Bronchoscopic Lung Biopsy Using Noninvasive Ventilatory Support: Case Series and Review of Literature of NIV-Assisted Bronchoscopy

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BACKGROUND: Fiberoptic bronchoscopy and lung biopsy are important diagnostic tools in patients with diffuse pulmonary infiltrates. However, these patients often have hypoxemic respiratory failure that makes this procedure hazardous. Noninvasive ventilation (NIV) has been shown to improve oxygenation in hypoxemic patients. OBJECTIVE: To report the efficacy and safety of an innovative technique of NIV-assisted bronchoscopic lung biopsy in a small case-series of hypoxemic subjects with diffuse parenchymal infiltrates; also to systematically review the literature on NIV-assisted bronchoscopy. METHODS: Subjects with bilateral diffuse parenchymal infiltrates and P_{aO_2}/F_{IO_2} < 200 mm Hg underwent bronchoscopic lung biopsy under NIV support. NIV was initiated 10 min before the procedure and continued for 30 min after the procedure. The primary outcomes were performance of successful procedure and episodes of decline in S_{pO_2} < 90%. Secondary end points were the change in the respiratory and hemodynamic parameters during the procedure and occurrence of complications such as pneumothorax, hemorrhage, and endotracheal intubation. RESULTS: Six subjects, with a mean ± SD age of 44.5 ± 11.6 years, were included in the study. The median (interquartile range [IQR]) P_{aO_2}/F_{IO_2} prior to lung biopsy was 164.5 mm Hg (146.3–176.3 mm Hg), and the median (IQR) inspiratory and expiratory positive airway pressures were 14 cm H_2O (12–15 cm H_2O) and 5 cm H_2O. Fiberoptic bronchoscopy was well tolerated and all subjects maintained S_{pO_2} > 92% during the procedure. One subject required endotracheal intubation due to hemoptysis. A definite diagnosis was obtained in 5 of the 6 subjects. A repeat procedure was performed in one subject, which again yielded no diagnosis. No other periprocedural complications were encountered. CONCLUSIONS: NIV-assisted bronchoscopic lung biopsy is a novel method for obtaining diagnosis in hypoxemic patients with diffuse lung infiltrates. However, this approach should be reserved for centers with extensive experience in NIV. More studies are required to define the utility of this approach. *Key words: noninvasive ventilation; NIV; bronchoscopy; respiratory failure; CPAP.* [Respir Care 2012;57(11):1927–1936. © 2012 Daedalus Enterprises]

Introduction

Fiberoptic bronchoscopy (FOB) is a valuable tool in evaluation of patients with diffuse pulmonary infiltrates. However, insertion of a flexible bronchoscope in the airway decreases the cross-sectional area proportional to the outer diameter of the flexible bronchoscope, and increases the resistance to air flow.[1] Usually inconsequential in patients without hypoxemia, a decrease in airway lumen size due to FOB can be detrimental in a hypoxemic patient, as it not only increases the work of breathing, but the P_{aO_2} also decreases by 10–20 mm Hg after an uncomplicated bronchoscopy.[2] Furthermore, suction during bronchoscopy reduces the end-expiratory lung volume, which leads to

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alveolar closure and ventilation-perfusion mismatch.[1-3] Thus, supplemental oxygen is recommended during bronchoscopy in hypoxemic patients to achieve an S_{pO_2} of at least 90%.[4] Severe hypoxemia ($P_{aO_2} \leq 60$ mm Hg despite F_{IO_2} of 0.5) in non-intubated patients is generally regarded as a contraindication to bronchoscopy, as these patients are at high-risk for developing hypoxia-related cardiorespiratory complications.[5]

Noninvasive ventilation (NIV) is the delivery of positive-pressure ventilation without an endotracheal airway. NIV is a safe and effective method of recruiting alveoli and augmenting ventilation, thereby ameliorating hypoxemia in patients with acute respiratory failure (ARF).[6] In fact, NIV used for pre-oxygenation is more effective at reducing arterial oxyhemoglobin desaturation than usual pre-oxygenation during endotracheal intubation in hypoxemic critically ill patients.[7] Several reports suggest that NIV can facilitate the performance of bronchoscopy in severely hypoxemic patients, by correcting the hypoxemia. However, all studies to date have used NIV for performance of bronchoalveolar lavage (BAL) in hypoxemic patients with pulmonary infiltrates.[8-16] No study has described the conduct of transbronchoscopic lung biopsy (TBLB) using NIV. We have wide experience with NIV and have found it suitable in correction of hypoxemia in diverse causes of respiratory failure.[17-20] Herein, we describe the first report of NIV-assisted TBLB in a small case-series of 6 patients. We also review the literature on the use of bronchoscopy performed using NIV support.

Methods

All patients with diffuse pulmonary infiltrates and ARF requiring NIV assistance during TBLB were included in the study. The study was approved by the local ethics committee, and written informed consent was taken from all subjects. Patients were included in the study if they met all of the following criteria: diffuse pulmonary opacities on high-resolution computed tomography of the chest; negative results on sputum cytology and cultures requiring lung biopsy for further diagnosis; and severe hypoxemia, defined by $P_{aO_2}/F_{IO_2} < 200$ mm Hg on high-flow air-entrainment mask. Patients were excluded from the study if any of the following was present: recent (< 1 month) acute myocardial infarction; platelet count < 75,000 cells/μL; coagulopathy, defined as prothrombin time or activated partial thromboplastin time > 1.5 times control; pH < 7.3 with $P_{aCO_2} > 50$ mm Hg; systolic blood pressure < 90 mm Hg or > 180 mm Hg; contraindication for NIV, including altered mental status, facial abnormality, or inability to fit the NIV mask.

QUICK LOOK

Current knowledge

Noninvasive ventilation (NIV) improves ventilation in hypercapnic respiratory failure and can improve oxygenation in select cases of hypoxemia. Fiberoptic bronchoscopy can be both an important diagnostic and therapeutic procedure in patients with respiratory disease. The use of bronchoscopic lung biopsy during NIV has not been studied systematically.

What this paper contributes to our knowledge

Bronchoscopic lung biopsy can be safely performed in patients with diffuse pulmonary infiltrates and acute respiratory failure receiving NIV. This approach should be performed only in centers with wide experience with both NIV and bronchoscopy.

Bronchoscopy Preparation

FOB was performed in the bronchoscopy suite by experienced faculty, using a wide channel videoscope (BF-1T 150, Olympus Optical, Tokyo, Japan). All subjects received nebulization with 4% lidocaine solution immediately before the procedure, and topical lidocaine jelly was applied in the nasal cavity. In addition, 2% lidocaine was instilled over the vocal cords, carina, and airways through the working channel of the flexible bronchoscope, to suppress cough during the procedure. No sedative was administered before or during the procedure.

NIV Protocol

NIV was delivered using a critical care ventilator (Servo-i, Maquet, Bridgewater, New Jersey) with an oronasal mask secured to the subject's face with elastic straps (Fig. 1). NIV was initiated at F_{IO_2} of 1.0, starting 10 min before the procedure, and continued for 30 min after the procedure. Ventilatory parameters were set at a continuous positive airway pressure (CPAP) of 5 cm H_2O and pressure support of 15 cm H_2O, adjusted to maintain S_{pO_2} of > 92%. The bronchoscope was inserted through a dual axis swivel adapter attached to the mask, with the tight disposable cap of the swivel adapter preventing air leak during the procedure (see Fig. 1). Initially, the mask was removed from the face and the flexible bronchoscope was inserted through the mask and then through the nasal passage, to ensure quick access. Once the vocal cords were visible, the mask was again applied over the subject's face and connected to the ventilator, and the bronchoscopy procedure was continued. While performing lung biopsy, the CPAP was re-

Fig. 1. Noninvasive ventilation was delivered using an oronasal mask, and the bronchoscope was inserted through the swivel adaptor.

duced to zero and only pressure support of 10 cm H_2O was given. During bronchoscopy, F_{IO_2} was maintained at 1.0, and after bronchoscopy was decreased to the pre-bronchoscopy level. The positive-pressure ventilation was maintained for at least 30 min after the procedure, following which the subject was shifted back to oxygen therapy with air-entrainment mask. The application of NIV was extended if the S_{pO_2} could not be maintained to $\geq$ 92% with air-entrainment mask.

Lung Biopsy

Bronchoscopy was performed in a standard fashion. The bronchoscope was wedged into the segmental bronchus of the desired biopsy site, determined from the radiologically abnormal areas on high-resolution computed tomography chest. Initially, BAL was performed with the tip of the bronchoscope wedged in the bronchial segment of interest, with sequential instillation of 20 mL saline aliquots. Subsequently, a conventional biopsy forceps (flexible bronchoscope 19C, Olympus Optical, Tokyo, Japan) was advanced through the working channel of the bronchoscope into the segmental bronchus until its tip was beyond bronchoscopic visualization. Once a gentle resistance was felt, the forceps was withdrawn by 1–2 cm proximally. The forceps was then opened and again advanced to the desired site and then closed and withdrawn while keeping the bronchoscope wedged in the same position. At least 4 biopsies were performed, unless there was any indication to terminate the procedure due to hypoxemia (S_{pO_2} < 90% on NIV) or bleeding.

Monitoring

We continuously monitored the S_{pO_2} and heart rate, while blood pressure was measured every 5 min during and 30 min after the procedure. An arterial blood gas analysis was performed before, during, and 15 min after the procedure. Chest radiograph and ultrasound examination were performed 2 hours after the procedure, to exclude pneumothorax. Facilities for endotracheal intubation and invasive ventilation were kept ready while performing the procedure.

End Points

The primary outcome was the performance of successful procedure, defined by completion of BAL and TBLB, and number of episodes of decline in S_{pO_2} to < 90%. Secondary end points were the change in the respiratory and hemodynamic parameters during the procedure and occurrence of complications like pneumothorax, hemorrhage, and endotracheal intubation.

Statistical Analysis

Data are presented in a descriptive fashion. The change in respiratory and hemodynamic variables over time were analyzed using the Friedman test.

Systematic Review

We first searched the literature for existing systematic reviews on NIV-assisted bronchoscopic biopsy. No reviews were found. Two authors (RA and AK) then independently searched the PubMed and EmBase databases for published papers reporting the use of NIV during bronchoscopy. We included relevant studies using the following free text terms: ("bronchoscopy" OR "fiberoptic bronchoscopy") AND ("niv" OR "noninvasive ventilation" OR "noninvasive ventilation" OR "nippv" OR "noninvasive positive-pressure ventilation" OR "noninvasive positive-pressure ventilation" OR "cpap" OR "continuous positive

Table 1. Baseline Characteristics of the Patients ($n = 6$)

Age, y	44.5 ± 11.6
Male/female, no.	3/3
Immunocompromised, no.	1
Heart rate, beats/min	104.3 ± 7.6
Respiratory rate, breaths/min	45.5 ± 2.4
Mean arterial blood pressure, mm Hg	84.3 ± 5.7
P_{aO_2}/F_{IO_2}, median (IQR) mm Hg	164.5 (146.3 − 176.3)
P_{aCO_2}, mm Hg	45.5 ± 2.4

± Values are mean ± SD.

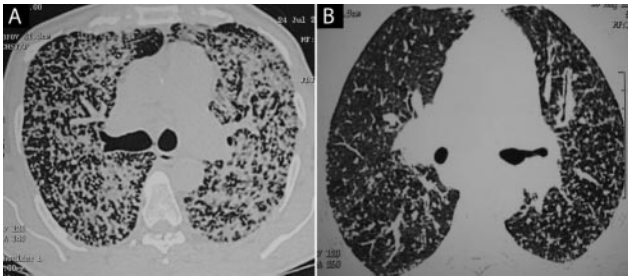

Fig. 2. High-resolution computed tomography images of 2 subjects who underwent noninvasive-ventilation-assisted transbronchoscopic lung biopsy. Panel A shows extensive nodular interlobular septal thickening, and this subject was found to have bronchoalveolar carcinoma on lung biopsy. Panel B shows interlobular septal thickening with ground glass opacities and randomly scattered nodules. Lung biopsy showed granulomatous inflammation and this subject was treated as sarcoidosis.

airway pressure" OR "bipap" OR "bi-level positive airway pressure" OR "bi-level positive airway pressure" OR "positive pressure therapy" OR "nipsv" OR "noninvasive pressure support ventilation" OR "noninvasive pressure support ventilation" OR "mask ventilation" OR "nasal ventilation" OR "non invasive ventilation" OR "non invasive positive-pressure ventilation" OR "non invasive pressure support ventilation"). In addition we reviewed our personal files. We included studies describing the performance of NIV-assisted bronchoscopy in patients with ARF. We excluded single patient case-reports or studies involving ≤ 5 patients.

Data were recorded on a standard data extraction form. The following items were extracted: publication details (title, authors, and other citation details), type of study (prospective or retrospective), demographic characteristics of the subjects, inclusion and exclusion criteria of individual studies, NIV settings and interface, bronchoscopy procedure and duration: diagnostic information from the bronchoscopy procedure, occurrence of hypoxemia (S_{pO_2} < 90%) during bronchoscopy, and endotracheal intubation related as a complication of the procedure (within 24 h of NIV-assisted bronchoscopy).

Results

Six subjects (3 males, 3 females) with a mean ± SD age of 44.5 ± 11.6 years were included in the study. All subjects were immunocompetent, except one, who was suffering from acquired immunodeficiency syndrome. The baseline characteristics of the subjects are shown in Table 1, and the representative computed tomography chest images of 2 subjects are shown in Figure 2. All subjects had severe hypoxemia, with the median P_{aO_2}/F_{IO_2} being 164.5 mm Hg. Most of the subjects had chronic symptoms, with a median of 160 d (range 14–240 d). The median (interquartile range) positive pressure used during bronchoscopy was 14 cm H_2O (12–15 cm H_2O)/5 cm H_2O. Bronchoscopy was well tolerated, and the bronchoscopy procedure was successfully completed in all the subjects. The changes in clinical and blood gas parameters are shown in Figure 3. There was significant improvement in respiratory rate and P_{aO_2}/F_{IO_2}, and significant decline in heart rate after application of NIV, which was maintained throughout the procedure. All subjects maintained S_{pO_2} > 92% during the procedure. The actual bronchoscopy procedure, including BAL and TBLB, took a median of 11.5 min (range 8–16 min). There was no evidence of pneumothorax on the post-procedure chest radiograph in any subject. One subject required elective endotracheal intubation following the procedure, due to hemoptysis. However, she did not require any additional blood transfusion and was extubated the same day. There was no mortality during the hospital stay.

A definite diagnosis was obtained in 5 (malignancy 2, lymphoma 1, sarcoidosis 1, pneumocystis pneumonia 1) of the 6 subjects with TBLB, while BAL was non-contributory in all these subjects. The results of TBLB enabled successful management of all subjects. A repeat procedure was performed in one subject, which again yielded no diagnosis. This subject was finally diagnosed as connective tissue disease-related non-specific interstitial pneumonia and started on glucocorticoid therapy.

Systematic Review of NIV-Assisted Bronchoscopy

Our initial search retrieved 113 citations, of which 20 studies involved NIV and bronchoscopy. Of these, 11 studies were further excluded as they were reviews, editorials, letters to the editor, or involved < 5 patients. Finally, 9 studies, involving 171 patients, were included for the systematic review.[8-16] All studies were prospective and observational, while 2 studies were randomized controlled trials (Table 2). Except for one study that used CPAP alone,[10] all studies utilized NIV for ventilation during FOB. The characteristics of patients and procedures in various studies are shown in Tables 2 and 3.

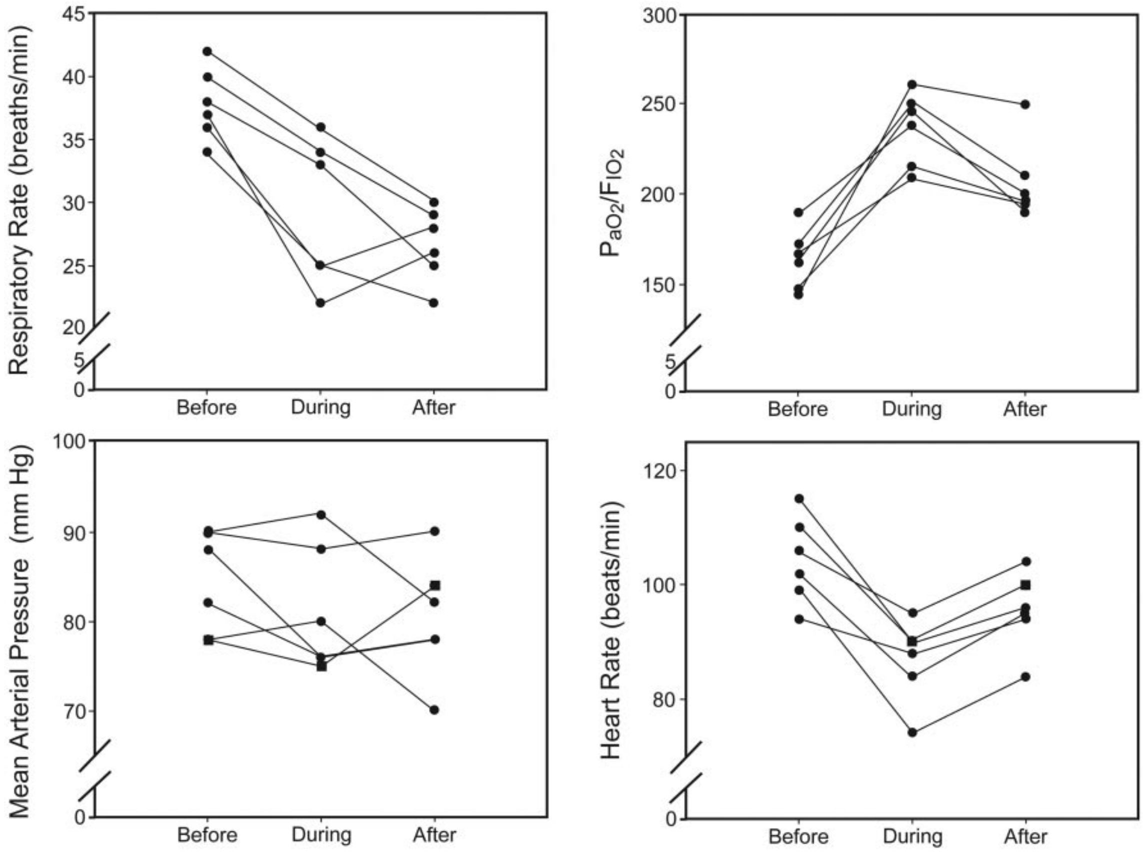

Fig. 3. Respiratory and hemodynamic parameters before, during, and after the procedure. There was substantial decline in respiratory rate and heart rate, and substantial improvement in P_{aO_2}/F_{IO_2} during and after the bronchoscopy procedure on NIV, compared to baseline. There was no important change in the mean arterial pressure

All studies employed positive pressure therapy 10–30 min prior to the procedure and continued NIV after the procedure for variable time periods.[8-16,21] Seven studies used only topical anesthesia during bronchoscopy without any sedation or analgesia.[8-14] In one study,[15] additional intravenous midazolam and propofol boluses were administered for sedation, while in another study intravenous target controlled propofol infusion was used.[16] There was improvement in S_{pO_2} following the application of NIV during bronchoscopy in the majority of the studies. Only in the study by Chiner et al[12] did the S_{pO_2} decrease to 86 ± 3% during FOB, while 3 patients in 2 other studies also developed hypoxemia during FOB.[13,15] In contrast to all studies where NIV was used to facilitate FOB, Baumann et al performed FOB in critically ill patients who were already on NIV support for underlying illness and showed improvement in P_{aO_2}/F_{IO_2} while the F_{IO_2} was increased to 1.0 during the bronchoscopy procedure.[15]

There were few complications. Of the 171 patients, 10 (5.8%) required endotracheal intubation related to the procedure (see Table 3). The diagnostic information obtained from bronchoscopy ranged from 60–100%, with the pooled information rate (Fig. 4) across the studies being 79% (95% CI 65–90%).

Discussion

The results of our study suggest that NIV-assisted bronchoscopy is a safe and effective method of obtaining lung biopsy in hypoxemic patients with diffuse pulmonary disease. Several investigators have shown that bronchoscopy is associated with temporary alterations in gas exchange, hemodynamics, and lung mechanics, due to diminution in the airway size.[1-3,22] The results of our study and the systematic review suggest that the use of NIV during bronchoscopy is associated with improvement in gas exchange, which can facilitate easy performance of BAL and lung biopsy.

In hypoxemic patients with diffuse pulmonary infiltrates, the options available include intubation and mechanical ventilation to ensure adequate ventilation during bronchoscopy, surgical lung biopsy, or institution of empirical treatment. Surgical lung biopsy allows direct sampling of lung tissue, with high sensitivity and specificity for the diag-

Table 2. Summary of Studies of Bronchoscopy With Noninvasive Ventilation

First Author	Year	Study	n	Age, mean ± SD, y	Male/Female	Inclusion Criteria	Exclusion Criteria
Antonelli[8]	1996	Prospective observational	8	40 ± 14	5/3	$P_{aO_2}/F_{IO_2} \leq 100$ mm Hg, pH ≥ 7.35, improvement in oxygenation during NIV before FOB	NA
Da Conceicao[9]	2000	Prospective observational	10	71 ± 5	7/3	$P_{aO_2} < 70$ mm Hg, $P_{aCO_2} > 50$ mm Hg on 3 L/min nasal O_2, improvement in oxygenation during NIV before FOB	Shock, impaired consciousness, acute respiratory distress, pH < 7.25, $P_{aCO_2} > 80$ mm Hg, $P_{aO_2} < 50$ mm Hg despite 3 L/min nasal oxygen, facial deformity, severe bronchospasm
Maitre[10]	2000	Randomized controlled	CPAP 15 Oxygen 15	Mean 58 IQR 35–78	11/4 10/5	Need for FOB for diagnosis, hypoxemia: $P_{aO_2} < 125$ mm Hg on 10 L/min O_2	Recent (< 1 week) acute myocardial infarction, pH < 7.3, $P_{aCO_2} > 60$ mm Hg, $P_{aO_2} < 50$ mm Hg at F_{IO_2} 10 L/min , platelet < 30 × 10^9 cells/L, systolic blood pressure < 80 mm Hg, encephalopathy or coma, contraindications for transbronchoscopic lung biopsy
Antonelli[11]	2002	Randomized controlled	NIV 13 Oxygen 13	NIV 52 ± 20 Oxygen 57 ± 10	8/5	$P_{aO_2}/F_{IO_2} \leq 200$ mm Hg, suspected nosocomial pneumonia	Emergency intubation (CPR, respiratory arrest, hemodynamic instability, or coma), respiratory failure due to neurological disease, status asthmaticus, > 2 new organ failures, facial deformities, or recent oral, esophageal, or gastric surgery
Chiner[12]	2010	Prospective observational	35	63 ± 17	26/9	Acute hypoxemic respiratory failure with $P_{aO_2}/F_{IO_2} \leq 200$ mm Hg or respiratory rate > 35 breaths/min, and FOB for diagnostic or therapeutic purpose	$S_{pO_2} < 90\%$ despite NIV, intolerance to NIV, clinical indication for invasive ventilation defined by hemodynamic instability, CPR, encephalopathy, or coma
Heunks[13]	2010	Prospective observational	12	64 ± 11	6/6	Indication for FOB and BAL with hypoxemia or respiratory distress	Recognized contraindications for NIV, such as reduced level of consciousness, recent facial or esophageal surgery, and inability to tolerate the face mask
Scala[14]	2010	Prospective case-control	NIV 15 Controlled mechanical ventilation 15	NIV 80 ± 5 Controlled mechanical ventilation 80 ± 5	12/3 9/6	Acutely decompensated COPD: pH < 7.33 and $P_{aCO_2} > 55$ mm Hg, $P_{aO_2}/F_{IO_2} \leq 250$ mm Hg, respiratory rate > 25 breaths/min, inability to clear airways from excessive secretions, and hypercapnic encephalopathy	Refusal of NIV, facial deformity, preexisting psychiatric or neurological disease, upper gastrointestinal bleed, upper-airway obstruction, acute coronary syndrome, tracheostomy or intubation, need for urgent intubation due to cardiorespiratory arrest, or requiring ventilation due to severe community-acquired pneumonia or septic shock
Baumann[15]	2011	Prospective observational	40	61 ± 15	26/14	Acute hypoxemic respiratory failure with $P_{aO_2}/F_{IO_2} \leq 300$ mm Hg on NIV, requiring NIV prior to bronchoscopy, requiring diagnostic or therapeutic FOB, age ≥ 18 y	Institution of NIV purely to facilitate bronchoscopy
Clouzeau[16]	2011	Prospective observational	23	60 ± 16	19/4	Adults with acute respiratory failure by clinical signs of respiratory failure (polypnea, use of accessory respiratory muscle), P_{aO_2}/F_{IO_2} < 250 mm Hg on NIV, who needed FOB with BAL for diagnosis	NIV contraindicated, acute coronary syndrome, thrombocytopenia < 30 × 10^9 cells/L, coagulation disorders, $P_{aO_2}/F_{IO_2} < 80$ mm Hg under NIV, persistent respiratory acidosis under NIV (pH < 7.32), systolic blood pressure < 80 mm Hg, propofol or xylocaine allergy, pregnancy, age < 18 y or > 90 y, or weight > 150 kg or < 30 kg

NIV = noninvasive ventilation
FOB = fiberoptic bronchoscopy
CPR = cardiopulmonary resuscitation
BAL = bronchoalveolar lavage
NA = not available

Table 3. NIV Settings, Details of Bronchoscopic Procedure and Complications in Studies in the Systematic Review

First Author	Year	Indication for NIV	IPAP/EPAP, (cm H_2O)	F_{IO_2} During FOB	NIV Duration	Interface	Bronchoscopic Procedure	Duration of Bronchoscopy	Complications Related to the Procedure
Antonelli[8]	1996	Immunocompromised with suspected pneumonia	17/4	Before 0.7 During 1.0 After 0.7	10 min before and 90 min after FOB	Oronasal mask	BAL	7 min (max 10 min)	None
Da Conceicao[9]	2000	COPD	16/NA	0.7	5 min before and 5 min after FOB	Oronasal mask	BAL	11 ± 4 min	None
Maitre[10]	2000	FOB required for diagnostic purpose in patients with hypoxemia	CPAP titrated in steps of 2.5 to 7.5	Before 10 L/min During NA After 10 L/min	5 min before and 30 min after FOB	Oronasal mask	BAL, bronchial biopsy in 2 patients	Oxygen group 305 ± 54 s CPAP group 311 ± 44 s	Oxygen group 7 CPAP group 1 (required intubation)
Antonelli[11]	2002	Suspected nosocomial pneumonia with acute hypoxemic respiratory failure	15–17/4	Before 0.5 During 0.9 After 0.7	10 min before and 30 min after FOB	Oronasal mask	BAL	11 ± 4 min	Oxygen group 2 NIV group 1 (required intubation)
Chiner[12]	2010	Acute respiratory failure where FOB is indicated	16 ± 1.5/6 ± 1	5–15 L/min regulated to maintain $S_{pO_2} \geq 90\%$	Before and during and 15 min after FOB	Nasal mask	Bronchoaspirate 35 Protected specimen brush 21 BAL 11 Bronchial biopsy 8	NA	No procedure had complications, but S_{pO_2} decreased to 86 ± 3% during FOB
Heunks[13]	2010	Non-ICU hypoxemic patients where FOB is indicated	10/6 F_{IO_2} 1.0	Before 1.0 During 1.0 After 0.1	20 min before FOB, until $S_{pO_2} > 92\%$ at F_{IO_2} 0.4	Novel full face mask	BAL	NA	Hypoxemia during procedure in 1 patient
Scala[14]	2010	COPD with pneumonia and encephalopathy	10–25/5	Before 0.7 During 1.0 After Decreased to maintain $S_{pO_2} > 90\%$	Before FOB until clinical improvement with gradual reduction of the pressure support	Oronasal mask	BAL	7.8 ± 3.1 min	None
Baumann[15]	2011	Critically ill with acute hypoxemic respiratory failure	10–25/5–10	Before 1.0 During 1.0 After 0.7	Prior to decision on FOB and continued after the procedure	Oronasal mask	BAL	7.8 ± 5.5 min	4 patients needed intubation 2 patients developed $S_{pO_2} < 90\%$ during the procedure
Clouzeau[16]	2011	Patients with acute respiratory failure	11 ± 3/6 ± 1	Before 0.7 During 1.0 After 1.0	Before and during FOB and 60 min after procedure	Oronasal mask	BAL	13.5 ± 5.5 min	4 patients needed intubation

NIV = noninvasive ventilation
FOB = fiberoptic bronchoscopy
BAL = bronchoalveolar lavage
EPAP = expiratory positive airway pressure
IPAP = inspiratory positive airway pressure
NA = not available

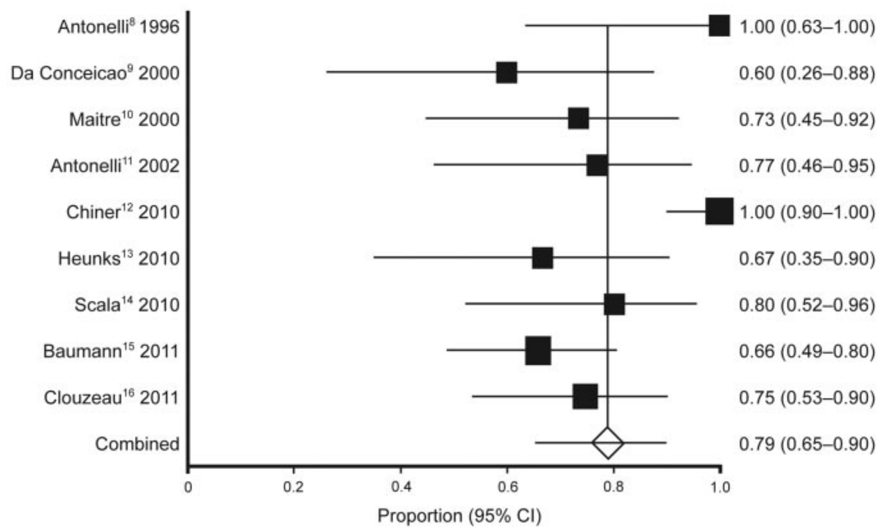

Fig. 4. Diagnostic information obtained from noninvasive-ventilation-assisted bronchoscopy. The yield in individual studies is represented by a square (percentage), through which runs a horizontal line (95% CI). The diamond at the bottom represents the pooled diagnostic information from the studies (79% [95% CI 65–90%]).

nosis of diffuse lung processes.[23,24] However, it is not readily available and there is often reluctance for this procedure in the ICU, both by the intensivists and the patients (or their relatives). An empiric treatment has been criticized due to the potential toxicities arising from unnecessary medical treatments, the excessive costs, and the risk of not treating an undiagnosed but reversible medical condition.[23,25] Hence, there is a need for alternative strategies for obtaining lung biopsy in these critically ill patients, as many of these represent therapeutic emergencies. Our study suggests that NIV-assisted TBLB is another alternative in hypoxemic patients with diffuse pulmonary infiltrates.

Several studies have reported the performance of NIV-assisted bronchoscopy (see Tables 2 and 3). Antonelli et al were the first to report an NIV-assisted bronchoscopic procedure, when they performed BAL in 8 immunocompromised patients with severe hypoxemia (P_{aO_2}/F_{IO_2} < 100 mm Hg). The use of NIV was associated with significant improvements in P_{aO_2}/F_{IO_2} during bronchoscopy.[8] Da Conceicao et al investigated 10 consecutive COPD patients with pneumonia and ARF admitted to the ICU. During FOB with NIV, the S_{pO_2} increased from 91 ± 4.7% at baseline to 97 ± 1.7%.[9] In a randomized controlled trial of 30 patients with $P_{aO_2} < 125$ mm Hg despite high flow mask, Maitre et al showed significantly higher S_{pO_2} values in the CPAP group, compared to oxygen therapy alone, using a new CPAP device. Not only did the patients in the oxygen group develop hypoxemia during the bronchoscopy procedure, 5 patients in the oxygen group (compared to none in the CPAP group) required ventilatory assistance following the procedure.[10] Subsequently, in another randomized study involving 26 patients with nosocomial pneumonia and $P_{aO_2}/F_{IO_2} \leq 200$ mm Hg, Antonelli et al found the use of NIV superior to conventional oxygen supplementation, with better hemodynamic tolerance.[11] Application of NIV was associated with increase in P_{aO_2}/F_{IO_2} by 82%, in contrast to decline in P_{aO_2}/F_{IO_2} by 10% in the oxygen therapy group during FOB. Furthermore, the P_{aO_2}/F_{IO_2} remained elevated in the NIV group, while it fell by a further 10% 60 min post procedure in the oxygen therapy group.[11] The same group also found the helmet interface for delivering NIV to be safe in avoiding gas exchange deterioration.[21]

Chiner et al evaluated nasal mask for delivering NIV while the FOB was performed orally using a bite block sealed with an elastic glove finger in 35 patients with a mean P_{aO_2}/F_{IO_2} of 168 mm Hg. In contrast to other studies, patients developed hypoxemia during the procedure, with S_{pO_2} decreasing to 86% during FOB.[12] Hence, this method cannot be routinely recommended for NIV-assisted FOB. Heunks et al reported the use of a novel full face mask for delivering positive pressure during diagnostic FOB in 12 patients with mean P_{aO_2}/F_{IO_2} of 192 mm Hg with hypoxemia. The procedure was successful in all patients, and in only one patient S_{pO_2} decreased to 86% during bronchoscopy.[13]

In an interesting study, Scala et al showed that in patients with decompensated COPD with hypercapnic encephalopathy due to community-acquired pneumonia, and inability to clear copious secretions, the use of NIV with therapeutic bronchoscopy was associated with improvement in P_{aO_2}/F_{IO_2} of similar magnitude, compared to a control group of patients requiring invasive ventilation. Moreover, the occurrence of septic complications and tracheostomy was less in the NIV group, due to decrease in the rate of endotracheal intubation, albeit with similar hospital mortality, duration of ventilation, and hospital stay as in the invasive ventilation group.[14] All the previously mentioned studies have used NIV to prevent respiratory deterioration in spontaneously breathing hypoxemic patients undergoing bronchoscopy not otherwise requiring NIV for ARF. In contrast, Baumann et al reported the performance of FOB in patients with hypoxemic ARF requiring NIV for management. In 40 patients with mean ± SD P_{aO_2}/F_{IO_2} of 176 ± 54 mm Hg on NIV, bronchoscopy was successfully completed in all patients. Oxygen saturation fell below 90% in 2 patients, while 4 patients required endotracheal intubation following the procedure.[15]

Our study is different from all the aforementioned studies in that it is the first study to report the performance of bronchoscopic lung biopsy under NIV support. In fact, need for TBLB has been considered as an exclusion criterion for NIV-assisted FOB.[10] Interestingly, BAL was non-contributory in all our subjects because, in contrast to the previous studies, which predominantly included subjects with suspected infection, the current study included predominantly non-infective subjects with relatively longer duration of hypoxia. This chronic nature of hypoxia might have also led them to tolerate higher levels of hypoxia and the conduct of the procedure. Although improvement with NIV was reassuring, more data are required in hypoxemic ARF of acute onset. In the majority of the studies, including our study, bronchoscopy was performed only with topical anesthesia, without any sedation or analgesia. However, Clouzeau et al performed FOB under NIV and propofol target-controlled infusion in hypoxemic patients, and found it not only to be safe but found it also to reduce patient discomfort.[16]

Bronchoscopy in patients with ARF can be challenging, as it is associated with an alteration of the respiratory mechanics and gas exchange, with resultant hypoxemia, which could be detrimental in these patients.[1,2] The causes of hypoxemia during bronchoscopy include ventilation-perfusion mismatch from obstruction by the bronchoscope, frequent suctioning of the airways, and lavage fluid in the alveoli. The performance of BAL alone has been shown to worsen the P_{aO_2} during FOB.[1,26] The current study and the systematic review of the literature suggest that FOB can be safely performed with NIV assistance in patients with ARF, with minimal complications. According to international consensus, NIV is defined as any form of ventilatory support applied without endotracheal intubation, and therefore includes CPAP as well.[27] The systematic review suggests that FOB can be safely performed with either CPAP[10] or NIV[11] assistance, depending on the availability, as no study has compared CPAP with NIV during bronchoscopy.

In our experience, the introduction of the bronchoscope into the nares through the face mask can be a difficult step, as the bronchoscope has to be considerably manipulated, which not only prolongs the procedure but can also cause trauma to the nasal mucosa. To facilitate easy passage, the bronchoscope is initially passed through the face mask, and the tip of bronchoscope is gently passed through the nose till the vocal cords are visible (see Fig. 1). The assistant then firmly secures the mask, avoiding substantial leakage. This simple modification facilitates quicker positioning of the bronchoscope. While performing lung biopsy, CPAP was reduced to zero and only pressure support was given in an attempt to avoid pneumothorax, and a similar approach has been used in intubated patients.[28] The rate of pneumothorax after TBLB in mechanically ventilated patients (14.3%)[28] is considerably higher than the reported frequency of 5% after TBLB in spontaneously breathing patients,[29,30] and hence one needs to be ready to manage this complication.

Conclusions

In conclusion, FOB can be safely performed in patients with ARF under NIV support, and the results of this pilot study suggest that NIV-assisted TBLB can be considered as an alternative in patients in patients with ARF and diffuse pulmonary infiltrates. However, this approach should be performed only in centers with wide experience with both NIV and bronchoscopy. More studies are required to adequately define the utility of NIV-assisted bronchoscopic lung biopsy.

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