Practical Application of Noninvasive Ventilation in the Hospital Setting:

A Supplement to the ERS/ATS Clinical Practice Guidelines for Noninvasive Ventilation for

Acute Respiratory Failure

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Introduction

Some important topics related to noninvasive ventilation (NIV) and its implementation are better suited to technical summaries than formal recommendations. The material that follows is a short review of material that is not based on a rigorous literature search/review and was not subjected to the GRADE process. Nonetheless, we believe this information will be useful to clinicians.

Interfaces

The choice of the interface for individual patients is critical to determining NIV success or failure, since poor tolerance is often related to the interface. Several kinds of interfaces are available. The most popular ones for use during acute respiratory failure are the oronasal mask, the total facemask, and the helmet (mainly used in Europe, rarely used in North America). [1] Nasal interfaces, such as a nasal mask or nasal pillows, are infrequently used in the acute setting due to air leaks through the mouth, especially during the first few hours of ventilation.

When choosing the appropriate interface, attention should be paid to minimizing non-intentional leaks, which can only be partially compensated for by the NIV software on critical care ventilators or bilevel ventilators. [2] Tightening of the straps to control leaks is not always entirely successful and may reduce patient comfort and tolerance, and contribute to facial skin breakdown. [3] Dead space has been raised as a concern with some masks, especially those with large volumes such as the helmet. However, physiological studies have not shown a greater volume of dead space in larger masks, including the helmet. This is likely due to air streaming directly into the upper airway. [4] Lemyze et al [5] conducted a prospective observational study of do-not-intubate patients evaluating the efficacy of a total face mask when an oronasal mask failed to reverse the patient's acute respiratory failure. They found that two thirds of patients survived to hospital discharge after switching to the total face mask. Patients switched earlier to the total face mask (in the first 12 hrs) developed fewer pressure sores

despite a greater time of NIV exposure within the first 48 hrs and less use of protective dressings. Another study reported greater odds of skin breakdown with an oronasal mask compared to a total facemask. [6] An RCT comparing the oronasal and total face mask found that both performed similarly when used to treat patients with acute respiratory failure deemed candidates for NIV. [7]

In total there are 9 RCTs comparing different interfaces (i.e., nasal mask, oronasal masks, total face mask, helmet, and open-mouthpiece), mostly for acute hypercapnic respiratory failure (**Table 1**). [7-15] No major clinical differences between interfaces were observed in these investigations, both in terms of patient tolerance and comfort or ability to reduce $PaCO_2$ levels. The exception is the study by Patel and colleagues, [14] who randomized 83 patients with ARDS to receive NIV by helmet or oronasal mask. They reported that treatment with helmet NIV resulted in a significant reduction in intubation rates and 90-day mortality. To date, the single center study by Patel and colleagues has not been replicated and thus the results should be interpreted with caution. Meta-analysis of these studies is not helpful due to clinical heterogeneity including factors such as the different types of interfaces used, differences within the specific interface types (e.g., oronasal mask) including different shapes, headgear, material, and position on the skin and the rapid evolution of interfaces over time.

Masks that cover the nose and mouth are the preferred initial choice as compared with nasal masks alone in the acute setting with the goal of minimizing mouth leaks. Nasal masks or the helmet may have a role in patients who are claustrophobic or expectorating frequently. Increasing the level of pressure-support and positive end-expiratory pressure, and using the highest pressurization rate (rise time) are advisable when providing NIV via helmet. [16] It is important to optimize fit and comfort of the selected interface, and ensure that straps are tight enough to minimize leak but not so tight that comfort and tolerance are compromised. Trying other interfaces, sometimes on a rotational basis, may be helpful if the initial device fails.

The Ventilator for NIV

Ventilator types for NIV include bilevel ventilators, intermediate ventilators, and critical care ventilators. These designs are described further in **Table 2**. Important is the ability to compensate for leaks. Large leaks and lack of adequate compensation reduces the effectiveness of NIV, contributes to asynchrony and reduces patient comfort. There are regional differences in the preference of ventilator for NIV. This is often based on the bias of the clinician and the ventilators available.

Published studies related to the ventilator type for NIV application are summarized in **Table 3**. [2, 17-46] Much of the evidence comes from bench studies. There are few human studies and no studies that have examined important patient outcomes such as the need for intubation or mortality. Also, 20 years ago, concern existed that the performance of bilevel ventilators was inferior to ICU ventilators. Interestingly, as the performance of bilevel ventilators improved, especially for leak compensation, more recent concerns relate to whether the performance of ICU ventilators for NIV is as good as that of bilevel ventilators. Based on the limited evidence available, it is not possible to state that one type of ventilator (bilevel vs critical care) is superior to the other, but making ventilator choices and adjustments according to the capabilities and limitations of the device being used, along with the ventilation and oxygenation needs of the patient, is important to NIV success.

A potential concern with the single limb circuits and a passive exhalation port used with bilevel ventilators is the potential for rebreathing (**Table 4**). Major determinants of rebreathing are the expiratory time and the flow through the circuit during exhalation. Increasing the expiratory pressure requires greater flow and thus decreases the amount of rebreathing. It is for this reason that the minimum expiratory pressure setting on many bilevel ventilators is 4 cm H_2O. Due to leak compensation, unintentional leak may increase flow through the circuit and decrease rebreathing. A dual limb circuit has separate inspiratory and expiratory limbs and an

active exhalation valve, so rebreathing should not occur. Note that a single limb circuit cannot be used with the helmet.

For acute care applications, it is desirable to use a ventilator with a blender allowing precise FiO_2 delivery from 0.21 to 1.0 (**Table 5**). Modern bilevel ventilators designed for acute care applications typically incorporate a blender for oxygen administration. Bilevel ventilators designed for use outside the acute care setting often do not have a blender, but rather provide supplemental oxygen by titration into the circuit or interface. The result is a variable FIO_2. with only modest concentrations of oxygen that can be achieved (e.g., <60%). With oxygen titration, the FIO_2 is affected by the site of the oxygen titration, type of exhalation port, ventilator settings, oxygen flow, breathing pattern, and leak. The interaction among these variables affecting FIO_2 when a titration method is used makes it difficult to deliver a precisely known FIO_2. Thus, continuous monitoring by pulse oximetry is needed, as changes to any of the variables listed previously might affect FIO_2. When NIV is used for hypoxemic respiratory failure, a ventilator that can provide a precise FIO_2 is desirable.

Important to the function of ventilators for NIV is their ability to tolerate leaks. Leaks include intentional leak through the passive exhalation port as well as unintentional leaks due to a loose-fitting interface. An important functional characteristic of bilevel ventilators is their ability to compensate for leaks. In the past, critical care ventilators were intolerant of leaks, however newer generation critical care ventilators have built-in leak compensation with NIV modes. The performance of critical care ventilators with NIV modes has been evaluated primarily in bench studies. In a laboratory and clinical study, Carteaux et al [25] suggested that, as a group, bilevel ventilators outperform critical care ventilators for NIV as it relates to patient-ventilator synchrony. However, the NIV modes on some, but not all, critical care ventilators, allow clinicians to make adjustments to improve synchrony such as trigger type and sensitivity and flow cycling criteria and inspiratory time with pressure support. Due to the differences in ability to compensate for leaks among ventilators used for NIV and the multiple adjustments available, it is important for

clinicians to appreciate the unique characteristics of the ventilators they use and how the adjustments available can be used to optimize delivery of NIV.

Some patients receiving NIV might also benefit from inhaled drug delivery, and if required, available evidence supports the efficacy and safety of delivering aerosols during NIV[47]. The inhaled bronchodilator response might be enhanced with the use of NIV in acute asthma (Soroksky ref), but the evidence is not sufficiently solid to recommend this as standard therapy.

Ventilator Modes and Settings for NIV

For many years, clinicians have preferred pressure-limited modes over volume-limited modes for application of NIV. In an epidemiologic survey conducted in the US, over 90% of NIV applications used bilevel type pressure-limited ventilators and approximately only 5% used critical care ventilators. [48] As early as 1993, a small randomized trial found that although non-invasive pressure support ventilation (PSV) and volume-limited ventilation yielded similar intubation rates and lengths of stay in patients with COPD exacerbations, compliance (or tolerance) was better with PSV. [49] Since then, pressure limited modes have dominated the delivery of NIV.

Pressure-limited modes

Pressure-limited modes used to deliver NIV include the following:

1) Continuous positive airway pressure (CPAP) – consisting of a single selected pressure applied via a noninvasive interface to the upper airway. Both in Europe and in the United States, CPAP constitutes about 10% of NIV applications to treat acute respiratory failure, mainly for cardiogenic pulmonary edema or prophylactically for postoperative patients. [48]. CPAP can be applied using bilevel ventilators or flow regulators using mixtures of compressed air and oxygen, usually at pressures between 5 and 10 cm H_2O. Advantages of

CPAP include low cost (if flow regulators are used) and a lack of issues related to asynchrony. The disadvantage of CPAP is that it provides no active respiratory assistance during inspiration, and thus less effectively reduces respiratory muscle workload than bilevel positive airway pressure.

2) Bilevel positive airway pressure (bilevel NIV) – the most commonly used mode to administer NIV, [48] consists of a higher inspiratory pressure (IPAP) and lower expiratory pressure (EPAP). This mode is similar to PSV as described below, with pressure support being the difference between IPAP and EPAP. IPAP is typically set to reduce respiratory rate to 20/min – 25/min and to increase tidal volume to 6 to 8 ml/kg predicted body weight (PBW). Average pressures, in a study from the United States, of those using bilevel NIV for acute respiratory failure [48] were 12 cm H_2O IPAP and 5 cm H_2O EPAP. When treating patients with hypoxemic respiratory failure, higher pressures may be necessary, as higher EPAP is used to improve oxygenation and higher pressure support to increase tidal volume and reduce dyspnea. [50] If EPAP is raised, then IPAP must be raised in parallel to maintain a steady pressure support. Advantages of bilevel NIV include leak compensation to maintain targeted pressures and special algorithms that help to facilitate synchrony in the face of air leaks.

3) Pressure support ventilation (PSV) – similar to bilevel NIV but is provided on critical care ventilators or a few dedicated NIV ventilators. Unlike PSV, bilevel NIV derives from devices that were originally designed to treat sleep apnea. [51] Both PSV and bilevel NIV are flow or pressure triggered and provide higher inspiratory and lower expiratory pressures. With PSV, breaths are flow cycled (from inspiratory to expiratory pressure) and there is no backup rate whereas with bilevel NIV, spontaneous (triggered) breaths are flow cycled and ventilator-triggered breaths are time-cycled and a backup rate can be applied. Ventilator settings in PSV are essentially the same as with bilevel NIV, but it is important to recall that the terminology is different; EPAP equals PEEP, but IPAP equals pressure support plus PEEP.

Thus, changing from PSV at settings of 10 cm H_2O pressure support and 5 cm H_2O PEEP prior to extubation would necessitate 15 cm H_2O IPAP and 5 cm H_2O EPAP if the patient is to be continued on the same level of pressure support using bilevel NIV following extubation. So called "NIV modes" are often used to administer PSV to patients using NIV via critical care ventilators, but it is important to consider that the specifications of these modes differ between ventilator manufacturers and adjustments may be necessary to optimize ventilator function, especially in the face of air leaks. It is important to consider that different specific functions of PSV differ between critical care ventilators. [2, 25, 27, 29]

4) Pressure Control Ventilation (PCV) – Similar to bilevel NIV or PSV, PCV is flow triggered and uses preset inspiratory and expiratory pressures but differs in that a backup rate is mandatory and breaths are time-cycled. Setting inspiratory and expiratory pressures with PCV is the same as with PSV, but inspiratory time is set using absolute time or an I:E ratio. This mode can be useful to improve expiratory synchrony when inspiratory pressure is prolonged in the face of air leaks [52] or a delayed drop in inspiratory flow as may be seen in COPD patients. [53]

5) Average Volume Assured Pressure Support (AVAPS) – a proprietary mode found on some noninvasive ventilators that uses an algorithm to enable the ventilator to automatically adjust inspiratory airway pressure (adaptive pressure support) to achieve a target tidal volume. The operator sets a target tidal volume, range of inspiratory pressures, EPAP and a backup rate and the ventilator seeks the lowest inspiratory pressure within the targeted pressure range that provides the target volume. Advantages include a higher likelihood that patients will reach the targeted tidal and minute volumes and therefore improve hypercarbia and coma faster than with bilevel NIV. This capability was confirmed in a small randomized trial of patients with obesity hypoventilation patients and acute on chronic hypercapnic respiratory failure. [54] A limitation of this mode is that support is reduced if patient effort results in a tidal volumes that exceeds the target and respiratory muscles of such patients may fatigue. In a

bench study, Lujan et al [21] found that the presence of dynamic unintentional leaks interfered with ventilator performance using adaptive pressure support modes. Inspiratory leaks resulted in a reduction in pressure support, with no guarantee of delivered tidal volume. In a multi-center RCT, Cao et al [55] reported no significant differences in the decrement of $PaCO_2$, need for intubation, or in-hospital mortality between pressure support and volume-targeted pressure-limited NIV. Clinical studies have reported mixed results with AVAPS and similar modes, [54, 56, 57] and their proper role in the management of NIV is yet to be determined. [58, 59]

6) intelligent Volume Assured Pressure Support (iVAPS) – another proprietary mode that is similar to AVAPS but targets alveolar ventilation (obtained by subtracting anatomic dead space from target tidal volume). This mode automatically adjusts backup rate within a narrow range to try to optimize breathing pattern and comfort.

Volume-targeted modes

Although used much less often than pressure-limited modes, volume-targeted modes can be used for NIV. Volume control can be applied, with set tidal volumes of 6 - 8 mL/kg PBW. The chief limitation of volume-targeted modes has been an inability to compensate for leaks, leading to failure to provide the targeted tidal volume and possible auto-cycling as the persisting leak triggers premature breaths. Some critical care ventilators have NIV modes that provide a volume-limited option that includes leak compensation, but these may require additional adjustment for optimal tidal volume delivery. [2]

Modes to enhance synchrony

1) Proportional Assist Ventilation (PAV) - was developed to match ventilator response with breathing effort. Based on the equation of motion, it tracks instantaneous inspiratory flow and its integral, tidal volume, and delivers flow and volume to match patient demand. [60] Ideally,

patient resistance and compliance are measured and PAV can then provide full support or a proportion as selected by the operator. An issue with PAV for NIV is the difficulty in measuring resistance and compliance, which is an important limitation of this mode for NIV. On some ventilators, PAV can be used during invasive ventilation, but not for NIV (e.g. PAV+). Theoretically, PAV has the ability to enhance synchrony and comfort in comparison to standard PSV modes but it shares limitations such as the inability to provide support in the face of auto-PEEP unless the patient lowers alveolar pressure below atmospheric which initiates triggering. Studies on PAV to treat acute respiratory failure using NIV largely confirm its ability to enhance synchrony and comfort relative to more conventional modes of ventilation, but most fail to show significant benefits in other outcomes such as intubation rate, hospital length of stay or mortality. [61-63] PAV should be avoided if patients have depressed drive to breathe or neuromuscular weakness. PAV is available on a number of different commercially available ventilators, generally as an add-on feature at additional expense, and has not become a standard part of the regimen for NIV.

2) Neurally adjusted ventilator assist (NAVA) - another approach to matching ventilator action to patient inspiratory demand. NAVA uses esophageal electrodes to track electrical activity of the diaphragm as an index of breathing effort. [64] Accordingly, it has the potential to use neural respiratory drive to control the ventilator, thereby optimizing synchrony. Because it tracks electrical activity rather than inspiratory flow, it delivers flow without delay, even in the face of auto-PEEP. Studies on NAVA during NIV have shown enhanced synchrony compared to conventional modes, [65-68] but no improvements in NIV success rates, lengths of stay or mortality. NAVA may be helpful in situations involving difficult synchrony during NIV such as COPD patients with auto-PEEP, [65, 66] but it has not gained very widespread use, perhaps because it requires a specialized gastric tube.

Monitoring

Patient comfort, accessory muscle use, respiratory and heart rates, blood pressure and oxygenation should be monitored carefully at the initiation of NIV and regularly thereafter. Sufficient personnel (nurses, respiratory therapists, physicians) should be available to guarantee patient safety during NIV administration. To assure the success of NIV, close monitoring is necessary, especially during the initiation period (**Table 6**). Frequency of subsequent assessments will depend on the evolution of patient status. When improvement is slow or if there is concern about deterioration, more frequent assessment should be made to guide ventilator settings or to make interface adjustments. Choosing the appropriate location (e.g., medical ward, respiratory care unit, or intensive care unit) for NIV requires consideration of the patient's need for monitoring, the monitoring capabilities of the unit, personnel resources (e.g., nursing and respiratory therapy), and staff skill and experience. [69]

The subjective response of the patient is very important to NIV success and should be monitored closely. Alleviation of dypnea depends on adequate provision of ventilator support and the ability of the patient to relax enough to allow the ventilator to assume some of the breathing workload. Some patients become very anxious or even claustrophobic when the mask is applied and need reassurance, coaching or even sedation. Comfort is important as well and is related to the interface type, how tightly the interface is applied, ventilator settings and synchrony, and humidification (see below). A decline in respiratory rate and in accessory muscle use are often good harbingers of a patient adapting well to NIV.

Monitoring of tidal volume is important to assure adequate alveolar ventilation. However, a high tidal volume during NIV might be problematic. Carteaux et al [70] reported that, in patients with moderate-to-severe hypoxemia, an exhaled tidal volume > 9.5 mL/kg PBW predicted NIV failure. It would thus seem reasonable to target tidal volumes of 6 – 8 mL/kg PBW in patients receiving NIV. Unfortunately, some bilevel ventilators don't accurately measure tidal volume. Contal et al [24] reported that, on average, tidal volume was underestimated with bilevel ventilators, with only 2 of the 7 devices tested underestimating by<100 mL.

Asynchrony occurs frequently during NIV, particularly in the presence of leaks, and is associated with NIV failure. [53] The difference between inhaled and exhaled tidal volume is used to determines the magnitude of the leak. Some ventilators, particularly bilevel ventilators, display the leak flow. Many ventilators designed for NIV have good leak compensation algorithms and thus reduce the frequency of asynchrony due to leak. Excessive leak can lead to auto-triggering and prolonged inspiration [71]. Ineffective efforts (patient respiratory rate greater than the ventilator response) often indicate the presence of intrinsic PEEP (e.g., COPD) or weak inspiratory effort (e.g., neuromuscular disease). Missed triggers due to intrinsic PEEP can be addressed through the use of applied PEEP and missed triggers due to weakness can be addressed by increasing trigger sensitivity. In a multicenter study, the analysis of the waveforms generated by ventilators had a significant positive effect on physiological and patient-centered outcomes during an exacerbation of COPD. [72]

Ventilator alarm settings during NIV should balance patient safety, noise disruption, and nuisance for care providers. If a backup respiratory rate is not set (e.g., pressure support), an apnea alarm is necessary. A disconnect alarm is needed in the event that the interface is accidentally removed or the circuit separates from the interface or the ventilator. Other alarms, such as low tidal volume and minute ventilation alarms, are important but less crucial.

Oxygen saturation by pulse-oximetry (SpO_2) should be maintained >88%. Since SpO_2 improves with the application of NIV, it should be continuously monitored for at least the first 24 hours of treatment. A lack of improvement in oxygenation after 1 hour of NIV is a predictor of NIV failure in patients with acute hypoxemic respiratory failure. [73, 74]

The response of $PaCO_2$ and pH after 1-2 hours of NIV is a predictor for NIV success in patients with acute hypercapnic respiratory failure. [75-77] Blood gases are useful at baseline prior to initiation of NIV to establish a baseline and after an hour or 2 to assess the patient's response. The necessity of subsequent blood gases is determined by changes in clinical condition or in ventilator settings, and when withdrawal of NIV is being considered. There is

increasing use of venous as opposed to arterial blood gases and use of noninvasive techniques to measure PCO2 such as end-tidal or transcutaneous, but their utility for management of NIV has not been established. End tidal measurements, in particular, have been problematic when measurement is made from the leak port incorporated into the interface, with poor agreement between $PaCO_2$ and end-tidal PCO_2.. Thus, the reliability of end-tidal PCO_2 has been questioned during NIV. [78]

Facial skin breakdown has been estimated to occur in 5 - 20% of NIV applications [79, 80] although newer interfaces and improving management techniques have probably lowered these rates. In the United States, stage 3 or 4 pressure ulcers acquired after hospital admission are considered serious reportable events. Thus, it is important to monitor skin condition and implement steps to minimize skin breakdown such as proper strap tightening, use of barrier tape or cushioning between mask and face, selection of an appropriate size and type of interface, and rotating interfaces. One study reported greater odds of skin breakdown with an oronasal mask compared to a total facemask. [6]

Humidification

A prior clinical practice guideline suggested use of active humidification (a heated humifidier) during NIV to improve comfort and adherence [81]. Although either active or passive (a heat-and-moisture exchanger (HME)) humidification can be used, active humidification has been thought to be more effective and does not introduce additional dead space into the circuit as an HME does. [82-83] One study reported that use of a HME decreased CO_2 elimination during NIV, despite increased minute ventilation, especially in hypercapnic subjects. [84] A short-term crossover study on healthy subjects found that gas humidified by either the heated humidifier or HME during NIV was sensed as more comfortable than unhumidified dry gas.[85] Furthermore, a multi-center RCT on patients, however, found no difference in intubation rate or PaCO2, even in hypercapneic patients, between subjects receiving NIV with a heated humidifier

compared to a HME. [86] While acknowledging that no studies have reported effects of humidification on intubation rates, mortality, or lengths of stay during NIV, we favor the routine use of humidification with a heated humidifier during NIV, with the possible exception of those (such a patients with cardiogenic pulmonary edema) who are require it for only a few hours or less.

Sedation and Analgesia

Sedation and analgesia can be used during NIV to enhance comfort and tolerance of the modality. According to an international survey, [87] a minority of pulmonary and critical care physicians (< 25%) in the United States and Europe routinely use sedation and analgesia for NIV. Physicians reluctant to use them expressed concerns about suppression of respiratory drive.

The most commonly used agents are short acting benzodiazepines and opiates via low dose intravenous bolus administration. [87] Several studies have evaluated a possible role for continuous intravenous dexmedetomidine that by virtue of its short half-life, analgesic properties and lack of respiratory suppression, has been considered an attractive agent for NIV. Huang et al [88] compared dexmedetomidine to midazolam in a cohort of 62 patients with cardiogenic pulmonary edema failing NIV due to intolerance. Those randomized to dexmedetomidine had fewer intubations, less time on mechanical ventilation, and less time in the ICU (all P < 0.05). However, patients receiving dexmedetomidine had more bradycardia, although it was not severe enough to necessitate cessation of therapy. Patient-ventilator synchrony may be improved with use of dexmedetomidine. [89]

In a more recent randomized pilot trial, Devlin et al [90] used dexmedetomidine as a routine sedative/analgesic agent starting within 8 hours of NIV initiation to determine whether

NIV tolerance and success rates would be improved. Compared to placebo and as needed midazolam, they found no improvement in NIV tolerance or time at desired sedation level, nor was the rate of intubation or length of time on mechanical ventilation reduced. The seemingly conflicting results of these latter two studies may be explained by the use of dexmedetomidine for routine sedation in patients starting on NIV in the Devlin study, in which it did not improve outcomes, as opposed to use as a rescue therapy in the Huang study in which it helped to avert intubations and shortened duration of time on the ventilator.

In one small open label trial on patients failing NIV, 9 of 13 avoided intubation after receiving a remifentanil infusion, which was associated with improved oxygenation and ventilation. [91] In a pilot prospective trial on 36 patients with acute hypoxemic respiratory failure uncomfortable on NIV and requesting cessation, Rocco et al [92] administered remifentanil (starting at 0.025 µg/kg/min and titrating up to 0.12 µg/kg/min as needed). With remifentanil, 22 of the patients tolerated NIV and avoided intubation. The tolerant patients also had greater improvements in PaO_2/FIO_2 on NIV and a lower mortality rate (14 versus 50%, $P < 0.05$) than those requiring intubation.

Available evidence supports that sedation/analgesia should be used to enhance comfort and tolerance of NIV in patients experiencing excessive discomfort and anxiety if initial non-pharmacologic measures have failed. Routine use of sedation/analgesia with the aim of improving comfort and tolerance upon initiation of NIV does not appear to be beneficial. Intermittent boluses of benzodiazepines and/or opiates are suitable sedative/analgesic agents, but if used must be given cautiously at the lowest effective doses due to the risk of respiratory depression. Intravenous infusions of agents such as dexmetetomidine and remifentanyl have theoretical advantages over intermittent bolus medications, but superiority has not been established in clinical trials.

NIV to prevent worsening of hypoxemia during fiberoptic bronchoscopy

NIV during fiberoptic bronchoscopy (FOB) has been considered in patients with severe hypoxemia to prevent complications related to endotracheal intubation and mechanical ventilation for the procedure. Observational studies [93-96] and 2 RCTs, one using bilevel NIV [97] and the other CPAP, [98] on small cohorts of patients support the usefulness of performing FOB during NIV in patients with acute respiratory failure of various origins (e.g., hypoxemic respiratory failure in immunocompromised patients, patients with COPD exacerbation).

The first RCT was conducted in 26 hypoxemic patients with suspected nosocomial pneumonia. [97] The authors concluded that bilevel NIV was superior to conventional oxygen supplementation in preventing gas-exchange deterioration during FOB, with associated improved hemodynamic tolerance. The second RCT, [98] using CPAP, was performed on 30 subjects with a PaO_2/FIO_2 <300. This RCT showed that the use of CPAP during FOB allowed minimal alterations in gas exchange and prevented subsequent respiratory failure, while this was not the case in the patients undergoing standard oxygen therapy. Use of bilevel NIV or CPAP could be considered in patients with moderate hypoxemia (i.e. PaO_2/FIO_2 150 - 300) to prevent a further deterioration during FOB. [95].

High flow nasal cannula (HFNC) has also been reported to minimize hypoxemia during bronchoscopy. [99]. When NIV was compared to HFNC during bronchoscopy, the latter was associated with a higher degree of desaturation. [100]

Summary

Much of the success of NIV relates to the skills of the clinician and the technical aspects of the application of NIV. In this paper we have reviewed some of the literature related to practical aspects on NIV, hoping that it will have value despite that formal recommendations cannot be made.

References

1. Crimi C, Noto A, Princi P, Esquinas A, Nava S. A European survey of noninvasive ventilation practices. *Eur Respir J* 2010: 36(2): 362-369.

2. Vignaux L, Tassaux D, Carteaux G, Roeseler J, Piquilloud L, Brochard L, Jolliet P. Performance of noninvasive ventilation algorithms on ICU ventilators during pressure support: a clinical study. *Intensive Care Med* 2010: 36(12): 2053-2059.

3. Schettino GP, Tucci MR, Sousa R, Valente Barbas CS, Passos Amato MB, Carvalho CR. Mask mechanics and leak dynamics during noninvasive pressure support ventilation: a bench study. *Intensive Care Med* 2001: 27(12): 1887-1891.

4. Fodil R, Lellouche F, Mancebo J, Sbirlea-Apiou G, Isabey D, Brochard L, Louis B. Comparison of patient-ventilator interfaces based on their computerized effective dead space. *Intensive Care Med* 2011: 37(2): 257-262.

5. Lemyze M, Mallat J, Nigeon O, Barrailler S, Pepy F, Gasan G, Vangrunderbeeck N, Grosset P, Tronchon L, Thevenin D. Rescue therapy by switching to total face mask after failure of face mask-delivered noninvasive ventilation in do-not-intubate patients in acute respiratory failure. *Crit Care Med* 2013: 41(2): 481-488.

6. Yamaguti WP, Moderno EV, Yamashita SY, Gomes TG, Maida AL, Kondo CS, de Salles IC, de Brito CM. Treatment-related risk factors for development of skin breakdown in subjects with acute respiratory failure undergoing noninvasive ventilation or CPAP. *Respir Care* 2014: 59(10): 1530-1536.

7. Ozsancak A, Sidhom SS, Liesching TN, Howard W, Hill NS. Evaluation of the total face mask for noninvasive ventilation to treat acute respiratory failure. *Chest* 2011: 139(5): 1034-1041.

8. Antonaglia V, Ferluga M, Molino R, Lucangelo U, Peratoner A, Roman-Pognuz E, De Simoni L, Zin WA. Comparison of noninvasive ventilation by sequential use of mask and helmet

versus mask in acute exacerbation of chronic obstructive pulmonary disease: a preliminary study. *Respiration* 2011: 82(2): 148-154.

9.   Chacur FH, Vilella Felipe LM, Fernandes CG, Lazzarini LC. The total face mask is more comfortable than the oronasal mask in noninvasive ventilation but is not associated with improved outcome. *Respiration* 2011: 82(5): 426-430.

10.   Cuvelier A, Pujol W, Pramil S, Molano LC, Viacroze C, Muir JF. Cephalic versus oronasal mask for noninvasive ventilation in acute hypercapnic respiratory failure. *Intensive Care Med* 2009: 35(3): 519-526.

11.   Girault C, Briel A, Benichou J, Hellot MF, Dachraoui F, Tamion F, Bonmarchand G. Interface strategy during noninvasive positive pressure ventilation for hypercapnic acute respiratory failure. *Crit Care Med* 2009: 37(1): 124-131.

12.   Kwok H, McCormack J, Cece R, Houtchens J, Hill NS. Controlled trial of oronasal versus nasal mask ventilation in the treatment of acute respiratory failure. *Crit Care Med* 2003: 31(2): 468-473.

13.   Pisani L, Mega C, Vaschetto R, Bellone A, Scala R, Cosentini R, Musti M, Del Forno M, Grassi M, Fasano L, Navalesi P, Nava S. Oronasal mask versus helmet in acute hypercapnic respiratory failure. *Eur Respir J* 2015: 45(3): 691-699.

14.   Patel BK, Wolfe KS, Pohlman AS, Hall JB, Kress JP. Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. *JAMA* 2016: 315(22): 2435-2441.

15.   Nicolini A, Santo M, Ferrari-Bravo M, Barlascini C. Open-mouthpiece ventilation versus nasal mask ventilation in subjects with COPD exacerbation and mild to moderate acidosis: a randomized trial. *Respir Care* 2014: 59(12): 1825-1831.

16.   Vargas F, Thille A, Lyazidi A, Campo FR, Brochard L. Helmet with specific settings versus facemask for noninvasive ventilation. *Crit Care Med* 2009: 37(6): 1921-1928.

17.   Garnier M, Quesnel C, Fulgencio JP, Degrain M, Carteaux G, Bonnet F, Similowski T, Demoule A. Multifaceted bench comparative evaluation of latest intensive care unit ventilators. *Br J Anaesth* 2015: 115(1): 89-98.

18.   Chen Y, Cheng K, Zhou X. Performance characteristics of seven bilevel mechanical ventilators in pressure-support mode with different cycling criteria: a comparative bench study. *Med Sci Monit* 2015: 21: 310-317.

19.   Nakamura MA, Costa EL, Carvalho CR, Tucci MR. Performance of ICU ventilators during noninvasive ventilation with large leaks in a total face mask: a bench study. *J Bras Pneumol* 2014: 40(3): 294-303.

20.   Oto J, Chenelle CT, Marchese AD, Kacmarek RM. A comparison of leak compensation in acute care ventilators during noninvasive and invasive ventilation: a lung model study. *Respir Care* 2013: 58(12): 2027-2037.

21.   Lujan M, Sogo A, Pomares X, Monso E, Sales B, Blanch L. Effect of leak and breathing pattern on the accuracy of tidal volume estimation by commercial home ventilators: a bench study. *Respir Care* 2013: 58(5): 770-777.

22.   Khirani S, Louis B, Leroux K, Delord V, Fauroux B, Lofaso F. Harms of unintentional leaks during volume targeted pressure support ventilation. *Respir Med* 2013: 107(7): 1021-1029.

23.   Carlucci A, Schreiber A, Mattei A, Malovini A, Bellinati J, Ceriana P, Gregoretti C. The configuration of bi-level ventilator circuits may affect compensation for non-intentional leaks during volume-targeted ventilation. *Intensive Care Med* 2013: 39(1): 59-65.

24.   Contal O, Vignaux L, Combescure C, Pepin JL, Jolliet P, Janssens JP. Monitoring of noninvasive ventilation by built-in software of home bilevel ventilators: a bench study. *Chest* 2012: 141(2): 469-476.

25.   Carteaux G, Lyazidi A, Cordoba-Izquierdo A, Vignaux L, Jolliet P, Thille AW, Richard JC, Brochard L. Patient-ventilator asynchrony during noninvasive ventilation: a bench and clinical study. *Chest* 2012: 142(2): 367-376.

26.   Ueno Y, Nakanishi N, Oto J, Imanaka H, Nishimura M. A bench study of the effects of leak on ventilator performance during noninvasive ventilation. *Respir Care* 2011: 56(11): 1758-1764.

27.   Ferreira JC, Chipman DW, Hill NS, Kacmarek RM. Bilevel vs ICU ventilators providing noninvasive ventilation: effect of system leaks: a COPD lung model comparison. *Chest* 2009: 136(2): 448-456.

28.   Borel JC, Sabil A, Janssens J-P, Couteau M, Boulon L, Lévy P, Pépin J-L. Intentional Leaks in Industrial Masks Have a Significant Impact on Efficacy of Bilevel Noninvasive Ventilation. *Chest* 2009: 135(3): 669-677.

29.   Vignaux L, Tassaux D, Jolliet P. Performance of noninvasive ventilation modes on ICU ventilators during pressure support: a bench model study. *Intensive Care Med* 2007: 33(8): 1444-1451.

30.   Battisti A, Tassaux D, Janssens JP, Michotte JB, Jaber S, Jolliet P. Performance characteristics of 10 home mechanical ventilators in pressure-support mode: a comparative bench study. *Chest* 2005: 127(5): 1784-1792.

31.   Vitacca M, Barbano L, D'Anna S, Porta R, Bianchi L, Ambrosino N. Comparison of five bilevel pressure ventilators in patients with chronic ventilatory failure: a physiologic study. *Chest* 2002: 122(6): 2105-2114.

32.   Tassaux D, Strasser S, Fonseca S, Dalmas E, Jolliet P. Comparative bench study of triggering, pressurization, and cycling between the home ventilator VPAP II and three ICU ventilators. *Intensive Care Med* 2002: 28(9): 1254-1261.

33.   Mehta S, McCool FD, Hill NS. Leak compensation in positive pressure ventilators: a lung model study. *Eur Respir J* 2001: 17(2): 259-267.

34.   Highcock MP, Shneerson JM, Smith IE. Functional differences in bi-level pressure preset ventilators. *Eur Respir J* 2001: 17(2): 268-273.

35.   Patel RG, Petrini MF. Respiratory muscle performance, pulmonary mechanics, and gas exchange between the BiPAP S/T-D system and the Servo Ventilator 900C with bilevel positive airway pressure ventilation following gradual pressure support weaning. *Chest* 1998: 114(5): 1390-1396.

36.   Bunburaphong T, Imanaka H, Nishimura M, Hess D, Kacmarek RM. Performance characteristics of bilevel pressure ventilators: a lung model study. *Chest* 1997: 111(4): 1050-1060.

37.   Szkulmowski Z, Belkhouja K, Le QH, Robert D, Argaud L. Bilevel positive airway pressure ventilation: factors influencing carbon dioxide rebreathing. *Intensive Care Med* 2010: 36(4): 688-691.

38.   Schettino GP, Chatmongkolchart S, Hess DR, Kacmarek RM. Position of exhalation port and mask design affect CO2 rebreathing during noninvasive positive pressure ventilation. *Crit Care Med* 2003: 31(8): 2178-2182.

39.   Lofaso F, Brochard L, Hang T, Lorino H, Harf A, Isabey D. Home versus intensive care pressure support devices. Experimental and clinical comparison. *Am J Respir Crit Care Med* 1996: 153(5): 1591-1599.

40.   Lofaso F, Brochard L, Touchard D, Hang T, Harf A, Isabey D. Evaluation of carbon dioxide rebreathing during pressure support ventilation with airway management system (BiPAP) devices. *Chest* 1995: 108(3): 772-778.

41.   Ferguson GT, Gilmartin M. CO2 rebreathing during BiPAP ventilatory assistance. *Am J Respir Crit Care Med* 1995: 151(4): 1126-1135.

42.   Storre JH, Huttmann SE, Ekkernkamp E, Walterspacher S, Schmoor C, Dreher M, Windisch W. Oxygen supplementation in noninvasive home mechanical ventilation: the crucial roles of CO2 exhalation systems and leakages. *Respir Care* 2014: 59(1): 113-120.

43.   Dai B, Kang J, Yu N, Tan W, Zhao HW. Oxygen injection site affects FIO2 during noninvasive ventilation. *Respir Care* 2013: 58(10): 1630-1636.

44.   Miyoshi E, Fujino Y, Uchiyama A, Mashimo T, Nishimura M. Effects of gas leak on triggering function, humidification, and inspiratory oxygen fraction during noninvasive positive airway pressure ventilation. *Chest* 2005: 128(5): 3691-3698.

45.   Schwartz AR, Kacmarek RM, Hess DR. Factors affecting oxygen delivery with bi-level positive airway pressure. *Respir Care* 2004: 49(3): 270-275.

46.   Thys F, Liistro G, Dozin O, Marion E, Rodenstein DO. Determinants of Fi,O2 with oxygen supplementation during noninvasive two-level positive pressure ventilation. *Eur Respir J* 2002: 19(4): 653-657.

47.   Hess DR. Aerosol Therapy During Noninvasive Ventilation or High-Flow Nasal Cannula. *Respir Care* 2015: 60(6): 880-891; discussion 891-883.

48.   Ozsancak Ugurlu A, Sidhom SS, Khodabandeh A, Ieong M, Mohr C, Lin DY, Buchwald I, Bahhady I, Wengryn J, Maheshwari V, Hill NS. Use and outcomes of noninvasive positive pressure ventilation in acute care hospitals in Massachusetts. *Chest* 2014: 145(5): 964-971.

49.   Vitacca M, Rubini F, Foglio K, Scalvini S, Nava S, Ambrosino N. Non-invasive modalities of positive pressure ventilation improve the outcome of acute exacerbations in COLD patients. *Intensive Care Med* 1993: 19(8): 450-455.

50.   L'Her E, Deye N, Lellouche F, Taille S, Demoule A, Fraticelli A, Mancebo J, Brochard L. Physiologic effects of noninvasive ventilation during acute lung injury. *Am J Respir Crit Care Med* 2005: 172(9): 1112-1118.

51.   Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask. Physiologic and clinical implications. *Chest* 1990: 98(2): 317-324.

52.   Calderini E, Confalonieri M, Puccio PG, Francavilla N, Stella L, Gregoretti C. Patient-ventilator asynchrony during noninvasive ventilation: the role of expiratory trigger. *Intensive Care Med* 1999: 25(7): 662-667.

53.   Hess DR. Patient-ventilator interaction during noninvasive ventilation. *Respir Care* 2011: 56(2): 153-165; discussion 165-157.

54.   Briones Claudett KH, Briones Claudett M, Chung Sang Wong M, Nuques Martinez A, Soto Espinoza R, Montalvo M, Esquinas Rodriguez A, Gonzalez Diaz G, Grunauer Andrade M. Noninvasive mechanical ventilation with average volume assured pressure support (AVAPS) in patients with chronic obstructive pulmonary disease and hypercapnic encephalopathy. *BMC Pulm Med* 2013: 13: 12.

55.   Cao Z, Luo Z, Hou A, Nie Q, Xie B, An X, Wan Z, Ye X, Xu Y, Chen X, Zhang H, Xu Z, Wang J, An F, Li P, Yu C, Liang Y, Zhang Y, Ma Y. Volume-Targeted Versus Pressure-Limited Noninvasive Ventilation in Subjects With Acute Hypercapnic Respiratory Failure: A Multicenter Randomized Controlled Trial. *Respir Care* 2016: 61(11): 1440-1450.

56.   Murphy PB, Davidson C, Hind MD, Simonds A, Williams AJ, Hopkinson NS, Moxham J, Polkey M, Hart N. Volume targeted versus pressure support non-invasive ventilation in patients with super obesity and chronic respiratory failure: a randomised controlled trial. *Thorax* 2012: 67(8): 727-734.

57.   Oscroft NS, Ali M, Gulati A, Davies MG, Quinnell TG, Shneerson JM, Smith IE. A randomised crossover trial comparing volume assured and pressure preset noninvasive ventilation in stable hypercapnic COPD. *COPD* 2010: 7(6): 398-403.

58.   Hill NS. Noninvasive ventilation for COPD: volume assurance not very reassuring. *COPD* 2010: 7(6): 389-390.

59.   Windisch W, Storre JH. Target volume settings for home mechanical ventilation: great progress or just a gadget? *Thorax* 2012: 67(8): 663-665.

60.   Younes M, Puddy A, Roberts D, Light RB, Quesada A, Taylor K, Oppenheimer L, Cramp H. Proportional assist ventilation. Results of an initial clinical trial. *Am Rev Respir Dis* 1992: 145(1): 121-129.

61.   Elganady AA, Beshey BN, Abdelaziz AAH. Proportional assist ventilation versus pressure support ventilation in the weaning of patients with acute exacerbation of chronic obstructive pulmonary disease. *Egypt J Chest Dis Tuberc* 2014: 63(3): 653-660.

62.   Gay PC, Hess DR, Hill NS. Noninvasive proportional assist ventilation for acute respiratory insufficiency. Comparison with pressure support ventilation. *Am J Respir Crit Care Med* 2001: 164(9): 1606-1611.

63.   Wysocki M, Richard JC, Meshaka P. Noninvasive proportional assist ventilation compared with noninvasive pressure support ventilation in hypercapnic acute respiratory failure. *Crit Care Med* 2002: 30(2): 323-329.

64.   Sinderby C, Navalesi P, Beck J, Skrobik Y, Comtois N, Friberg S, Gottfried SB, Lindstrom L. Neural control of mechanical ventilation in respiratory failure. *Nat Med* 1999: 5(12): 1433-1436.

65.   Doorduin J, Sinderby CA, Beck J, van der Hoeven JG, Heunks LM. Automated patient-ventilator interaction analysis during neurally adjusted non-invasive ventilation and pressure support ventilation in chronic obstructive pulmonary disease. *Crit Care* 2014: 18(5): 550.

66.   Liu L, Xia F, Yang Y, Longhini F, Navalesi P, Beck J, Sinderby C, Qiu H. Neural versus pneumatic control of pressure support in patients with chronic obstructive pulmonary diseases at different levels of positive end expiratory pressure: a physiological study. *Crit Care* 2015: 19: 244.

67.   Piquilloud L, Tassaux D, Bialais E, Lambermont B, Sottiaux T, Roeseler J, Laterre PF, Jolliet P, Revelly JP. Neurally adjusted ventilatory assist (NAVA) improves patient-ventilator interaction during non-invasive ventilation delivered by face mask. *Intensive Care Med* 2012: 38(10): 1624-1631.

68.   Schmidt M, Dres M, Raux M, Deslandes-Boutmy E, Kindler F, Mayaux J, Similowski T, Demoule A. Neurally adjusted ventilatory assist improves patient-ventilator interaction during postextubation prophylactic noninvasive ventilation. *Crit Care Med* 2012: 40(6): 1738-1744.

69.   Hill NS. Where should noninvasive ventilation be delivered? *Respir Care* 2009: 54(1): 62-70.70.   Carteaux G, Millan-Guilarte T, De Prost N, Razazi K, Abid S, Thille AW, Schortgen F, Brochard L, Brun-Buisson C, Mekontso Dessap A. Failure of Noninvasive Ventilation for De Novo Acute Hypoxemic Respiratory Failure: Role of Tidal Volume. *Crit Care Med* 2016: 44(2): 282-290.

71.   Vignaux L, Vargas F, Roeseler J, Tassaux D, Thille AW, Kossowsky MP, Brochard L, Jolliet P. Patient-ventilator asynchrony during non-invasive ventilation for acute respiratory failure: a multicenter study. *Intensive Care Med* 2009: 35(5): 840-846.

72.   Di Marco F, Centanni S, Bellone A, Messinesi G, Pesci A, Scala R, Perren A, Nava S. Optimization of ventilator setting by flow and pressure waveforms analysis during noninvasive ventilation for acute exacerbations of COPD: a multicentric randomized controlled trial. *Crit Care* 2011: 15(6): R283.

73.   Antonelli M, Conti G, Moro ML, Esquinas A, Gonzalez-Diaz G, Confalonieri M, Pelaia P, Principi T, Gregoretti C, Beltrame F, Pennisi MA, Arcangeli A, Proietti R, Passariello M, Meduri GU. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. *Intensive Care Med* 2001: 27(11): 1718-1728.

74.   Spada C, Gandhi R, Patel SR, Nuccio P, Weinhouse GL, Lee PS. Oxygen saturation/fraction of inspired oxygen ratio is a simple predictor of noninvasive positive pressure ventilation failure in critically ill patients. *J Crit Care* 2011: 26(5): 510-516.

75.   Anton A, Guell R, Gomez J, Serrano J, Castellano A, Carrasco JL, Sanchis J. Predicting the result of noninvasive ventilation in severe acute exacerbations of patients with chronic airflow limitation. *Chest* 2000: 117(3): 828-833.

76.   Carlucci A, Richard JC, Wysocki M, Lepage E, Brochard L, Ventilation SCGoM. Noninvasive versus conventional mechanical ventilation. An epidemiologic survey. *Am J Respir Crit Care Med* 2001: 163(4): 874-880.

77.   Plant PK, Owen JL, Elliott MW. Non-invasive ventilation in acute exacerbations of chronic obstructive pulmonary disease: long term survival and predictors of in-hospital outcome. *Thorax* 2001: 56(9): 708-712.

78.   Piquilloud L, Thevoz D, Jolliet P, Revelly JP. End-tidal carbon dioxide monitoring using a naso-buccal sensor is not appropriate to monitor capnia during non-invasive ventilation. *Ann Intensive Care* 2015: 5: 2.

79.   Nava S. Behind a mask: tricks, pitfalls, and prejudices for noninvasive ventilation. *Respir Care* 2013: 58(8): 1367-1376.

80.   Nava S, Navalesi P, Gregoretti C. Interfaces and humidification for noninvasive mechanical ventilation. *Respir Care* 2009: 54(1): 71-84.

81.   American Association for Respiratory C, Restrepo RD, Walsh BK. Humidification during invasive and noninvasive mechanical ventilation: 2012. *Respir Care* 2012: 57(5): 782-788.

82.   Branson RD, Gentile MA. Is humidification always necessary during noninvasive ventilation in the hospital? *Respir Care* 2010: 55(2): 209-216; discussion 216.

83.   Esquinas Rodriguez AM, Scala R, Soroksky A, BaHammam A, de Klerk A, Valipour A, Chiumello D, Martin C, Holland AE. Clinical review: humidifiers during non-invasive ventilation--key topics and practical implications. *Crit Care* 2012: 16(1): 203.

84.   Lellouche F, Pignataro C, Maggiore SM, Girou E, Deye N, Taille S, Fischler M, Brochard L. Short-term effects of humidification devices on respiratory pattern and arterial blood gases during noninvasive ventilation. *Respir Care* 2012: 57(11): 1879-1886.

85. Lellouche F, Maggiore SM, Lyazidi A, Deye N, Taillé S, Brochard L. Water content of delivered gases during non-invasive ventilation in healthy subjects. Intensive Care Med. 2009; 35(6):987-95.

86.   Lellouche F, L'Her E, Abroug F, Deye N, Rodriguez PO, Rabbat A, Jaber S, Fartoukh M, Conti G, Cracco C, Richard JC, Ricard JD, Mal H, Mentec H, Loisel F, Lacherade JC, Taille S, Brochard L. Impact of the humidification device on intubation rate during noninvasive ventilation with ICU ventilators: results of a multicenter randomized controlled trial. *Intensive Care Med* 2014: 40(2): 211-219.

87.   Devlin JW, Nava S, Fong JJ, Bahhady I, Hill NS. Survey of sedation practices during noninvasive positive-pressure ventilation to treat acute respiratory failure. *Crit Care Med* 2007: 35(10): 2298-2302.

88.   Huang Z, Chen YS, Yang ZL, Liu JY. Dexmedetomidine versus midazolam for the sedation of patients with non-invasive ventilation failure. *Intern Med* 2012: 51(17): 2299-2305.

89.   Conti G, Ranieri VM, Costa R, Garratt C, Wighton A, Spinazzola G, Urbino R, Mascia L, Ferrone G, Pohjanjousi P, Ferreyra G, Antonelli M. Effects of dexmedetomidine and propofol on patient-ventilator interaction in difficult-to-wean, mechanically ventilated patients: a prospective, open-label, randomised, multicentre study. *Crit Care* 2016: 20(1): 206.

90.   Devlin JW, Al-Qadheeb NS, Chi A, Roberts RJ, Qawi I, Garpestad E, Hill NS. Efficacy and safety of early dexmedetomidine during noninvasive ventilation for patients with acute respiratory failure: a randomized, double-blind, placebo-controlled pilot study. *Chest* 2014: 145(6): 1204-1212.

91.   Constantin JM, Schneider E, Cayot-Constantin S, Guerin R, Bannier F, Futier E, Bazin JE. Remifentanil-based sedation to treat noninvasive ventilation failure: a preliminary study. *Intensive Care Med* 2007: 33(1): 82-87.

92.   Rocco M, Conti G, Alessandri E, Morelli A, Spadetta G, Laderchi A, Di Santo C, Francavilla S, Pietropaoli P. Rescue treatment for noninvasive ventilation failure due to interface intolerance with remifentanil analgosedation: a pilot study. *Intensive Care Med* 2010: 36(12): 2060-2065.

93.   Antonelli M, Conti G, Riccioni L, Meduri GU. Noninvasive positive-pressure ventilation via face mask during bronchoscopy with BAL in high-risk hypoxemic patients. *Chest* 1996: 110(3): 724-728.

94.   Chiner E, Sancho-Chust JN, Llombart M, Senent C, Camarasa A, Signes-Costa J. Fiberoptic bronchoscopy during nasal non-invasive ventilation in acute respiratory failure. *Respiration* 2010: 80(4): 321-326.

95.   Clouzeau B, Bui HN, Guilhon E, Grenouillet-Delacre M, Leger MS, Saghi T, Pillot J, Filloux B, Coz S, Boyer A, Vargas F, Gruson D, Hilbert G. Fiberoptic bronchoscopy under noninvasive ventilation and propofol target-controlled infusion in hypoxemic patients. *Intensive Care Med* 2011: 37(12): 1969-1975.

96.   Heunks LM, de Bruin CJ, van der Hoeven JG, van der Heijden HF. Non-invasive mechanical ventilation for diagnostic bronchoscopy using a new face mask: an observational feasibility study. *Intensive Care Med* 2010: 36(1): 143-147.

97.   Antonelli M, Conti G, Rocco M, Arcangeli A, Cavaliere F, Proietti R, Meduri GU. Noninvasive positive-pressure ventilation vs. conventional oxygen supplementation in hypoxemic patients undergoing diagnostic bronchoscopy. *Chest* 2002: 121(4): 1149-1154.

98.   Maitre B, Jaber S, Maggiore SM, Bergot E, Richard JC, Bakthiari H, Housset B, Boussignac G, Brochard L. Continuous positive airway pressure during fiberoptic bronchoscopy in hypoxemic patients. A randomized double-blind study using a new device. *Am J Respir Crit Care Med* 2000: 162(3 Pt 1): 1063-1067.

99.   Lucangelo U, Vassallo FG, Marras E, Ferluga M, Beziza E, Comuzzi L, Berlot G, Zin WA. High-flow nasal interface improves oxygenation in patients undergoing bronchoscopy. *Crit Care Res Pract* 2012: 2012: 506382.

100.   Simon M, Braune S, Frings D, Wiontzek AK, Klose H, Kluge S. High-flow nasal cannula oxygen versus non-invasive ventilation in patients with acute hypoxaemic respiratory failure undergoing flexible bronchoscopy--a prospective randomised trial. *Crit Care* 2014: 18(6): 712.

Table 1. Studies comparing interfaces for NIV.

Study	Design	Major Findings
Antonaglia [8]	53 subjects with COPD exacerbation randomized to mask or helmet. Physiologic parameters, need for intubation, length of stay, and complications recorded.	The sequential use of a mask and helmet reduced the incidence of failure; use of helmet increased length of stay and duration of mechanical ventilation.
Chacur [9]	60 subjects randomized to oronasal or total facemask. Clinical and laboratory parameters, as well as the level of ventilatory support, were recorded. Mask tolerance and need for intubation were compared.	The total facemask was more comfortable, allowing the patients to tolerate NIV longer, but this did not translate into a better outcome.
Cuvelier [10]	34 subjects randomly assigned to total facemask or oronasal mask. The main outcome variable was improvement of arterial pH 24 h after NIV initiation.	Total facemask had the same clinical efficacy as the oronasal mask during acute hypercapnic respiratory failure.
Girault [11]	90 subjects randomized to oronasal or nasal mask. The main end point was mask	Mask failure occurred significantly more often in the group who received the nasal mask, mainly because of the need for mask change

	failure. Secondary end points were tolerance, change in respiratory parameters, and patient outcome.	because of the occurrence of major buccal air-leaks in 94% of cases. Improvement in respiratory parameters was similar in the two groups. Respiratory comfort was assessed as lower and complications more frequent by the staff in the oronasal mask group.
Kwok [12]	35 subjects randomized to nasal or oronasal mask.	Both masks performed similarly with regard to improving vital signs and gas exchange and avoiding intubation. Nasal mask was less well tolerated than the oronasal mask.
Ozsancak [7]	60 subjects with acute respiratory failure randomized to oronasal mask or total facemask. Mask comfort and dyspnea were assessed using visual analog scores. Other outcomes included time required to apply, vital signs and gas exchange at set time points, and early NIV discontinuation rates.	The oronasal mask and total facemask were equally comfortable and had similar application times. Early NIV discontinuation rates, improvements in vital signs and gas exchange, and intubation and mortality rates were similar.
Nicolini [15]	50 subjects were randomized to NIV via nasal mask or mouthpiece. The	The 2 groups had similar trends in arterial blood gases and breathing frequency. No differences in duration of NIV or hospital stay

	primary outcome was improvement in arterial blood gases.	were noted. Significantly more subjects preferred mouthpiece ventilation.
Pisani [13]	80 subjects with COPD and acute hypercapnic respiratory failure randomized to helmet or oronasal mask; compared changes in arterial blood gases, tolerance, dyspnea, vital signs, intubation rate.	Changes in blood gases and comfort were similar, while dyspnea decreased more using the oronasal mask. Intubation rate and the need for interface change were low and not different between groups.
Patel [14]	83 subjects with ARDS randomized to helmet or oronasal mask.	Helmet NIV resulted in a significant reduction of intubation rates and a significant reduction in 90-day mortality.

Table 2. A comparison of ventilator designs for NIV.

Design	Description
Bilevel ventilator	Bilevel ventilators use internal blowers to generate flow through a single limb circuit during both inhalation and exhalation. A passive leak port, either in the circuit or the interface, is open throughout the respiratory cycle. An active exhalation valve is not needed because the exhaled gas passes through the leak port.
Intermediate ventilator	These ventilators are most commonly used for patient transport or home care ventilation. They utilize a single limb circuit with either an active exhalation valve near the patient or a passive leak port. In the past, these devices have been leak intolerant. However, newer designs offer leak compensation.
Critical care ventilator without NIV mode	In the past, critical care ventilators were designed primarily for invasive ventilation. As such, they were leak intolerant. Although these ventilators have been used for NIV, the absence of leak compensation often resulted in asynchrony and much clinician time and effort to minimize leak.
Critical care ventilator with NIV mode	Newer generation critical care ventilators have NIV modes, with dual limb circuits that separate the inspiratory from expiratory gases. NIV modes offer leak compensation, but the ability of the ventilator to compensate for leaks varies among manufacturers. Additional embellishments available from some manufactures include an adjustable flow termination and a maximum inspiratory time during pressure support, both of which improve synchrony with pressure support in the presence of leak. Some manufactures also provide leak compensation in all modes, including

	volume control and pressure control. The nomenclature for ventilator modes during NIV is typically the same as that used during invasive ventilation.

Table 3. Studies of ventilator type

Study	Design	Major Findings
Garnier [17]	Bench study of 13 ICU ventilators with and without leak.	Eleven devices failed to compensate V_T and 4 failed to compensate for PEEP with leak. Inspiratory delays differed among ventilators. NIV algorithms efficiently prevented the decrease in pressurization capacities and PEEP levels induced by leaks in 10 and 12 of the 13 ventilators, respectively.
Chen [18]	Bench study compared performance of 7 bilevel ventilators in the presence of leaks.	Performance and triggering workload varied among bilevel ventilators. Adjusting cycle criteria can improve patient-ventilator synchrony.
Nakamura [19]	Bench study of 8 ICU ventilators equipped with NIV mode.	Four ventilators had significant issues with (auto-triggering or inappropriate shut down due to misdetection of disconnection); 3 worked with some problems (low PEEP or high cycling delay); and 1 worked properly.
Oto [20]	Bench evaluation of leak compensation in acute care ventilators during invasive and noninvasive ventilation	Leak compensation in invasive and noninvasive modes had wide variations between ventilators. The PB840 and the V60 were the only ventilators to acclimate to all leaks, but there were differences in performance between these 2 ventilators.

Lujan [21]	Bench study to assess the reliability of V_T provided by 5 ventilators under different conditions of respiratory pattern, inflation pressure, and leakage.	All tested ventilators underestimated V_T.
Khirani [22]	Bench study to determine the ability of home ventilators to maintain the preset V_T during unintentional leaks volume targeted pressure support.	Most of the ventilators with a single-limb circuit with intentional leak correctly estimated V_T. Volume-targeted pressure support, when used with ventilators with expiratory valve or double-circuit, can paradoxically exacerbate the V_T drop during unintentional leaks.
Carlucci [23]	Bench study to determine the ability of home ventilators to maintain the preset V_T during unintentional leaks volume targeted pressure support.	In a vented circuit configuration all 3 ventilators kept constant or increased inspiratory pressure in leak conditions to guarantee V_T. In a non-vented circuit configuration, all tested ventilators showed a reduction in delivered tidal volume.
Contal [24]	Testing study 7 home ventilators to simulate NIV and unintentional leaks, to evaluate accuracy of data provided.	For assessing leaks, three of the devices tested were highly reliable. V_T was underestimated by all devices and increased with higher pressures.
Carteaux [25]	A bench and clinical study to compare patient-ventilator	Dedicated NIV ventilators allowed better patient-ventilator synchrony than ICU and

	synchrony during NIV between ICU, transport, and dedicated NIV ventilators.	transport ventilators, even with their NIV algorithms. The NIV algorithm improved, at least slightly and with a wide variation among ventilators, trigger and/or cycle synchronization.
Ueno [26]	Bench study of 3 NIV ventilators and 2 ICU ventilators, to assess how they coped with 2 leak levels and no leak during NIV	Some of the ventilators compensated for leak better than others. With the larger leak none of the ventilators maintained the set PEEP or pressure support.
Vignaux [2]	Clinical evaluation of NIV algorithms available with ICU ventilators on the incidence of asynchrony.	NIV algorithms provided by ICU ventilators can reduce the incidence of asynchrony due to leaks, but some of these algorithms can generate premature cycling.
Ferreira [27]	Bench study of 9 ICU ventilators in the presence of leaks, compared with a bilevel ventilator.	Only 2 ICU ventilators required no adjustments as they adapted to increasing leaks. Thus, in the presence of leaks, ICU ventilators may require adjustments to maintain an adequate tidal volume.
Borel [28]	Bench study of 7 interfaces connected to 4 ventilators.	The level of intentional leaks in the masks ranged from 30 to 45 L/min at IPAP of 14 cm H2O. Leaks did not affect trigger performance. Ability to achieve and maintain IPAP was decreased with all ventilators and in all simulated lung conditions when intentional

		leak increased. Cycle was not affected by intentional leaks except in obstructive lung conditions.
Vignaux [29]	Bench study to evaluate NIV modes on ICU ventilators.	Leaks interfered with key functions of ICU ventilators. NIV modes corrected part or all of these issues, but with variations between ventilators.
Battisti [30]	Bench study to compare characteristics of 10 bilevel ventilators with conditions of different respiratory mechanics.	All devices had very short trigger delays and trigger workload. Pressurization capability varied among the ventilators. Cycle was often not synchronous when the default settings were used, but was improved by modifying cycle settings when that option was available.
Vitacca [31]	Clinical study to compare patient-ventilator interaction and comfort with 5 bilevel ventilators.	All of the studied ventilators were well tolerated and performed well in terms of inspiratory muscle unloading. The number of ineffective triggers was similar among the studied ventilators.
Tassaux [32]	Bench study to compare trigger, pressurization, and cycle of a bilevel ventilator and 3 ICU ventilators.	The bilevel ventilator performed as well as one of the ICU ventilators, but not as well as the other two.
Mehta [33]	Bench study of leak compensating abilities of 6 different ventilators used for	Leak-compensating capabilities differed markedly among ventilators, but bilevel devices were preferred for patients with

	NIV.	substantial air leaking.
Highcock [34]	Bench study of 4 bilevel ventilators.	Differences found in the ventilators' responses to a leak and to changes in simulated patient effort.
Patel [35]	Clinical study comparing a bilevel ventilator to an ICU ventilator.	The performance of the bilevel ventilator was equally efficacious to that of the ICU ventilator in supporting respiratory muscles.
Bunburaphong [36]	Bench study evaluated the performance of 9 bilevel ventilators to an ICU ventilator.	Most bilevel ventilators evaluated were able to respond to high ventilatory demands and outperformed the ICU ventilator; in the clinical study, there were no differences in $PaCO_2$, V_T, respiratory rate, or minute ventilation between a bilevel and ICU ventilator.

Table 4. Studies evaluating rebreathing with bilevel ventilators.

Study	Design	Major Findings
Szkulmowski [37]	Clinical study of rebreathing with a bilevel ventilator and single limb circuit.	A single limb circuit presents a rebreathing risk to patients, but that risk is modest if expiratory pressure is applied.
Schettino [38]	Bench study to evaluate the effect of exhalation port location and mask design on rebreathing with bilevel ventilator.	Face mask with exhalation port in the mask and the smallest mask volume resulted in less rebreathing than the face mask with the leak port in the circuit or the total face mask.
Lofaso [39]	Bench and clinical study evaluating 6 bilevel ventilators.	Rebreathed volume decreased with increasing expiratory pressure level, but remained substantial at a level of 5 cm H_2O.
Lofaso [40]	Bench and clinical study to evaluate rebreathing in bilevel ventilators.	No significant effect on blood gases between bilevel and ICU ventilators, but with increases in V_T, minute ventilation, and work of breathing for the bilevel ventilator.
Ferguson [41]	Clinical study of rebreathing with a bilevel ventilator.	The use of a standard exhalation device with a bilevel ventilator results in rebreathing. Use of a plateau exhalation device or a non-rebreathing valve eliminated rebreathing.

Table 5. Studies evaluating oxygen delivery with bilevel ventilators

Study	Design	Major Findings
Storre [42]	Daytime measurements in 20 subjects receiving NIV with supplemental oxygen.	The use of a leak port circuit and leak around the interface significantly reduced oxygen concentration at the mask and negatively impacted gas exchange.
Dai [43]	Bench study of factors affecting FIO_2 with bilevel ventilators.	Oxygen flow, inspiratory and expiratory pressure, and exhalation valve type all affected FIO_2. For a given oxygen flow, the injection site was the most important factor that affected FIO_2. The injection site that was closest to the patient (on the mask) had the higher FIO_2.
Miyoshi [44]	Bench study of the effects of gas leak on FIO_2, trigger, and humidification.	The bilevel ventilators triggered properly at all levels of gas leak. Increased leak caused FIO_2 to decrease. With large gas leaks, relative humidity was maintained, but absolute humidity decreased.
Schwartz [45]	Bench study evaluating delivered oxygen concentration with bilevel ventilator.	Delivered oxygen concentration with a bilevel ventilator is a complex interaction between the leak port type, the site of oxygen injection, the ventilator settings, and the oxygen flow. The highest FIO_2 was achieved with oxygen added to the mask, with the leak port in the circuit, and with the lowest settings of inspiratory and expiratory pressure.

| Thys [46] | Bench study to evaluate the determinants of FIO_2 with a bilevel ventilator. | When all other variables were constant, the connection closest to the leak port resulted in the highest FIO_2. Increases in IPAP led to decreases in FIO_2. FIO_2 increased with increased oxygen flow, although it was difficult to obtain an $FIO_2 >$ 0.3 unless very high oxygen flows were used. |

Table 6. NIV monitoring requirements.

Subjective Responses: respiratory distress, dyspnea, anxiety, claustrophobia, discomfort with mask or air pressure, dryness of mouth or eyes, gastric insufflation.

- At NIV intiation

- Every 15 to 30 min for first 2 hours of therapy

- Hourly or as needed after first 2 hours

Physical findings: respiratory rate, heart rate, blood pressure, level of consciousness, accessory muscle use, abdominal paradox, comfort, skin breakdown.

- At NIV initiation

- Every 15 - 30 min for first 2 hours of therapy

- If stable after 2 hours of therapy, then hourly assessments.

Ventilator parameters: tidal volume, minute ventilation, leak under mask or through mouth, inspiratory pressure setting, expiratory pressure setting, FIO_2, synchrony

- At NIV initiation

- Every 15 - 30 min for first 2 hours of therapy

- If stable after 2 hours of therapy, then assessments every 4 - 6 hours.

Gas Exchange: pulse oximetry, arterial blood gases, end-tidal PCO_2, transcutaneous PCO_2

- Continuous pulse oximetry

- Arterial blood gases at baseline, 30 - 60 min after initiation, and with changes in clinical condition