# Special Article

### Brazilian recommendations of mechanical ventilation 2013. Part 2

Recomendações brasileiras de ventilação mecânica 2013. Parte 2

The present recommendations are a joint initiative of the Mechanical Ventilation Committee of the Brazilian Intensive Care Medicine Association (*Associação de Medicina Intensiva Brasileira* - AMIB) and the Commission of Intensive Therapy of the Brazilian Thoracic Society (*Sociedade Brasileira de Pneumologia e Tisiologia* - SBPT).

#### **Abstract**

Perspectives on invasive and noninvasive ventilatory support for critically ill patients are evolving, as much evidence indicates that ventilation may have positive effects on patient survival and the quality of the care provided in intensive care units in Brazil. For those reasons, the Brazilian Association of Intensive Care Medicine (Associação de Medicina Intensiva Brasileira - AMIB) and the Brazilian Thoracic Society (Sociedade Brasileira de Pneumologia e Tisiologia - SBPT), represented by the Mechanical Ventilation Committee and the Commission of Intensive Therapy, respectively, decided to review the literature and draft recommendations for mechanical ventilation with the goal of creating a document for bedside guidance as to the best practices on mechanical ventilation available to their members. The document was based on the available evidence regarding 29 subtopics selected as the most relevant for the subject of interest. The project was developed in several stages, during which the selected topics were distributed among experts recommended by both societies with recent publications on the subject of interest and/or significant teaching and research activity in the field of mechanical ventilation in Brazil. The experts were divided into pairs that were charged with performing a thorough review of the international literature on each topic. All the experts met at the Forum on Mechanical Ventilation, which was held at the headquarters of AMIB in São Paulo on August 3 and 4, 2013, to collaboratively draft the final text corresponding to each sub-topic, which was presented to, appraised, discussed and approved in a plenary session that included all 58 participants and aimed to create the final document.

**Keywords:** Recommendations; Mechanical Ventilation; Respiratory Insufficiency.

### Resumo

O suporte ventilatório artificial invasivo e não invasivo ao paciente grave tem evoluído e inúmeras evidências têm surgido, podendo ter impacto na melhora da sobrevida e da qualidade do atendimento oferecido nas unidades de terapia intensiva no Brasil. Isto posto, a Associação de Medicina Intensiva Brasileira (AMIB) e a Sociedade Brasileira de Pneumologia e Tisiologia (SBPT) - representadas por seu Comitê de Ventilação Mecânica e sua Comissão de Terapia Intensiva, respectivamente, decidiram revisar a literatura e preparar recomendações sobre ventilação mecânica, objetivando oferecer aos associados um documento orientador das melhores práticas da ventilação mecânica na beira do leito, com base nas evidências existentes, sobre os 29 subtemas selecionados como mais relevantes no assunto. O projeto envolveu etapas que visaram distribuir os subtemas relevantes ao assunto entre *experts* indicados por ambas as sociedades, que tivessem publicações recentes no assunto e/ ou atividades relevantes em ensino e pesquisa no Brasil, na área de ventilação mecânica. Esses profissionais, divididos por subtemas em duplas, responsabilizaram-se por fazer uma extensa revisão da literatura mundial. Reuniram-se todos no Fórum de Ventilação Mecânica, na sede da AMIB, na cidade de São Paulo (SP), em 3 e 4 de agosto de 2013, para finalização conjunta do texto de cada subtema e apresentação, apreciação, discussão e aprovação em plenária pelos 58 participantes, permitindo a elaboração de um documento final.

Descritores: Recomendações; Ventilação Mecânica; Insuficiência Respiratória.

#### Introduction

Invasive or non-invasive mechanical ventilation (MV) must be performed in an adequate and safe

manner to avoid the occurrence of ventilationinduced lung injury. Based on physiological

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Conflicts of interest: With the help of the Brazilian Thoracic Society, the AMIB Division of Scientific Issues procured financial support from industrial companies and laboratories, distributed as sponsorship quotas, to cover part of the event costs (participants' air tickets, food and lodging). None of those companies participated in the drafting of the present document, nor had access to its content until it was disclosed (after its final format was approved) as brochures distributed at the Brazilian Congress of Intensive Care Medicine in Rio de Janeiro in 2013. The companies that collaborated with the present project are: Air Liquide, Covidien, GE, Intermed, Magnamed, Mindray and Philips.

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principles, evidence collected in laboratory experiments, and randomized clinical or observational studies involving actual patients that were available in the literature, current MV recommendations indicate that ventilatory support should be performed at a tidal volume (Vt) of 6 mL/kg predicted body weight, with a delta between plateau pressure and positive end-expiratory pressure (PEEP) not greater than 15 cmH<sub>2</sub>O, and end-expiratory pressure levels sufficient to avoid airway and alveolar collapse and ensure adequate gas exchange. Other recommendations include positioning the patient to guarantee adequate and harmless ventilation (such as prone positioning in cases of severe acute respiratory distress syndrome - ARDS) and the use of advanced support techniques (such as extracorporeal carbon dioxide (CO<sub>2</sub>) removal) in cases of refractory ARDS. The development of increasingly more sophisticated ventilators allow for fine adjustment of sensitivity and include several trigger mechanisms, different inspiratory flow speeds, acceleration, mechanisms for ending inspiratory time, and monitoring options, which enable adjustment of the patient-ventilator synchrony and MV as a function of the patient's disease. In this regard, the possibility of providing differential ventilatory support for restrictive and obstructive conditions stands out.

For that reason, joint analysis of the available evidence on ventilatory support by Brazilian experts who deal with mechanical ventilation like anesthesiologists, intensivists, pulmonologists, physical therapists, nurses, nutritionists and speech therapists was necessary. Such evidence, taken together with experience gathered by the various specialties, may provide guidance to health care professionals in Brazilian intensive care units (ICU) on how to provide safe and effective respiratory support for patients with respiratory failure, based on the best evidence available, in order to avoid the occurrence of ventilator-associated lung injury.

Therefore, the aim of the present study was to review the available literature on 29 subtopics related to ventilatory support for individuals with respiratory failure, and following presentation, discussion, and approval at a plenary session including all 58 participating specialists, to present the results in the form of recommendations and suggestions.

### Methods

Literature available from Medline (2003-2013) and the Cochrane Central Register of Controlled Trials (CENTRAL) was reviewed by specialists with a higher education (intensivists, anesthetists, pulmonary specialists, physical therapists, and nurses) who were distributed in pairs for review of each of the 29 selected subtopics related to non-invasive and invasive ventilatory support for patients with respiratory failure.

After reviewing the articles available in the literature, each pair answered the questions formulated by the organizing commission (composed by Carmen Silvia Valente Barbas, President of the Committee of Respiratory Failure and Mechanical Ventilation of AMIB, Alexandre Marini Isola, National Coordinator of the Course of MV in ICU - VENUTI, and Augusto Manoel de Carvalho Farias, Coordinator of the Department of Intensive Care of the SBPT) according to criteria previously suggested by other authors. (1-4) Thus, the term recommendation was used when the level of evidence was high, i.e., derived from randomized studies conducted with more than 100 participants, meta-analyses, all-or-nothing effect, or patient safety. The term suggestion was used when the available evidence was weak, i.e., based on observational or case-control studies. case series, or on the experience of specialists to provide guidance for efficient and safe ventilatory support in Brazil. We therefore hoped that these evidence-based recommendations would help to avoid potential deleterious effects associated with inadequate ventilatory support in our patients.

The 58 participating specialists were requested to answer the proposed questions during an eight-hour session conducted at the Brazilian Intensive Care Medicine Association (Associação de Medicina Intensiva Brasileira - AMIB) on August 3, 2013. The answers were formulated based on the evidence available in the literature and on the experience of the specialists and were then presented at a plenary session that included all 58 participating specialists, which was held on August 4, 2013 at AMIB headquarters. During that session, the answers were discussed, modified when needed, voted on, and approved in accordance with the suggestions and observations of the specialists who attended the meeting.

The reports made by all the pairs of specialists were gathered by the project organizing commission, which revised, formatted and

drafted the final document, following the authors' revisions. The document was then printed in the form of a bedside manual of recommendations to be distributed to ICUs all across Brazil, and it was also sent for publication in the Brazilian Journal of Intensive Care (Revista Brasileira de Terapia Intensiva - RBTI) and the Brazilian Journal of Pulmonology (Jornal Brasileiro de Pneumologia).

### Mechanical ventilation in chest trauma

#### Noninvasive mechanical ventilation

**Recommendation** – Noninvasive ventilation (NIV) is contraindicated in patients with upper airway injury, in the presence of hemodynamic instability, and in severe craniocerebral trauma. (5-10)

**Recommendation** – In patients with isolated chest trauma, early application of NIV can improve gas exchange, prevent orotracheal intubation (OTI), and reduce complications and ICU length of stay.<sup>(5-10)</sup>

**Recommendation -** The use of NIV should be monitored at the bedside by a healthcare professional within 30 minutes to 2 hours. For NIV to be considered successful, the following criteria should be met: reduction of the respiratory rate (f), increase in the tidal volume (Vt), improvement of the level of consciousness, reduction or cessation of the use of accessory muscles, increase in the partial pressure of oxygen (PaO<sub>2</sub>) and/or the peripheral oxygen saturation (SpO<sub>2</sub>), and reduction of the partial pressure of carbon dioxide (PaCO<sub>2</sub>) without significant abdominal distension. In unsuccessful cases, OTI and invasive MV should be performed immediately.

#### Invasive mechanical ventilation(11)

**Recommendation –** Patients with severe chest trauma, respiratory failure, and specific contraindications to NIV should be promptly intubated and ventilated.

**Recommendation –** Initially, use an assist-control mode of ventilation, i.e., volume-cycled ventilation (VCV) or pressure-control ventilation (PCV), in chest trauma with severe respiratory failure.

**Recommendation** - Regardless of the mode selected (VCV or PCV), patients with chest trauma should be initially ventilated with a Vt of 6 mL/kg predicted body weight, an f of 16-20 breaths/

min, and a fraction of inspired oxygen (FiO<sub>2</sub>) that is sufficient to maintain an  $SpO_2 > 92\%$  and a PEEP of 5-10 cmH<sub>2</sub>O. In cases of ARDS, follow the instructions in the related section of the present Recommendations.

**Recommendation -** In cases of high output bronchopleural fistula, use the PCV mode, which will compensate for the leak. Another option is the use of high frequency oscillatory ventilation, only in centers with this capability and specialized personnel. In cases that are more severe, asynchronous independent lung ventilation can be either used or not, and the lung with the fistula is ventilated in the PCV mode with a distending pressure of < 15 cmH<sub>2</sub>O and low PEEP levels (< 10cmH<sub>2</sub>O).

### Pain control

**Suggestion** – Thoracic epidural analgesia, as part of a multimodal strategy, is recommended. If epidural analgesia cannot be used or is contraindicated, patient-controlled i.v. analgesia or intercostal nerve blockade can be used.<sup>(11)</sup>

**Suggestion** - Administration of intermittent analgesia can be used in cases of less severe pain.

## Mechanical ventilation during surgical procedures

**Comment** - Postoperative pulmonary complications (PPC) contribute to a substantial proportion of the risks associated with surgery and anesthesia, being the major cause of morbidity and mortality in the postoperative period. (12) PPC, which include respiratory infections, respiratory failure, pleural effusion, atelectasis, pneumothorax, bronchospasm, and aspiration pneumonitis, affect approximately 5% of patients undergoing surgery. (12,13)

### Specific care before intubation

Preoperative risk stratification

**Recommendation -** All patients should be assessed for risk of PPC by using a specific scale. The American Society of Anesthesiology (ASA) classification is a scale that is subjective and imprecise. Among the scales suggested for stratifying patient risk for PPC are the European Surgical Outcomes Study (EuSOS) scoring system and the Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT).<sup>[13]</sup>

### Pre-oxygenation during induction of anesthesia

**Recommendation** - Pre-oxygenation with an  ${\rm FiO}_2$  of approximately 100% for all patients aims at increasing reserve and reducing the risk of hypoxemia. <sup>(14)</sup>

### Use of noninvasive ventilation during induction of anesthesia

**Suggestion –** Use NIV during induction of anesthesia for elective surgery in patients with decreased abdominal compliance and in those in whom it is necessary to use an  ${\rm FiO}_2$  of 100% for pre-oxygenation. The use of NIV can prevent the development of atelectasis in patients with decreased abdominal compliance and in those undergoing pre-oxygenation with an  ${\rm FiO}_2$  of 100%.<sup>(14)</sup>

<u>Use of positive end-expiratory pressure</u> and alveolar recruitment maneuvers during induction of anesthesia

**Suggestion –** Use recruitment maneuvers and a PEEP of approximately 5–8 cmH<sub>2</sub>O after induction of anesthesia in patients with decreased abdominal compliance or in those who develop hypoxemia.<sup>(14)</sup>

### Specific care during the intraoperative period

#### Mode of ventilation

**Suggestion** – Use PCV to improve pulmonary mechanics in patients undergoing video-assisted laparoscopic surgery. Observe appropriate expired Vt values. (15,16) In the remaining scenarios, there is no benefit of a mode of ventilation over another, provided that respiratory mechanics are respected.

#### Tidal volume

**Recommendation** – The use of MV with a Vt of 6 mL/kg predicted body weight should be considered in all patients. Various studies in various scenarios (abdominal, thoracic, and cardiac surgery) have demonstrated the benefit of using low Vt during surgery.<sup>(17-19)</sup>

### Positive end-expiratory pressure

**Suggestion -** The use of a PEEP of approximately 5-8 cmH<sub>2</sub>O should be considered. All

studies assessing conventional MV strategies versus protective strategies in patients undergoing surgery considered using a low Vt and a high PEEP in the protective strategies. In general, the use of a high PEEP results in better oxygenation and a lower incidence of PPC. (17,20)

#### Alveolar recruitment maneuvers

**Suggestion -** Use alveolar recruitment maneuvers (RM) during the intraoperative period to reverse alveolar collapse and improve oxygenation. The use of RM, in association with maintenance of high PEEP levels, reduces the amount of collapsed lung and improves patient oxygenation during surgery. Among the RM most often cited in the literature is maximum recruitment strategy (MRS), which seeks to maintain a high plateau pressure (Pplat) in the airway (approximately 40-45 cmH<sub>2</sub>0) for 60 seconds (as described in Part 1 of the present Recommendations).

### Fraction of inspired oxygen

**Suggestion** - The lowest  ${\rm FiO}_2$  level that can maintain  ${\rm SpO}_2$  at approximately 96-98% should be used. The combination of an  ${\rm FiO}_2$  of approximately 30-40% and high PEEP levels can maintain adequate oxygenation and reduce lung atelectasis. The role of high levels of oxygen in preventing surgical wound infection remains controversial.<sup>(14)</sup>

### Respiratory rate

**Recommendation -** Use f to maintain  $PaCO_2$  at 38-43 mmHg (end-tidal  $CO_2$  [ $CO_2$  at end-expiration] of approximately 35-40 mmHg). The trend to use a low Vt during surgery requires the adoption of a high f.<sup>(17,19)</sup>

### Discontinuation of mechanical ventilation

**Recommendation -** Discontinue MV in the postoperative period as early and as quickly as possible, as soon as the patient is hemodynamically stable, is under adequate analgesia, has no electrolyte disturbances, and has regained a sufficient level of consciousness to ensure maintenance of ventilatory drive and airway protection. Extubation can be performed in the operating room, in the post-anesthesia care unit, or in the ICU.<sup>(21)</sup>

#### Noninvasive ventilation after extubation

**Suggestion -** The use of NIV should be considered in patients undergoing cardiac, thoracic, bariatric, or upper abdominal surgery, because it is associated with better oxygenation and a lower incidence of atelectasis. It should be performed with low pressure levels in upper abdominal and esophageal surgery. NIV should not delay reintubation.

**Recommendation –** NIV should not be used following the onset of an acute respiratory failure episode after extubation. (22)

## Mechanical ventilation in obese patients

**Comment -** Patients with a body mass index (BMI)  $\geq$  30 kg/m² are considered obese. This condition is characterized by a series of physiological changes, such as decreased lung compliance, which is caused by the direct mechanical effect of fat distribution and an abnormal position of the diaphragm, because of increased intra-abdominal pressure (IAP), reduced functional residual capacity (FRC), and reduced total lung capacity (TLC), and by the increased work of breathing, because of increased airway resistance (Raw) and increased chest wall resistance, as well as a need for high minute volumes, leading to an increase in PaCO<sub>3</sub>. (23,24)

**Recommendation** – Consider every obese patient as potentially difficult airway. In obese patients with a Malampatti score  $\geq 3$  and a Cormack score of 3-4, as well as increased neck circumference, consider difficult airway and prepare the necessary infrastructure to manage this condition.<sup>(25)</sup>

**Suggestion** - Use the reverse Trendelenburg position during ventilation. <sup>(26)</sup> The goal is to improve  $PaO_2$ , static respiratory system compliance (Crs), and cardiac output, as well as reducing the development of atelectasis.

**Suggestion** - Avoid the supine position, because of reduced FRC, cardiac output, and increased work of breathing. If it is possible to use it, the beach chair position is suggested.<sup>(27)</sup>

**Suggestion** – Use NIV in cases of hypercapnic respiratory failure, taking the necessary precautions. Care should be exercised in the use of NIV in patients with a BMI  $\geq 45 \text{kg/m}^2$ , because there is a higher risk of failure in this group.

**Suggestion** - In invasive MV, no mode is superior to another mode. It is suggested that the assist-control mode (AC) as either PCV or VCV be initially used. <sup>(28)</sup>

**Suggestion** - Monitor respiratory mechanics. Monitoring of IAP should be considered in cases of increased PaCO<sub>2</sub> levels and/or increased airway pressures that cannot be explained by pulmonary causes.

**Recommendation** – Use a Vt of 6mL/kg predicted body weight;<sup>26-29)</sup> for FiO<sub>2</sub>, it is suggested that the lowest level that can maintain oxygen saturation (SatO<sub>2</sub>)  $\geq$  92% be used.

**Suggestion** - For PEEP/recruitment maneuvers, <sup>(30,31)</sup> the goal is to increase FRC, prevent the development of atelectasis, and reduce the risk of ventilation-induced lung injury. In addition, it is suggested that MRS be performed in cases of hypoxemia, decreased Vt, or increased PaCO<sub>2</sub> levels.

**Suggestion –** Use PEEP levels  $\geq$  10 cmH<sub>2</sub>0. **Recommendation –** Maintain Pplat at  $\leq$  35 cmH<sub>2</sub>0.<sup>(32)</sup>

**Suggestion** – In cases of moderate and severe ARDS, a Pplat of up to 40 cm $H_2O$  may be tolerable, provided that the distending pressure is maintained at  $\leq$  15 cm $H_2O$ .

**Recommendation** – Extubate patients as soon as their clinical status allows, and NIV can be used to facilitate it.

# Mechanical ventilation in patients with central nervous system involvement

### Gas exchange - oxygen

**Recommendation** – Avoid hypoxemia in patients with acute neurological injury, because it leads to increased morbidity and mortality. (33,34)

**Suggestion -** Avoid hyperoxia in cases of anoxic-ischemic encephalopathy.<sup>(35)</sup>

### Gas exchange - carbon dioxide

**Recommendation** - Do not use prophylactic or prolonged hyperventilation, and maintain  $PaCO_2$  between 35 and 40 mmHg during the acute phase of injury. (36-38)

**Recommendation** - Acute hyperventilation is indicated as rescue therapy in cases of cerebral herniation. (36-38)

**Recommendation** - Monitor CO<sub>2</sub> by capnography. When this tool is unavailable, assess PaCO<sub>2</sub> levels through blood gas sampling, more frequently during the acute phase.

**Suggestion** – In patients with acute ischemic stroke, avoid  $PaCO_2 < 35$  mmHg because of risk of ischemia in the penumbra region.

### Acute respiratory distress syndrome

**Recommendation** - Use a protective ventilation strategy for the treatment of ARDS in patients with neurological injury, accompanied by intracranial pressure (ICP) and cerebral perfusion pressure monitoring.<sup>(29,39)</sup> More details are provided in the related section of the present Recommendations.

**Suggestion** – In cases of severe ARDS, the use of a high PEEP should be individualized and ICP should be monitored, because increased ICP can occur when there is a concomitant decrease in lung and brain compliance. (40,41)

### Modes of ventilation

**Suggestion** – Use the VCV mode for patients with severe neurological injury during the acute phase, <sup>(42)</sup> to avoid oscillations in Vt.

**Recommendation** - Patients with severe neurological injury, with intracranial hypertension (ICH) during the acute phase, should not be maintained on a spontaneous mode of ventilation. (43)

### Airway approach

**Recommendation** – Intubate patients with a Glasgow Coma Scale score  $\leq$  8 and in whom the cough reflex is absent. (44)

**Suggestion -** Use rapid sequence intubation in patients with ICH or with suspected ICH, minimizing the risk of secondary brain injury due to increased intracranial pressure. This technique uses a combination of sedatives that have minimal cardiodepressant effects, such as ketamine (1-2 mg/kg i.v.) or etomidate (0.3 mg/kg i.v.), particularly in patients with hypotension or at risk of hypotension, and short-acting neuromuscular blocking agents (succinylcholine, 1.5 mg/kg i.v.) so that, within 45 to 60 seconds, the goal of paralysis and sedation is achieved.

### Unconventional ventilation strategies

**Suggestion** – In patients with severe pulmonary involvement, individualize the use of new venti-

lation strategies such as recruitment maneuvers, prone positioning, arteriovenous extracorporeal membrane CO<sub>2</sub> removal (AV-ECCO<sub>2</sub>R), and extracorporeal membrane oxygenation (ECMO), assessing risk versus benefit on a case-by-case basis. (45-47)

#### Head of the bed between 30° and 45°

**Recommendation** – Maintain the head of the bed between 30° and 45° because this improves cerebral venous return and reduces the effect of PEEP on ICP. (48)

## Mechanical ventilation in patients with neuromuscular diseases

**Comment** - In respiratory failure from neuromuscular disease, ventilatory support depends on the location of the injuries (from spinal cord injuries to direct muscle involvement) (Chart 1).

### Acute polyradiculoneuritis (Guillain-Barré syndrome)

**Comment -** One third of patients with acute polyradiculoneuritis (Guillain-Barré syndrome) require MV during the course of the disease. Generalized weakness, rapid progression, and bulbar involvement are associated with the need for MV in such patients. (49-52)

**Suggestion** – Patients with acute polyradiculoneuritis should be periodically assessed by measuring maximum inspiratory pressure (Plmax) from residual volume, maximum expiratory pressure (PEmax) from TLC, and vital capacity (VC). Patients with Plmax < –30 cmH<sub>2</sub>O, PEmax < 40 cmH<sub>2</sub>O, and VC < 20 mL/kg or a reduction of more than 30% in VC should be electively intubated to prevent emergency OTI. (49-52)

**Recommendation** – NIV should be used with care because of the instability of acute polyradiculoneuritis. Therefore, OTI and invasive MV should not be delayed when there is deterioration of lung function. (49-52)

**Suggestion** – The decision to tracheostomize patients with Guillain-Barré syndrome may be postponed for 2 weeks. If, after 2 weeks, lung function test results do no improve significantly, tracheostomy should be considered. If lung function test results are improving, tracheostomy may be postponed until weaning is achieved. [49-52]

**Chart 1** – Location of the neuromuscular injuries and examples.

Location	Examples	
Spinal cord	Transverse myelitis, trauma, and extrinsic compression	
Motor neuron	Amyotrophic lateral sclerosis and poliomyelitis	
Peripheral nerves	Acute polyradiculoneuritis and critical illness polyneuropathy	
Neuromuscular junction	Myasthenia gravis, botulism, and organophosphate intoxication	
Muscles	Muscular dystrophies, myopathies, and myositis	

### Myasthenia gravis

**Comment** - Acute respiratory failure results from a myasthenic crisis precipitated by neuromuscular junction failure, usually accompanied by bulbar weakness. Myasthenic-specific treatment with immunoglobulin or plasmapheresis should be initiated early. (53-55)

**Suggestion** - Consider using NIV (bilevel positive airway pressure [BiPAP]) in patients with myasthenic crisis in an attempt to prevent OTI, with PCO<sub>2</sub> > 50mmHg being a predictor of BiPAP failure; the use of NIV can be considered in persistent or recurrent weakness following extubation. (63-55)

**Suggestion** - Periodically assess patients with myasthenic crisis by measuring Plmax, PEmax, and VC. Patients with VC < 20 mL/kg, Plmax <  $-30 \text{ cmH}_2\text{O}$ , and PEmax > 40 cmH $_2\text{O}$  can undergo a trial treatment with NIV (BiPAP) and, if there is failure, they should be electively intubated to prevent emergency OTI. (53-55)

**Suggestion** – Conduct an intensive respiratory program, including sighs, use of PEEP, frequent aspiration of the bronchial tree, respiratory therapy, body position change, and administration of antibiotic therapy (in cases of documented infection), in patients placed on MV for a myasthenic crisis. (53-55)

### Duchenne muscular dystrophy

**Comment** - Duchenne muscular dystrophy (DMD) is a recessive X-linked disease that affects 1:3,000 male births. It is characterized by progressive loss of muscle strength, with VC decreasing progressively until the onset of respiratory failure, usually between 18 and 20 years of age, with a consequent need for ventilatory

support. Most patients develop cardiomyopathy. Forced VC (FVC) < 1L and the onset of nocturnal hypoventilation are signs of poor prognosis, and NIV can be used to improve survival and quality of life outcomes. (56-58)

**Suggestion -** Use NIV in cases of nocturnal hypoventilation and/or decreased VC (< 1L).

**Suggestion** – Invasive ventilation via elective tracheostomy is indicated for patients who do not tolerate NIV or who have been intubated for an acute event. (56-58)

### Amyotrophic lateral sclerosis

**Comment -** Amyotrophic lateral sclerosis (ALS) is a degenerative motor neuron disease, during the course of which respiratory failure due to muscle failure may occur. Chronic aspiration due to bulbar muscle dysfunction and ineffective cough are additional complications. Most patients die from respiratory complications that vary in course.<sup>[59,60]</sup>

**Recommendation -** Use NIV in patients with ALS, except in the subgroup of patients with severe bulbar dysfunction.

**Recommendation** - Invasive MV via tracheostomy is indicated in patients with impaired airway protection and severe bulbar dysfunction, and it should only be instituted after its complications, as well as its social and logistical implications, are discussed in detail with the patients and their families.

**Recommendation** – Indications for ventilatory support include VC < 50% of predicted, Plmax <  $-30 \text{ cmH}_2\text{O}$  or < 60% of predicted, peak expiratory flow (PEF) < 270 L/min, PCO $_2$  > 45 mmHg, and nocturnal hypoventilation. (59,60)

**Suggestion** - The parameters for invasive and NIV are as follows. An oral or nasal mask can be used provided that it is properly fitted. BiPAP should be used. Invasive MV via tracheostomy is usually carried out in the ventilation mode that is most suitable for the type of demand, if there is associated lung disease. Patients should be monitored for episodes of atelectasis, accumulation of secretions, and pneumonias.<sup>(61)</sup>

### Mechanical ventilation in patients with cardiovascular disease

**Comment** - The goal of MV in patients with cardiovascular disease is to adjust oxygenation and ventilation and to ensure cardiac output.

**Recommendation** - Achieve an  $SpO_2 \ge 94\%$  by using the lowest possible  $FiO_2$ .

**Recommendation** – Noninvasive MV with either continuous positive airway pressure (CPAP) or BiPAP is safe, and both modes have similar effects and are effective in preventing OTI. They should be applied as a form of ventilatory support during acute pulmonary edema. (62-68)

**Recommendation –** Apply the protective strategy to MV patients with cardiovascular disease. <sup>[69,70]</sup>

**Recommendation** – Applying recruitment maneuvers is safe in patients with cardiovascular disease provided that there is proper monitoring and appropriate care. <sup>(69,70)</sup>

**Suggestion** – Monitoring of cardiac output and measurement of extravascular lung water are suggested in MV patients with cardiovascular disease and ARDS, with the aim of volume adjustment and hemodynamic optimization.<sup>(71)</sup>

**Suggestion** - Monitoring of cardiac output, in patients with cardiovascular disease, can be performed with a pulmonary artery catheter (PAC) or noninvasively, by means of pulse contour analysis. (69,70)

**Suggestion** - Transthoracic echocardiography can be performed in MV patients with cardiovascular disease who are hemodynamically unstable. (70)

**Suggestion** - Perform transthoracic echocardiography in patients who exhibit hemodynamic instability after undergoing RM, in order to assess them for volume status and right ventricular (RV) dysfunction. (69,70)

**Recommendation** - Discontinuation of MV in patients with cardiovascular disease follows the recommendations for patients with no cardiovascular disease. The use of NIV should be prioritized to facilitate the process of discontinuation of MV, and NIV should be applied immediately after extubation. (62-70)

**Suggestion** - Increased brain natriuretic peptide (BNP) levels during weaning from ventilation in patients with cardiovascular disease show accuracy in predicting weaning failure. (70,72)

**Recommendation** - A positive fluid balance should be avoided in MV patients with cardiovascular disease who are hemodynamically stable.<sup>(70)</sup>

**Recommendation** – Inhaled nitric oxide is an effective strategy in MV patients with cardiovascular disease, RV dysfunction, and pulmonary hypertension. (70)

**Recommendation** – No mode of ventilation is recommended over another in patients with cardiovascular disease. (70)

**Suggestion** – In patients on inotropic support, this support may be continued until after extubation.<sup>(70)</sup>

# Mechanical ventilation in patients with cardiovascular disease undergoing surgery

Tidal volume

**Recommendation** - The use of a Vt of 6 mL/kg predicted body weight, in the volume-control mode or peak/plateau inspiratory pressure, is sufficient to maintain this same volume in PCV.<sup>(70)</sup>

Positive end-expiratory pressure

**Recommendation** - Apply PEEP during general anesthesia, because it is associated with improved oxygenation and prevention of atelectasis.<sup>(70)</sup>

Alveolar recruitment maneuvers

**Suggestion –** RM can be used intraoperatively to prevent alveolar collapse. (69)

Fraction of inspired oxygen

**Recommendation** - At induction of anesthesia, use an  $FiO_2$  of 100% to ensure adequate oxygenation for intubation. Fractions of oxygen needed to maintain  $SpO_2 > 94\%$  are recommended.<sup>(70)</sup>

Discontinuation of mechanical ventilation

**Recommendation** - Discontinuation of MV should be gradual, and pressure support ventilation (PSV) can be used. NIV is an important resource, which should be used immediately after extubation. (62-70)

Postoperative analgesia

**Recommendation** – Achieving adequate postoperative analgesia is associated with optimization of postoperative pulmonary function.

## Mechanical ventilation in interstitial lung diseases

**Comment -** Interstitial lung diseases (ILDs) are a heterogeneous group of diseases that

predominantly affect the lung interstitium, with varying degrees of inflammation and fibrosis, <sup>(73,74)</sup> and that can progress with varying degrees of hypoxemia and gradual reduction in lung volumes. Patients with ILD may require MV because of a number of factors, including the anesthesia process in surgical procedures, such as open lung biopsy and other elective or emergency operations, respiratory infections leading to respiratory failure, and acute exacerbations (AEs – noninfectious) of the underlying interstitial disease. <sup>(75,76)</sup>

#### Indications for mechanical ventilation

**Comment -** Respiratory failure in patients with ILD should be divided into two groups: progression of the underlying disease and AEs. AEs are characterized by acute, unexplained worsening of clinical symptoms of ILD, especially dyspnea and cough, usually in the last 30 days, accompanied by radiological worsening, often in the form of ground-glass changes superimposed on previous changes. AEs were initially described in patients with idiopathic pulmonary fibrosis (IPF), but they can occur in other forms of ILD.<sup>[76-79]</sup> The onset of AEs seems to occur at some point in the course of IPF in 5 to 10% of patients, and mortality in those requiring MV is nearly 100%.

**Recommendation** - Before diagnosing an AE, it is necessary to exclude infections, pulmonary thromboembolism, cardiac dysfunction, druginduced pulmonary toxicity, etc.<sup>(76-80)</sup>

### Acute complication

**Suggestion** - In AEs of ILD, the patient's previous status should be assessed. Invasive MV is indicated if the cause of acute respiratory failure is diagnosed as not being due to progression of the underlying disease.

### Progression of the underlying disease

**Recommendation –** ICU admission and invasive MV should be avoided, and any decision in this regard should be discussed with the patients or their families.

#### Noninvasive mechanical ventilation

**Suggestion -** NIV can be used as initial ventilatory support in patients with ILD who develop acute respiratory failure or as palliative ventilatory support in patients who have previ-

ously expressed the desire not to be intubated. Either CPAP or bilevel NIV can be used and should be applied early.

**Recommendation** - The use of NIV should be monitored at the bedside by a healthcare professional within thirty minutes to two hours. For NIV to be considered successful, the following criteria should be met: reduction of f, increase in Vt, improvement of the level of consciousness, reduction or cessation of the use of accessory muscles, increase in PaO<sub>2</sub> and/or SpO<sub>2</sub>, and reduction of PaCO<sub>2</sub> without significant abdominal distension. In unsuccessful cases, OTI and invasive MV should be performed immediately. Success is expected in 50% of this population. [80]

#### Noninvasive mechanical ventilation

**Comment -** Since the histological finding in AEs is diffuse alveolar damage (DAD), similar to that observed in patients with ARDS, and given the lack of prospective studies, some authors have suggested that strategies used for ARDS could be extrapolated to patients with AEs of ILD. Therefore, some experts advocate the use of protective ventilation, with a low Vt, set at approximately 6 mL/kg ideal body weight, and a Pplat  $\leq$  30 cmH<sub>2</sub>O.<sup>(80-84)</sup> The use of a high PEEP in patients with ILD has not been investigated in any study. Two retrospective studies found an association between PEEP and the outcome of patients with ILD who underwent MV: Suh et al. reported low mortality in a group of patients with acute interstitial pneumonia who received an early intervention strategy, which involved a series of measures, including MV with a low Vt and a moderate PEEP, with a median of 11 cmH<sub>2</sub>0.<sup>(79)</sup> In contrast, in a more heterogeneous group of patients with ILD who underwent MV, Fernandez-Perez et al. observed that a PEEP > 10 cmH<sub>2</sub>O on the first day of MV was associated with high mortality, but they themselves comment that a high PEEP may be a marker of greater respiratory failure severity. (76)

**Suggestion** - Patients with ILD who require MV should be ventilated with a low Vt, set at approximately 6 mL/kg ideal body weight, and a Pplat  $< 30 \text{ cmH}_2\text{O}$ ; a high f (> 30 breaths/min) and a short inspiratory time can be used to prevent hypercapnia. Use a PEEP between 5 and 10 cmH<sub>2</sub>O.

**Suggestion -** The use of a high PEEP can be attempted with caution and should be indi-

vidualized for each patient. Rescue therapies for refractory hypoxemia, such as prone positioning, RM, and nitric oxide, can be used in referral centers with expertise in these therapies.

## Discontinuation of mechanical ventilation

### Identifying patients who are ready to wean

**Recommendation** – Discontinue patients from invasive MV as soon as it is clinically possible. [85,86]

**Recommendation** – The definitions of terms related to discontinuation of MV must be made clear in ICU guidelines. The concept of "successful weaning" refers to a patient successfully completing the spontaneous breathing trial (SBT) while still connected to the ventilator. "Successful extubation" refers to a patient having the endolaryngeal tube removed (extubation) after passing the SBT and not being reintubated in the following 48 hours. In tracheostomized patients, successful extubation means tolerating being disconnected from the ventilator after passing the SBT and not needing to be reconnected to the ventilator in the following 48 hours. (87-89)

**Recommendation -** Assess and identify patients daily (active surveillance by means of internal guidelines established by a multidisciplinary team) with a view to the possibility of discontinuing ventilation, in order to reduce duration of MV and decrease costs. (90-94)

### Sedation

**Recommendation** – Sedation should be interrupted daily to assess the patient's ability to maintain spontaneous ventilation<sup>(95)</sup> (see the "Sedation and Analgesia" section in Part 1 of the present Recommendations).

### Criteria required for assessment of readiness to wean

**Recommendation** – Perform active surveillance, including the topics in Chart 2.<sup>(88,90-96)</sup>

#### Predictive indices

**Recommendation** - The most accurate weaning-predictive indices are the rapid shallow breathing index (RSBI), i.e., f divided by Vt (f/Vt), and the integrative weaning index (IWI) (Chart 3).

They should only be calculated in situation in which the decision is difficult and must NOT be used as the sole tool in the decision-making process regarding the SBT. [97-99]

### Autonomous breathing trial (spontaneous breathing trial)

**Recommendation** – In the SBT, patients should be placed on T-tube or ventilated with PSV of 5-7 cmH<sub>2</sub>O for 30-120 minutes. During the SBT, patients should be monitored for signs of failure. (85-94) Successful SBTs are defined as those in which patients maintain an adequate breathing pattern, as well as adequate gas exchange, hemodynamic stability, and comfort (Chart 4). (85-94,100-102)

**Recommendation** - After a successful SBT, determine whether the airways are patent and whether the patient is able to protect them.

### How to determine the timing of extubation

Assessment of airway protection

**Recommendation** - Determine whether the patient has the required level of consciousness (a Glasgow coma scale score > 8), an effective cough (a positive white card test result and a peak flow > 60 lpm), and a small amount of secretions (with no need for suctioning every 1 or 2 hours). (103)

### Assessment of airway patency

**Suggestion** – Test airway patency in patients at higher risk for laryngeal stridor and airway obstruction (prolonged ventilation and trauma); to that end, a qualitative or quantitative approach can be used. Perform thorough suctioning of the mouth and larynx before deflating the tube cuff for the test, in order to prevent unwanted material from entering the lower airways iatrogenically (Chart 5).<sup>(104)</sup>

#### Use of corticosteroids

**Recommendation** – In patients at high risk for laryngeal stridor and laryngeal edema, as identified by the cuff leak test, the preventive use of corticosteroids may be beneficial. The prescribed doses range from 20 to 40 mg of i.v. methylprednisolone every 4 to

**Chart 2 –** Topics that are to be routinely assessed during active surveillance in mechanically ventilated patients.

 $PaO_2 \ge 60$ mmHg on  $FIO_2 \le 0.4$  and  $PEEP \le 5$  to 8 cmH $_2O$  Hemodynamic stability, with good tissue perfusion, with or without low doses of vasopressors, and absence of decompensated coronary artery disease or arrhythmias with hemodynamic effects

Resolution or control of the cause of respiratory failure Capability to initiate an inspiratory effort

Zero or negative fluid balance in the last 24 hours Normal acid-base and electrolyte balance

Delay extubation when patients are scheduled to be taken to tests or surgery requiring general anesthesia in the next 24 hours

PaO<sub>2</sub>: partial pressure of oxygen; FlO<sub>2</sub>: fraction of inspired oxygen; and PEEP: positive end-expiratory pressure.

**Chart 3** – Significant parameters for predicting successful weaning.

Parameter	Number	Threshold value				
	of studies					
Measured in the ventilator						
Minute volume	20	< 10-15 L/min				
Negative	10	$< -20 \text{ to } -30 \text{ cmH}_20$				
inspiratory force		-				
Plmax	16	$< -15 \text{ to } -30 \text{ cmH}_2 \text{ 0}$				
Airway occlusion	4	< 0.30				
pressure (P <sub>0.1</sub> ) /						
Plmax						
CROP index	2	< 13				
Measured during spontaneous ventilation (1-2 min)						
f	24	< 30-38				
Vt	18	> 325-408 mL (4-6 mL/kg)				
f/Vt index	20	< 105 breaths/min./L				
Integrative	2	> 25 mL/cmH <sub>2</sub> 0				

CROP: compliance, respiratory rate, oxygenation, and pressure; Plmax: maximum inspiratory pressure; f: respiratory rate; and Vt: tidal volume.

breaths/min./L

weaning index

6 hours, started at least 4 hours, more commonly 12 to 24 hours, before extubation. (105)

### Use of noninvasive ventilation in the discontinuation of mechanical ventilation

Use of noninvasive ventilation to facilitate discontinuation of mechanical ventilation - early weaning (noninvasive ventilation as a facilitation technique)

**Recommendation** – It is recommended that NIV be used to facilitate early discontinuation of MV in patients with chronic obstructive pulmonary

**Chart 4 -** Signs of intolerance to the spontaneous breathing trial.

Respiratory rate > 35 breaths/min

Arterial de  $O_2$  saturation < 90%Heart rate > 140 bpm

Systolic blood pressure > 180 mmHg or < 90 mmHg

Signs and symptoms of agitation, sweating, altered level of consciousness

disease (COPD), even in those who fail the SBT, provided that their clinical status is adequate. The patient should be managed in centers with experience in the use of NIV (Figure 1).<sup>(106)</sup>

<u>Use of noninvasive ventilation to prevent</u> <u>extubation failure (noninvasive ventilation as</u> <u>a preventive technique)</u>

**Recommendation** – NIV should be used immediately after extubation, in a preventive manner, in patients identified as high risk, especially in hypercapnic patients (Figure 1 and Chart 6). (107-111)

Use of noninvasive ventilation in respiratory failure after extubation (noninvasive ventilation as a curative technique)

**Recommendation** - Avoid the use of NIV in extubated patients who again develop respiratory failure within 48 hours. Do not delay reintubation in this situation, except in surgical patients who develop respiratory failure in the postoperative period (Figure 1).<sup>(112)</sup>

How to manage patients with weaning failure (patients who fail their first spontaneous breathing trial)

**Recommendation** – Reinstate ventilatory support that provides patients with comfort and adequate gas exchange, maintaining it for 24 hours, so that the SBT can be repeated. Try to identify the causes of failure<sup>(86)</sup> (for difficult-to-wean patients and those requiring long-term weaning, see the related section of the present Recommendations).

### Gradual weaning methods

**Recommendation** - Avoid the use of synchronized inspiratory mandatory ventilation, because it can increase the time to discontinuation of invasive MV. (113)

### How to manage patients with extubation failure

**Recommendation** – Reintubate patients as soon as possible; identify and treat the causes of failure; and, as soon as possible, restart the discontinuation process (exception: noninvasive ventilation as a curative technique may be tried in surgical patients).

### Patients with prolonged weaning

**Suggestion** – Use classification definitions for the duration of the weaning process to categorize your patients as undergoing simple weaning<sup>(114)</sup> (when patients successfully complete their first SBT), difficult weaning (when patients fail their first SBT and require up to three SBTs or up to seven days of MV following the first SBT), and,

**Chart 5** – How to perform the endotracheal tube cuff-leak test in mechanically ventilated patients.

- 1. Before performing the cuff-leak test, perform suctioning of tracheal and oral secretions and set the ventilator to assist-control mode (VCV).
- 2. With the cuff inflated, record Vti and Vte and observe whether they are similar.
- 3. Deflate the cuff.
- 4. Record Vte during six consecutive breaths; observe that Vte will reach a plateau after the first breaths.
- 5. With the cuff deflated, Vte is expected to be < 90% of (the preset) Vti, situation in which the test is considered adequate.

VCV: volume-cycled ventilation; Vte: expired tidal volume; and Vti: inspired tidal volume.

finally, prolonged weaning (when patients fail more than three consecutive SBTs or require >7 days of MV following the first SBT).

**Suggestion** – Use the concept of prolonged MV defined as MV that is needed for  $\geq 21$  consecutive days for 6 hours daily.

**Recommendation –** Identify causes of failure to discontinue MV (Chart 7). (88,114-130)

### Muscle disorders

**Suggestion** - Assess the possibility of critical illness polyneuropathy and of phosphorus, magnesium, calcium, and potassium disorders.

### Endocrine and metabolic diseases

**Recommendation** - Adequately control diabetes, hypothyroidism, and adrenal failure.

**Chart 6 -** Noninvasive ventilation as a preventive technique: risk factors for respiratory failure.

Hypercapnia after extubation (> 45 mmHg)

Heart failure

Ineffective cough

Copious secretions

More than one consecutive failed weaning trial

More than one comorbidity

Upper airway obstruction

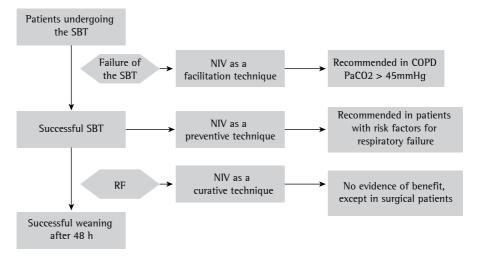
Age greater than 65 years

Heart failure as the cause of intubation

APACHE score > 12 on the day of extubation

Patients on IMV for more than 72 hours

IMV: invasive mechanical ventilation.



**Figure 1 –** Use of noninvasive ventilation for discontinuation of mechanical ventilation. SBT – spontaneous breathing trial; NIV – noninvasive ventilation; COPD – chronic obstructive pulmonary disease; RF – acute or exacerbated respiratory failure.

**Comment –** Obesity can be an additional factor for prolonged weaning, because it is characterized by an increase in  $O_2$  consumption  $(VO_2)$  and  $CO_2$  production  $(VCO_2)$ , a decrease in static compliance, VC, and TLC, and a possible increase in IAP and Raw.

### Electrolyte and acid-base disturbances

**Recommendation - Monitor, diagnose, and** treat states of hyperhydration, which are associated with increased morbidity, mortality, and ICU length of stay. Identify and treat cases of metabolic alkalosis, the most common causes of which are chronic respiratory acidosis and use of diuretics. Metabolic alkalosis is associated with increased mortality, decreased respiratory drive, decreased 0 delivery (DO<sub>2</sub>), shift of the oxyhemoglobin curve to the left, ventilation/perfusion (V/Q) mismatch, and systemic vasoconstriction. Provide an adequate means of nutrition (see the related section of the present Recommendations) to prevent malnutrition, increased protein catabolism, reduced body muscle mass and decreased effectiveness of the thoracic pump mechanism, with reduced strength and endurance and increased VO2, and perpetual dependence on the ventilator. Decreased albumin is associated with prolonged weaning and should be monitored.(114-130)

### Rehabilitation strategies and strategies to facilitate discontinuation from mechanical ventilation

Reassessment of the underlying disease and comorbidities

**Recommendation -** Treat cardiac, pulmonary, psychiatric, and infectious underlying diseases as much as possible, and maintain clinically adequate nutrition.

**Chart 7 -** Causes of failure to discontinue mechanical ventilation. (89,115-131)

Age ≥ 65 years

Decreased diaphragmatic function

Presence of comorbidities

Presence de delirium, depression, anxiety

Persistent infection/inflammatory states

Decompensated cardiac, respiratory, neurological, and psychiatric diseases

Specific care for discontinuation of mechanical ventilation

**Suggestion** – Transfer patients undergoing prolonged weaning to a unit specializing in discontinuation of MV, if available.

**Recommendation** - Tracheostomy is indicated in patients who repeatedly fail SBTs, from the tenth day of MV onward, as part of a discontinuation protocol and in accordance with specifications in the related section of the present Recommendations.

**Suggestion** - Perform SBTs daily, using a tracheostomy collar or T-piece. In cases of tolerance (f < 35 breaths/minute or over 35 breaths/minute for less than 5 consecutive minutes; SaO2 > 90%; HR < 140 beats/minute or a sustained change of 20% in any direction; 90 mmHg > blood pressure < 180 mmHg with no anxiety or diaphoresis), gradually increase the duration of T-piece use and rest the patient overnight on assist-control ventilation. In cases of failure, return the patient to an assist-control mode for rest, in order to make a second attempt within 24 hours. (123)

**Suggestion** – Long-term MV is characterized when there is failure of the entire discontinuation process, especially in patients with spinal trauma, end-stage COPD, advanced dementia, pulmonary fibrosis, and irreversible neuromuscular disease. In these situations, explain the concept of futile treatment and palliative care to patients and families in order to arrive at a joint decision regarding the best approach.<sup>(114)</sup>

**Recommendation** – Early physical therapy and passive mobilization should be performed during MV and also during the discontinuation process. These activities are considered safe and are associated with better functional results and shorter duration of  $MV^{(121,130)}$  (see the related section of the present Recommendations).

**Suggestion** – Inspiratory muscle training can be considered in patients who fail to wean, in order to increase Plmax and facilitate discontinuation of ventilatory support.<sup>[130,131]</sup>

### Hemodynamic changes and hemodynamic care in patients on invasive mechancial ventilation

**Comment -** The cardiovascular effects of positive pressure MV are described in Chart 8.

### Hemodynamic care in mechanically ventilated patients

**Recommendation -** Resuscitation aimed at restoration of tissue perfusion begins in the early acute phase, in which resuscitation should be performed as soon as possible to achieve mixed venous  $O_2$  saturation  $(SvO_2) > 65\%$  or central venous saturation  $(SvO_2) > 70\%$ , blood lactate concentration < 2 mmol/L (18 mg/dL), and adequacy of  $DO_2/VO_2$ . The process should continue in the post-resuscitation phase (when adequate tissue perfusion is achieved), and fluid restriction should be performed to maintain a zero or negative fluid balance.

**Suggestion** – In ARDS patients receiving PEEP  $\geq$  15 cmH<sub>2</sub>O and < 20 cmH<sub>2</sub>O, perform echocardiography at least once and, if necessary, monitor cardiac output. (137,138) In ARDS patients receiving PEEP  $\geq$  20 cmH<sub>2</sub>O or experiencing hemodynamic instability, perform monitoring with serial echocardiography and/or with a volumetric PAC, if available. (137,138)

**Suggestion** - During MRS with decremental PEEP titration, use invasive blood pressure monitoring; perform echocardiography after 6 hours, or earlier if the patient exhibits hemodynamic instability, to assess RV dysfunction. (137,138)

**Suggestion** - In moderate/severe ARDS, consider extravascular lung water monitoring (if available). (139,140)

**Suggestion -** Avoid systemic systemic vasodilators in refractory hypoxemia (they inhibit hypoxic vasoconstriction).<sup>[141]</sup>

**Suggestion** - Interpret  $SvO_2$  by considering  $PaO_3$ . High  $PaO_3$  values can increase  $SvO_3$ . (142)

### Mechanical ventilation in patients with left ventricular failure

**Recommendation -** For the diagnosis of left ventricular (LV) failure, use Doppler

**Chart 8** - Cardiovascular effects of positive pressure mechanical ventilation.

Hemodynamic effect		Likely effect on cardiac	
of positive pressure		output	
ventilation		Preload	Afterload
		dependent	dependent
RV	Decreases preload		
	Increases afterload	<b>V</b>	<b>V</b>
LV	Decreases preload		<b>^</b>
	Decreases afterload	<b>V</b>	ı

RV: right ventricle; and LV: left ventricle.

echocardiography, which should show ejection fraction, velocity-time integral, as well as assess diastolic function [E/A, E/E', global end-diastolic volume]. If you use a PAC, a pulmonary artery occlusion pressure >18 mmHg and a cardiac index <  $2.2 \text{ L/min/m}^2$  characterize LV failure.

**Recommendation –** Use inotropes, vasopressors if necessary, diuretics, and vasodilators when possible. In selected cases, use mechanical circulatory support.<sup>(143)</sup>

**Suggestion –** Favor the use of high PEEP (because of decreased LV preload and afterload). If there is concomitant RV failure, increase PEEP carefully (monitor the RV and RV flow). (144) Prevent severe hypercapnia (pH < 7.15 or  $PaCO_2 > 80$  mmHg). Consider kidney ultrafiltration for achieving a negative fluid balance in situations of refractoriness to diuretics. (146)

### Mechanical ventilation in patients with right ventricular failure

**Recommendation** - Regarding diagnosis, use Doppler echocardiography (RV diastolic diameter > 3.5 cm, RV/LV ratio > 1, intraventricular septal flattening or paradoxical interventricular septal motion, pulmonary artery systolic pressure > 35 mmHg, tricuspid annular plane systolic excursion < 1.8 cm)<sup>(147)</sup> or a PAC (a volumetric PAC, if available): central venous pressure > pulmonary artery occlusion pressure; mean pulmonary artery pressure > 25 mmHg; systolic index < 30 mL.min<sup>-1</sup>.m<sup>-2</sup>; RV end-diastolic volume index > 140 mL.m<sup>-2</sup>.<sup>(137)</sup>

**Suggestion** - Details regarding monitoring, treatment, and specific care are shown in Chart 9 and Figure 2.

# Resources available for hemodynamic monitoring in mechanically ventilated patients

**Suggestion** - Suggested methods of hemodynamic monitoring in MV patients include predicting the response to fluid loading (a > 15% increase in the cardiac index) in patients with the following characteristics: PEEP < 10 cmH<sub>2</sub>0; Vt of 8-10 mL.kg-1 ideal body weight; f < 30 min-1; respiratory compliance > 30 mL.cmH<sub>2</sub>0; no arrhythmias; no respiratory effort; no cor pulmonale; delta pulse pressure > 13%; systolic volume variation > 10%; delta velocity time integral > 15%; superior vena cava collapsibility

> 36%; and inferior vena cava distensibility > 18%. (153,154) Also perform the expiratory port occlusion maneuver – in spontaneously breathing patients receiving PEEP  $\leq$  10 cmH $_2$ 0, (155) with a delta central venous pressure > 1 mmHg (1.36 cmH $_2$ 0). (156) In patients receiving high PEEP and/or low Vt, passive leg raising maneuver, (157) fluid challenge with small aliquots of fluid (250 mL), and cardiac index monitoring can be used (Figure 2). (158)

### Speech-language pathology care in the rehabilitation of patients after mechanical ventilation

**comment** - The role of speech-language pathologists in the ICU is endorsed by Resolution-RDC 07/2010 of the Brazilian *Agência Nacional de Vigilância Sanitária* (ANVISA, National Health Oversight Agency). In dysphagia, the role of speech-language pathologists in the ICU is

**Chart 9** – Suggestions for monitoring, treatment, and specific care in patients with right ventricular failure. (146,148-152)

Perform monitoring with a PAC (a volumetric PAC, if available).  $^{(148)}$ 

Prevent hypervolemia (reverse Bernheim effect), promote a negative fluid balance. [149]

Favor the use of a low PEEP (< 10cmH<sub>2</sub>O) and a Vt of 6 mL/kg predicted weight or lower.<sup>(149)</sup>

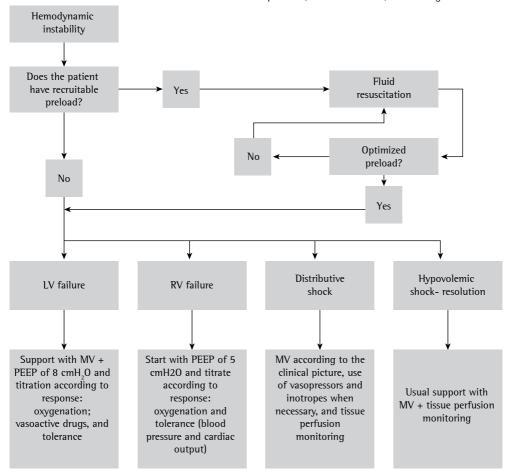
Prevent hypoxemia (it increases pulmonary vascular resistance caused by hypoxic vasoconstriction). (149)

Prevent severe hypercapnia (it increases RV afterload).<sup>(150)</sup> Consider using dobutamine at low doses (to prevent tachycardia) or milrinone.<sup>(149)</sup>

Use nitric oxide/sildenafil testing associated with monitoring with a PAC or transthoracic echocardiography. In centers where nitric oxide is unavailable, a therapeutic trial of sildenafil can be used. (151)

Avoid abrupt withdrawal of inhaled nitric oxide. [152] Consider kidney ultrafiltration for achieving a negative fluid balance in situations of refractoriness to diuretics. [146]

PAC: pulmonary artery catheter; PEEP: positive end-expiratory pressure; Vt: tidal volume; and RV: right ventricular.



**Figure 2** – Hemodynamic management algorithm in mechanically ventilated patients. LV: left ventricular; RV: right ventricular; MV: mechanical ventilation; PEEP: positive end-expiratory pressure.

regulated by Resolution 356 of the Brazilian Federal Speech-Language Pathology Council, passed on December 6, 2008, and published in the *Diário Oficial da União* (Official Federal Government Gazette) on December 9, 2008. In a multidisciplinary team, the speech-language pathologist evaluates the safety of oral feeding/swallowing and manages swallowing difficulties, thereby contributing to the prevention of aspiration pneumonia and to the tracheostomy weaning process.

**Suggestion –** Request a speech-language pathology evaluation<sup>(159-165)</sup> for all patients who required OTI  $\geq$  48 hours, for patients who underwent repeated OTI, and for those with tracheostomy (whether or not they are mechanically ventilated).

**Recommendation** – Regarding the timing for speech-language pathology evaluations after extubation, it is recommended that patients be evaluated 24<sup>(166)</sup> to 48 hours after extubation and that those who have dysphagia and are at risk for aspiration be started on speech therapy. (167-171)

**Suggestion -** Do NOT perform speech-language therapy in orotracheally intubated patients, because there is a lack of clinical evidence regarding its benefits to the swallowing function; however, early identification of patients who, even during OTI, have several associated risk factors that may compromise swallowing dynamics (patients with cardiovascular disease, patients with Parkinson's disease, post-stroke patients, and patients with dementia) is indicated.

**Suggestion** – Perform clinical speech-language evaluations (structural and functional) at the bedside<sup>(163,172)</sup> and determine the need for instrumental examination of swallowing (functional nasal fiberoptic endoscopy and modified barium swallow test).<sup>(173)</sup>

**Suggestion** – The speech-language pathologist should define the type of food consistency and the need for the use of thickeners for the administration of fluids, in collaboration with the Nutrition Service, when the patient is ready to initiate oral intake.

**Suggestion** – Fit a speaking valve into the mechanical ventilator circuit or directly into the tracheostomy, with the aid of a physical therapist and/or a physician, provided that cuff deflation is feasible and patient tolerance is assessed. (174,175)

**Suggestion** - In tracheostomized patients, use a blue food dye in the food delivered orally

and/or in the saliva swallowing test, to evaluate the occurrence of discharge of blue saliva and/or secretions through the tracheostomy, characterizing an aspiration event. (176-178)

**Suggestion** – Assess for signs and symptoms of dysphagia during the delivery of oral nutrition, especially those that may be associated with bronchial aspiration, such as choking, cough, and wet voice. (179-181)

**Suggestion -** Discuss with the medical team the use of xerostomic medications in patients on MV and/or with tracheostomy who do not tolerate cuff deflation or who experience significant aspiration of saliva. (182)

**Suggestion** – Perform direct and indirect swallowing therapy in patients who have dysphagia and/or are at risk for aspiration. (183)

# Nursing care in patients receiving invasive or noninvasive ventilatory support

**Comment -** The nursing team, as part of the multidisciplinary ICU team, actively participates in the administrative and healthcare activities involving invasive and noninvasive support in MV patients.

#### Care of circuits, filters, and humidifiers

**Recommendation -** Maintain the lower airways warm and moist during MV.

**Recommendation** - Replace (hygroscopic and hydrophobic) heat and moisture exchangers every 7 days, provided that appropriate height and positioning of the devices relative to the endotracheal tube are maintained (the devices should be connected vertically to the tube and the circuit so that they are not flooded with droplets and dirt). If there is dirt, condensation, or damage, the filter should be replaced. (184)

**Recommendation** – Do not replace the mechanical ventilator circuit routinely; replace it only when there is dirt visible to the naked eye, when there is damage, or in cases of prolonged ventilation (> 30 days). (185,186)

# Cleaning and maintenance of the equipment

**Recommendation -** Mechanical ventilator circuits require high-level disinfection (5% sodium

hypochlorite and a contact time of 60 minutes) or sterilization. (187)

### Precautions during bed bath and patient repositioning

**Recommendation** - Assess the vital signs, analyze and record the MV parameters (ventilation mode, peak pressure, PEEP, f, Vt, and FIO<sub>2</sub>), and check the alarms and clinical parameters before a bed bath and before patient repositioning. Continue cardiac monitoring and SatO<sub>2</sub> monitoring during the bed bath and during patient repositioning. Allow a 5- to 10-minute equilibrium period before determining hemodynamic intolerance/instability due to patient repositioning and/or a bed bath. (188,189)

**Recommendation** - Work with the multidisciplinary team to determine the most appropriate time to perform a bed bath in critically ill, clinically unstable patients. The nurse should assess the patient before allowing the bath, postponing it in cases of severity that can compromise patient safety.

**Recommendation** - Perform patient repositioning every 2 hours, with a lift sheet and at least two nursing professionals. (190)

**Suggestion** - Perform continuous lateral rotation therapy with the use of a bed for kinetic therapy, when available.<sup>(191)</sup>

**Recommendation** - Maintain the head of the bed between 30° and 45° in MV patients. The evidence is conflicting as to aspiration of gastric content (45°) and pressure ulcers (30°). Positioning at 30° is preferred as long as it does not pose risks to or cause conflict with medical and nursing procedures. (192)

**Suggestion** – Use the beach chair position 2 to 4 times/day; it requires less personnel than do other interventions and therefore allows early mobility of ICU patients and improvement in pulmonary function. (193)

**Recommendation** – Maintain the cuff pressure of the endotracheal tube between 18 and 22 mmHg or between 25 and 30 cmH<sub>2</sub>O (cuff meter) in order to prevent air leaks without excessive compression of the tracheal mucosa. Avoid cuff pressures > 22 mmHg or 30 cmH<sub>2</sub>O. Check the cuff pressure at least 4 times/day and before performing oral hygiene.

**Recommendation -** Maintain the endotracheal tube secured and centralized by using an adhesive device or a shoelace so that the cuff pressure is

homogeneously distributed in the trachea. Pay attention to lesions in the oral cavity, in the corners of the lips, and on the face. (194)

**Recommendation** – The precautions to be followed during patient repositioning and while tilting the patient laterally in a bed bath are described in Chart 10.<sup>(195)</sup>

**Recommendation** - In patients being placed in the prone position, it is recommended that the procedure be performed in the presence of at least five members of the ICU team, including at least one physician and one nurse. The skin of the frontal region, nose, knees, iliac crest, genitalia, and nipples should be protected. Patient rotation should be performed in two steps, with total attention being paid to the invasive devices. The dorsal electrocardiogram should be monitored, and the reverse Trendelenburg position may be used to decrease facial edema. (194,195)

**Recommendation –** Use a closed suctioning system to perform tracheal suctioning in hemodynamically unstable patients, in order to prevent desaturation in at-risk patients (i.e., patients with cardiovascular disease) and to maintain alveolar recruitment and prevent atelectasis in ARDS patients receiving PEEP  $\geq$  10 cmH $_2$ O. The system should be changed every 7 days. Closed suctioning systems have not been shown to reduce the occurrence of ventilatorassociated pneumonia, mortality, or ICU length of stay, when compared with open systems. [196]

### Specific instructions for oral hygiene, oral feeding, and enteral feeding

**Recommendation** – It is recommended that oral hygiene with brushing be performed every 12 hours, with an aqueous solution containing 0.12% chlorhexidine gluconate. In the intervals, oral hygiene should be performed with distilled or filtered water and/or alcohol-free mouthwash four times/day. (196-198)

**Recommendation** – Check the cuff pressure of the endotracheal tube or tracheostomy before performing oral hygiene. (189)

**Recommendation** – The gastric and post-pyloric routes can be used for enteral feeding in MV patients, with post-pyloric tube placement being reserved for patients with gastric intolerance and/or contraindication.<sup>(200)</sup>

**Recommendation -** Secure the nasogastric tube with a securing device (a commercially available nasal bridle or an adhesive device) in

**Chart 10 -** Precautions during patient repositioning and while tilting the patient laterally in a bed bath.

Visualize all of the stretchers and equipment that are connected to the patient.

Be careful not to pull the mechanical ventilator circuit during head-of-bed elevation, lateral tilting for patient repositioning and/or a bed bath, in order to prevent accidental extubations. Check whether the ventilatory device is fixed; release the ventilator circuit from the rack.

Maintain the head of the bed at 30°.

Pull the patient up in bed, keeping your eyes on the ventilator.

Tilt the patient laterally with his/her head supported by the headrest.

Perform hygiene of the patient's back and buttocks, most of it already with the patient placed in the lateral decubitus position, facing the side where the ventilator is.

Elevate the head of the bed and fix the circuit to the ventilator rack loosely so that, if the patient is moved in bed, the ventilator circuit is not pulled.

order to reduce the rate of unintentional tube dislodgement. (201)

**Suggestion -** Monitor the difference between prescribed and delivered enteral nutrition as a marker of dietary compliance. (202)

# Physical therapy care in patients on ventilatory support

**Comments -** ICU patients may experience respiratory and muscle dysfunction and, over time, develop neuromuscular weakness and complications of immobility, which can make discontinuation of MV difficult. Prolonged immobility leads to loss of motor function and loss of quality of life, both of which can be minimized with the institution of early mobilization and respiratory care. The incidence of ICU-acquired muscle weakness (neuromuscular weakness) in patients requiring prolonged MV ranges from 25 to 60%, (203) which contributes to increasing ICU and hospital length of stay. Physical therapy works to maintain and/or restore the functionality of the patient by preventing musculoskeletal changes and respiratory complications.

**Recommendation** - A physical therapy diagnosis should precede any intervention. (204)

**Recommendation** - Physical therapy in MV patients in the ICU should be delivered 24 hours/day, having benefits in reducing duration of MV,

ICU and hospital length of stay, hospital costs, and mortality. (200,205)

# Physical therapy maneuvers and approaches in mechanically ventilated patients

**Recommendation** – Bronchial hygiene therapy (positioning, manual inflation, vibration, and chest compression): indicated in patients with increased Raw due to the presence of secretions, causing asynchrony of MV and/or reduced oxygenation; and mandatory in lobar atelectasis. (206)

**Suggestion** - Lung expansion techniques can be used in the presence of lung collapse, with reduced compliance and oxygenation.<sup>(207)</sup>

**Recommendation** – Perform inspiratory muscle training in patients with inspiratory muscle weakness who are undergoing prolonged MV, in order to improve muscle strength. The role of inspiratory muscle training in reducing duration of MV and successfully discontinuing MV has yet to be established.<sup>[208]</sup>

### Early mobilization in noninvasive and invasive mechanical ventilation

**Recommendation** – Early mobilization should be initiated less than 72 hours following the initiation of mechanical ventilation, because it is feasible, safe, and results in significant functional benefits.<sup>(206)</sup>

**Suggestion** - Neuromuscular electrical stimulation and a cycle ergometer can be considered as a complement to the early mobilization program. (208)

**Suggestion** – Training for transfer from sitting to standing can be included in the treatment plan and precede ambulation, taking the correlation with functional limitation into account, as consensually determined by the multidisciplinary team. (209)

**Suggestion** - Intervention in functional decline can be used to increase the chances of a return to independent performance of activities of daily living after discharge. (209)

# Nutritional care in mechanically ventilated patients

### Determination of caloric needs

**Suggestion** – Use indirect calorimetry or predictive formulas (equations or a pocket formula)

to determine the caloric needs of critically ill MV patients. Indirect calorimetry should be considered when available, but it is necessary to take the patient's clinical status into account, as well as the frequency it will be used. There is not enough evidence to indicate that any of the available formulas in the literature is superior to the others. (210-214) Chart 11 suggests the formulas most commonly used in daily practice.

**Recommendation** – Initiate the enteral diet by delivering a small amount (20 to 25% of the target dose) and progressively increase it until achieving the target dose within 48 to 72 hours, in order to avoid the risk of refeeding syndrome. Before each increase, assess tolerability.

### Determination of protein needs

**Suggestion** – Determine the amount of protein for MV patients on the basis of their BMI, <sup>210-215)</sup> as shown in Chart 12.

**Suggestion** - Individualize the protein needs for critically ill MV patients with acute renal dysfunction. An important aspect to consider is that these patients should not receive a protein-restricted diet as a means to prevent or delay renal replacement therapy. Consider that patients on renal replacement therapy experience a significant loss of amino acids (10 to 15 g) during a dialysis session. (210-216) In patients who are not candidates for dialysis, special diets formulated for nephropathic patients can be used.

#### Routes of administration

**Recommendation** – Use the enteral route as the primary option, whenever there is viability of the gastrointestinal tract.<sup>(211,217)</sup>

**Suggestion** - Avoid using parenteral nutrition in critically ill MV patients until all strategies to optimize enteral nutrition (EN) have been attempted.

#### Early enteral nutrition

**Recommendation** - Initiate early EN (within 24 to 48 hours after admission to the ICU), provided that the patient is hemodynamically stable. Early EN therapy has been shown to reduce the mortality rate in critically ill MV patients and has been associated with a reduction in infectious complications and hospital length of stay.<sup>(208-211,217,218)</sup>

# Strategy to optimize delivery of enteral nutrition and minimize risks in mechanically ventilated patients<sup>(219)</sup>

#### Elevation of the head of the bed

**Recommendation** – The head of the bed should be maintained between 30° and 45°, unless there is a contraindication, for all intubated patients receiving EN.<sup>(200,210,220)</sup>

### Tube placement for nutrition

**Recommendation -** Two routes (gastric and/ or post-pyloric) should be considered in MV patients, with post-pyloric tube placement being reserved for patients with gastric intolerance and/or contraindication.<sup>(200,211)</sup>

**Chart 11 -** Pocket formula and the Harris-Benedict equation.

Pocket formula
Initial phase (acute): 20-25 kcal/kg of body weight (achieve this target dose within 48 to 72 hours)
Sequential phase: 25-30 kcal/kg of body weight
Obesity BMl >30: 11 to 14 kcal/kg/day of the actual body weight or 22 to 25 kcal/kg/day of the
ideal body weight

**Harris-Benedict** equation (validated for healthy subjects) requiring a correction factor for the stress caused by the disease and/or treatment

Men: BEE =  $66.47 + (13.75 \times W) + (5 \times H) - (6.755 \times A)$ Women: BEE =  $655.1 + (9.563 \times W) + (1.85 \times H) - (4.676 \times A)$ Stress factor: multiply by 1.2 to 1.5 (Suggestion - start at 1.2)

BM1: body mass index; BEE: basal energy expenditure; W: weight; H: height; and A: age.

**Chart 12 -** Amount of protein for mechanically ventilated patients, by body mass index.

	, 0 0	
BMI	Gram/kg of body	Note
	weight/day	
<30	1.2-2.0 (actual	It can be increased
	body weight)	in trauma patients,
		burn patients, and
		multiple trauma
		patients
Class 1 and 11	$\geq$ 2.0 (ideal body	
(30-40)	weight)	
Class 111 >40	$\geq$ 2.5 (ideal body	
	weight)	

**Suggestion** – Consider gastrostomy or jejunostomy in MV patients requiring EN < 4 weeks, according to the patient's clinical status. (221)

### Monitoring of gastric residuals in mechanically ventilated patients

**Recommendation** – Do not use monitoring of gastric residual volumes in MV patients with the aim of preventing ventilator-associated pneumonia. (222,223) As a positive effect, early EN without monitoring of gastric residuals in MV patients has been shown to improve delivery of EN.

### Continuous enteral nutrition compared with other methods

**Suggestion** - The continuous method using an infusion pump<sup>(210)</sup> can be used in critically ill MV patients with intolerance to EN.

### Establishing a nutritional therapy protocol

**Suggestion** - Guidelines can be implemented in the facility to optimize EN in MV patients, in order to mitigate the calorie-protein deficit. (224)

**Suggestion -** Prokinetic agents (preferably metoclopramide) can be used to improve tolerance, in order to attain the enteral caloric goal. (210)

### Specific care

#### Lipid-rich, carbohydrate-poor diet

**Suggestion** - (Lipid-rich, carbohydrate-poor) formulations designed to manipulate the respiratory quotient and reduce CO<sub>2</sub> production can be used in selected patients (COPD patients with CO<sub>2</sub> retention, patients with severe ARDS and permissive hypercapnia receiving borderline protective ventilation, those with CO<sub>2</sub> retention undergoing difficult or prolonged weaning). Efforts should be made to prevent excess total calories. (200,210,225)

### Enteral feeding enriched with fish oil, borage oil, antioxidant vitamins

**Suggestion** – Enteral formulations with an anti-inflammatory lipid profile and with oxidants can be used in MV patients with ARDS. (200,211,226-229) High doses of omega-3 should be avoided in patients who have coagulation disorders. (200,211,226-229)

### Phosphorus replacement

**Suggestion** - Correction of phosphorus deficit is desirable in MV patients. This is justified by the association between hypophosphatemia and failure to discontinue MV. (230)

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### Individual conflicts of interest:

Carmen Silvia Valente Barbas - received honorary for lectures from Covidien and Mindray. Alexandre Marini Isola - received honorary for lectures from Covidien and Mindray. Augusto Manoel de Carvalho Farias - received funds for CAPTIVATE study from Novartis and support to attend the AMIB congress from Sanofi-Aventis and Expressa. Ana Maria Casati Gama - received grant support from Boehringer company for lectures and for attending ATS congress in 2014. Arthur Oswaldo de Abreu Vianna - received funding support to attend critical care congress from E. Tamussino. Carlos Roberto Ribeiro Carvalho - is a stake holder of TIMPEL. Corine Taniguchi - received honoraria for a lecture on ventilator-associated pneumonia from Covidien and for two classes on automatic weaning from mechanical ventilation from Draeger. Diogo Oliveira Toledo - received honoraria from Danone and Nestlé for lecutres. Gustavo Faissol Janot de Matos - received financial support from Edwards Lifescience for training lecture given to company employees. Jorge Luis Valiatti - received honoraria from Intermed Brazil for consulting and training during the years 2005-2012. José Mario Meira Teles - received honoraria for lectures from Hospira. Juliana Carvalho Ferreira - received grants to her Institution. Marcelo Brito Passos Amato - declares that his laboratory (LIM-09 USP) has received funding for research in the last 5 years from the following companies: a) Covidien 2012-2014 (for experimental studies and simulations on patient-ventilator synchrony), b) Dixtal Biomedical / Philips 2009-2013 (for experimental studies on Electrical Impedance Tomography), c) the SA Timpel 2013-2014 (for experimental studies on Electrical Impedance Tomography). Marcelo Alcântara Holanda - declares he is the founder and owner of the platform and the virtual simulator for teaching XLung Mechanical Ventilation. Marcelo Park - receivedfunding for lectures on ECMO from Maquet and Nipro. Murillo Santucci César Assunção - received honoraria for lectures from the following industries: Edwards Lifescience, Eli Lilly, Pfizer, Astrazeneca, Roche, Thermo-Fisher, Astellas, Novartis, and Baxter and research grants and monitors from Edwards Lifescience, Dixtal-Philips, Masimo and Eli Lilly. Alexandre Biasi Cavalcanti, Antonio Duarte, Ary Serpa Neto, Bruno Bravin, Bruno do Vale Pinheiro, Bruno Franco Mazza, Carlos Toufen, Cid Marcos David, Débora Dutra da Silveira Mazza, Desanka Dragosavac, Eduardo Leite, Eliana Caser, Eliezer Silva, Fabio Amorim, Felipe Saddy, Filomena Galas, Gisele Sampaio, João Claudio Emmerich, Josué Victorino, Luciana Prodomo, Ludhmila Abrahão Hajjar, Luis Claudio Martins, Luis Marcelo Malbouisson, Mara Ambrosina Vargas, Marco Antonio Soares Reis, Marcia Jacomelli, Marcos Soares Tavares, Marta Cristina Paulette Damasceno, Moyzes Pinto Coelho Duarte Damasceno, Nazah Youssef, Paulo José Zimmermann, Pedro Caruso, Péricles Almeida Delfino Duarte, Octavio Messeder, Raquel Caserta Eid, Ricardo Goulart Rodrigues, Rodrigo Francisco de Jesus, Ronaldo Adib Kairalla, Sandra Justino, Sergio Nemer, Simone Barbosa Romero and Verônica Amado - have no conflict of interest.

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