New Aspects in Mechanical Ventilation

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Abstract

We present a short overview on what is state of the art in mechanical ventilation with emphasis on acute lung injury and acute respiratory distress syndrome as well as on some newer trends for weaning of the patients from mechanical ventilation.

Key Words

IC treatment · ARDS · Ventilation

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Introduction

Since its introduction in the early fifties of the last century, mechanical ventilation has become a unique tool to save life especially in, but by no means limited to, respiratorily compromised patients. Nowadays, the recognition that mechanical ventilation, although life-saving, can contribute to patient morbidity and mortality has been the most important advance in the management of patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). Like that, many other dogmas of mechanical ventilation have dramatically changed only within a couple of years. The application of external positive end expiratory pressure (PEEP) in patients with exacerbated chronic obstructive pulmonary disease (COPD) or asthma, having been abandoned over decades with respect to the risk of lung overdistension, now has become a standard procedure, provided external PEEP is set below the level of the so-called intrinsic PEEP. Similarly, the acceptance of elevated arterial carbon dioxide partial pressure ($PaCO_2$) in patients with ALI or ARDS (known as permissive hypercapnia) has been widely accepted to prevent potentially harmful ventilatory settings otherwise necessary to keep the $PaCO_2$ within physiological ranges (i.e., within normal values for the healthy subject). The same holds true for the concept of intermittent application of sights which was smiled at for years and now has been resurrected in the form of recruitment maneuvers. Furthermore, the trend to allow for supported spontaneous breathing instead of the fully controlled mechanical ventilation early and thus the less stable phase of ALI and ARDS is another example of a dogma that becomes increasingly changed. Last but not least, there is increasing evidence that noninvasive ventilatory support via a face mask or similar devices can successfully augment ventilation and prevent tracheal intubation in patients with acute cardiogenic pulmonary edema, exacerbated COPD, or possibly also in patients suffering from ALI. In this context it has to be noted that the apparently never-ending struggle of volume-targeted versus pressure-targeted mechanical ventilation seems to be over as with the introduction of the so-called dual-control modes (i.e., volume-targeted, pressure-limited, and time-cycled ventilation) the advantages of volume and pressure control have been ideally combined.

In the following, a short overview is given about the state of art in mechanical ventilation with emphasis to ALI and ARDS as well as on some newer trends for weaning of the patients from mechanical ventilation. Other promising modalities of ventilatory support that are still subjected to experimental investigations and therefore far beyond clinical practice will not be addressed in this review.

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Ventilatory Management of ALI and ARDS

As no specific pharmacologic intervention has been proven effective for ALI or ARDS yet, therapy is largely supportive with the use of mechanical ventilation. Within the last years there has been growing evidence that mechanical ventilation, although necessary to save life, can potentiate or directly injure the lungs, i.e., due to high inflation pressures or overdistention (barotrauma or volutrauma [1]), repetitive opening and closing of alveoli (atelectrauma [2]), and upregulation of cytokine release resulting in a systemic inflammatory response (biotrauma [3]). These mechanisms collectively have been subsumed under the term "ventilator-associated lung injury" or VALI [4–6].

Observations show that the lungs of patients with ALI or ARDS are heterogeneously affected (some areas are atelectatic, and therefore less available for ventilation while others appear and behave normal) leading to the "baby lung" concept which suggests that lung volume available for ventilation in ALI/ARDS is markedly reduced [7, 8]. This could explain why barotrauma or volutrauma results when volumes and pressures adapted to a normal adult lung are forced in an ARDS lung. Furthermore, shear forces at the interface between the open and closed lung units result. Both of these injuries additionally promote release of cytokines from the lung resulting in adverse systemic effects (i.e., contributing to the development of multisystem organ failure [2, 3]).

The better understanding of ALI, ARDS and ventilator-associated lung injury has lead to lung-protective mechanical ventilation strategies recently tested in a number of important clinical trials.

Conventional Lung-Protective Ventilation

This strategy is designed to prevent further lung injury in patients with ALI or ARDS using a standard mechanical ventilator.

Five randomized controlled trials have compared lung-protective ventilation with conventional mechanical ventilation [9–13]. Three of these did not find a difference in mortality between the treatment and control groups [10–12]. One study including 53 patients applied higher PEEP and recruitment maneuvers combined with pressure- and volume-limited ventilation in the intervention group [9]. This study demonstrated a significant reduction in 28-day mortality. However, there was no significant difference in mortality at hospital discharge, and a high mortality rate (71%) in the control arm may have attributed to the survival difference. The fifth largest trial, with 861 patients, of volume- and pressure-limited ventilation was conducted by the ARDS Network (ARDSNet) [13]. It demonstrated a 9% absolute decrease in mortality (31 vs. 40%; $p = 0.007$) when patients were ventilated with reduced tidal volumes (target of 6 ml/kg of predicted body weight with a range of 4–8 ml/kg depending on plateau pressure and pH) and reduced pressures (plateau pressure, measured after a 0.5 s end-inspiratory pause, ≤ 30 cm H_2O).

Although it can be criticized that the control groups of the two trials showing a survival advantage did not reflect "standard of care", they strongly suggest that ventilatory strategies have an impact on mortality [14]. This is supported by two subsequent meta-analyses, providing some evidence that volume-limited ventilation, particularly in the setting of elevated plateau pressure (>30 cm H_2O), has a short-term survival benefit [15, 16].

In addition to lung-protective ventilation, higher PEEP and the use of recruitment maneuvers may be adjunctive components. Recruitment refers to the reopening of collapsed alveoli through an intentional increase in transpulmonary pressure, which may be achieved through a variety of mechanisms. However, optimal pressure, duration, and frequency of recruitment maneuvers have not been defined and tested in clinical trials. Factors as the type (e.g., primary vs. secondary) and stage (e.g., early vs. late) of ALI or ARDS and recruitment technique used [17, 18] may be responsible for the variable results yielded in human studies [19–23]. It has to be emphasized that the safety of recruitment maneuvers requires careful evaluation. Although transient oxygen desaturation and hypotension are the most common adverse effects, other clinically significant events such as barotrauma (e.g., pneumothorax), arrhythmia, and bacterial translocation may occur [22, 24].

Alternative Ventilatory Approaches to Lung Protection

The precise role of high-frequency ventilation (HFV) and airway pressure release ventilation (APRV) has not been established. HFV allows for higher mean airway pressures, lower peak airway pressures and for markedly reduced tidal volumes (1–3 ml/kg) [25, 26]. Only high-frequency oscillatory ventilation (HFOV) has been studied in moderately sized randomized trials [27]. In two trials (148 and 61 patients, respectively) there were no significant differences with respect to major adverse outcomes (i.e., new air leakage, intractable hypotension) and mortality between HFOV and conventional mechanical ventilation.

Airway pressure release ventilation not only provides higher mean airway pressures but also allows for spontaneous breathing, which may be associated with better gas exchange, improved hemodynamics, and reduced sedation requirements [28].

Adjunctive Therapies to Lung-Protective Ventilation

The use of prone positioning may lead to recruitment of dorsal (nondependent) atelectatic lung units, improved respiratory mechanics, decreased ventilation–perfusion mismatch, increased secretion drainage, and reduced injurious mechanical forces [29].

There are three randomized trials of prone positioning in adults with ALI or ARDS [30–32]. In the first study including 304 patients a significant improvement of oxygenation in the prone group could be demonstrated but no significant difference in mortality or any secondary outcome [30]. However, a post hoc analysis showed decreased mortality for the most severely ill patients assigned to the prone position at day 10, but this benefit did not persist beyond intensive care unit discharge. The second study including 791 patients (48% with ALI or ARDS) also demonstrated improved oxygenation without a survival benefit at 28 days [31]. The third study was stopped early (133 of 200 patients) due to problems with enrolment. It revealed a large, but statistically insignificant, difference in intensive care unit mortality between the two groups (supine, 58.6% vs. prone, 44.4%; $p = 0.43$) [32].

At this time, other adjunctive therapies such as inhaled vasodilators (e.g., NO), surfactant, and extracorporeal life support should be limited to future clinical trials and rescue therapy for patients with ALI or ARDS with life-threatening hypoxemia failing maximal conventional lung-protective ventilation as there is insufficient scientific evidence to support their use in daily practice.

Ventilatory Management for Weaning from Mechanical Ventilation

At the latest after there has been a lasting improvement in the underlying causes for ventilatory impairment, the process of weaning from mechanical ventilation should be initiated. To this end, two distinct concepts have been established of which the one gives preference to a more controlled modality of mechanical ventilation interrupted by a daily preextubation trial [33]. In this 2 h trial, the patient is breathing spontaneously with sufficient oxygen delivery and PEEP via the endotracheal tube but without any additional ventilatory support. The other concept is based on a gradual reduction of ventilatory support whereby the patient is expected to concomitantly increase his effort step by step [34]. Although the latter sounds very physiological, some pitfalls have to be addressed.

First of all, competence for successfully managing ventilation is not only limited to the ability to deal with the work of breathing but also to deal with breathing control that still might be hampered in the very early phase of weaning, e.g., due to after-effects of analgosedation.

Secondly, the endotracheal or tracheostomy tube (ETT) as the smallest part of the connecting system between the ventilator and patient imposes an additional work of breathing for the patient [35–37]. *Additional* means that this work of breathing is imposed to the work the patient already has, i.e., to overcome impaired mechanical properties of his diseased respiratory system, and also that this kind of work will no longer be present after the removal of ETT. Due to its resistive nature, the ETT-related additional work of breathing mainly depends on the gas flow through and the inner diameter of the ETT: the higher the gas flow and the smaller the ETT, the higher the pressure drop across the ETT and, thus, the bigger the additional work of breathing for the patient [38–40]. As the gas flow in spontaneous breathing is far from being constant, ETT resistance can, by principle, not be compensated for by a constant inspiratory pressure support, e.g., with the pressure support ventilation (PSV) mode [35, 47]. In addition, it has to be highlighted that the ETT-related additional work of breathing is not restricted to inspiration but also present during expiration and therefore can change the otherwise passive process of exhalation to an active (i.e., power consuming) one [37, 39]. If so, expiratory time will be prolonged and air trapping and intrinsic PEEP might be promoted [41].

A third point that has to be addressed for the concept of gradual weaning from ventilatory support goes along the patient's increasing competence to participate in both the work and the control of breathing. Unlike controlled mechanical ventilation in the sedated patient where ventilation is defined exclusively by the settings of the ventilator and the mechanical properties of the patient's respiratory system, a third contributor, i.e., the patient's behavior, interacts with the compound of ventilatory settings and respiratory mechanics. As long as the patient's behavior goes along the preset ventilatory modalities, external (i.e., by the ventilator) and internal (i.e., by the patient) contribution of breathing support ideally supplies each other. If this is not the case, the patient and the ventilator are more or less in asynchrony (fighting each other [42, 43]) and the resulting effect on ventilation might be very less than that entered by either contributor. Obviously, sensitive algorithms for the triggering of inspiration and expiration are necessary to improve patient–ventilator synchrony [35, 42, 43]. By the way, optimized synchronization between the ventilator's response and the neural intention of the patient to start inspiration and expiration is increasingly subjected to ongoing research [44].

Connected with, but not restricted to, the problem of asynchrony, another pitfall of the concept of gradual weaning from ventilatory support has to be addressed, i.e., the time that has to be spent for adapting the ventilatory settings during the course of weaning to (1) the resolving mechanical properties of the respiratory system, (2) the patient's behavior, and (3) planned withdrawal of ventilatory support. This task will be even more time-consuming for noninvasive ventilation (NIV). To entirely fulfill that task, a nearly continuous bedside presence of a respiratory therapist (nurse, doctor) seems to be a prerequisite.

In summary, the concept of weaning from mechanical ventilation by a gradual withdrawal of ventilatory support in connection with a concomitant increasing participation of the patient sounds very physiological and thus might be preferred in case the pitfalls related with have been successfully overcome. Of note, these pitfalls are the more important in more diseased patients whereas they are of minor importance or even neglectable in less diseased patients, e.g., in patients subjected to a short course of postsurgical ventilation.

The concept of allowing patients to breathe spontaneously while receiving mechanical ventilation, interspersing their own efforts with those of the machine, evolved in the early 1970s with the introduction of assist/control (A/C), intermittent mandatory ventilation (IMV) and later on with synchronized intermittent mandatory ventilation (SIMV) and PSV. Despite their usefulness and broad acceptance in clinical practice (especially PSV), the application of these ventilatory modalities has unmasked the pitfalls mentioned above rather than helped to circumvent them. Meanwhile some newer ventilatory modes are available in clinical practice being especially designed to overcome some of these disadvantages.

Automatic Tube Compensation

Automatic tube compensation [ATC; also known as tube compensation, (TS) and other acronyms] is a new option to compensate for the nonlinearly flow-dependent pressure drop across an ETT during inspiration and, in some ventilators, also during expiration. In doing so, ATC compensates for the tube-related additional work of breathing ("electronic extubation"). ATC is based on a closed-loop working principle [45]. For expiratory tube compensation (if at all in place), either a negative pressure source is mandatory [45] or the preset PEEP level is used as a rather limited source of "negative" pressure [46]. ATC is not a true ventilatory mode but rather a new option that can be combined with virtually all ventilatory mode whereby the level of pressure assistance in that mode then has to be reduced [46]. As of yet, ATC has been associated with certain benefits for the tracheally intubated spontaneously breathing patient. Among these, reduced work of breathing [47, 48], preservation of the natural "noisy" breathing pattern [46–49], enhanced synchronization between the patient and the ventilator [46, 50], and improved respiratory comfort [49, 51] seem to be the most important. Moreover, sufficient spontaneous breathing with ATC alone, i.e., without any additional ventilatory assist, might help to predict more accurately the readiness for extubation in the last phase of weaning from mechanical ventilation [52]. Furthermore, it has been shown in patients with acute lung disease that ATC unloads the inspiratory muscles and increased alveolar ventilation without adversely affecting cardiorespiratory function [53]. Of note, however, it has been demonstrated in an experimental setting that the flow-adapted tube compensation in different commercially available ventilators was more or less adequate for inspiratory but not for expiratory tube compensation [54]. Expiratory ATC should not be used in the presence of active airway obstruction as it might then facilitate airway collapse [46, 50]. A further limitation of ATC is given when the ETT becomes (partly) obstructed by tube kinking or mucous deposition [55]. If so, resistance of the ETT will be inevitably undercompensated (as with any other ventilatory modes such as PSV) because the algorithm behind ATC is based on the physical conditions of a native, i.e., unobstructed, ETT [46]. With a bedside maneuver, accuracy of ATC can be easily regained [56].

Proportional Assist Ventilation

In an effort to adapt the breathing assistance of the ventilator closer to the needs of the spontaneously breathing patient (e.g., to avoid patient–ventilator asynchrony and to solve triggering problems) proportional assist ventilation [PAV; also known as proportional pressure support, (PPS) and other acronyms] has been developed [57–60]. PAV was first described in 1962 by Tyler and Grape [61]. Instead of a preset pressure support (as with PSV) the patient receives support in proportion to his instantaneous effort without any preselected target for volume or pressure. Consequently, PAV is the only ventilatory mode that adapts pressure assistance instantaneously and thus continuously to the patient's needs. The patient's instantaneous effort is determined by the (patient-generated) instantaneous airflow and volume and is supported by a flow- and volume-proportional pressure support, respectively [57, 58]. In doing so, flow-proportional pressure support compensates for increased airway resistance and volume-proportional pressure support for reduced compliance of the respiratory system. In other words, flow-proportional pressure support unloads the resistive burden of the patient whereas volume-proportional pressure support does it for elastic burden. With PAV the pressure applied to inflate the respiratory system results from a combination of the patient's inspiratory effort and the positive jet proportional pressure applied by the ventilator. In doing so, PAV works in a positive feedback manner (like an amplifier) whereby the gain of amplification has to be set by the caregiver. PAV does not need an inspiratory or expiratory trigger [50]. Furthermore, if PAV is applied as pure flow-proportional pressure support, there is no end-inspiratory positive pressure load (otherwise inevitable with any other ventilatory mode except negative pressure ventilation with iron lung or similar devices) [50]. As PAV provides flow-proportional pressure support in a linear manner, it can, by principle, not adequately compensate for the nonlinear pressure drop across the ETT in intubated patients [48, 50]. Therefore, PAV should always be combined with ATC.

In clinical studies, PAV has been shown to fulfill most of the promises coming along, such as to avoid patient–ventilator asynchrony and triggering failure [50, 62], to reduce airway pressure at preserved alveolar ventilation [63, 64], and to allow for a more physiological (i.e., variable) breathing pattern [64–68] and increased comfort [69]. Alongside the highly appealing advantages of PAV, a number of limitations and disadvantages also need to be depicted. First of all, full advantages of the PAV mode could be drawn only, if current compliance and resistance of patient's respiratory system are known [50, 58]. As during spontaneous breathing this is not an easy task, especially in the clinical setting, the level of unloading with PAV cannot be properly defined. As a consequence, under-compensation and over-comepensation ("run-away") of the elastic and resistive burden might result [58]. Furthermore, as PAV allows the patient complete freedom in determining his breathing pattern and thus in selecting his respiratory rate and the depth of his breaths, this freedom presupposes that the patient's respiratory control center is able to handle this degree of freedom [50, 58]. This will hardly be the case in the very early phase of weaning (e.g., because of ongoing or just discontinued sedation therapy) and definitely not in patients with periodic breathing or the Cheyne–Stokes breathing pattern [70] which both can be intensified by PAV to a more severe degree. Furthermore, PAV should not be applied in the presence of leakage in the pneumatic ventilator–patient system, as the control algorithm behind PAV then will proportionally support also the leak flow and thus might promote lung overdistention [58].

Adaptive Support Ventilation

The philosophy behind adaptive support ventilation (ASV; available with the Galileo ventilators from Hamilton Medical) is to improve the patient–ventilator interaction by allowing the patient to determine the ventilatory support required, whereby the ventilator automatically adapts to the changing requirements for support [71–73]. ASV is analogous to modern closed-loop technology in aviation such as autopilot and automatic landing system. ASV is based on pressure-targeted SIMV with pressure support, using a computerized lung function analyzer to determine the patient's requirement online breath-by-breath [74] and a programmed computer-driven ventilator to supply the best pressure, flow, and ventilation pattern as precisely as possible for each breath [74–79]. The cornerstones for determining the best pressure, flow, and ventilation pattern are based on the preset (by the caregiver) minimum alveolar ventilation, well-defined boundaries for safety, the concept of maximal energetic benefit (i.e., minimal work of breathing of the patient–ventilator unit [75]), and measurements of current lung mechanics included therein series dead space and expiratory time constant [74]. ASV can be used for controlled mechanical ventilation as well as for supported spontaneous breathing, but over and above that, also for the proper transition from the former to the latter and vice versa [71, 72]. With that feature in place, ASV can be used to deliver full or partial ventilatory support during the initiation, maintenance, and weaning phase of mechanical ventilation whereby the entire process of mechanical ventilation and weaning (with respect to ventilatory support but not to oxygenation) is widely automated. Not surprisingly, ASV has been designated with the catchword automatic weaning [71]. However, because of the complexity of the weaning process, ASV was designed and, as yet, has been demonstrated to work properly in easy-to-wean rather than in difficult-to-wean patients. One of the major disadvantages of ASV lies in the fact that in the presence of an increased minute ventilation the ASV controller is unable to differentiate between increased ventilatory demand (e.g., fever, infection, etc.) and regaining competence of the patient to deal with the work of breathing. Any increase in alveolar minute ventilation will be answered by the ASV controller by a reduction of the ventilatory support level, which is adequate in the latter but deleterious in the former, i.e., in case of increased ventilatory demand. May be that, with the incorporation of airway occlusion pressure into the algorithm ($P_{0.1}$ controller [80]), ASV could overcome such problems and, in connection with ATC, might be able to govern weaning also in more difficult-to-wean patients.

SmartCare

This ventilatory option is commercially available only in the Evita XL ventilators from Dräger and was designed to automatically wean the pressure support (PSV) in ventilator-dependent spontaneously breathing patients. In contrast to ASV, which is based on well-defined rules, SmartCare is rather based on a clinical protocol for weaning being elaborated by experts in respiratory care [81–83]. In doing so, SmartCare firstly regulates the level of pressure support in order to have the patient's breathing rate, tidal volume, and end-tidal CO_2 within well-defined ranges (the so-called zone of comfort). In a second step, the pressure support is automatically reduced step by step provided all of the above-mentioned respiratory variables remain within the zone of comfort. If one or more of the respiratory variables leave the zone of comfort, the pressure support level is increased stepwise up to its preset upper limit or backup apnea ventilation is initiated. If the pressure support has been reduced to a minimal level being considered to compensate for ETT resistance and all of the respiratory variables were within the zone of comfort, removal of the ETT can be considered. Note, that the settings for oxygenation (i.e., PEEP and FiO_2) must be adapted manually as they are not in the scope of automated weaning. As of jet, SmartCare has been demonstrated to work well in not difficult-to-wean patients [84, 85]. It has also been shown that SmartCare significantly shortens duration of weaning, which holds especially true in intensive care units with limited personal resources [85, 86].

Non-invasive Ventilation

Non-invasive ventilation (NIV) delivers mechanical ventilatory support to the lungs with a non-invasive interface (i.e., face mask) between patient and ventilator instead of an ETT. Proper use of nasal or face masks is crucial to avoid air leakage, pressure sores, eye irritation, and poor patient compliance. The use of nasal masks carries a great risk of leakage if the patient breathes through the mouth, a markedly impairing effectiveness. Various ventilation modes can be applied in NIV. Continuous positive airway pressure (CPAP) is the simplest one and can be used for the treatment of cardiogenic pulmonary edema and in postoperative respiratory complications but probably not for acute respiratory failure. To effectively support a patient with acute respiratory failure, a combination of pressure support (PSV) with PEEP is used. Another promising mode of NIV assistance is the application of PAV currently being under investigation. Tolerance of NIV depends not only on the patient's mental and respiratory status but also on the attention given by caregivers. Poor tolerance of NIV by the patient has been found to be an independent predictor of failure [87].

Patients with hypercapnic acute respiratory failure are most likely to benefit from NIV [88, 89]. The pathophysiology of acute decompensation episodes of chronic respiratory failure involves an inability of the respiratory muscles to generate adequate alveolar ventilation. Therefore, such patients have a small tidal volume, which is inadequately compensated for by an increase in respiratory rate. Their rapid shallow breathing with a limited carbon dioxide removal may be improved by NIV and it can reverse clinical abnormalities related to hypoxemia, hypercapnia, and acidosis [90, 91] resulting in avoidance of endotracheal intubation and reduction of complications, length of stay, and finally improving survival in patients with COPD [92–94]. Furthermore, NIV can be considered in patients with a do-not-intubate order, especially in those with a diagnosis of congestive heart failure or chronic obstructive pulmonary disease, who have strong coughing, or who are not sedated due to a better prognosis [95].

Some patients with acute cardiogenic pulmnary edema may require short-term ventilatory support. Several NIV modalities have been used to prevent endotracheal intubation in these cases. Non-invasive CPAP increases intrathoracic pressure, decreases arterio-venous shunting, and improves arterial oxygenation [96, 97]. Furthermore, CPAP may lessen the work of breathing by decreasing the left ventricular afterload in non-preload-dependent patients [98]. Randomized trials comparing CPAP with PSV plus PEEP found equal effects of both CPAP and PSV plus PEEP. Moreover, they could show a significant reduction in the need of endotracheal intubation and mechanical ventilation compared to standard medical treatment [99, 100].

Most recently, an increasing number of studies have been presented where NIV has been studied in patients with predominately hypoxemic respiratory failure. In some of these studies it could be shown that in selected patients with ALI in the absence of hemodynamic and neurological impairment, NIV may reduce the need for intubation and improve outcomes [93, 101, 102].

One of the benefits of NIV may be the reduction of infectious complications. NIV potentially reduces the risk of nosocomial pneumonia because the natural glottic barrier is not bypassed by an endotracheal tube. Lower rates of mortality, intubation, infection, and lower length of stay could be shown in solid organ recipients or in patients with severe immune suppression [103, 104]. Whether NIV is effective for postextubation respiratory distress is still a matter of debate. The first randomized controlled trial performed in a heterogeneous group of patients did not show any benefit from the use of NIV to prevent the need for re-intubation [105].

Risks of NIV: In an emergency department study, a trend toward poor outcome in the NIV group suggested that endotracheal intubation was perhaps delayed by inappropriate or inadequate use of NIV [106]. In the study from Antonelli et al. [101] that found overall benefits of NIV, the mortality rate was still high in patients who were initially given NIV but eventually required intubation, raising the possibility that delayed intubation may have adversely affected the outcomes. Identifying early predictors of NIV failure may be useful to minimize this risk.

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