

# Noninvasive Positive-Pressure Ventilation and Ventilator-Associated Pneumonia

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There is much interest in the use of noninvasive positive-pressure ventilation (NPPV) to prevent intubation and afford a survival benefit for patients. The risk of pneumonia in patients receiving NPPV has been reported in 12 studies. Compared to patients receiving invasive mechanical ventilation (4 studies), the pneumonia rate is lower with the use of NPPV (relative risk [RR] 0.15, 95% confidence interval [CI] 0.04 to 0.58,  $p = 0.006$ ). Compared to patients assigned to invasive mechanical ventilation (3 studies), in which some of the patients assigned to NPPV did not respond and were eventually intubated, there was also a benefit for the use of NPPV (RR 0.24, 95% CI 0.08 to 0.73,  $p = 0.01$ ). In studies in which patients assigned to NPPV were compared to patients assigned to standard therapy (5 studies), in which some of the patients in each group were eventually intubated, there was benefit shown for the use of NPPV (RR 0.56, 95% CI 0.31 to 1.02,  $p = 0.06$ ). When this meta-analysis is repeated without the results of the negative study for NPPV (extubation failure), there is a stronger benefit in support of NPPV to decrease the risk of pneumonia in the remaining 4 studies (RR 0.38, 95% CI 0.20 to 0.73,  $p = 0.003$ ). A meta-analysis combining the results from the 12 studies reviewed shows a strong benefit for NPPV (RR 0.31, 95% CI 0.16 to 0.57,  $p = 0.0002$ ). One randomized controlled trial of continuous positive airway pressure compared with standard treatment in patients who developed acute hypoxemia after elective major abdominal surgery reported a lower rate of pneumonia with continuous positive airway pressure (2% vs 10%, RR 0.19, 95% CI 0.04 to 0.88,  $p = 0.02$ ). In patients who are appropriate candidates for NPPV or continuous positive airway pressure, the available evidence suggests a benefit in terms of a lower risk of pneumonia. Perhaps “endotracheal-tube-associated pneumonia” is a better term than “ventilator-associated pneumonia.” *Key words: continuous positive airway pressure, mechanical ventilation, noninvasive positive-pressure ventilation, ventilator-associated pneumonia.* [Respir Care 2005;50(7): 924–929. © 2005 Daedalus Enterprises]

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Table 1. Studies Reporting Nosocomial Pneumonia Rates Associated With NPPV

Study	Patient Population	Design	Patients (n)		Pneumonia Rate (%)	
			NPPV	Control	NPPV	Control
Brochard et al <sup>10</sup>	COPD exacerbation	Randomized controlled trial	43	42	5	17
Guerin et al <sup>11</sup>	Medical intensive care unit	Prospective cohort	30	199	0	8
Antonelli et al <sup>12</sup>	Acute hypoxemic respiratory failure	Randomized controlled trial	32	32	3	25
Nava et al <sup>13</sup>	Intubated COPD patients randomized to extubation and NPPV or remained intubated	Randomized controlled trial	25	25	0	28
Nourdine et al <sup>14</sup>	All mechanically ventilated patients during study period	Prospective cohort	129	607	0	13
Antonelli et al <sup>15</sup>	Acute respiratory failure in patients with solid-organ transplantation	Randomized controlled trial	20	20	10	20
Hilbert et al <sup>16</sup>	Acute respiratory failure in immunocompromised patients	Randomized controlled trial	26	26	8	23
Girou et al <sup>17</sup>	Medical intensive care unit	Matched case control	50	50	8	22
Carlucci et al <sup>1</sup>	All mechanically ventilated patients during study period	Prospective cohort	65	380	2	19
Keenan et al <sup>18</sup>	Post-extubation respiratory failure	Randomized controlled trial	39	42	41	40
Ferrer <sup>19</sup>	Persistent weaning failure	Randomized controlled trial	21	22	24	59
Ferrer <sup>20</sup>	Acute hypoxemic respiratory failure	Randomized controlled trial	51	54	10	24

NPPV = noninvasive positive-pressure ventilation  
COPD = chronic obstructive pulmonary disease

## Introduction

There has been much clinical and academic interest in the use of noninvasive positive-pressure ventilation (NPPV). Arguably, there is more and better evidence for this therapy than perhaps any other respiratory care modality. A prospective survey<sup>1</sup> for 3 weeks in 42 intensive care units found that NPPV was used in 16% of mechanically ventilated patients as first-line therapy. In that survey, NPPV was never used for patients in coma, but was used in 14% of patients with hypoxemic respiratory failure, 27% of patients with pulmonary edema, and 50% of patients with hypercapnic respiratory failure. Endotracheal intubation was eventually performed in 40% of patients receiving intubation (ie, a 60% success rate).

Five systematic reviews have been published related to the use of NPPV for acute respiratory failure.<sup>2-6</sup> They reached the same conclusions: NPPV decreases intubation rate and mortality, with the greatest benefit being for exacerbations of chronic obstructive pulmonary disease (COPD) and for more severe exacerbations.

Nosocomial pneumonia in mechanically ventilated patients is often due to aspiration of pharyngeal secretions around the cuff of the endotracheal tube (ETT), rather than to what is breathed from the ventilator through the airway.<sup>7-9</sup> It then follows that the risk of nosocomial pneumonia should be decreased if mechanical ventilation is provided with NPPV rather than through an ETT. Several studies have reported the risk of pneumonia in patients

receiving NPPV, compared to patients receiving invasive mechanical ventilation (Table 1). The purpose of this paper is to systematically review the evidence for reduced risk of pneumonia in patients receiving NPPV.

## Methods

I searched PubMed and the reference lists of systematic reviews to identify studies that reported pneumonia as an outcome, used NPPV as a treatment group, and had a control group. From each study I extracted the methodology, patient population, method used to diagnose pneumonia, and the pneumonia rates in the NPPV and control groups. I conducted a meta-analysis for pneumonia rate comparing NPPV to the control group, using a random-effects model to calculate relative risk and 95% confidence intervals for the pooled results of the studies (RevMan Analyses software, version 1.0 for Windows, in Review Manager [RevMan] 4.2.7, The Cochrane Collaboration, Oxford, England, 2004).

## NPPV and Ventilator-Associated Pneumonia

In a randomized controlled trial of NPPV, Brochard et al<sup>10</sup> evaluated its use in patients with acute exacerbations of COPD. Although the criteria for diagnosis of pneumonia were not stated, it was reported that 2/43 (5%) patients assigned to NPPV developed pneumonia, compared to 7/42 (17%) assigned to standard treatment.

In a prospective epidemiological survey, Guerin et al<sup>11</sup> evaluated the impact of NPPV on pneumonia rate in a medical intensive care unit. Respiratory failure was associated with a variety of primary diagnoses, including respiratory, neurological, poisoning, cardiovascular, infection, gastrointestinal, metabolic disturbances, and miscellaneous causes. Pneumonia was diagnosed when, after satisfying classical clinical and radiological criteria, bronchoalveolar lavage and/or protected-specimen-brush samples grew  $\geq 10^4$  and  $\geq 10^3$  colony forming units (CFU)/mL, respectively, of at least one microorganism. The incidence of pneumonia was 7/38 (18%) in patients receiving NPPV, then tracheal intubation; 5/23 (22%) in patients receiving tracheal intubation, then NPPV; 15/199 (8%) in patients receiving only tracheal intubation; and 0/60 in patients receiving only NPPV ( $p < 0.0001$ ).

In a randomized controlled trial, Antonelli et al<sup>12</sup> compared NPPV and invasive mechanical ventilation in patients with acute hypoxemic respiratory failure. Causes of respiratory failure included pneumonia, trauma, cardiogenic pulmonary edema, and postoperative respiratory failure. Patients in whom clinical manifestations of pneumonia developed (radiographic evidence of persistent pulmonary infiltrates, hyperthermia or hypothermia, purulent tracheobronchial secretions, a high white-cell count, and worsening of pulmonary gas exchange) underwent bronchoscopy with bronchoalveolar lavage. Pneumonia was diagnosed when at least 100,000 CFU/mL were measured in bronchoalveolar-lavage. Pneumonia occurred in 1/32 (3%) receiving NPPV and 8/32 (25%) patients receiving invasive mechanical ventilation.

Nava et al<sup>13</sup> conducted a multicenter randomized controlled trial to determine whether NPPV improves the outcome of weaning from invasive mechanical ventilation. The study population included intubated patients with COPD and acute hypercapnic respiratory failure. A spontaneous breathing trial was conducted 48 hours after intubation. If this failed, extubation to NPPV or invasive pressure-support ventilation were compared. Pneumonia was defined as the presence of a new and persistent infiltrate on chest radiography, combined with at least two of the following conditions: fever, peripheral leukocyte count higher than 10,000 cells/ $\mu$ L, and tracheal aspirate in which a Gram-stain showed one or more types of bacteria. The pneumonia rate was 0/25 in patients extubated to NPPV and 7/25 (28%) in patients who received conventional weaning with an ETT in place ( $p < 0.001$ ).

Nourdine et al<sup>14</sup> conducted a prospective epidemiologic survey to observe the pneumonia rate in patients receiving NPPV, compared to those receiving invasive ventilatory support. The diagnosis of pneumonia was based on clinical criteria. Pneumonia occurred in 0/129 patients who received only NPPV, 4/25 (16%) patients who received NPPV

but were subsequently intubated, and 80/607 (13%) in patients receiving only invasive ventilatory support ( $p < 0.01$ ).

Girou et al<sup>17</sup> studied the association of NPPV with nosocomial infections in critically ill patients, using a matched case-control study. Fifty patients with COPD or cardiogenic pulmonary edema treated with NPPV were compared to 50 patients who received invasive mechanical ventilation. Patients were matched on diagnosis, Simplified Acute Physiology Score II, Logistic Organ Dysfunction score, age, and no contraindications to NPPV. Patients with new and persistent lung infiltrates on chest radiographs, temperature  $> 38^\circ\text{C}$ , and macroscopically proven purulent tracheal secretions were suspected of having pneumonia. In patients receiving invasive mechanical ventilation, the diagnosis of pneumonia was confirmed by quantitative protected catheter culture, defined as  $\geq 10^3$  CFU/mL. In patients receiving NPPV, the diagnosis of pneumonia was based on the administration of new antibiotics in the absence of other sites of infection. The pneumonia rate was 4/50 (8%) in patients receiving NPPV and 11/50 (22%) in patients receiving invasive ventilation ( $p = 0.04$ ). The rates of urinary tract infections and catheter-related infections were also lower in patients receiving NPPV.

Antonelli et al<sup>15</sup> conducted a randomized controlled trial of NPPV for the treatment of acute respiratory failure in patients undergoing solid-organ transplantation (liver, lung, kidney). Patients received either NPPV or standard therapy with supplemental oxygen. The diagnosis of pneumonia was made when  $> 10^4$  CFU/mL were measured in the bronchoalveolar lavage fluid. The pneumonia rate was 2/20 (10%) for patients in the NPPV group and 4/20 (20%) for patients in the standard therapy group.

Hilbert et al<sup>16</sup> evaluated the use of NPPV in immunosuppressed patients (hematologic cancer and neutropenia, drug-induced, acquired immune deficiency syndrome) with pulmonary infiltrates, fever, and acute respiratory failure. This was a prospective randomized trial of NPPV compared to standard treatment with supplemental oxygen. The diagnosis of pneumonia was determined from radiographic findings of persistent new pulmonary infiltrates, hyperthermia or hypothermia, worsening of gas exchange, and confirmed by bronchoalveolar lavage. Pneumonia occurred in 2/26 (8%) patients receiving NPPV and 6/26 (23%) patients receiving standard therapy.

Carlucci et al<sup>1</sup> conducted a prospective survey over a 3-week period of 42 intensive care units to assess the use and effectiveness of NPPV. Although no specific criteria were used for the diagnosis of pneumonia, all centers reported using clinical, biologic, and radiologic criteria together with quantitative cultures of protected-brush specimens for endotracheally intubated patients. For patients receiving NPPV, clinicians did not require quantitative cultures of protected-brush specimens in every case, and the diagnosis was based on clinical (fever, sputum, lung

crackles), radiologic (new infiltrate), and biologic (increase in white blood cells, bacteria in the sputum or in bronchial aspirates) criteria. Pneumonia occurred in 1/65 (2%) patients successfully avoiding intubation with the use of NPPV and 82/423 (19%) patients receiving invasive ventilatory support ( $p < 0.002$ ). Of all patients receiving NPPV, 11/108 (10%) developed pneumonia (43 of 108 patients failed NPPV) compared to 72/380 (19%) of patients receiving only invasive mechanical ventilation ( $p < 0.05$ ).

Keenan et al<sup>18</sup> conducted a randomized controlled trial of the effectiveness of NPPV compared with standard medical therapy to prevent the need for reintubation in patients who develop respiratory distress within 48 hours after extubation. Patients were assigned to receive standard medical therapy or NPPV. The diagnosis of pneumonia was based on clinical criteria. Pneumonia occurred in 16/39 (41%) patients assigned to the NPPV group and 17/42 (40%) of patients assigned to the standard therapy group ( $p = 0.61$ ). It should also be noted that this study also reported no benefit for NPPV for reintubation rate ( $p = 0.79$ ) or mortality ( $p = 0.34$ ).

Ferrer et al<sup>19</sup> conducted a randomized controlled trial to assess the efficacy of NPPV in intubated patients who failed a spontaneous breathing trial for 3 consecutive days. Patients were extubated to NPPV or remained intubated and received daily spontaneous breathing trials. Diagnoses included exacerbation of chronic pulmonary disorders (77% of cases), congestive heart failure, community-acquired pneumonia, hospital-acquired pneumonia, postoperative respiratory failure, acute lung injury, thoracic trauma, hemoptysis, and cardiac arrest. Diagnosis of pneumonia was based on clinical criteria. Pneumonia occurred in 5/21 (24%) patients extubated to NPPV and 13/22 (62%) who remained intubated.

A randomized controlled trial by Ferrer et al<sup>20</sup> evaluated the use of NPPV in patients with severe hypoxemic respiratory failure. Causes of respiratory failure included pneumonia, cardiogenic pulmonary edema, thoracic trauma, acute respiratory distress syndrome, acute severe asthma, postoperative respiratory failure, and interstitial pneumonitis. Patients were assigned to NPPV or high-concentration oxygen therapy. Diagnosis of pneumonia was based on clinical criteria. Pneumonia occurred in 5/51 (10%) of patients assigned to NPPV and 13/54 (24%) of patients assigned to oxygen therapy.

### Observations

Three types of studies are reported in this review. In the first type, the pneumonia rate in patients receiving NPPV is compared to the pneumonia rate in patients receiving invasive mechanical ventilation (4 studies). A meta-analysis of these studies shows a very strong benefit for the use of NPPV (relative risk [RR] 0.15, 95% confidence interval

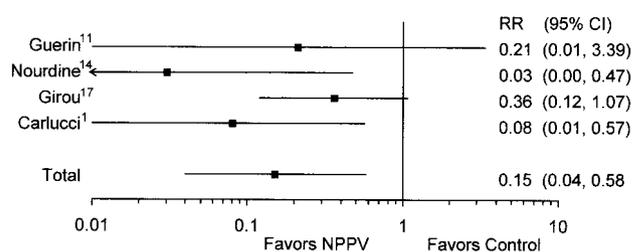


Fig. 1. Pooled analysis of pneumonia in studies comparing noninvasive positive-pressure ventilation (NPPV) with invasive mechanical ventilation.  $p = 0.13$  for heterogeneity.  $p = 0.006$  for overall effect. RR = relative risk. CI = confidence interval.

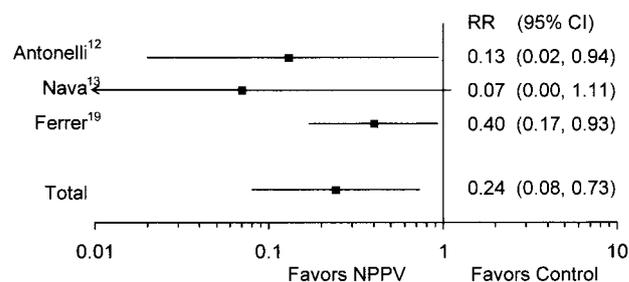


Fig. 2. Pooled analysis of pneumonia in studies where patients were assigned to noninvasive positive-pressure ventilation (NPPV) or invasive mechanical ventilation.  $p = 0.25$  for heterogeneity.  $p = 0.01$  for overall effect. RR = relative risk. CI = confidence interval.

[CI] 0.04 to 0.58,  $p = 0.006$ ) (Fig. 1). In the second type of study, the pneumonia rate in patients assigned to NPPV is compared to the rate of pneumonia in patients assigned to invasive mechanical ventilation (3 studies). In this type of study, some of the patients assigned to NPPV were eventually intubated. A meta-analysis of these studies shows benefit for the use of NPPV (RR 0.24, 95% CI 0.08 to 0.73,  $p = 0.01$ ) (Fig. 2). In the third type of study, the rate of pneumonia in patients assigned to NPPV is compared to the rate of pneumonia in patients assigned to standard therapy. In this type of study, some of the patients in each group are eventually intubated; typically, more patients in the standard therapy group were intubated. A meta-analysis of these studies shows a benefit for the use of NPPV (RR 0.56, 95% CI 0.31 to 1.02,  $p = 0.06$ ) (Fig. 3A). This meta-analysis includes the results of a study<sup>18</sup> in which there was no difference in intubation rate or mortality rate between patients assigned to NPPV or standard therapy, suggesting that these patients (extubation failure) are not good candidates for NPPV. When the meta-analysis is repeated excluding the results of that study,<sup>18</sup> there is a stronger benefit in support of NPPV to decrease the risk of pneumonia (RR 0.38, 95% CI 0.20 to 0.73,  $p = 0.003$ ) (see Fig. 3B). A meta-analysis combining the data from the 12 studies reviewed shows a benefit for NPPV (RR 0.31, 95% CI 0.16 to 0.57,  $p = 0.0002$ ).

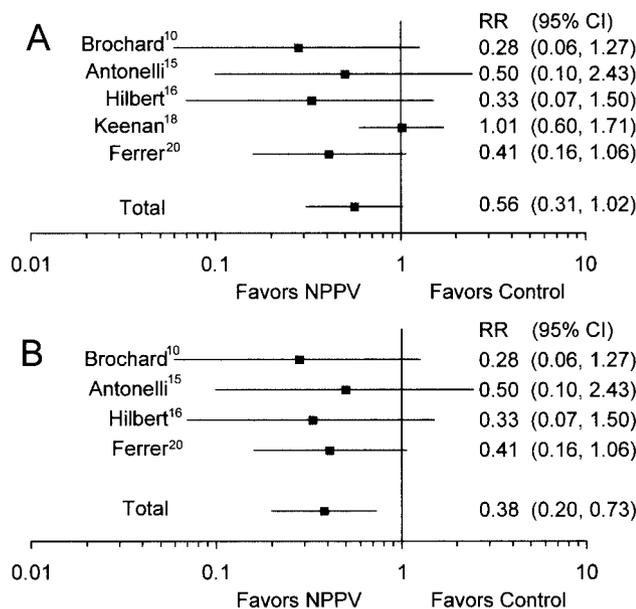


Fig. 3. A: Pooled analysis of pneumonia in studies comparing patients assigned to noninvasive positive-pressure ventilation (NPPV) or assigned to standard therapy.  $p = 0.19$  for heterogeneity.  $p = 0.06$  for overall effect. B: Pooled analysis of pneumonia in studies comparing patients assigned to NPPV or assigned to standard therapy after removal of the study showing no benefit for noninvasive positive-pressure ventilation (NPPV) (failed extubation).  $p = 0.96$  for heterogeneity.  $p = 0.003$  for overall effect. RR = relative risk. CI = confidence interval.

Although a few of these studies were designed specifically to assess the effect of NPPV on pneumonia rate,<sup>11,14,17</sup> in most of the studies pneumonia rate was a secondary outcome. Accordingly, many of the studies are underpowered to detect significant differences in pneumonia rates. The strength of the meta-analyses reported here is the ability to pool results from several small studies. These studies differ in their design and in the populations of patients enrolled (see Table 1). Despite this, statistical tests for heterogeneity of results between studies are not significant for any of the meta-analyses (see Figs. 1–3).

Most but not all of the randomized controlled trials of NPPV versus standard therapy report a lower intubation rate for patients assigned to receive NPPV. What is not known is whether patients who were intubated were also the patients who developed pneumonia. Likewise, mortality rate is lower for patients assigned to NPPV, compared to those assigned to standard therapy, but we do not know that the patients who die are also the patients with pneumonia.

### Continuous Positive Airway Pressure and Pneumonia

Squadroni et al<sup>21</sup> conducted a randomized controlled trial of the effectiveness of continuous positive airway pressure compared with standard treatment to prevent the

need for intubation and mechanical ventilation in patients who develop acute hypoxemia after elective major abdominal surgery. Pneumonia was reported as a secondary outcome, and its presence was determined by clinical criteria. Consecutive patients were enrolled who developed severe hypoxemia after major elective abdominal surgery. The trial was stopped for efficacy after 209 patients were enrolled. Patients who received continuous positive airway pressure had a lower intubation rate (1% vs 10%, RR 0.099, 95% CI 0.01 to 0.76,  $p = 0.005$ ) and had a lower rate of pneumonia (2% vs 10%, RR 0.19, 95% CI 0.04 to 0.88,  $p = 0.02$ ).

### Summary

In patients who are appropriate candidates for NPPV or continuous positive airway pressure, the available evidence suggests a benefit in terms of a lower risk of pneumonia. The available evidence suggests that NPPV is associated with lower rates of pneumonia, intubation, and mortality. What remains unknown is whether the lower mortality rate in patients receiving NPPV is related to a lower pneumonia rate. The available evidence does suggest that the lower rate of pneumonia is probably related to the avoidance of intubation. Thus ventilator-associated pneumonia is probably related to the presence of an ETT rather than the use of a ventilator. Perhaps “endotracheal tube-associated pneumonia” is a better term than “ventilator-associated pneumonia.”

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## Discussion

**Maki:** I think you are going to find that the investigators are a little unsure of their data with respect to mortality reduction independent of pneumonia. I think it's very likely to be true. The question that we must ask ourselves about these randomized trials is, are we killing people by unnecessarily intubating them? And why are we killing them, or how are they dying if they are not dying due to pneumonia?

**Hess:** I think that with the appropriate analysis we will see that the mortality is not related to the VAP. There are other very compelling reasons to use noninvasive ventilation, such as because it affords a survival benefit to patients, whether or not they are dying because they developed pneumonia.

**MacIntyre:** I want to go back to some of the points I was exploring yesterday, arguing that the ventilator and the ventilator settings are an important part of the problem—not just the tube. With noninvasive ventilation, as we all know well, the limited amount

of pressure and volume you can put into your patient effectively forces the clinician to use a lung-protective strategy, because you just can't put excessive pressures and volumes into the airway without excessive leak.

**Hess:** Or put it into the belly.

**MacIntyre:** Or put it into the belly via the pressure-relief system there.

**Pierson:**\* I just wanted to reemphasize something that you have already pointed out, which is how many patients often have to be screened—as in the Brochard et al paper<sup>1</sup>—in order to complete the studies that yield the compelling data you have shown. I think that—while it is great that noninvasive ventilation appropriately applied is associated with much better outcomes—even in the hands of good investigators only a relatively small portion of all the patients they take care of would fit the description of those included in their studies. And in

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the hands of most practitioners, noninvasive ventilation is still not thought of nearly often enough or applied successfully nearly often enough, because of lack of experience and expertise with the technique.

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**Hess:** One of the things I glossed over was patient selection. Patient selection is incredibly important. In the hour-long talks I give on noninvasive ventilation I spend about half of the time talking about patient selection, and I spend the other half of the time on technical application.

**Maki:** I think Neil [MacIntyre] may have hit on something very important. I have been impressed by how few physicians caring for ventilated patients follow the concept of lung-protective strategies for ventilatory support. It's one further variable. The NIH [National Institutes of Health] trial<sup>1</sup> certainly shows that lung-protective strategies are beneficial—and that may

be the problem—an increased risk of VAP with conventional ventilation may not be appreciated. Are we putting people at risk for VAP by intubating and using conventional ventilation because not very close attention is paid to lung-protective strategies?

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**Hess:** I can say something and Neil can add to it. To support your point is the paper from Mayo Clinic a few months ago.<sup>1</sup> They looked at patients who were initially intubated who did not have ALI or ARDS, and the strongest risk factor for developing ALI or ARDS was the tidal volume the patient was placed on when mechanical ventilation was initiated. The greater the tidal volume was above 6 mL/kg, the greater the odds of developing ALI/ARDS.

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**Pierson:** Following up on Dennis's [Maki] comment, I think there are now several studies, including one from Harborview,<sup>1</sup> one from Vermont,<sup>2</sup> and one from Minnesota,<sup>3</sup> that have shown how poorly we apply known, proven, effective therapies with respect to lung-protective ventilation, even after widespread dissemination of the results of the first ARDS Network study.<sup>4</sup> The majority of patients with ARDS, recognized as such in the hands of the people managing them—sometimes in those same investigative centers—were not getting anywhere close to the management protocol used in the study.<sup>5</sup>

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**MacIntyre:** We discussed this yesterday, but I think it deserves repeating. A lot of people feel that the ARDS Network trial results apply only to specific ARDS patients. Clinicians at the bedside often argue that the patient they are looking at that day doesn't meet ARDS Network entry criteria. I think the important thing to remember when you think about lung-protective strategies is that what you're protecting is the normal lung regions. So it doesn't matter what the disease is; what matters is to protect what's left behind, or what is still salvageable. The more normal regions of the lung need protection, and that is why I think these lung-protective strategies apply to all patients with lung disease who require mechanical ventilation.

**Hess:** One of the talks that I give for our residents is on protecting the lungs of mechanically ventilated patients. I first talk about noninvasive ventilation, then I talk about high tidal volumes and plateau pressures, and then I talk about getting the patient off the ventilator as soon as you can.

I think of all of these things in the context of lung-protective ventilation strategies, much the same as you talked about yesterday.

**Kollef:** The simple message is that the ventilator and the endotracheal tube are bad things, and you want to minimize patient exposure to them, so noninvasive ventilation is one approach. The next approach is to get them extubated as quickly as possible, sometimes even using noninvasive ventilation, as demonstrated in the study by Nava et al,<sup>1</sup> where patients were randomly assigned to have standard weaning or to be extubated within 1 to 2 days of intubation for an exacerbation of COPD and placed on noninvasive ventilation, or possibly even using other strategies, such as weaning protocols, optimizing sedation, and potentially even early tracheostomy, all of which could provide a package for minimizing exposure to this harmful medium.

#### REFERENCE

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**Hess:** Very nice way of encapsulating a whole bunch of talks over the last days.

**Branson:** The benefit seems to be the maintenance of the intact airway, but what is the role of humidifiers, HMEs [heat-and-moisture exchangers], or the ventilator circuit in preventing VAP during noninvasive ventilation?

**Hess:** I think humidification during noninvasive ventilation is important; you can get a lot of drying of the upper airway with noninvasive ventilation. We routinely use humidification when we provide noninva-

sive ventilation. We don't do that with an HME. I think an HME can be very problematic during noninvasive ventilation, as far as triggering and adding additional dead space; plus, if you have a nasal interface and you are exhaling through your mouth, the HME essentially becomes nonfunctional.

**Niederman:** I don't think you have to make this question even as complicated as we're making it. I think the issue that you raised—that you couldn't prove that excess mortality is related to pneumonia—may not be the right question. I'm sure you could prove that if you're ventilated and you get pneumonia, you spend more time on the ventilator than if you are ventilated and you don't get pneumonia. That alone may be the factor that contributes to mortality, because the

longer you are on the ventilator, the more likely other things will happen. I don't think you have to say that if you ask if the pneumonia killed the patient that means they died from septic shock or refractory hypoxemia due to that pneumonia. If you ask, are you better off to be ventilated without pneumonia than with pneumonia, the answer is pretty obvious. Since there are such a myriad of things that have happened to patients on ventilators, it's just not a good thing to get pneumonia, and it leads to other bad things that ultimately lead to their death.

**Pierson:** If I can just add one more thing as we're about to move the conference into interventions for people who have VAP—

**Hess:** I guess mine was sort of lack of intervention.

**Pierson:** It strikes me that many of the most effective things that we have been talking about at this conference to reduce the incidence of VAP have been—rather than specific interventions or products or innovations—changes in clinician behavior. I think you can put noninvasive ventilation into that, in that one has to know how to do it, think about doing it, and so forth, and one already has the equipment, by and large. Certainly in our previous discussions, lower-tidal-volume ventilation doesn't need any new equipment: you just set it differently. Increase hand hygiene, elevate the head of the bed, monitor the cuff pressure; these are not products; these are not expensive new things to order; these are changes in clinician behavior that all have pretty good evidence bases at this point.