Complications of Noninvasive Ventilation in Acute Care

Peter C Gay MD

The use of noninvasive ventilation (NIV) for acute respiratory failure has become widespread, but with the newfound beneficial treatments come complications. There is credible although somewhat disparate evidence to support the concept that, compared to invasive ventilation, NIV can reduce the incidence of infectious complications. In selected populations, nosocomial pneumonia appears to be significantly less common with NIV than with endotracheal intubation. NIV complications range from minor (eg, mask-related difficulties) to serious (eg, aspiration and hemodynamic effects). Evidence shows that if NIV is inappropriately applied for too long, the consequences may lead to death, presumably due to excessive delay of intubation. Despite apparently similar costs of treatment for patients with equivalent severity of illness, there is substantially less reimbursement for NIV than for intubation. The use of sedation in NIV patients has not been systematically studied, and sedation is generally underutilized, to avoid complications. Do-not-intubate patients pose a special ethical dilemma with regard to NIV, because NIV may conflict with a preexisting directive not to use life-support measures in the terminally ill patient. *Key words: noninvasive ventilation, mechanical ventilation, acute respiratory failure, complications, nosocomial pneumonia, mask.* [Respir Care 2009;54(2):246–257. © 2009 Daedalus Enterprises]

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Introduction

The assigned objective of my contribution to this conference was to discuss the role of noninvasive ventilation (NIV) in reducing the incidence of nosocomial infection and the complications associated with NIV. Most studies of NIV have reported some of the observed complications, and, when added to those that have commented on nosocomial pneumonia, the total is in the thousands. It is not possible to address all of these herein, so there will be an inherent selection bias, for which I am solely responsible.

The following discussion has 2 sections: the first on whether NIV decreases the incidence of nosocomial pneumonia, compared to endotracheal intubation; the second on NIV complications.

Endotracheally intubated patients have a much higher likelihood of developing nosocomial pneumonia than those not intubated, so it was natural to ask whether NIV might reduce the incidence of nosocomial pneumonia. It is commonly stated that nearly every effective therapy has risks and potential complications; NIV is no exception. I will review the less serious complications (typically related to the equipment, such as the mask), then the more serious complications, which may occur particularly with misapplication of NIV (eg, inappropriately extended use of NIV). Also, today's cost-containment demands on all medical therapy have to be evaluated in any calculation of an intervention's effectiveness and complications, and NIV has some unique considerations, which I will discuss. Lastly I will remark on ethical complications of NIV in certain patients.

The Case for Lower Incidence of Nosocomial Infection With Noninvasive Ventilation

It is easy to argue that the endotracheal tube can promote nosocomial infection by impairing cough and secretion clearance, which allows continued accumulation of secretions/microorganisms around the cuff and into the lower airways. In a retrospective study of 118 consecutive non-neutropenic adult patients with ventilator-associated pneumonia (VAP) and overall fatality rate of 36.6%, the insertion of an endotracheal tube was a crucial single factor that contributed to the development of the pneumonia.[1] Other significant factors included depressed level of consciousness, underlying chronic lung disease, thoracic or upper-abdominal surgery, prior episode of a large-volume aspiration, and age > 70 years. An early prospective observational study evaluated the impact of NIV on VAP in a medical intensive care unit (ICU) with a cohort of 320 consecutive patients with ICU stay > 2 days and mechanically ventilated for ≥ 1 day.[2] The patients were treated with either NIV, intubation, or both in either order. The VAP incidence rates were: 22% in the group that had intubation, then NIV; 18% in the group that had NIV, then intubation; 8% in the group that had only intubation; and 0% in the group that had only NIV ($P < .001$). ICU stay and type of ventilation were associated with VAP, via logistic regression analysis. Celis et al[1] concluded that, compared to intubation, NIV significantly lowered the incidence of VAP, but this was largely explained by differences in disease severity and risk exposure.

Subsequent prospective studies of VAP evaluated large groups of patients with various causes of respiratory failure and compared NIV to intubation. A French study included 761 patients who required some form of mechanical ventilation for >48 hours.[3] There were 129 NIV patients, 607 intubation patients, and 25 patients who required intubation after NIV, who were studied for VAP and other forms of nosocomial infection, including catheter-related infection, urinary tract infection, and bacteremia. The incidence of all nosocomial infections was lower in the NIV group than in the intubation group (14.2 vs 30.3 infections per 1,000 patient-days, $P < .01$). When adjusted for the severity of illness, NIV markedly reduced the VAP risk (hazard ratio 4.07).

The next large prospective study of NIV in clinical practice was performed over a 3-week period in 42 intensive care units, and included 689 patients (581 intubated and 108 NIV) with various respiratory failure causes.[4] NIV indications included hypoxemic acute respiratory failure (14% of the patients), pulmonary edema (27%), and hypercapnia (50%). The NIV patients had a lower incidence of nosocomial pneumonia (10% vs 19%, $P = .03$) and mortality (22% vs 41%, $P < .001$). NIV success was associated with a lower risk of pneumonia (odds ratio = 0.06, 95% confidence interval 0.01–0.45) and death (odds ratio = 0.16, 95% confidence interval 0.05–0.54).

A longitudinal evaluation of routine clinical NIV practice in a 26-bed ICU, from 1994 to 2001, included 479 consecutive patients ventilated specifically for exacerbation of chronic obstructive pulmonary disease (COPD) or severe cardiogenic pulmonary edema.[5] NIV use significantly increased during the study period, in parallel with a decrease in mortality and ICU-acquired infection rate. NIV was an independent factor associated with lower risk of death (odds ratio 0.37, 95% confidence interval 0.18–0.78). The rate of ICU-acquired pneumonia decreased from 20% in 1994 to 8% in 2001 ($P = .04$).

Hypoxia

A randomized controlled trial compared NIV to intubation in 64 patients with acute hypoxic respiratory failure, enrolled from a pool of 486 patients.[6] The study had well-defined end points and a standardized weaning protocol. There was no significant difference in ICU mortality (47% in the intubation group vs 28% in the NIV group, $P = .19$),

but ICU stay was shorter in the NIV patients (16 ± 17 d vs 9 ± 7 d, $P = .04$), and the surviving NIV patients had shorter ventilation ($P = .006$). The NIV patients had fewer serious complications (38% vs 66%, $P = .02$); pneumonia or sinusitis related to the endotracheal tube was > 90% lower (3% vs 31%, $P = .003$). This was the first randomized controlled trial to highlight the lower rate of nosocomial pneumonia with NIV. Another important feature common to NIV randomized controlled trials is the large number of patients excluded. The generalizability of the study results must therefore be considered with caution, and additional studies are warranted.

Mixed Population

A randomized controlled trial in 7 multipurpose ICUs examined NIV versus intubation in 64 patients with various causes of respiratory failure.[7] NIV reduced the intubation rate (58% vs 100%, relative risk reduction 43%, $P < .001$). Complications occurred in 52% of the NIV patients and 70% of the intubated patients ($P = .07$), which is a nonsignificant trend toward fewer ICU complications, including pneumonia.

Another randomized controlled trial was designed to determine the effectiveness of NIV versus standard medical therapy in preventing reintubation in a mixed population of patients at high risk for post-extubation respiratory distress. Eighty-one patients developed respiratory distress within 48 hours of extubation, and were randomized to supplemental oxygen ($n = 42$) or NIV via face mask plus standard medical therapy ($n = 39$). There was no difference in the rate of reintubation (72% vs 69%) or pneumonia (16% vs 17%) between the NIV and control subjects.[8]

Persistent Weaning Failure

A prospective randomized controlled trial assessed the efficacy of NIV in 43 patients with persistent weaning failure, who had failed a 3-day weaning trial.[9] The patients were randomly assigned to either extubation and NIV or continued intubation and a conventional weaning program with daily weaning attempts. The NIV group had shorter invasive ventilation (9.5 ± 8.3 d vs 20.1 ± 13.1 d, $P = .003$), ICU stay (14.1 ± 9.2 d vs 25.0 ± 12.5 d, $P = .002$), and hospital stay (27.8 ± 14.6 d vs 40.8 ± 21.4 d, $P = .03$). There was a lower incidence of nosocomial pneumonia (24% vs 59%, $P = .04$) and septic shock (2 [10%] vs 9 [41%], $P = .045$).

Meta-Analysis

A meta-analysis of 12 studies reviewed the risk of pneumonia in NIV patients.[10] Four studies compared NIV patients to intubated ventilated patients. The pneumonia rate was lower in the NIV patients (relative risk 0.15, $P = .006$). In 3 studies that included patients who initially failed NIV and were then intubated, there was benefit from the use of NIV first (relative risk = 0.24, $P = .01$), compared to immediate intubation. Five studies compared NIV to standard therapy. When comparing the patients in each group who failed NIV and required intubation, there was less pneumonia in those who initially received NIV (relative risk 0.56, $P = .06$). In essence, there was compelling evidence that in various clinical scenarios NIV significantly reduces the occurrence of nosocomial pneumonia.

Table 1 summarizes the above-described studies.

Clinical Complications of Noninvasive Ventilation

The complications of NIV were comprehensively reviewed in a textbook edited by Hill.[11] I will review the complications similarly, organized by complications related to the mask, pressure, and air flow, and more serious concerns such as hemodynamic consequences, aspiration, and other potentially fatal complications. The complications of individual studies are not always included. A review[12] of 28 randomized trials of NIV for acute respiratory failure was done in 2005, and its results are summarized and further updated with 10 new references in Table 2. Note in the far right column that 17 studies did not report any separate complications beyond the specified end points.[8,13,14,18,21,25,28,30,31,33,37-39,41,44-46] Ten studies found no difference in complications, 9 studies found fewer complications with NIV, and 2 studies found more complications with NIV.[6,7,9,15-17,19,20,22-24,26,27,29,32,34-36,40,42,43]

Complications Related to the Mask

Table 3 lists NIV complications related to masks. The incidence of subjective mask discomfort may be as high as 50%, but in most cases this can be treated with mask adjustment or change of mask. Skin rashes may develop due to hypersensitivity or infection, and typically respond to topical steroids or antibiotics. One of the more serious mask-related complications is ulcer on the nasal bridge (Fig. 1), many of which respond to special dermal application materials, but there have been cases extreme enough to require skin graft. Oronasal masks have higher likelihood of causing claustrophobia and have greater dead space, which may require special valving to promote greater bias flow. Helmets (available only in Europe) and full-face masks may avoid claustrophobia, presumably because they do not impede the patient's vision and do not contact near the eyes or nasal bridge. The theoretical concern about asphyxiation in case of respirator-blower failure or aspiration should be reduced by the requirement of quick-release straps on oronasal and full-face masks. Aerophagia

Table 1. Studies of Noninvasive Ventilation and Nosocomial Pneumonia

Study Year	Design	Location and/or Patients	Patients *n*	Findings and Conclusions
Celis[1] 1988	Retrospective	Single-center medical ICU Patients with VAP	118	VAP 36.6% overall mortality. Crucial pneumonia factors included intubation, depressed consciousness, chronic lung disease, surgery, aspiration, and old age.
Guérin[2] 1997	Prospective cohort	Single-center medical ICU	320	VAP 8% in intubated patients, 0% in NIV patients. Duration of ICU stay and intubation related to VAP.
Nourdine[3] 1999	Prospective survey	Multicenter mixed ICU	761	Nosocomial infection was lower with NIV than with intubation (14.2 vs 30.3 per 1,000 patient-days). NIV reduced VAP risk 4-fold.
Carlucci[4] 2001	Prospective survey	Multicenter mixed ICU	689	NIV reduced nosocomial pneumonia (10% vs 19%) and mortality (22% vs 41%). NIV success associated with less pneumonia and mortality.
Girou[5] 2003	Longitudinal survey	Single center Patients with COPD or pulmonary edema	479	NIV greatly increased over the 7-y study, while mortality and ICU infection decreased. NIV was related to lower mortality.
Antonelli[6] 1998	RCT	Single center Patients with hypoxic respiratory failure	64	NIV had shorter ventilation and fewer complications
Honrubia[7] 2005	RCT	Multicenter Mixed medical ICU patients	64	NIV reduced intubation rate and had a trend toward fewer complications, including pneumonia.
Keenan[8] 2002	RCT	Single-center mixed medical ICU patients	81	No difference in rate of reintubation or pneumonia.
Ferrer[9] 2003	RCT	Single-center mixed medical ICU patients	43	NIV reduced ICU and hospital days, duration of ventilation, and rate of nosocomial pneumonia and septic shock.
Hess[10] 2005	Meta-analysis	Multicenter RCTs	NA	Majority of studies concluded that NIV reduced pneumonia rate.

ICU = intensive care unit
VAP = ventilator-associated pneumonia
NIV = noninvasive ventilation
RCT = randomized controlled trial
NA = not applicable

and sialorrhea can occur, but are usually self-limiting or respond to simethicone or anti-sialorheics.

Complications Related to Pressure and Flow

Table 4 lists NIV complications related to pressure and flow. Pressure-related symptoms include discomfort, ear or sinus pain, and (with higher pressure support) gastric insufflation. All of these are alleviated by decreasing the pressure. No study has revealed an optimal target pressure, and seeking maximum inspiratory pressure on the basis of tolerance and comfort seems appropriate. The most serious pressure effects may be pneumothorax and pneumocephalus, which have been reported anecdotally but are uncommon.[47,48] Flow-related concerns are similar; the symptoms include nasal dryness, congestion, or obstruction, which may be due to nasal or sinus irritation. Consider topical decongestants or corticosteroids. Most patients benefit from heated humidification, but proper cleaning instructions should be followed. Eye irritation can be avoided with careful attention to air leaks, which may be particularly annoying to patients.

Aspiration and Mucus Plugging

Aspiration is a potentially more serious complication of NIV, and is best avoided with careful attention to patient selection. The impact of over-sedation on aspiration is discussed separately below. For fear of this complication, during early historical application of NIV, cautious clinicians considered frequent or universal placement of nasogastric drainage tubes. Mucus plugging was also a concern, but mandatory humidification/hydration and chest physiotherapy/cough assistance were thought to be protective. Ultimately, neither the true incidence of this complication nor the utility of the interventions suggested above are known or well documented (Table 5).

Table 2. Randomized Controlled Trials of Noninvasive Ventilation

Study	Year	Patient Population	Location	Type of NIV	Control	Patients (*n*)		Complications
						NIV	Control	
Bersten[13]	1991	ACPE	ED or ICU	CPAP	Usual care	19	20	NR
Bott[14]	1993	COPD	Ward	ACV	Usual care	30	30	NR
Wysocki[15]	1995	Hypercapnic ARF (no COPD)	ICU	PSV + PEEP	Usual care	21	20	No difference
Brochard[16]	1995	COPD	ICU	PSV	Usual care	43	42	Fewer with NIV
Kramer[17]	1995	Hypercapnic ARF	ICU	IPAP + EPAP	Usual care	16	15	No difference
Barbé[18]	1996	COPD	Ward	IPAP + EPAP	Usual care	20	20	NR
Mehta[19]	1997	ACPE	ED or ICU	IPAP + EPAP	CPAP	14	13	More with NIV
Nava[20]	1998	COPD (ventilator weaning)	ICU	PSV + PEEP	Invasive PSV + PEEP	25	25	Fewer with NIV
Celikel[21]	1998	COPD	ICU	PSV + PEEP	Usual care	15	15	NR
Antonelli[6]	1998	Hypoxemic ARF	ICU	PSV + CPAP	ACV + PEEP, SIMV + PSV + PEEP	32	32	Fewer with NIV
Wood[22]	1998	Hypercapnic ARF, Hypoxemic ARF	ED	IPAP + EPAP	Usual care	16	11	No difference
Confalonieri[23]	1999	Community-acquired pneumonia + hypercapnic ARF, Hypoxemic ARF	Intermediate respiratory care unit	PSV + CPAP	Usual care	28	28	No difference
Girault[24]	1999	Hypercapnic ARF (ventilator weaning)	ICU	PSV + PEEP, ACV + PEEP	Invasive PSV + PEEP	17	16	No difference
Jiang[25]	1999	Post-extubation	ICU	IPAP + EPAP	Usual care	47	46	NR
Antonelli[26]	2000	Hypercapnic ARF, solid-organ transplantation	ICU	PSV + PEEP	Usual care	20	20	Fewer with NIV
Martin[27]	2000	Hypercapnic ARF, Hypoxemic ARF	ICU	IPAP + EPAP	Usual care	32	29	No difference
Plant[28]	2000	COPD	Ward	Pressure-cycled	Usual care	118	118	NR
Delclaux[29]	2000	Non-hypercapnic ARF	ICU	CPAP	Usual care	62	61	More with NIV
Masip[30]	2000	ACPE	ICU	PSV + CPAP	Usual care	20	20	NR
Auriant[31]	2001	Postoperative hypoxemic ARF	ICU	IPAP + EPAP	Usual care	24	24	NR
Hilbert[32]	2001	Hypoxemic ARF in immunosuppressed patients	ICU	PSV + CPAP	Usual care	26	26	Fewer with NIV
Levitt[33]	2001	ACPE	ED	IPAP + EPAP	Usual care	19	19	NR
Keenan[8]	2002	Hypercapnic ARF, Hypoxemic ARF after extubation	ICU	IPAP + EPAP	Usual care	39	42	NR
Conti[34]	2002	COPD	ICU	PSV + CPAP	ACV + PEEP, PSV + PEEP	23	26	No difference
Ferrer[9]	2003	Hypoxemic ARF	ICU	IPAP + EPAP	Usual care	51	54	Fewer with NIV
Nava[35]	2003	ACPE	ED	PSV + CPAP	Usual care	33	31	No difference
L'Her[36]	2004	ACPE in patients > 75 y old	ED	CPAP	Usual care	43	46	Fewer with NIV
Esteban[37]	2004	ARF, Post-extubation hypoxemic ARF	ICU	PSV + CPAP	Usual care	114	107	NR
Crane[38]	2004	ACPE	ED	CPAP IPAP + EPAP	Usual care	20/20	20	NR
Bellone[39]	2005	Hypercapnic ACPE	ED	PSV + CPAP	CPAP	18	18	NR
Squadrone[40]	2005	Post-operative hypoxemic ARF	ICU	CPAP	Usual care	105	104	Fewer with NIV
Nava[41]	2005	To prevent reintubation	ICU	PSV + CPAP	Usual care	48	49	NR
Honorubia[7]	2005	Hypercapnic ARF	ICU	PSV + CPAP	ACV + PEEP	31	33	No difference
Kindgen-Milles[42]	2005	To prevent reintubation after surgery	ICU	Continuous CPAP	Intermittent CPAP	25	25	Fewer with NIV
Ferrer[43]	2006	To prevent reintubation after surgery	ICU	IPAP + EPAP	Usual care	79	83	No difference
Ferrari[44]	2007	ACPE		PSV + CPAP	CPAP	25	27	NR
Moritz[45]	2007	ACPE	ED	IPAP + EPAP	CPAP	50	59	NR
Gray[46]	2008	ACPE	ED	CPAP IPAP + EPAP	Usual care	78/77	79	NR

NIV = noninvasive ventilation
ACPE = acute cardiogenic pulmonary edema
ED = emergency department
ICU = intensive care unit
CPAP = continuous positive airway pressure
NR = not reported
COPD = chronic obstructive pulmonary disease
ACV = assist-control (volume-cycled) ventilation
ARF = acute respiratory failure
PSV = pressure support ventilation
PEEP = positive end-expiratory pressure
IPAP = inspiratory positive airway pressure
EPAP = expiratory positive pressure
Weaning = studies that used NIV to facilitate weaning from mechanical ventilation
SIMV = synchronized intermittent mandatory ventilation

Table 3. Problems Related to Noninvasive Ventilation Interfaces

Problem	Incidence	Remedies
Nasal mask		
Mask discomfort	30–50%	Decrease strap tension Re-seat mask Try different mask size or type
Skin rash	10–20%	Topical steroids or clindamycin Dermatologic consultation
Nasal-bridge sores	5–10%	Minimize strap tension Use forehead spacer Artificial skin Switch to different mask type
Nasal obstruction	Occasional	Topical decongestant Try oronasal mask
Oronasal mask		
Mask discomfort	30–50%	Minimize strap tension Try different mask size or type
Claustrophobia	10–20%	Reassure patient Try different mask type
Skin rash, nasal bridge sores	10–20%	Same as for nasal mask sores
More dead space	Depends on mask	Insert foam rubber to reduce dead space Anti-asphyxia valve
Aspiration of vomit	Rare	Quick-release straps
Mouthpiece		
Discomfort	Common	Reassure patient Diminishes with adaptation
Hypersalivation, salivary retention	Common	Reassure patient Diminishes with adaptation
Aerophagia	Common	Reassure patient Simethicone
Pressure sores on lips, gums	Infrequent	Decrease strap tension Consider custom fitting
Orthodontic problems	After prolonged use	Remodel mouthpiece Consult orthodontist
Head straps		
Discomfort	10–30%	Try different strap system
Unstable mask	Common with 2-strap system	Try different mask or strap system

Inadequate Gas Exchange

Aside from equipment failure, the greatest difficulties with both oxygenation and ventilation occur under the circumstances of suboptimal patient-ventilator synchrony. The problems fall into 2 categories: failure to trigger the ventilator, and failure to cycle the ventilator, of which the possible causes are many.[49] Though most NIV ventilators have leak-compensation, air leaks can compromise triggering and cycling. If a patient desires to cycle (ie, end inspiration) at a higher end-inspiratory flow than the ventilator's cycling criterion, the patient has to use expiratory muscles unnecessarily. Failure to trigger (ie, begin inspiration) is also problematic, and the patient-ventilator dyssynchrony it causes can lead to inadequate gas exchange, though this is highly dependent on the rise time (initial inspiratory flow), which was not adjustable on most early-generation NIV devices. Both excessive and inadequate initial flow led to dyssynchrony during pressure-targeted assisted ventilation. This problem was addressed in later NIV ventilators by incorporating adjustable rise time. In intubated patients recovering from acute lung injury, during pressure-support ventilation the shortest rise time significantly reduces the work of breathing.[50] In a study with 6 patients with hypoxemic respiratory failure from AIDS-related opportunistic pneumonia, Calderini found better patient-ventilator synchrony and less patient effort with time-cycled ventilation than with flow-cycled ventilation.[51] The difficulty with time-cycled ventilation is that respiratory rate is often variable, which causes dyssynchrony. Attention to the cycling time criterion likewise has important effects in different patient populations. In the intubated patients with acute respiratory failure noted above, the lowest cycle criterion (5% of the peak inspiratory flow)

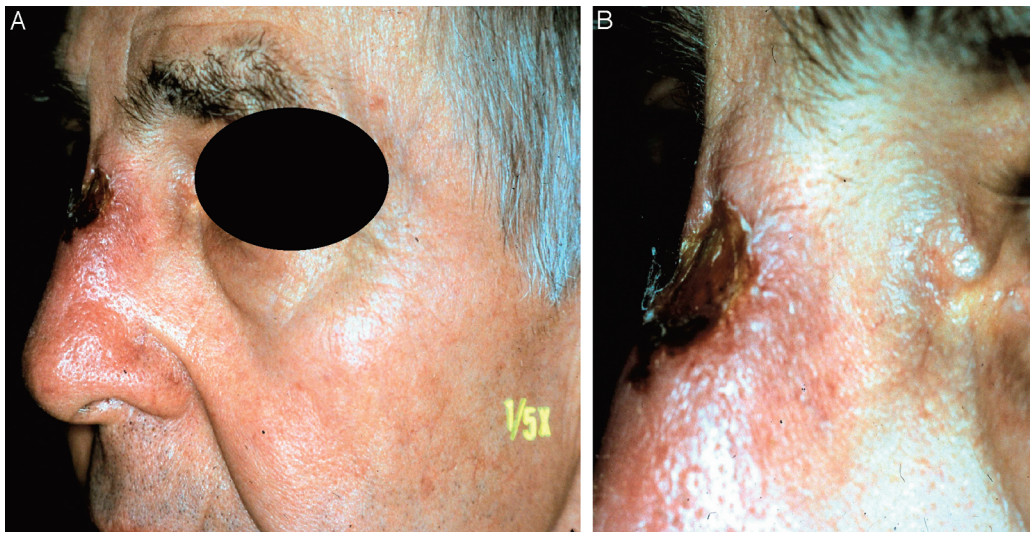

Fig. 1. A. Nasal bridge ulcer caused by a mask. B. Enlargement of the bridge of the nose.

Table 4. Problems Related to Air Pressure and Flow During Noninvasive Ventilation

Problem	Incidence (%)	Remedy
Pressure		
Discomfort	20–50	Reduce inspiratory pressure
Ear or sinus pain	10–20	Reduce inspiratory pressure
Gastric insufflation	30–40	Reduce pressure Simethacone Gastric suctioning if ventilation is impaired
Pneumothorax	Rare	Avoid excessive inflation pressure Consider thoracostomy tube drainage
Flow		
Nasal/oral congestion	50	Topical steroid, decongestant, antihistamine/decongestant combination
Nasal/oral dryness	30–50	Nasal saline Humidification Reduce air leaks
Eye irritation	33	Eye emollient Adjust strap tension Different mask

Table 5. Major Complications of Noninvasive Ventilation

Problem	Incidence	Remedies
Aspiration	5%	Careful patient selection Gastric drainage when appropriate
Mucus plugging	Infrequent	Careful patient selection Adequate rehydration Cough assistance Respiratory treatments
Severe hypoxemia	Depends on etiology of respiratory failure	Careful patient selection High-flow oxygen Increase expiratory pressure
Hypotension	Infrequent	Careful patient selection Adequate hydration Lower inspiratory pressure

significantly reduced respiratory rate and increased tidal volume (V_T).[50] In intubated patients with severe COPD, a high cycle criterion (40% of peak flow) reduced dynamic hyperinflation and inspiratory effort.[52]

Oxygen delivery must provide adequate oxygenation, but very few NIV ventilators contain an oxygen blender capable of delivering high-flow oxygen, so oxygen delivery may be limited to the flow available from the hospital-room oxygen source, which could be inadequate for some patients with severe hypoxemia.

Hemodynamic Compromise

A rare but serious NIV problem can occur in patients with compromised cardiac output. The airway pressure applied to the upper airway during NIV increases the intrathoracic pressure and right-ventricular after-load and reduces pre-load, which can cause hypotension in a susceptible patient. Confalonieri et al used echocardiography to evaluate the acute hemodynamic effects of initiating NIV in 16 patients with COPD and acute ventilatory failure.[53] In 4 patients (21%) NIV reduced cardiac output $>$ 15%. Other than poor tolerance of mask ventilation and failure to increase respiratory rate with NIV, there was no

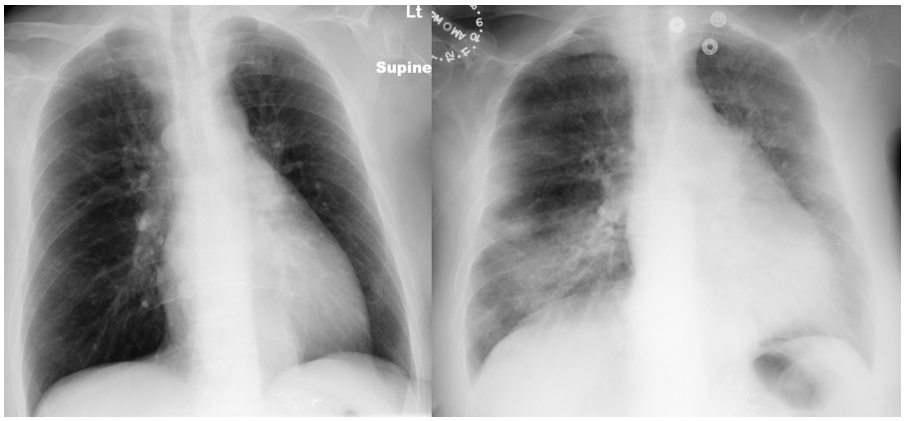

Fig. 2. Left: Hospital-admission chest radiograph is unremarkable. Right: Intensive-care-unit admission radiograph shows bilateral infiltrates, most dense in the right lower lobe.

other identifying risk factor in the patients who had decreased cardiac output. That study emphasizes the need to be aware of the potential for blood pressure changes in patients with poor initial respiratory-rate response to NIV and perhaps compromised cardiac status and/or hypovolemia (see Table 5).

When You "Go Too Far"

A frequent argument in favor of NIV is that there is little down side to its application because you can always resort to invasive ventilation at any time. There have been studies that denied the efficacy of NIV, and in particular for patients with post-extubation respiratory failure, in whom there was disappointing lack of efficacy.[8] More disturbing were the later findings from Esteban et al, in a multicenter investigation of 221 patients who were electively extubated after $\geq$ 48 hours of mechanical ventilation and subsequently developed respiratory failure within 48 hours.[37] One hundred fourteen NIV patients were compared to 107 patients who received standard medical therapy, but the trial was stopped early, after an interim analysis. Although there was no difference in reintubation between the NIV group and the standard-therapy group (reintubation rate 48% in both groups), the ICU death rate was higher in the NIV group (25% vs 14%, $P = .048$) and the median time from respiratory failure to reintubation was longer in the NIV group (12 h vs 2.5 h, $P = .02$).

The following (not previously reported) case example shows that delaying intubation of a patient with hypoxic respiratory failure can lead to complications. The patient was a 54-year-old woman admitted for pain-control, related to a small proximal femur fracture from a fall at home. She had undergone gastric bypass several years ago, and was now suffering from severe fibromyalgia that had required increasing narcotic support over the past month, and she had poor home compliance with continuous positive airway pressure. She developed acute hypoxemic respiratory failure, presumably from aspiration, and was transferred to the ICU and started on NIV. Over the next 48 hours that she continued on NIV her chest radiograph progressed to show bilateral infiltrates, she required a fraction of inspired oxygen (F_{IO_2}) of 1.0, and her expired V_T was in excess of 12 mL/kg (Fig. 2). She was reluctant to be intubated, but after 50 hours of NIV she opted for intubation, which allowed us to lower the F_{IO_2} to 0.50 and to set V_T at 6 mL/kg (Fig. 3). She required prolonged mechanical ventilation and tracheotomy, which was eventually removed, and she later recovered to home NIV at night alone. Although there are no data to identify an unsafe V_T, there is theoretical concern about the large unregulated V_T allowed by NIV. Most would accept that a continuous high F_{IO_2} can lead to oxygen toxicity in patients with acute hypoxic respiratory failure. My contention here is that intubating the patient sooner might have avoided the deleterious effects of high F_{IO_2} and large V_T.

The "Cost of Business"

An often overlooked issue regarding NIV is reimbursement. What has largely remained a non-concern to clinicians is that failure to intubate equates to failure to achieve maximum reimbursement. Of course we cannot make clinical decisions based on reimbursement factors, and no good clinician would think that way, but a quirk of the Diagnosis-Related Group (DRG) designations for patients with respiratory failure relates to the fact that intubation alone obtains a far higher reimbursement than any NIV treatment, regardless of severity of illness (Table 6). The most common DRGs for NIV are 189 (former DRG 87) "pulmonary edema and respiratory failure" and 190-192 (former DRG 88) "COPD," which, on a national reimbursement status, pay under $7,000. Any respiratory system diagnosis that requires ventilatory support for either $<$ 96 hours

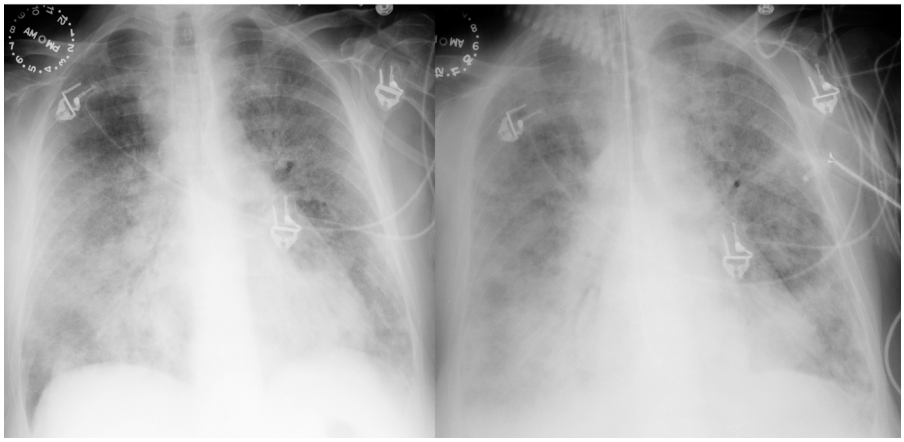

Fig. 3. Left: Worsening infiltrates after 24 hours on noninvasive ventilation and near-100% oxygen. Right: Patient had already met criteria for severe acute respiratory distress syndrome, and after intubation we were able to reduce the fraction of inspired oxygen and tidal volume.

Table 6. Diagnosis-Related Groups and National Average Payments

Current DRG	Former DRG	Description	Payment* ($)	Type of Ventilation
189	87	Pulmonary edema and respiratory failure	6,780	NIV
190-192	88	Chronic obstructive pulmonary disease	5,528	NIV
208	566	Respiratory system diagnosis: intubation and ventilatory support < 96 h	11,150	Intubation
207	565	Respiratory system diagnosis: ventilatory support ≥ 96 h	25,429	Intubation
004	483	Tracheostomy, except for face, mouth, and neck diagnoses	56,694	Tracheostomy and mechanical ventilation

* Payment assumes a 2008 standardized amount of $4,963.64, a hospital with a wage index of 1.000, and does not include capital payment or any add-on payments for teaching, disproportionate share, et cetera. The amount does not take into account the current blended-payment formula, under which payment is based on both old and new Diagnosis-Related Groups (DRGs).

(DRG 208 [former DRG 566]) or $>$ 96 hours (DRG 207 [former DRG 565]) reimburses 2–3 times higher, respectively, despite similar predicted outcome and attendant complicating medical diagnoses. Whenever a tracheostomy is done for a reason other than a face, mouth, or neck diagnosis (DRG 004 [former DRG 483]), then the base reimbursement (not including usual additional outlier supplement) is about 8 times higher than any NIV-related DRG. Clearly the patient expenses are more dependent on the co-existing medical illnesses and severity of illness, but this is not considered for reimbursement. NIV has not been shown to require more personnel time or to prolong hospital stay or increase costs.[19] Because NIV is associated with fewer complications, several medical societies are working to change this reimbursement prejudice against NIV and make reimbursement more dependent on the cause of respiratory failure and attendant comorbidities.

Sedation

One unsettled topic is sedation during NIV. With little data to guide practice, complications are inevitable when the airway remains unprotected. There have been no systematic studies on sedation during NIV, but there was a recent international, Web-based survey[54] of practices and attitudes about sedation during NIV. Seven hundred ninety (27%) of 2,985 physicians responded. Fifteen percent, 6%, and 28%, respectively, never used sedation, analgesia, or hand restraints at any time with NIV patients, and the large majority of respondents reported using those interventions in $\leq$ 25% of patients. Sedation was usually administered as an intermittent intravenous bolus, outside of a protocol, and sedation was assessed by nurses, with clinical end points rather than a sedation scale. Devlin et al[54] concluded that most physicians infrequently use sedation or analgesia during NIV for acute respiratory failure, but practice varies widely between specialties and geographic regions. Clinicians who use NIV should be wary of excessive sedation and the risk of aspiration, hypoventilation, and possible hypotension. From an opposing standpoint, inadequate sedation could also contribute to undue anxiety, increased work of breathing, and poor patient-ventilator synchrony.

Ethics: the Final Consideration

Many questions arise about the efficacy of NIV in do-not-intubate patients. Schettino et al studied 131 do-not-intubate patients who had 137 episodes of respiratory failure at their university-affiliated hospital over a 1-year period.[55] Hospital mortality was 38% in the 24 patients who had COPD exacerbation, 39% in the 28 patients who had acute cardiogenic pulmonary edema, 68% in the 9 patients who non-COPD hypercapnic ventilatory failure, 77% in the 13 post-extubation respiratory-failure patients, and 86% in the 57 patients with hypoxemic respiratory failure. Forty of the patients had advanced cancer, which was associated with high risk of death (85% mortality rate, $P = .002$). These investigators created a scoring system that included the Simplified Acute Physiology Score II and serum albumin level. That score could be calculated before NIV was applied, and it was predictive of hospital outcome. They concluded that NIV can reverse acute respiratory failure and prevent hospital mortality in do-not-intubate patients with COPD and cardiogenic pulmonary edema, but not in patients with post-extubation failure, hypoxemic respiratory failure, or end-stage cancer. A strong argument might be made to avoid NIV in a subset of these terminally ill-patients.

Summary

The innate comfort benefit from avoiding intubation by using NIV is obvious, but a very attractive discovery was the accompanying reduction in nosocomial pneumonia. There is a believable case that NIV reduces the incidence of infectious complications, although not all studies support this view. It is appropriate to ask, where are we with NIV in the acute-care setting?[56] NIV complications range from minor to severe, and there is now evidence that if NIV is applied inappropriately (eg, for too long), you may face a situation where you have "gone too far." There is a disconnect between cost and reimbursement when NIV is selected instead of intubation, though this "fiduciary misanthropy" is being challenged. There is a paucity of data on when and how much sedation is advisable during NIV. NIV for do-not-intubate patients creates unique ethical dilemmas because NIV may prolong life in otherwise terminal conditions. Nearly every effective therapy has risks and complications, and, usually, the more effective the treatment, the more the potential adverse effects. As with any other treatment, the clinician must exercise judgment to balance the risks and benefits of NIV to deliver the best service to the patient.

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Discussion

Kallet: If they re-code NIV reimbursement, would that take away the financial incentive to use it, or decrease costs? Or do you think it would still favor overall reduction of costs?

Gay: The cost of taking care of these really sick patients is high; they're getting dialysis and procedures, they're in the ICU, their SAPS [Simplified Acute Physiology Score II] and APACHE II [Acute Physiology and Chronic Health Evaluation] scores are equivalent to intubated patients. The only difference is that they don't have a tube in their throat. Their costs can be very similar. The problem is that reimbursement is tagged to something completely different, and unless those codes are changed, they're going to be reimbursed at about one tenth of what intubated patients are.

Hill: A cynical physician would say, "If you want to maximize your revenues, the best approach is to tracheotomize everybody on a ventilator within the first 2 or 3 days."

You showed the data from the Rana et al study,[1] and it seems we're going too far with NIV sometimes, particularly in patients with acute hypoxic respiratory failure. Patients who are in shock or have multi-system failure should not be put on NIV, and yet they are being put on NIV. I think the biggest risk—and this is a medical/legal risk too—is an unanticipated cardiorespiratory arrest that results in morbidity or death. We must avoid that, and I think education has a lot to do with preventing it.

1. Rana S, Gay P, Buck C, Hubmayr R, Gajic O. Failure of noninvasive ventilation in patients with acute lung injury: observational cohort study. Crit Care 2006;10(3):R79.

Gay: This is a 2-way street: both the patient and the physician are making decisions.

Hill: There certainly are patients on the fringe, and if you have a lot of skill and experience with NIV and feel that the patient is responding—oxygenating better, stabilizing, and so forth—maybe in those circumstances it's OK to use NIV. But there are situations where I think it's pretty clear that we've gone too far: arrests have occurred, severe morbidity and mortality ensue.

Kacmarek: You're right. We can't expect NIV to work miracles and not be willing to accept that it failed and the patient needs to be intubated. Some patients respond to NIV, and their clinical status and oxygenation improve, but in many situations the patient is simply "flogged" with NIV and should be intubated. If the patient is obviously not benefiting from NIV, and is fighting for every breath, hour after hour, they should be intubated. We have all stressed that if you start NIV on somebody with hypoxemic respiratory failure and you do not see a change in their clinical presentation within an hour or two, you should intubate. The key is not just P_{O_2} but clinical presentation. I'm not sure that concept is not getting across to all clinicians.

Hess: I was intrigued by your suggestion, which I happen to agree with, that during NIV large tidal volumes—essentially the control group of the ARDS [acute respiratory distress syndrome] Network study—might cause lung injury. I've observed that there are a lot of clinicians who believe that if the patient is on pressure support with the mask, or even with an endotracheal tube, and the patient generates a big tidal volume on their own, that's OK. So I was very interested in your observation that we might be inducing ventilator-induced lung injury while allowing these patients to take tidal volumes of 12 mL/kg with a face mask.

Gay: I think there's more to it than that. I have some people taking liter tidal volumes, and that makes me nervous: excessive lung stretch is lung stretch. But there are others who say at least activate the diaphragm and decrease some of the atelectasis. Well, there still may be some advantage to having the diaphragm work with you. I don't know if the answer is somewhere in the middle, but I think that tidal volumes of 10 to 15 mL/kg will cause lung stretch and acute lung injury.

Epstein: But in these spontaneously breathing patients it's hard to know what volume to use and where that

volume's going. It's a different situation than the ARDS Network study's patients.

Keenan: Why is that?

Epstein: In a patient whose diaphragm is functioning, a lot of that tidal volume may be expanding dependent areas of atelectatic lung, versus the sedated or maybe paralyzed patient lying on his back in the ICU. Christian Putensen's group looked at spontaneous breathing.[1] I'm not sure.

1. Wrigge H, Zinserling J, Neumann P, Muders T, Magnusson A, Putensen C, Hedenstierna G. Spontaneous breathing with airway pressure release ventilation favors ventilation in dependent lung regions and counters cyclic alveolar collapse in oleic-acid-induced lung injury: a randomized controlled computed tomography trial. Crit Care 2005;9(6):R780-R789.

Kallet: I think you have to look really carefully at some of the data from those who promote spontaneous breathing in all clinical situations. In one study that compared APRV [airway pressure-release ventilation] to controlled ventilation in ARDS [acute respiratory distress syndrome],[1] the shunt improved with APRV, so it re-recruited lung. But when you look at the amount of tidal volume going to areas of high ventilation-to-perfusion, which would be the areas we'd assume are overdistended anyway, there was no difference. We don't know the answer to this, and it'll take years to get it. With someone actively breathing on pressure support I don't necessarily think it makes a big difference if they're taking large tidal volumes; I still think they may be overdistending some lung areas. The jury's still out on that. I'm not satisfied with the evidence.

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Hill: I also think we don't know the answer to that one.

Epstein: We agree that we don't know.

Gay: The F_{IO_2} changed as well. We were able to decrease it from 100% to 40% once she was intubated. There are several things that you're limited to changing until you have airway control.

Keenan: I want to mention a problem that we are beginning to see at our center, which I think can kind of creep up on you if you have marked restriction on access to beds where patients can be conventionally ventilated. We invasively ventilate patients in our ICU and noninvasively ventilate in our high-dependency unit. It is not uncommon for us to have all ICU beds occupied with ventilated patients, with other patients ventilated in the emergency department and post-anesthesia unit waiting for ICU beds.

Lately we've had a few patients admitted to our high-dependency unit with cardiogenic pulmonary edema and managed on NIV, who initially settle but decompensate if they come off NIV, and they need to return to NIV support. They have a small rise in troponin level and need cardiac angiography and possible stenting, but to do that safely we believe they need to be intubated, although other centers may feel comfortable supporting them on NIV alone. As they are on NIV and comfortable, and we have no place to recover them, their investigations become delayed.

This is another "complication" of NIV. The ability to support patients on NIV who cannot progress towards hospital discharge without a specific treatment that requires conventional ventilation can delay their treatment in centers where access to ICU beds is a problem. This may be unique to our center or health-care system, but I raise this point because others may find themselves with patients who have responded well to NIV but deteriorate if removed from it.

The focus clearly should always be to provide the patient with the necessary investigations and treatment, even if it means intubation and mechanical ventilation. Ideally this should not be influenced by access to ICU beds.