι αδιαμφισβήτητα μία σωτήρια παρέμβαση, όμως η απόφαση ποιος και πότε θα υποστηριχθεί παραμένει μια πρόκληση. Οι ενδείξεις περιλαμβάνουν την αναπνευστική ανεπάρκεια, το shock, το κώμα και χειρουργικές παρεμβάσεις που απαιτούν αναλγησία και καταστολή. Η ενδοτραχειακή διασωλήνωση μπορεί να είναι δυσχερής και ο μηχανικός αερισμός συνοδεύεται και από επιπλοκές που ίσως επιδεινώσουν τον ήδη ασταθή ασθενή. Επιπλέον, αν δεν υπάρχει συγχρονισμός μεταξύ ασθενούς και αναπνευστήρα είναι δύσκολο να επιτευχθεί επαρκής ανταλλαγή αερίων και να υποστηριχθεί το έργο της αναπνοής. Ο κλινικός ιατρός είναι επιφορτισμένος με το να υποψιάζεται , να αναγνωρίζει και να επιλύει τυχόν επιπλοκές του μηχανικού αερισμού. Τέλος, με την ευρεία διάδοση του μηχανικού αερισμού προκύπτουν και ηθικά διλήμματα; ασθενείς με τελικού σταδίου νόσημα μπορεί να παραμείνουν εν ζωή χωρίς την προοπτική βελτίωσης του υποκείμενου νοσήματος. Σε αυτές τις περιπτώσεις είναι σημαντικό οι ίδιοι οι ασθενείς να συμμετέχουν στην απόφαση για περαιτέρω υποστήρι-

ξη εφόσον έχουν ενημερωθεί για τις δυνατότητες και τους περιορισμούς αυτής της παρέμβασης.Θ.
Πνεύμων 2020, 33(1):13-24.

Λέξεις - Κλειδιά: *Επεμβατικός μηχανικός αερισμός, Ενδείξεις , Επιπλοκές*

REFERENCES

1. Pham T, Brochard LJ, Slutsky AS. Mechanical Ventilation: state of the Art. Mayo Clinic proceedings 2017; 92:1382-400.
2. Roussos C, Koutsoukou A. Respiratory failure. Eur Respir J Suppl 2003; 22(47 Suppl):3s-14s.
3. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J 2017; 50:1602426.
4. Masip J, Roque M, Sánchez B, Fernández R, Subirana M, Expósito JA. Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis. JAMA 2005; 294:3124-30.
5. Kreppein U, Litterst P, Westhoff M. Hypercapnic respiratory failure. Pathophysiology, indications for mechanical ventilation and management. Medizinische Klinik, Intensivmedizin und Notfallmedizin 2016; 111:196-201.
6. Lightowler JV, Wedzicha JA, Elliott MW, Ram FS. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. BMJ 2003; 326:185.
7. Cohen CA, Zagelbaum G, Gross D, et al. Clinical manifestations of inspiratory muscle fatigue. Am J Med 1982; 73:308.
8. Slutsky AS. Mechanical ventilation. American College of Chest Physicians' Consensus Conference. Chest 1993; 104:1833.
9. Kangelaris KN, Ware LB, Wang CY, et al. Timing of intubation and clinical outcomes in adults with acute respiratory distress syndrome. Critical Care Medicine 2016; 44:120-9.
10. Hussain S, Roussos Ch. Distribution of respiratory muscle and organ blood flow during endotoxin shock in dogs. J Appl Physiol 1985; 59:1802-8.
11. Berger RE, Rivers E, Levy MM. Management of Septic Shock. N Engl J Med 2017; 376:2282-5.
12. Bernard SA, Smith K, Porter R, et al. Paramedic rapid sequence intubation in patients with non-traumatic coma. Emerg Med J: EMJ 2015; 32:60-4.
13. Schultz MJ, Abreu MG, Pelosi P. Mechanical ventilation strategies for the surgical patient. Curr Opin Crit Care 2015; 21:351-7.
14. Janssens, G. Hartstein. Management of difficult intubation. Eur J Anaesthesiol 2001; 18:3-12.
15. Practice Guidelines for Management of the Difficult Airway. Anesthesiology 2013; 118:251-70
16. Higgs A, McGrath BA, Goddard C, et al. Guidelines for the management of tracheal intubation in critically ill adults. Br J Anaesth 2018; 120:323–52.
17. Thomas AN, McGrath BA. Patient safety incidents associated with airway devices in critical care: A review of reports to the UK National Patient Safety Agency. Anaesthesia 2009; 64:358-65.
18. Kalanuria AA, Zai W, Mirski M. Ventilator-associated pneumonia in the ICU. Crit Care 2014; 18:208.
19. Gattinoni L, Protti A, Caironi P, Carlesso E. Ventilator-induced lung injury: The anatomical and physiological framework. Crit Care Med 2010; 38(10Suppl):539-48.
20. Benjamin B, Holinger LD. Laryngeal complications of endotracheal intubation. Ann Otol Rhinol Laryngol 2008; 117(9Suppl):2–20.
21. Pacheco-Lopez PC, Berkow LC, Hillel AT, Akst LM. Complications of airway management. Respir Care 2014; 59:1006-19.
22. Qvist J, Pontoppidan H, Wilson RS, et al. Hemodynamic responses to mechanical ventilation with PEEP: the effect of hypervolemia. Anesthesiology 1975; 42:45.
23. Fougères E, Teboul JL, Richard C, et al. Hemodynamic impact of a positive end-expiratory pressure setting in acute respiratory distress syndrome: importance of the volume status. Crit Care Med 2010; 38:802.
24. Bersten AD, Holt AW, Vedig AE, et al. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. N Engl J Med 1991; 325:1825.
25. Boussarsar M, Thierry G, Jaber S, et al. Relationship between ventilatory settings and barotrauma in the acute respiratory distress syndrome. Intensive Care Med 2002; 28:406.
26. Pingleton SK. Barotrauma in acute lung injury: is it important? Crit Care Med 1995; 23:223.
27. International consensus conferences in intensive care medicine: Ventilator-associated Lung Injury in ARDS. This official conference report was cosponsored by the American Thoracic Society, The European Society of Intensive Care Medicine, and The Societé de Réanimation de Langue Française, and was approved by the ATS Board of Directors, July 1999. Am J Respir Crit Care Med 1999; 160:2118.
28. Hughes KT, Beasley MB. Pulmonary Manifestations of Acute Lung Injury: More Than Just Diffuse Alveolar Damage. Arch Pathol Lab Med 2017; 141:916.
29. Caironi P, Cressoni M, Chiumello D, et al. Lung opening and closing during ventilation of acute respiratory distress syndrome. Am J Respir Crit Care Med 2010; 181:578.
30. Dreyfuss D, Soler P, Saumon G. Mechanical ventilation-induced pulmonary edema. Interaction with previous lung alterations. Am J Respir Crit Care Med 1995; 151:1568.
31. Gajic O, Dara SI, Mendez JL, et al. Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. Crit Care Med 2004; 32:1817.
32. Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with

traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342:1301-8.
33. Simonis FD, Serpa Neto A, Binnekade JM, et al. Effect of a Low vs Intermediate Tidal Volume Strategy on Ventilator-Free Days in Intensive Care Unit Patients Without ARDS: A Randomized Clinical Trial. JAMA 2018; 320:1872.
34. Fan E, Del Sorbo L, Goligher EC, et al. An Official American Thoracic Society/European Society of Intensive Care Medicine/ Society of Critical Care Medicine Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med 2017; 195:1253-63.
35. Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015; 372:747-55.
36. Gattinoni L, Protti A, Caironi P, Carlesso E. Ventilator-induced lung injury: the anatomical and physiological framework. Crit Care Med 2010; 38:S539.
37. Muscedere JG, Mullen JB, Gan K, Slutsky AS. Tidal ventilation at low airway pressures can augment lung injury. Am J Respir Crit Care Med 1994; 149:1327.
38. Tremblay LN, Slutsky AS. Ventilator-induced injury: from barotrauma to biotrauma. Proc Assoc Am Physicians 1998; 110:482.
39. Tremblay L, Valenza F, Ribeiro SP, et al. Injurious ventilatory strategies increase cytokines and c-fos m-RNA expression in an isolated rat lung model. J Clin Invest 1997; 99:944.
40. von Bethmann AN, Brasch F, Nüsing R, et al. Hyperventilation induces release of cytokines from perfused mouse lung. Am J Respir Crit Care Med 1998; 157:263.
41. Ranieri VM, Suter PM, Tortorella C, et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA 1999; 282:54.
42. Cabrera-Benítez NE, Parotto M, Post M, et al. Mechanical stress induces lung fibrosis by epithelial-mesenchymal transition. Crit Care Med 2012; 40:510.
43. Plötz FB, Slutsky AS, van Vught AJ, Heijnen CJ. Ventilator-induced lung injury and multiple system organ failure: a critical review of facts and hypotheses. Intensive Care Med 2004; 30:1865.
44. Jaber S, Petrof BJ, Jung B, et al. Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. Am J Respir Crit Care Med 2011; 183:364.
45. Goligher EC, Dres M, Fan E, et al. Mechanical Ventilation-induced Diaphragm Atrophy Strongly Impacts Clinical Outcomes. Am J Respir Crit Care Med 2018; 197:204
46. Goligher EC, Dres M, Fan E, et al. Mechanical ventilation–induced diaphragm atrophy strongly impacts clinical outcomes. Am J Respir Crit Care Med 2018; 197:204-13.
47. Freeman BA, Crapo JD. Hyperoxia increases oxygen radical production in rat lungs and lung mitochondria. J Biol Chem 1981; 256:10986.
48. Chu DK, Kim LH, Young PJ, et al. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. Lancet 2018; 391:1693.
49. O'Driscoll BR, Howard LS, Earis J, et al. BTS guideline for oxygen use in adults inhealthcare and emergency settings. Thorax 2017; 72:ii1.
50. American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005; 171:388-416.
51. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002; 165:867-903.
52. Leung P, Jubran A, Tobin MJ. Comparison of assisted ventilator modes on triggering, patient effort, and dyspnea. Am J Respir Crit Care Med 1997; 155:1940-8.
53. Laghi F, Goyal A. Auto-PEEP in respiratory failure Minerva. Anestesiol 2012; 78:201-21.
54. Mutlu GM, Mutlu EA, Factor P. GI complications in patients receiving mechanical ventilation. Chest 2001; 119:1222.
55. Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA 2005; 294:813.
56. Kuiper JW, Groeneveld AB, Slutsky AS, Plötz FB. Mechanical ventilation and acute renal failure. Crit Care Med 2005; 33:1408.
57. Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373:1874.
58. Ozsancak A, D'Ambrosio C, Garpestad E, et al. Sleep and mechanical ventilation. Crit Care Clin 2008; 24:517-31.
59. Psarologakis C, Kokkini S, Georgopoulos D. Sleep and mechanical ventilation in critically ill patients. In: Vincent JL, editor. Annual update in intensive care and emergency medicine. Cham (Switzerland): Springer International Publishing; 2014. p. 133–46.
60. Devlin JW, Skrobik Y, Gélinas C, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/ Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med 2018; 46:e825.
61. Blissitt PA. Sleep and Mechanical Ventilation in Critical Care. Crit Care Nurs Clin North Am 2016; 28:195-203.
62. Thille AW, Rodriguez P, Cabello B, et al. Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive Care Med 2006; 32:1515-22.
63. Murias G, Lucangelo U, Blanch L. Patient-ventilator asynchrony. Curr Opin Crit Care 2016;22:53-9.
64. Hansen-Flaschen JH. Dyspnea in the ventilated patient: a call for patient-centered mechanical ventilation. Respir Care 2000; 45:1460.
65. Georgopoulos D, Prinianakis G, Kondili E. Bedside waveforms interpretation as a tool to identify patient-ventilator asynchronies. Intensive Care Med 2006; 32:34.
66. Bulleri E, Fusi C, Bambi S, Pisani L. Patient-ventilator asynchronies: types, outcomes and nursing detection skills. Acta Biomed 2018; 89(7-S):6-18.
67. Leung P, Jubran A, Tobin MJ. Comparison of assisted ventilator modes on triggering, patient effort, and dyspnea. Am J Respir Crit Care Med 1997; 155:1940-8.

68. Navalesi P, Longhini F. Neurally adjusted ventilatory assist. Curr Opin Crit Care 2015; 21:58–64.
69. Demoule A, Clavel M, Rolland-Debord C, et al. Neurally adjusted ventilatory assist as an alternative to pressure support ventilation in adults: a French multicentre randomized trial. Intensive Care Med 2016; 42:1723–32.
70. Colombo D, Cammarota G, Bergamaschi V, et al. Physiologic response to varying levels of pressure support and neutrally adjusted ventilatory assist in patients with acute respiratory failure. Intensive Care Med 2008; 34:2010-8.
71. Liu L, Xia F, Yang Y, et al. Neural versus pneumatic control of pressure support in patients with chronic obstructive pulmonary diseases at different levels of positive end expiratory pressure: a physiological study. Crit Care 2015; 19:244.
72. Xirouchaki N, Kondili E, Vaporidi K, et al. Proportional assist ventilation with load-adjustable gain factors in critically ill patients: comparison with pressure support. Intensive Care Med 2008; 34:2026-34.
73. Jecker NS. Medical futility and care of dying patients, In Caring for Patients at the End of Life. West J Med 1995; 163:287-91.
74. Standards for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC): Part V. Medicolegal considerations and recommendations. JAMA 1974; 227(suppl):864-6.
75. Standards and Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiac Care (ECC). Part VII: Medicolegal considerations and recommendations. JAMA 1980; 244: 504-8.
76. Nava S, Sturani C, Hartl S, et al. End-of-life decision-making in respiratory intermediate care units: a European survey. Eur Respir J 2007; 30:156-64.
77. Esbensen KL. What matters most when considering noninvasive ventilation for patients with do-not-intubate or comfort-measures-only orders? Crit Care Med 2018; 46:1367-70.
78. Vilaça M, Aragão I, Cardoso T, Dias C, Cabral-Campello G. The Role of Noninvasive Ventilation in Patients with "Do Not Intubate" Order in the Emergency Setting. PLoS One 2016; 11:e0149649.
79. Dales RE, O'Connor A, Hebert P, Sullivan K, McKim D, Llewellyn-Thomas H. Intubation and mechanical ventilation for COPD: development of an instrument to elicit patient preferences. Chest 1999; 116:792-800.
80. Charles S, Bara R, Christiane S, et al. Changes in End-of-Life Practices in European Intensive Care Units From 1999 to 2016. JAMA 2019; 322:1692-704.
81. McIntyre KM. Loosening criteria for withholding prehospital cardiopulmonary resuscitation. Futility of prehospital cardiopulmonary resuscitation: like beauty, in the eyes of the beholder. Arch Intern Med 1993; 153:2189-92.
82. Chen YC, Fan HY, Curtis JR, Lee OK, Liu CK, Huang SJ. Determinants of receiving palliative care and ventilator withdrawal among patients with prolonged mechanical ventilation. Crit Care Med 2017; 45:1625-34.
83. Rigopoulou A, Bechrakis P. Oxygen toxicity and the lung. Pneumon 2004; 17:18-28.