Noninvasive Positive-Pressure Ventilation in Patients with Acute Hypoxemic Respiratory Failure and HIV/AIDS

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Keywords

Noninvasive ventilation • Acute hypoxemic respiratory failure • Hypoxemic respiratory failure • Respiratory failure in HIV/AIDS • NIV • NIPPV

10.1 Introduction

Pulmonary complications, especially acute respiratory failure (ARF), contribute to morbidity and mortality in immunocompromised patients. The etiology, pathophysiology, and reversibility of lung injury and the severity of ARF are key to the therapeutic response and prognosis for these patients.

An essential notion is that evolution of ARF depends on a causal disease and that noninvasive ventilation (NIV) does not correct the primary process. It should be considered a measure that allows us to gain the time needed to reverse the primary process. The longer NIV is needed, the less chance there is of success, suggesting that perhaps that patient is not an appropriate one to subject to NIV.

It is advisable to identify the various scenarios in which immunosuppression may be associated with ARF.

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- Patients with a malignancy or inflammatory diseases, among whom we can identify two groups: (1) those on immunosuppressive therapy, in whom ARF is mainly associated with infections, recurrence of the underlying disease, drug toxicity, or other noninfectious diseases; (2) those without immunosuppressive therapy, among whom ARF is predominantly related to progression of the underlying disease or other noninfectious disease.
- Transplant patients with predominantly infectious pulmonary complications related to drug immunosuppression, drug toxicity, or other noninfectious diseases.
- Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) patients, among whom ARF is related predominantly to lung infections (bacterial pneumonia, *Pneumocystis jirovecii* pneumonia, lung infections caused by opportunistic agents other than *P. jirovecii*) or other noninfectious diseases.

In HIV/AIDS patients, ARF is the leading cause of hospitalization in intensive care units (ICUs), with bacterial pneumonia and *P. jirovecii* pneumonia the most frequently associated entities. Survival in this situation depends on having the means to diagnose and manage ARF and the causal disease and the methods to support vital functions (including respiratory function) while the causative disease is being reversed. Support of respiratory function might include the use of oxygen therapy, noninvasive positive-pressure ventilation (NIV), intubation and mechanical ventilation (MV), and/or extracorporeal oxygenation devices.

Although MV is an effective, reliable method, it is associated with increased short-, medium-, and long-term morbidity and mortality related to ventilation-associated pneumonia and upper airway injury. Reducing the incidence of these complications associated with effectiveness at least equivalent to that of MV are the rational foundations for the development and implementation of NIV in these patients. Throughout this text, NIV refers to positive-pressure mechanical ventilation without airway invasion. NIV basically includes pressure support ventilation (PSV) with positive end-expiratory pressure (PEEP), also referred to as bilevel pressure ventilation, and continuous positive airway pressure (CPAP).

10.2   Underlying Pulmonary Injury in ARF Patients

The retrospective analysis of 4,710 autopsies of patients who died with ARF (which constituted 18 % of autopsies between 1990 and 2008) showed the following: The patients' average age was 52 years, and 58 % were male. Overall, 38 % of the deceased patients had a single associated disease, 32 % had two, 17 % had three, and 11 % had more than three. In all, 62 % of the patients had two or more associated diseases.

Histopathology revealed lung injury compatible with acute respiratory distress syndrome (ARDS) in 75 % of cases (41 % diffuse alveolar damage, 24 % pulmonary edema, 10 % alveolar hemorrhage). Inflammatory involvement described as interstitial pneumonia (edema of alveolar septa; infiltration with mononuclear cells, histiocytes, plasma cells, and polymorphonuclear neutrophils) was evident in 5 % of cases.

The most frequent associated diseases were bacterial pneumonia in 34 % of cases, malignancies in 28 %, sepsis and/or septic shock in 14 %, and HIV/AIDS in 10 %. The pattern described as interstitial pneumonia was seen predominantly in patients with HIV/AIDS [1].

The retrospective analysis of 250 autopsies of HIV/AIDS patients who died with ARF between 1990 and 2000, showed the following: Histopathology showed acute intersticial pneumonia (edema of the alveolar septa; infiltration of mononuclear cells, histiocytes, plasma cells, polymorphonuclear neutrophils) in 40 % of the cases. It also revealed injuries consistent with ARDS (diffuse alveolar damage 36 %, pulmonary edema 13 %, and alveolar hemorrhage 12 %) in 60 % of the deceased patients.

In addition to HIV/AIDS, a single disease associated with ARF was identified in 40 % of patients, two diseases or more in 44 %, and none in 16 %. Bacterial pneumonia was the most frequently associated disease (36 % of patients), and *P. jirovecii* pneumonia was the second most frequently seen (27 %). Pulmonary or disseminated tuberculosis (TB) was found in 15 %, sepsis and/or septic shock in 14 %, and cytomegalovirus (CMV) pneumonia in 13 %. The most frequent malignant disease was Kaposi's sarcoma, seen in 4.5 % of cases. *P. jirovecii* pneumonia was associated primarily with the injury described as acute interstitial pneumonia and sepsis and/or septic shock with diffuse alveolar damage [2].

Lung infection has a significant impact among the causes of ARF in HIV/AIDS patients. The risk of developing each infection is related to the severity of the immunosuppression, regional epidemiology, and prophylaxis against most frequently isolated agents. A clear example related to regional epidemiology is the comparison of the prevalence of pulmonary TB among different populations. The epidemiology of lung infection has changed in recent decades. Prophylaxis against *P. jirovecii* since 1989 and the availability of highly active antiretroviral therapy (HAART) since 1996 are the most obvious reasons. Although *P. jirovecii* pneumonia has been replaced by bacterial pneumonia as the most common lung infection, both continue to be leaders among causes of ARF.

Infection with HIV increases the incidence of bacterial pneumonia tenfold. Recurrent bacterial pneumonia has been included as an indicative disease for AIDS since 1992. Bacterial pneumonia, especially that caused by *Streptococcus pneumoniae*, and pulmonary TB can develop when the number of CD4+ T-cells is still acceptable (e.g., 500 cells), although the incidence increases as immune function declines. For this reason, during the initial stages of disease Bacterial pneumonia and TB are clearly predominant.

As in the general population, *S. pneumoniae* is the most frequently isolated agent in HIV/AIDS patients with community-acquired pneumonia, 20 % of all bacterial pneumonias, and 40 % of those with isolation of a known agent. Infection by opportunistic agents develops when the CD4+ T-lymphocyte number is <200 cells.

Haemophilus influenzae is isolated in 10–15 % of bacterial pneumonias, especially in patients with significantly lowered immune function. In 30 % of them, the evolution is subacute, and in more than half of these patients there are bilateral radiologically identified lung lesions.

Staphylococus aureus is the third single agent to cause bacterial pneumonia. It is advisable to remember that intravenous drug users may develop endocarditis of the tricuspid valve due to *S. aureus*, with pulmonary seeding manifested by multiple cavitary nodules.

Pseudomonas aeruginosa infections have been significantly reduced. The acquisition of this agent was mostly nosocomial, and patients today have less frequent and shorter hospitalizations. Pneumonias due to *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae* appear to be relatively uncommon in this population but have not been systematically studied.

Importantly, there is still a significant population of patients with undiagnosed HIV. There is yet another group with a diagnosis of HIV but who are not taking HAART or any other type of prophylaxis. Both the incidence of infections and related agents continue to be as described before effective treatment came available [3].

A prospective assessment of 57 HIV-positive patients hospitalized with lung injury and ARF between 1993 and 1998 showed the following results: Among the 57 patients, 30 had a diagnosis of bacterial pneumonia and 21 of *P. jirovecii* pneumonia. In all, 23 of the 30 with bacterial pneumonia had CAP. The most frequently isolated agent was *S. pneumoniae*. *Mycobacterium tuberculosis* was isolated in four patients. Most of the patients with *P. jirovecii* pneumonia did not have a diagnosis of HIV and had not received specific prophylaxis or HAART. In all, 33 % of the patients were under HAART compared with 80 % of those monitored regularly in the hospital. Pulmonary lesions seen by chest radiography were bilateral interstitial involvement in 35 patients, bilateral consolidation in 14, and unilateral consolidation in 8. The radiological lesions were bilateral in 100 % of those with *P. jirovecii* pneumonia and in 80 % with bacterial pneumonia. CD4 cell counts in patients with *P. jirovecii* pneumonia compared to those with bacterial pneumonia were 29 and 157, respectively. Mortality in this sample was 40 % and was higher for patients with *P. jirovecii* pneumonia. The only data associated with increased mortality was a low PaO_2/FiO_2 at admission.

Comparing these results with those from previous studies shows that 30 % patients with *P. jirovecii* pneumonia in this study developed ARF versus 70 % in earlier studies of episodes. Only 7 % required intensive care in this study compared with 19 % in the earlier studies. The number and severity of bacterial pneumonias were also reduced after the introduction of HAART [4].

A retrospective evaluation of 147 hospitalized patients with HIV/AIDS and ARF between 1996 and 2006 was conducted. The presence of ARF revealed the diagnosis of HIV in 30 % of the patients. The causes of ARF were bacterial pneumonia in 74 patients (50 %). The most frequently isolated agent was *S. pneumoniae*, with 38 % of these patients developing septic shock. *P. jirovecii* caused pneumonia in 52 (30 %) patients and in 60 % of patients with no previous diagnosis of HIV. Other opportunistic infections were seen in19 patients (12 %), more often TB and noninfectious diseases in 33 patients—predominantly heart failure and chronic obstructive pulmonary disease (COPD), perhaps related to the improved survival of these patients today. Related diseases did not change throughout the study period. Two or more causes were identified in 33 patients (22 %), such as an association of bacterial

pneumonia with *P. jirovecii* or other opportunistic or noninfectious diseases or *P. jirovecii* with CMV. The 43 patients who were under HAART more frequently had bacterial pneumonia or noninfectious diseases than opportunistic infections. In all, 49 patients (33 %) underwent NIV, and 30 % of them required MV. In total, 30 % of patients required MV and 26 % vasopressors. The in-hospital mortality rate was around 20 % and did not change over study period. It was not different for each of the four diagnostic categories. Mortality was related to the need for MV or vasopressors, the greater interval between hospital admission and transfer to the ICU, and the number of causes of ARF. There was no identified association between the CD4 cell count or viral load and mortality [5].

10.3 ARF Physiopathology

Patients with HIV/AIDS develop ARF related to multiple etiologies. Lung injury, however, is limited to a few patterns. We must not forget that ARF treatment through MV can, through alveolar overdistension and cyclical opening and closing of airspaces, generate similar lung lesions. The result of these processes is hypoxemia with or without hypercapnia and multiple organ failure in some cases. Among the described mechanisms of hypoxemia, ventilation/perfusion imbalance and intrapulmonary shunt (i.e., perfusion of alveolar units with little or no ventilation) are typical. They are related to ARDS.

The evolution of ARDS is described in three stages. The *exudative stage* is characterized by alterations in alveolar/capillary membrane permeability and passage of fluid rich in proteins, cytokines [e.g., interleukins 1 and 8, tumor necrosis factor α (TNFα)], lipid mediators (e.g., leukotriene B4), and cells (especially activated neutrophils) to the alveolar space. They are involved in the initiation, maintenance, and progression of an uncontrolled alveolar interstitial inflammatory process. The increased permeability of the alveolar-capillary membrane seems to be a consequence of an alteration in the homophilic union between VE-cadherin molecules, a critical protein in maintaining endothelial cells union. The anti-VE-cadherin antibody, inflammatory mediators such as TNFα, thrombin, and vascular endothelial growth factor (VEGF) interrupt these unions and allow pulmonary edema [6]. Moreover, aggregates of plasma proteins, remnants of necrotic cells, and altered surfactant accumulate, forming intra-alveolar hyaline membranes, which contribute to reducing lung compliance and generating areas of atelectasis. Impaired gas exchange results, causing increased work to breathe and dyspnea.

Pathophysiological phenomena in the pulmonary vasculature can lead to pulmonary arterial hypertension. These phenomena include the following [7].
- Endothelial dysfunction, which involves an imbalance between the vasodilator and vasoconstrictor mediators.
- Pulmonary vascular occlusion, intravascular neutrophil kidnapping, and propensity for intravascular coagulation.
- Increased vascular tone related to alterations in the control of hypoxic vasoconstriction, which generates irregular areas of vasoconstriction and increased

pulmonary vascular resistance, together with vasodilation that exaggerates the ventilation/perfusion imbalance and intrapulmonary shunt. Dysfunctional hypoxic vasoconstriction, which may be correlated with specific factors in the pathological process (e.g., endotoxins, hypothermia, alkalosis, elevated left atrial pressure) or the treatment instituted (e.g., β-adrenergic agonists agents, calcium channel blockers, nitroprusside, PEEP).

- Extrinsic vascular occlusion related to the increase in alveolar volume (PEEP), areas of atelectasis, and alveolar edema.
- Vascular remodeling (in later stages).

During the exudative stage, lung inflammation seems to be driven mainly by activation of the innate immune response through the union of microbial products or endogenous molecules associated with cell damage—danger-associated molecular patterns (DAMPs)—to recognition receptor patterns (e.g., Toll-like receptors) in the pulmonary epithelium and macrophages [8]. Other pathways may also participate, affecting the inflammatory process intensity, such as enzyme converters of angiotensin 1 and 2 balance during the course of viral infections and sepsis [9]. Alveolar surfactant abnormalities, including reduced production, changes in the phospholipid composition, and its inhibition by alveolar plasma proteins promote atelectasis [10].

The *proliferative stage* begins about day 7 and lasts about 2 weeks. During this phase of evolution, most of the surviving patients have been weaned from mechanical ventilation, and lung repair begins. However, in some cases there is progressive lung damage and early changes of pulmonary fibrosis. Histologically, the phase is characterized by organization of alveolar exudates, progressive replacement of neutrophils by lymphocytes, and proliferation of type II pneumocytes over the basal membrane.

Resolution of inflammation requires clearance of neutrophils from the alveoli, a process led by alveolar macrophages and known as "Eferocitosis" [6]. The emergence of alveolar type III procollagen at this stage, a marker of pulmonary fibrosis, is associated with prolongation of the clinical picture and increased mortality.

In the *fibrotic stage*, the alveolar architecture is profoundly altered. Acinar and ductal fibrosis is apparent. It impairs lung compliance and increases alveolar dead space. Fibrotic proliferation of the intima contributes to vascular occlusion, pulmonary hypertension, and its potential impact on right ventricular function [11].

10.4 Physiological Effects of NIV During ARF

The basic objectives of NIV implementation in these patients are to correct pulmonary gas exchange and reduce the work of breathing.

The physiological effects of NIV implementation were evaluated in ten patients with bilateral pulmonary infiltrates associated with lung infections and an average PaO_2/FiO_2 of 131.

CPAP or PEEP of at least 10 cmH₂O significantly increased the PaO_2/FIO_2.

This result suggest that implementation of PEEP or CPAP has favorable effects on oxygenation but only from certain levels. Also, it would be related to the increase
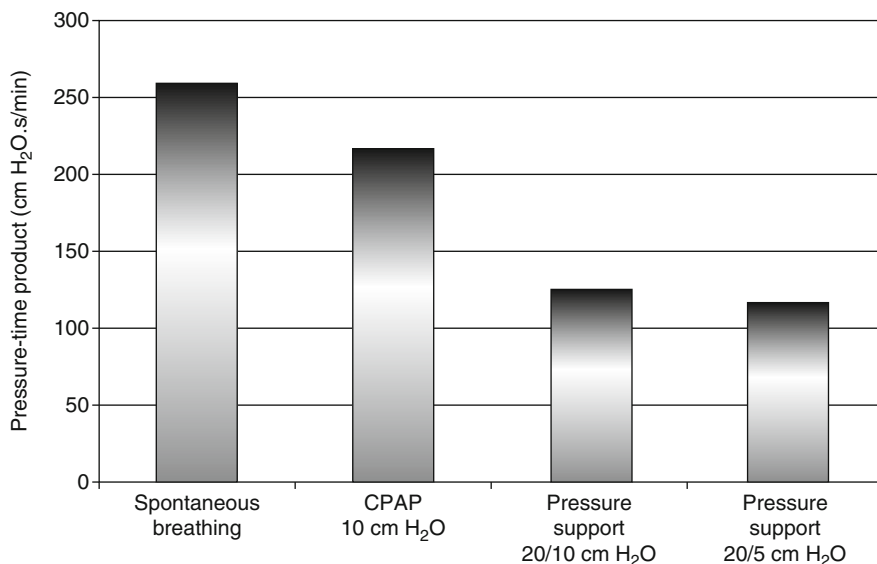
Fig. 10.1 Changes in respiratory muscles loading (pressure–time product) after continuous positive airway pressure (CPAP) application and two levels of pressure support ventilation related to spontaneous breathing in patients with acute respiratory failure [12, 13]

in functional residual capacity, dependent on the alveolar recruitment and stabilization.

Applying a PSV of 10 cmH$_2$O significantly reduced the PCO$_2$, alleviated the dyspnea, and reduced the burden on respiratory muscles, work of breathing, and respiratory drive, proportional to the PSV level applied [12].

Through increasing the tidal volume (Vt), NIV and particularly CPAP or PEEP improves respiratory system compliance by recruiting and stabilizing partially or totally collapsed alveoli. The Vt increase is associated with intensity and duration reduction of the respiratory muscles contraction, reducing the work of breathing. NIV reduces the inspiratory effort. The mean esophageal pressure (Pes) was reduced 8–15 cmH$_2$O (50–76 %), the average transdiaphragmatic pressure (Pdi) by 5–10 cmH$_2$O (42–62 %), and electromyographic activity of the diaphragm ranging from 17 to 93 %. The diaphragmatic time pressure product (PTPdi) was reduced on average 55 % and the work of breathing by 31–69 %. These results are explained by the reduction in the spontaneous transpulmonary pressure during inspiration (PSV), the threshold load for inspiration that is achieved by balancing the intrinsic PEEP, and the elastic load for inspiration by increasing respiratory compliance (CPAP or PEEP).

The PTPdi and the work of breathing are improved most effectively by combining PSV (10–20 cmH$_2$O) and CPAP or PEEP (5 cmH$_2$O), rather than using either alone. In patients with ARF and ARDS, CPAP reduced the PTPdi by about 16 %, whereas the combination of PSV (10–15 cmH$_2$O) with PEEP (5–10 cmH$_2$O) reduced it by more than 50 % (Fig. 10.1).

There seems to be no differences in the reduction of the work of breathing if PSV or proportional assisted ventilation applies. Furthermore, the most effective PSV settings for work of breathing reduction (e.g., the pressurization rate, or rise time) are not always the most comfortable for the patient.

Implementation of PSV with values that enable progressive improvement in indicators of the work of breathing reduction is related to a U-shaped tolerance curve. The lowest and highest values have the worst tolerance. The best results are obtained with PEEP values of 0–5 and a PSV of 5 or 10 cmH$_2$O.

The hemodynamic impact of positive pressure seems to be related to PEEP or CPAP of at least 10 cmH$_2$O and an interface that does not allow leakage. The operational mechanisms depends on the balance between the reduction of the venous return and afterload for the left ventricle.

The results suggest that the operator should seek the best combination between the levels of PEEP or CPAP and PSV that offer improved oxygenation and relieve stress on the respiratory muscles, limiting the peak pressure (up to 20 cmH$_2$O) and thus reduce the leaks and facilitate the patient's adaptation to the method [13]. However, the more pulmonary compliance is reduced (as in ARDS), the less are the chances of successful implementation of NIV.

10.5   Patient Selection, Starting, Failure Prediction, Mechanical Ventilation Indications

A reduction in the incidence of nosocomial infection rates is a proven advantage of applying NIV relative to MV in immunocompetent and especially immunocompromised patients. ARF in immunosuppressed patients (who are particularly predisposed to infections, mainly respiratory) is an indication of the need for NIV. According to recent international recommendations, NIV should be used in this context whenever possible [14].

Other noteworthy advantages of NIV are that it does not require the use of muscle relaxants or hypnotics, it allows swallowing and speech, and it does not produce upper airway injuries. Relevant aspects to consider when evaluating the results of starting NIV are team training in NIV indications, considering the importance of correct patient selection; the skills needed for its application (timing and modes); monitoring the trend in the evolution of the disease and the patient's response to the method applied; and finally a comparison of the results obtained by usual care with those obtained in clinical trials with NIV that may show marked differences.

10.5.1 Patient Selection

Patient selection must include consideration of the indications and contraindications for using NIV, both absolute and relative [15]. It is advised that the operator understand the benefits of the method before making decisions regarding the indications and starting it.

Indications for NIV
  Moderate or severe dyspnea
  Respiratory rate of ≥ 30
  Use of accessory muscles or paradoxical breathing
  $PaO_2/FiO_2 < 200$
  $PaO_2/FiO_2 < 300$ in patients at risk
  Underlying disease reversible in the short term
  Acceptable consciousness
  Hemodynamic stability
  No major organ dysfunction other than the lungs
  Disease categories globally not too high [Simplified Acute Physiology Score II
    (SAPS II) < 35]
Precautions
  ARDS and pneumonia
  Arrhythmias or cardiac ischemia
  Difficulty managing bronchorrhea
Exclusions
  Respiratory or cardiac arrest
  Lack of patient cooperation
  Uncontrollable vomiting or active gastrointestinal bleeding
  Mask or method intolerance
  Facial deformity or injury that prevents applying the mask
  Immediate orofacial, esophageal, or gastric surgery

10.5.2 Starting Ventilation

For initiating NIV in a patient with ARF [15–17], we recommend the use of equipment that provides a precise, stable FiO_2 and offers the possibility of monitoring the effects of ventilation through graphs and measures. It also should have alarm programming, leakage compensation, and various ventilation modes. The best interfaces are the total face mask, the oronasal mask, or a helmet. The recommended starting mode is PSV with PEEP.

Recommendations for implementation of PSV with PEEP suggest that once the interface is secured the level of PSV should be progressively increased until the expired tidal volume is 7–10 ml/kg and the respiratory rate is <25–35 cycles per minute. PEEP should progressively increase by increments of 2 cmH_2O to reach and maintain the SaO_2 at 90–92 % with up to 10 cmH_2O and an FiO_2 of up to 60 %. The peak pressure should be kept below 20–25 cmH_2O. Ideally, the patient is monitored continuously during the first 24 h. *Strict monitoring of the patient's evolution is needed in all units where NIV is being applied.*

Note: Based on the patient's evolution and tolerance, periods of spontaneous breathing can be initiated, with special care to avoid too rapid progress, which is usually harmful.

10.5.3 Failure Prediction

Several factors can predict NIV failure [15–17].
Age >40 years
ARDS or NAC
SAPS II $\geq$ 35 or APACHE II $\geq$ 17
Respiratory rate >25 at 1 h after NIV was initiated
Shock
Severe hypoxemia at admission
$PaO_2/FiO_2 \leq 175$ at 1 h after starting NIV

10.5.4 Indications for MV [15–18]

There are several indications for switching from NIV to MV [15–18].
Failure to maintain PaO_2 of 60 mmHg on FiO_2 of 60 %
Requirement of high pressure peaks
Lack of improvement trend regarding dyspnea and/or gas exchange
Mask or method intolerance
Difficulty managing respiratory secretions
Hemodynamic deterioration
Neurological impairment

10.6 Results

Numerous studies have confirmed the effectiveness of NIV in patients with COPD, acute hypercapnic respiratory failure, and cardiogenic pulmonary edema. Studies that have evaluated results in noncardiogenic hypoxemic ARF are scarce, as are those that have analyzed results of NIV implementation for ARF in immunosuppressed patients, HIV/AIDS, or other conditions. It is advisable to note that there is a considerable gap between scientific evidence and actual clinical situations to evaluate results of this method.

Consider a patient with HIV/AIDS in the emergency room with dyspnea and fever of 24 h, tachycardia, tachypnea, hypoxemia, and bilateral lung consolidation. We are subject to numerous limitations on data that would be needed to support decision making in this case, including current deterioration, degree of immunity, etiology of the disease, lung injury in evolution (pneumonia, ARDS, alveolar hemorrhage, or some combination), histopathology (acute interstitial pneumonia, diffuse alveolar damage). The need to make immediate decisions must be considered when overlaid with the data provided by the literature and their impact on the final result, rather than the efficacy of NIV itself. The parameters used by researchers to evaluate the results of NIV application during ARF includes clinical variables, measures of gas exchange, duration of hospitalization, need for MV, complications, and survival. The study designs have been heterogeneous with respect to patient and control selection and globally are grouped into two categories: NIV compared to conventional treatment for ARF (drug and oxygen therapy) or NIV compared to MV.

Starting NIV early during ARF has proved crucial for better results in immunosuppressed patients without HIV/AIDS [19, 20]. In a group of patients with ARF, among whom 20 % were immunosuppressed, Torres et al. showed that NIV is better than oxygen therapy in terms of improving the respiratory rate, oxygenation, need for MV, incidence of septic shock, and short-term mortality [21].

Uncontrolled studies evaluated CPAP and PSV in *P. jirovecii* pneumonia-related ARF and demonstrated a significant improvement in parameters such as dyspnea, respiratory rate, and gas exchange. They were associated with a reduction in MV indication and mortality [22–25].

Hilbert et al. established the effectiveness of NIV during ARF in immunosuppressed patients compared to conventional treatment in terms of MV indication (46 % vs. 77 %), short-term mortality (38 % vs. 69 %), and in-hospital mortality (50 % vs. 81 %). The number of HIV/AIDS patients in this sample was low [17].

Antonelli et al. randomized immunosuppressed patients (solid organ transplantation) with ARF to receive NIV or conventional treatment. They showed that NIV reduced the rate of MV indication (20 % vs. 70 %), ICU stay (5.5 vs. 9.0 days), and ICU mortality (20 % vs. 50 %). There was no difference in hospital mortality [26].

Confalonieri et al. showed that NIV and MV are equally effective in improving the respiratory rate and gas exchange in *P. jirovecii* pneumonia patients. Both methods significantly reduced the rate of associated complications [27].

In noncontrolled studies of ARF and *P. jirovecii* infection in immunosuppressed HIV/AIDS patients, the success rate for avoiding MV was 72 % with CPAP and 77 % with PSV. With NIV patient survival was 100 % versus 38 % for patients who required MV [28].

Dantas Anjos et al. demonstrated that CPAP improved gas exchange (oxygen) PSV, relieving the sensation of dyspnea in patients with HIV/AIDS during ARF [29]. Starting NIV during ARF, both moderate and severe, reduced the number of MV indications by 23 %, the ICU stay by 2 days, and short-term mortality by 17 % [30]. Both studies showed the benefit for NIV compared to MV. The results of studies showing noninferiority of NIV when considering conventional parameters can be regarded as results in favor of applying NIV, especially if we also take into consideration the avoidance of complications associated with MV, mainly respiratory infections [31, 32].

Key Major Recommendations
- Even if NIV seems to be a simple method with encouraging results and of low risk, it is important to note that these features are dependent on the technique being employed by an optimally trained and updated team. Success also depends on properly selected patients, the method being suitably applied, and, especially, failure quickly acknowledged.
- Not recognizing failure of the method to obtain the desired results and delay in applying MV in a timely fashion are main sources of serious complications related to NIV.

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