Role of Noninvasive Ventilation in Acute Lung Injury/Acute Respiratory Distress Syndrome: A Proportion Meta-analysis

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BACKGROUND: The role of noninvasive ventilation (NIV) in the management of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) is controversial. OBJECTIVE: To assess the efficacy of NIV in patients with ALI/ARDS, using a meta-analytic technique. METHODS: We searched the PubMed and Embase databases for relevant studies published between 1995 and 2009, and included studies that reported endotracheal intubation rate and/or mortality in patients with ALI/ARDS treated with NIV. We calculated the proportions and 95% CIs to assess the outcomes in the individual studies and pooled the results with a random effects model. RESULTS: Our search yielded 13 eligible studies (540 patients). The intubation rate ranged from 30% to 86%, and the pooled intubation rate was 48% (95% CI 39–58%). The mortality rate ranged from 15% to 71%, and the pooled mortality rate was 35% (95% CI 26–45%). There was significant statistical heterogeneity (assessed via the I^2 test and Cochran Q statistic) in both intubation rate and mortality. There was no evidence of publication bias. CONCLUSIONS: Our results suggest an almost 50% NIV failure rate in patients with ALI/ARDS, so NIV should be cautiously used in patients with ALI/ARDS. There is a need for a uniform NIV protocol for patients with ALI/ARDS. *Key words: acute lung injury; ALI; acute respiratory distress syndrome; ARDS; noninvasive ventilation; NIV; CPAP; meta-analysis.* [Respir Care 2010;55(12):1653–1660. © 2010 Daedalus Enterprises]

Introduction

The mainstay of treatment for patients with acute lung injury/acute respiratory distress syndrome (ALI/ARDS) progressing to acute respiratory failure (ARF) is intubation and mechanical ventilation. However, endotracheal intubation is associated with substantial morbidity, including upper-airway trauma, barotrauma, and pneumonia.[1-3] Noninvasive ventilation (NIV) is the application of ventilatory support without an invasive endotracheal airway. NIV has revolutionized the management of diverse causes of ARF. In selected situations, including COPD exacerbation,[4] NIV

avoids endotracheal intubation, reduces the risk of ventilator-associated pneumonia, shortens intensive care unit (ICU) stay, and reduces the overall cost of hospitalization.[5] There are 2 types of noninvasive mechanical ventilatory support: continuous positive airway pressure (CPAP), which delivers one set pressure throughout the respiratory cycle; and bi-level positive airway pressure (BPAP), which delivers one pressure during inspiration

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(the peak inspiratory positive airway pressure [IPAP]) and another pressure during expiration (the expiratory positive airway pressure [EPAP], which is similar to PEEP). The pressure support is the difference between IPAP and EPAP. Theoretically, BPAP seems to confer an advantage over CPAP by reducing the work of breathing during inspiration by providing additional inspiratory pressure.

The role of NIV in ALI/ARDS is controversial. In fact, recent studies have suggested that ALI/ARDS is an independent factor of NIV failure in patients with acute hy-

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poxemic respiratory failure.[6-8] One recent systematic review found NIV efficacious in decreasing the need for endotracheal intubation and improving ICU survival in patients with acute hypoxemic respiratory failure,[9] but that review did not specifically include patients with ALI/ARDS, and there was substantial heterogeneity; the evidence did not support the use of NIV in hypoxemic respiratory failure. Subsequently, we conducted a meta-analysis of randomized controlled trials (RCTs) and included only patients with ALI/ARDS.[10] The results suggested that patients with ALI/ARDS were unlikely to have important outcome benefits from NIV added to standard therapy, but the analysis included only 3 studies (with a total of 111 patients), which introduced a chance of type I and type II errors.

We systematically analyzed the effect of NIV on the rate of endotracheal intubation and ICU mortality in patients with ARDS/ARDS. Because of a paucity of RCTs, we analyzed data from both observational studies and RCTs.

Methods

Search Strategy

Our search strategy aimed to identify studies that described the efficacy of NIV (defined for this meta-analysis as either CPAP or BPAP) in patients with ALI/ARDS, based on the American-European consensus conference criteria.[11] We reviewed all studies (both retrospective and prospective) that reported the intubation-rate and ICU-mortality outcomes of NIV in patients with ALI/ARDS. Each of us independently searched the PubMed and Embase databases for relevant studies, using the following terms: nippv, bipap, cpap, niv, nipsv, noninvasive positive-pressure ventilation, noninvasive positive-pressure ventilation, non invasive positive-pressure ventilation, noninvasive ventilation, noninvasive ventilation, non invasive ventilation, bi-level positive airway pressure, bi-level positive airway pressure, continuous positive airway pressure, mask ventilation, nasal ventilation, noninvasive pressure-support ventilation, non invasive pressure-support ventilation, non-invasive pressure-support ventilation. The search was limited to studies published in 1995–2009, studies that included only adults ($\geq$ 19 y old), in English, clinical trial, and randomized controlled trial.

We also hand-searched the indices of *Critical Care Medicine*, *Intensive Care Medicine, The American Journal of Respiratory and Critical Care Medicine*, and *Chest* from 1995 to 2009; reviewed the reference lists of primary studies, reviews, and editorials; and reviewed our personal files. We excluded abstracts, editorials, reviews, case reports, studies conducted before the American-European consensus conference ALI/ARDS definitions were laid down, and studies in children.

Initial Review of Studies

The initial database created from the PubMed and Embase searches was compiled, and all duplicate citations were eliminated. Two of us (RA and ANA) screened those citations, without blinding, by title and abstract review, to capture the relevant studies. Any disagreement was resolved via discussion. This database was then screened again to include only primary articles, and the full text of each citation was obtained and reviewed. Studies were eligible for inclusion if they reported the efficacy of NIV in patients with ALI/ARDS.

Data Extraction

On a standard data-extraction form, we recorded:

- Publication details: title, authors, and other citation details

- Type of study: prospective or retrospective

- Details of the ALI/ARDS diagnosis criteria

- Baseline data on the study subjects: age, sex, respiratory rate, pH, P_{aO_2}/F_{IO_2}, and P_{aCO_2}

- Type of NIV interface

- NIV mode: CPAP or BPAP

- Intubation rate in patients with ALI/ARDS managed with NIV: the numerator was the number of patients intubated, and the denominator was the number of patients with ALI/ARDS

- Mortality in patients with ALI/ARDS managed with NIV: the numerator was the number of patients who died, and the denominator was the number of patients with ALI/ARDS

Determination of the Pooled Effect

We used statistics software (StatsDirect 2.7.7, StatsDirect, Cheshire, United Kingdom, and Meta-Analyst 3.13, BMC Medical Research Methodology, Boston, Massachusetts) for the statistical analysis. We measured the outcomes by calculating proportions and 95% CIs for each study, then pooled the data to derive a pooled proportion and 95% CI. For the purpose of proportion meta-analysis, the proportions were first turned into a quantity (the Freeman-Tukey variant of the arcsine square root transformed proportion) suitable for the usual fixed and random effects summaries.[12,13] The pooled proportion was calculated as the back-transform of the weighted mean of the transformed proportions, using DerSimonian weights for the random effects model[14] in the presence of significant heterogeneity.

Assessment of Heterogeneity

The impact of heterogeneity on the pooled estimates of the individual outcomes of the meta-analysis was assessed with the Cochran Q statistic and I^2 test, which measure the inconsistency between the study results, which was interpreted as the approximate proportion of total variation in the study estimates that was due to heterogeneity rather than sampling error.[15] An I^2 value more than 40% indicates significant heterogeneity. As the Cochran Q test has a low sensitivity for detecting heterogeneity, a P value of $< .1$ was considered significant for the presence of statistical heterogeneity.[16]

Assessment of Publication Bias

We checked for the presence of publication bias with the Begg funnel plot,[17] which plots the proportion (in the X axis) against the standard error of the proportion (in the Y axis). In the absence of publication bias, the proportion estimates from smaller studies are expected to be scattered above and below the summary estimate, producing a triangular or funnel shape.

We also checked for publication bias with 3 statistical tests:

- The Egger test,[18] which tests for asymmetry of the funnel plot. This is a test for Y intercept = 0 from a linear regression of normalized effect estimate (estimate divided by its standard error) against precision (reciprocal of the standard error of the estimate).

- The Harbord test,[19] which is similar to the Egger test but uses a modified linear regression method to reduce the false-positive rate.

- The Begg and Mazumdar test,[20] which tests the interdependence of variance and effect size with a rank correlation method.

Institutional review board clearance was not required because this study was a meta-analysis of published studies.

Results

Our initial database search retrieved 2,345 citations (Fig. 1), of which 1,770 were excluded because they did not involve ALI/ARDS. Finally, 13 studies (540 patients) that met our inclusion criteria and reported intubation rate and/or mortality in patients with ALI/ARDS were included in the final analysis.[6,7,21-31] The studies came from around the globe; 12 were prospective and one was retrospective (Table 1). All the studies included patients that had ALI/ARDS by the American-European consensus conference
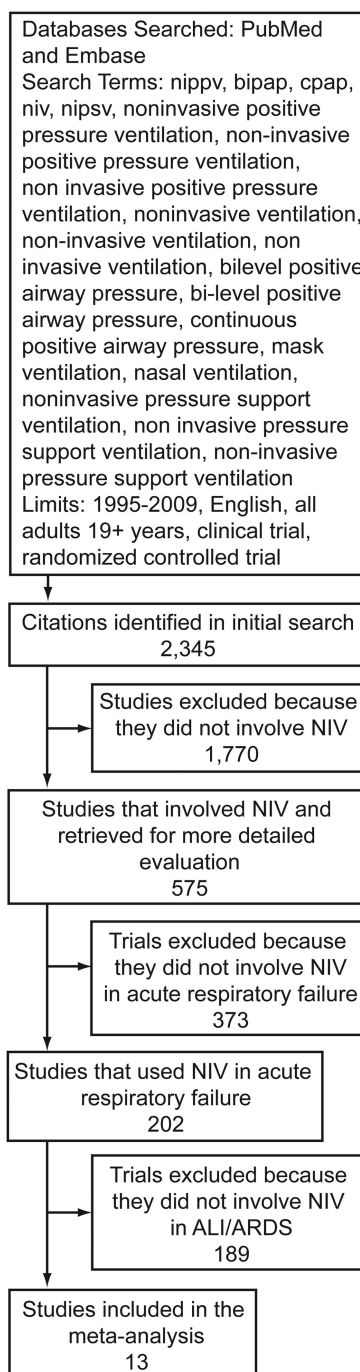
criteria, and reported intubation rate and mortality. Table 1 shows the baseline characteristics, including age, sex, ICU severity score, respiratory rate, and blood gas values. Table 2 shows the etiologies of ALI/ARDS, the NIV interfaces, and the ventilation modes. The studies included diverse causes of ALI/ARDS, and the majority of the studies used oronasal mask. Most studies used BPAP, whereas 2 studies[23,24] exclusively used CPAP (see Table 2).

Fig. 1. Citation selection process. NIV = noninvasive ventilation.

Databases Searched: PubMed and Embase
Search Terms: nippv, bipap, cpap, niv, nipsv, noninvasive positive pressure ventilation, non-invasive positive pressure ventilation, non invasive positive pressure ventilation, noninvasive ventilation, non-invasive ventilation, non invasive ventilation, bilevel positive airway pressure, bi-level positive airway pressure, continuous positive airway pressure, mask ventilation, nasal ventilation, noninvasive pressure support ventilation, non invasive pressure support ventilation, non-invasive pressure support ventilation
Limits: 1995-2009, English, all adults 19+ years, clinical trial, randomized controlled trial

Citations identified in initial search
2,345

Studies excluded because they did not involve NIV
1,770

Studies that involved NIV and retrieved for more detailed evaluation
575

Trials excluded because they did not involve NIV in acute respiratory failure
373

Studies that used NIV in acute respiratory failure
202

Trials excluded because they did not involve NIV in ALI/ARDS
189

Studies included in the meta-analysis
13

Table 1. Baseline Characteristics

First Author, Year	Total Patients (N)	Patients With ALI/ARDS (n)	Age (mean ± SD y)	Female No. (%)	APACHE or SAPS Score (mean ± SD)	Respiratory Rate (mean ± SD) breaths/min	pH (mean ± SD)	P_{aO_2}/F_{IO_2} (mean ± SD mm Hg)	P_{aCO_2} (mean ± SD mm Hg)
Rocker[21] 1999	10	10	47 ± 23	7 (70)	APACHE II 17 ± 5	ND	ND	102 ± 57	ND
Antonelli[22]* 2000	20	8	45 ± 19	7 (35)	SAPS 13 ± 4	38 ± 3	7.46 ± 0.05	129 ± 30	42 ± 10
Delclaux[23]* 2000	40	40	60 (18–88)†	23 (39)	SAPS II 32 (6–87)†	34 (20–60)†	7.42 (7.21–7.62)†	140 (59–288)†	37 (23–61)†
Hilbert[24] 2000	64	64	45 ± 16	29 (45)	SAPS II 56 ± 16	ND	ND	128 ± 32	ND
Antonelli[6] 2001	354	86	ND	ND	ND	ND	ND	ND	ND
Confalonieri[25] 2002	24	24	37 ± 9	ND	SAPS II 37 ± 9	35 ± 7	7.44 ± 0.06	122 ± 44	29 ± 7
Ferrer[7]* 2003	51	7	61 ± 17	21 (41)	SAPS II 34 ± 10	37 ± 6	7.42 ± 0.06	102 ± 21	37 ± 7
Cheung[26] 2004	20	20	51 ± 14	9 (45)	ND	29 ± 6	ND	138 ± 52	34 ± 5
Rana[27] 2006	54	54	60 (46–84)‡	21 (39)	APACHE III 56 (43–104)‡	23 (21–39)‡	7.37 (7.26–7.45)‡	112 (70–209)‡	36 (32–48)‡
Antonelli[28] 2007	147	147	53 ± 17	54 (37)	SAPS II 35 ± 9	36 ± 5	7.4 ± 0.1	111 ± 34	40 ± 13
Domenighetti[29] 2008	12	12	66 ± 8	7 (58)	SAPS II 44 ± 12	34 ± 4	7.39 ± 0.07	104 ± 42	37 ± 9
Yoshida[30]§ 2008	47	47	69 ± 11	13 (28)	APACHE II 18 ± 8	29 ± 6	7.35 ± 0.07	124 ± 47	38 ± 10
Agarwal[31] 2009	40	21	42 ± 24	12 (57)	APACHE II 15 ± 3	48 ± 9	7.42 ± 0.06	131 ± 46	32 ± 7

* Data on all patients who received noninvasive ventilation, not specifically patients with acute lung injury/acute respiratory distress syndrome (ALI/ARDS).
† In this report, this value was expressed as median and 5th–95th percentile.
‡ In this report, this value was expressed as median and range.
§ This was the only retrospective study. All the others were prospective.
APACHE = Acute Physiology and Chronic Health Evaluation
SAPS = Simplified Acute Physiology Score
ND = no data available

Outcomes

The intubation rate ranged from 30% to 86%. The pooled intubation rate was 48% (95% CI 39–58%) by the random effects model (Fig. 2). The mortality rate ranged from 15% to 71%. The pooled mortality rate was 35% (95% CI 26–45%) by the random effects model (Fig. 3).

Heterogeneity

There was significant clinical heterogeneity in the ALI/ARDS etiologies (see Table 1). There was also significant statistical heterogeneity for both intubation (I^2 76, 95% CI 55–85, Cochran Q statistic 50, $P < .001$) and mortality (I^2 79, 95% CI 61–86, Cochran Q statistic 56, $P < .001$).

Publication Bias

The funnel plots showed evidence of publication bias (Fig. 4), but the statistical tests showed no evidence of publication bias for the outcome of intubation (Begg-Mazumdar: Kendall's tau −0.026, $P = .86$; Egger: bias −0.922, $P = .56$; Harbord-Egger: bias −0.616, $P = .66$) or mortality (Begg-Mazumdar: Kendall's tau 0.333, $P = .13$; Egger: bias 0.791, $P = .61$; Harbord-Egger: bias 0.376, $P = .81$), which suggests overdispersion, rather than any meaningful bias.

Discussion

The results of this study show that application of NIV in ALI/ARDS is associated with at least a 50% success rate

Table 2. Etiology of ALI/ARDS, Type of NIV Interface, Intubation, and Mortality

First Author, Year	Etiology of ALI/ARDS	NIV Interface	NIV Mode	Intubated (No.)	ICU Mortality (No.)
Rocker[21] 1999	Malaria, fat emboli, postpartum thrombotic microangiopathy, inhalation injury, near drowning, pneumonia (infective, aspiration)	Oronasal	BPAP	4	3
Antonelli[22]* 2000	Complicated pneumonia, extrapulmonary sepsis, massive blood transfusion, acute pancreatitis (transplant recipients)	Oronasal	BPAP	3	3
Delclaux[23]* 2000	Pneumonia, aspiration, near-drowning, sepsis, shock, others	Oronasal	CPAP	15	9
Hilbert[24] 2000	Infectious and non-infectious pneumonia (in neutropenic patients)	Oronasal	CPAP	48	44
Antonelli[6] 2001	Both pulmonary and extrapulmonary ARDS, but exact etiology not stated	Oronasal	BPAP	44	26
Confalonieri[25] 2002	Pneumocystis pneumonia (in patients with acquired immune deficiency syndrome)	Oronasal	BPAP	8	6
Ferrer[7]* 2003	Not stated	Oronasal	BPAP	6	5
Cheung[26] 2004	Severe acute respiratory syndrome	Oronasal	BPAP	6	3
Rana[27] 2006	Pneumonia, nonpulmonary sepsis, vasculitis, exacerbation of interstitial lung disease	Oronasal	CPAP, BPAP	38	26
Antonelli[28] 2007	Pulmonary ARDS and extrapulmonary ARDS, but exact etiology not stated	Oronasal or helmet	BPAP	68	41
Domenighetti[29] 2008	Pneumonia, near-drowning, toxic ARDS	Oronasal	BPAP	4	5
Yoshida[30] 2008	Pulmonary ARDS and extrapulmonary ARDS, but exact etiology not stated	Oronasal	CPAP, BPAP	14	9
Agarwal[31] 2009	Both pulmonary and extrapulmonary ARDS but exact etiology not stated	Oronasal	BPAP	12	7

* Immunocompromised patients
ALI/ARDS = acute lung injury/acute respiratory distress syndrome
NIV = noninvasive ventilation
ICU = intensive care unit
BPAP = bi-level positive airway pressure
CPAP = continuous positive airway pressure

in preventing intubation and is successful in 65% of the cases in preventing death. These results are limited by the presence of significant clinical and statistical heterogeneity, but there was no evidence of publication bias.

The main goals of NIV in patients with ALI/ARDS are to improve oxygenation, to unload the respiratory muscles, and to relieve dyspnea, all of which should decrease the intubation rate. In patients with hypoxemic respiratory failure, NIV is as effective as conventional ventilation in correcting gas exchange.[32] There is also a strong physiologic basis for NIV in ARDS.[33] BPAP was associated with increased tidal volume, whereas tidal volume decreased with CPAP. Neuromuscular drive, inspiratory muscle effort, and relief of dyspnea significantly improved with BPAP, compared to CPAP, but oxygenation was better with higher CPAP (10 cm H_2O).[33] In patients with ALI/ARDS, BPAP reduces inspiratory muscle effort and dyspnea, and an optimized EPAP can improve oxygenation.[33] However, one has to balance EPAP to improve oxygenation on the one hand, and increase the IPAP (above the EPAP) to augment the tidal volume, relieve dyspnea, and decrease respiratory muscle effort on the other hand.

A recent systematic review suggested that the addition of NIV to standard medical therapy in patients with acute hypoxemic respiratory failure reduces the intubation rate, ICU stay, and ICU mortality.[9] However, because of significant heterogeneity, those results cannot be extrapolated to clinical practice. Patients with ALI/ARDS have diffuse alveolar damage and the most severe form of hypoxemic respiratory failure. Only 3 RCTs, with a total of 111 patients, have studied the effects of NIV in ALI/ARDS.[7,22,23] A meta-analysis of those 3 studies suggested that the addition of NIV to standard care in patients with ALI/ARDS did not reduce the intubation rate or ICU mortality.[10] However, that meta-analysis was limited by its small sample size.

Antonelli et al investigated NIV in patients undergoing solid-organ transplantation who developed ARF. More patients in the NIV group had improved P_{aO_2}/F_{IO_2}.[22] Also there was a significantly lower intubation rate and ICU mortality overall, but those differences were not signifi-
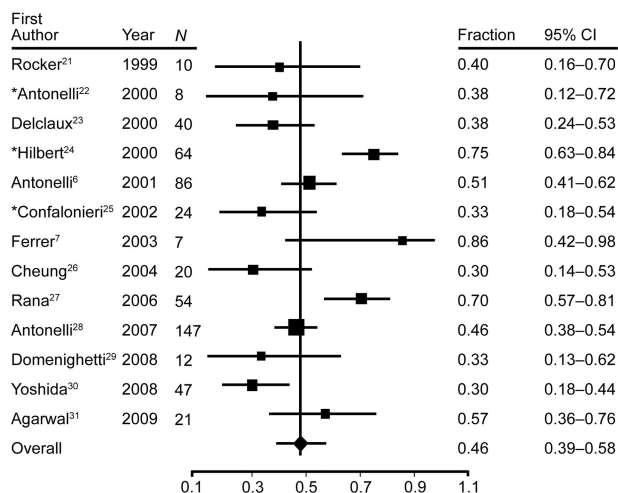
Fig. 2. Intubation rate in patients with acute lung injury/acute respiratory distress syndrome managed with noninvasive ventilation (random effects model). The intubation rates (percentages) in the individual studies are represented by squares, through which the horizontal lines represent the 95% CIs. The diamond at the bottom represents the pooled intubation rate from these studies. * The study was with immunocompromised patients.
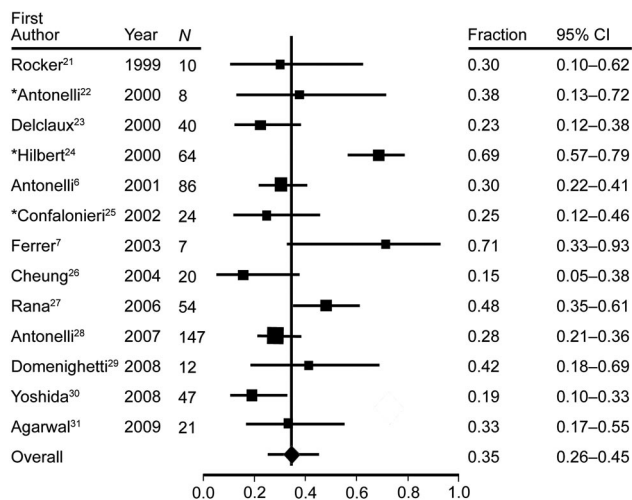

Fig. 3. Mortality rate in patients with acute lung injury/acute respiratory distress syndrome managed with noninvasive ventilation. The mortality (percentages) in the individual studies are represented by squares, through which the horizontal lines represent the 95% CIs. The diamond at the bottom represents the pooled intubation rate from these studies. * The study was with immunocompromised patients.

cant if only the subgroup of patient with ALI/ARDS was included. Another study observed that, despite early physiologic improvements, CPAP did not improve the intubation rate or outcomes in patients with ALI/ARDS.[23] In a large multicenter study of predictors of NIV failure in hypoxemic ARF, the intubation rate was 30% overall, but was 51% in patients with ARDS.[6] That study identified the following predictors of NIV failure:

- Age > 40 years

- $P_{aO_2}/F_{IO_2} < 146$ mm Hg

- Simplified acute physiology score (SAPS) II > 34

- ARDS/pneumonia as an etiology of hypoxemic ARF

In a series of patients with severe pneumocystis-pneumonia-related ARF, Confalonieri et al found that NIV avoided intubation in two thirds of the patients.[25] Avoidance of intubation was associated with better survival (100% vs 38%) and NIV decreased the need for invasive devices and decreased the ICU-related work load.[25] In an interesting observational study, Rana et al[27] observed NIV failure in all patients with ARDS and concomitant shock. In the subgroup of patients with ARDS without shock, metabolic acidosis and severe hypoxemia predicted NIV failure. In a recently published multicenter study[28] of 147 patients with ARDS, NIV decreased the intubation rate in 54% of patients. The factors independently associated with NIV failure (ie, need for intubation) were SAPS II score > 34 and $P_{aO_2}/F_{IO_2} < 175$ mm Hg after 1 hour of NIV.[28] Our experience has been similar. In a prospective study of 40 patients with hypoxemic ARF, we observed NIV failure in 57% (12/21) in the ALI/ARDS group and 37% (7/19) in the patients with ARF due to other causes. In the univariate logistic regression model, the only factor associated with NIV failure was the baseline P_{aO_2}/F_{IO_2}.[31]

In ARDS, transient loss of PEEP (EPAP) during mechanical ventilation can compromise lung recruitment and gas exchange. Because of unavoidable air leaks during NIV, transient PEEP losses are inevitable, and ARDS has repeatedly been found to be an independent variable associated with NIV failure.[6-8] However, our results suggest that NIV can reduce the intubation rate almost 50% in patients with ALI/ARDS, so NIV can benefit carefully selected ALI/ARDS patients. The issue is the selection of patients who are likely to benefit from NIV. Another important issue is early identification of the patient who is failing NIV, so we avoid intubation delay, which is associated with worse survival.[34] A reasonable clinical approach is to use NIV judiciously in patients with ALI/ARDS (Table 3). It is important to select patients properly, because some patients (eg, those with ARDS and shock) have uniformly poor NIV outcomes.[27] Also, the NIV trial requires close monitoring, and patients who do not respond to NIV should be intubated early, because the mortality risk increases with intubation delay. Although the optimal duration of the NIV trial remains uncertain, we believe that a response within 1–4 hours is a reasonable expectation.

Limitations

The major limitation of the present meta-analysis is the heterogeneity of patients and the statistical heterogeneity in the included trials. Another limitation is that some of the
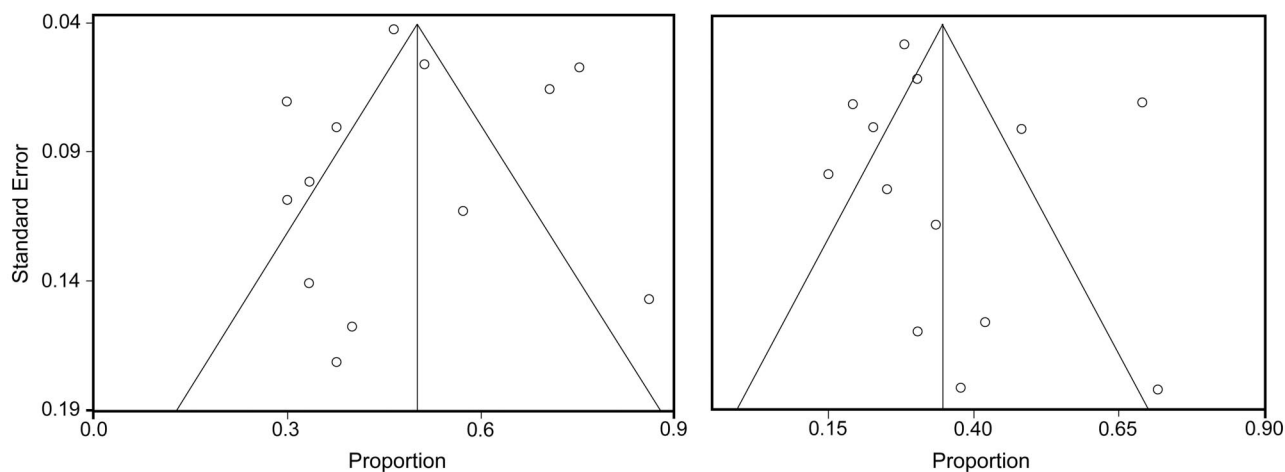
Fig. 4. Funnel plots of the proportion versus the standard error of the proportion for the outcome of intubation (left graph) and mortality (right graph). The circles represent the trials included in the meta-analysis. The line in the center indicates the summary proportion. The other lines represent the 95% CIs. Asymmetry about the pooled proportion line is consistent with the presence of minimal publication bias.

Table 3. Practical Approach to the Use of NIV in Patients With ALI/ARDS

1. Use NIV cautiously and only in an ICU where facilities for intubation and invasive ventilation are readily available.
2. Use NIV as early as possible in the ALI/ARDS course, but only in the following carefully selected patients:
   No severe hypoxemia at the outset
   No major organ dysfunction[24] (eg, acute renal failure that requires dialysis)
   No hypotension[27] or cardiac arrhythmias
   Simplified Acute Physiology Score (SAPS) II ≥ 34[28]
3. BPAP is preferred to CPAP.[33]
4. A critical-care ventilator with an oxygen blender is preferred to a domiciliary ventilator with an external oxygen supply.
5. Position: Elevate the head of the bed to 45°.
6. Interface: Oronasal mask is preferred to nasal mask
7. Protocol:
   Start with IPAP/EPAP of 8/4 cm H_2O
   Increase IPAP in increments of 2–3 cm H_2O, to a maximum of 16–18 cm H_2O, to obtain an exhaled tidal volume of 6 mL/kg and a respiratory rate of 30 breaths/min.
   Increase EPAP in increments of 1–2 cm H_2O, to a maximum of 8 cm H_2O, to obtain an oxygen saturation of $\geq 92\%$ with the lowest possible F_{IO_2}.[28]
8. BPAP trial for 1–4 hours, with close observation:
   Monitor respiratory rate, pH, and P_{aO_2}/F_{IO_2}.
   High likelihood of NIV failure if $P_{aO_2}/F_{IO_2} \leq 175$ mm Hg after 1 h.[28]
   Watch for late NIV failure, even if patient shows early improvement.
9. Weaning:
   During the initial period use NIV continuously; then use NIV the majority of the time, until oxygenation and clinical status improve.
   Progressively reduce the percent of time on NIV, in accordance with the patient's clinical improvement.
   Once EPAP requirement decreases to 4 cm H_2O, evaluate the patient on supplemental oxygen only (without ventilatory support) for 15 min.
   Discontinue BPAP if the patient maintains a respiratory rate ≤ 30 breaths/min and a $P_{aO_2} \geq 60$ mm Hg, on F_{IO_2} 0.3 without ventilatory support or use of the accessory muscles of respiration.[35]

NIV = noninvasive ventilation
ALI/ARDS = acute lung injury/acute respiratory distress syndrome
ICU = intensive care unit
BPAP = bi-level positive airway pressure
CPAP = continuous positive airway pressure
IPAP = inspiratory positive airway pressure
EPAP = expiratory positive airway pressure

studies used CPAP whereas others used BPAP, which are different approaches.

Another interesting aspect of NIV is to evaluate its efficacy in the 2 pathophysiologic subsets of ALI/ARDS: pulmonary and non-pulmonary. Unfortunately, none of the individual studies gave details on differences in outcomes in those 2 categories, so analysis of pulmonary versus non-pulmonary ALI/ARDS was not possible in this study.

One strength of the present meta-analysis was its systematic approach to searching the literature and specifically

including patients with ALI/ARDS as per the American-European consensus conference criteria.

Conclusions

NIV should be used cautiously in patients with ALI/ARDS. A large RCT is needed to determine the role of NIV in ALI/ARDS. A protocol needs to be developed wherein NIV is used in carefully selected and monitored patients, preferably in the earliest stages of ALI/ARDS, in patients with no or minimal major organ dysfunction. Finally, in patients with ALI/ARDS, the use of NIV should be limited to the protected environment of the ICU, where prompt intubation is available round the clock.

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