Use and Outcomes of Noninvasive Ventilation for Acute Respiratory Failure in Different Age Groups

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BACKGROUND: The prevalence of chronic disease and do-not-intubate status increases with age. Thus, we aimed to determine characteristics and outcomes associated with noninvasive ventilation (NIV) use for acute respiratory failure (ARF) in different age groups. METHODS: A database comprising prospective data collected on site on all adult patients with ARF requiring ventilatory support from 8 acute care hospitals in Massachusetts was used. RESULTS: From a total of 1,225 ventilator starts, overall NIV utilization, success, and in-hospital mortality rates were 22, 54, and 18% in younger (18–44 y); 34, 65, and 13% in middle-aged (45–64 y); 49, 68, and 17% in elderly (65–79 y); and 47, 76, and 24% in aged (≥80 y) groups, respectively ($P < .001$, $P = .08$, and $P = .11$, respectively). NIV use for cardiogenic pulmonary edema and subjects with a do-not-intubate order increased significantly with advancing age (25, 57, 57, and 74% and 7, 12, 18, and 31%, respectively, in the 4 age groups [$P < .001$ and $P = .046$, respectively]). For subjects receiving NIV with a do-not-intubate order, success and in-hospital mortality rates were similar in different age groups ($P = .27$ and $P = .98$, respectively). CONCLUSIONS: NIV use and a do-not-intubate status are more frequent in subjects with ARF ≥65 y than in those <65 y, especially for subjects with cardiogenic pulmonary edema. However, NIV success and mortality rates were similar between age groups. (ClinicalTrials.gov registration NCT00458926.) *Key words: noninvasive ventilation; acute respiratory failure; elderly; aged; middle-aged.* [Respir Care 2016;61(1):36–43. © 2016 Daedalus Enterprises]

Introduction

Based on the United States National In-patient Sample database, the number of hospitalizations for acute respiratory failure (ARF), one of the most frequent reasons for hospitalization,[1] almost doubled between 2001 and 2009.[2] The overall rate of mechanical ventilation remained steady at approximately 50%, but noninvasive ventilation (NIV) increased from 3.8 to 10.1%, whereas the use of invasive mechanical ventilation fell from 48.5 to 42.1%. Older patients (>85 y) more often received NIV than younger ones (12.7% vs 7%),[2] and were also more apt to have do-not-intubate orders than younger ones.[3] Considering that NIV is frequently offered for management of ARF in patients

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with do-not-intubate orders as a ceiling of ventilator care or palliative therapy,[4-9] this also would be expected to favor greater use of NIV in the elderly.

Most prior studies on NIV use in the elderly have been retrospective or based on questionnaires or databases collected on the basis of billing codes,[2,3,10-13] limiting the ability to identify clinical characteristics associated with NIV use. Additionally, current data regarding NIV use in the elderly has been derived mainly from hypercapnic subjects treated in ICUs or intermediate care units,[4,6,7] whereas elderly and do-not-intubate patients are not uncommonly treated on regular medical wards.[5]

In the present study, we used a database collected on site at a group of acute care hospitals in Massachusetts including all patients receiving ventilatory assistance for ARF (hypercapnic/hypoxic) in any hospital location and recorded multiple clinical and physiologic variables. Using this unique database, we sought to determine the utilization rate of NIV as a percentage of all ventilator starts for ARF in each age group and to confirm the hypothesis that NIV is used more often in older age groups. We also assessed subject characteristics and outcomes associated with NIV use in different age groups.

QUICK LOOK

Current knowledge

Noninvasive ventilation (NIV) represents a standard of care in the treatment of exacerbations of COPD and cardiogenic pulmonary edema. The use of NIV in other causes of acute respiratory failure has met with less success and can delay definitive treatment. NIV has also been used successfully in patients with a do-not-intubate status as part of palliative care.

What this paper contributes to our knowledge

In a review of an existing database, NIV was used more frequently in subjects older than 65 y compared with those < 65, approaching 50% of ventilator starts for acute respiratory failure. The use of NIV in these subjects reflects the greater prevalence of chronic lung disease and cardiogenic pulmonary edema in this group. The outcome of do-not-intubate subjects was associated with a higher mortality in both age groups.

Methods

Setting and Population

Our database was designed to study the impact of an educational intervention on NIV utilization and its outcomes for subjects with ARF in 8 hospitals previously found to be low NIV utilizers at the time of a prior NIV survey taken in Massachusetts and Rhode Island.[12] Of the hospitals, 3 were randomly designated as control, whereas 5 of them were educational intervention sites. The results of the intervention study will be reported separately. The institutional review boards of participating institutions approved the study (Tufts ID 7642) and waived the need for patient consent because it was observational only.

The study was conducted at each institution during sequential 3-month data collection periods at baseline (before) between January 1, 2004, and August 3, 2007, and after the intervention or control periods (after) between August 25, 2005, and December 26, 2009. All subjects receiving mechanical ventilation (either NIV [continuous positive airway pressure or pressure-support ventilation and PEEP] or invasive mechanical ventilation) for ARF were prospectively enrolled hospital-wide, unless they met exclusion criteria (Fig. 1). Subjects were allocated to one of 4 groups based on age: (1) younger (18–44 y), (2) middle-aged (45–64 y), (3) elderly (65–79 y), and (4) aged (≥80 y).

Data Collection

On-site respiratory therapists filled out standardized data forms at the time of mechanical ventilation initiation, including subject demographics and characteristics, etiology of ARF, time and location of initiation, and equipment and settings used. Investigators recorded any missing information post hoc by reviewing medical records on site and recorded duration of use, diagnoses, complications, and clinical outcomes.

The etiology of ARF was allocated to one of 6 subgroups, as described previously[14]: (1) acute-on-chronic lung disease (ie, COPD and other chronic lung diseases); (2) de novo ARF (ie, pneumonia and ARDS); (3) cardiogenic pulmonary edema; (4) ARF associated with neurologic diseases (including drug or alcohol overdose); (5) cardiopulmonary arrest; and (6) others (postextubation failure, immunosuppressed with ARF, sepsis, shock, and other diseases).

Outcome Variables

The primary outcome was the utilization rate of NIV as a percentage of all ventilator starts for ARF in each age group. The secondary outcomes were NIV success (defined as avoidance of intubation or death during use of NIV or the subsequent 48 h)[14] and in-hospital mortality rates per age group. Other secondary outcomes included subject characteristics and physiologic variables, location of use, duration of mechanical ventilation use, and length of stay

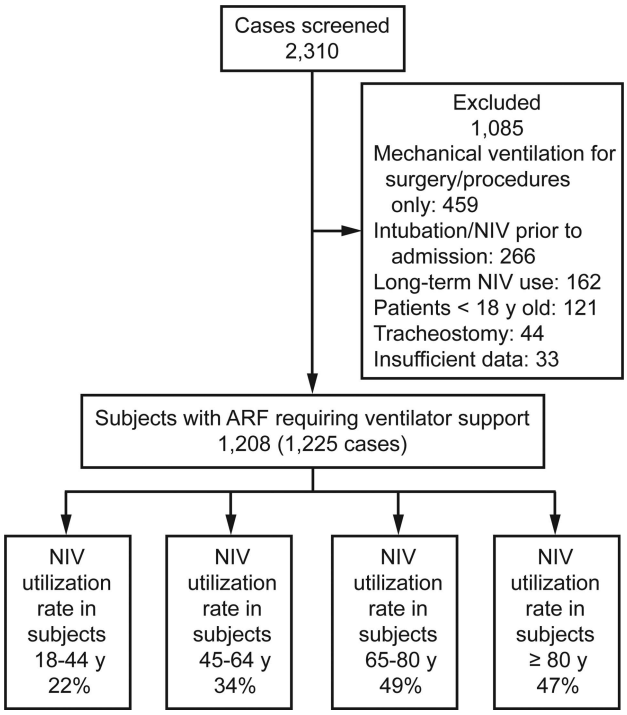

Fig. 1. Flow chart. IMV = invasive invasive mechanical ventilation; ETI = intubation; NIV = noninvasive ventilation; ARF = acute respiratory failure.

in hospital. Outcomes were also assessed for subjects with do-not-intubate orders in the different age groups.

Statistical Analysis

Statistical analysis was performed using SPSS 12.0 (SPSS, Chicago, Illinois). The educational intervention did not consider age, and given that there were no significant differences within age groups between the before and after surveys, we combined subjects from the before and after groups to maximize our numbers.

Continuous variables were expressed as median with interquartile range and compared using the Mann-Whitney *U* test or Kruskal-Wallis test. The chi-square test (with the Monte Carlo method) was used for categorical data when appropriate. A 2-tailed *P* value of $<.05$ was considered statistically significant.

Results

NIV Utilization Rates Per Age Group

As shown in Figure 1, 1,225 cases of ARF were enrolled into our study. Utilization rate of NIV as a first-line ventilator modality was 41% among all ventilator starts and 22, 34, 49, and 47% for younger, middle-aged, elderly, and aged groups, respectively ($P < .001$).

Subject Characteristics

Compared with invasive mechanical ventilation subjects, NIV subjects were older and more tachypneic with higher systolic and diastolic blood pressures and higher body mass indexes (Table 1). All NIV age groups had lower Simplified Acute Physiology Score II (SAPS II) and more often had a do-not-intubate status than the corresponding invasive mechanical ventilation age groups, as would be expected.

Among subjects receiving NIV, the older age groups had significantly lower body mass indexes, heart rates, and pH values and higher P_{CO_2} values, SAPS II, and rates of do-not-intubate orders than the younger and middle-aged groups (Table 1). However; after adjusting for the age effect on SAPS II, the severity of illness was highest in the younger group ($P = .02$).

NIV subjects were admitted mainly from home in all age groups, followed by other acute care hospitals in younger and nursing/group homes in the other age groups (Table 2). The location of NIV initiation did not differ within the age groups (Table 2). On the other hand, the greatest portion of subjects with a do-not-intubate status initiated on NIV were elderly in the ICU and aged on regular wards (0, 10, 51, and 39% ($P = .030$) and 0, 14, 38, and 48% ($P = .22$), respectively). Additionally, irrespective of age, there was an increased use of NIV outside of the ICU for do-not-intubate subjects compared with subjects without a do-not-intubate order (68% vs 56%, respectively, $P = .03$) (Table 2).

Overall, the most common etiology for ARF was neurologic (mainly drug overdoses) in the younger age group, acute-on-chronic lung disease in the elderly, and cardiogenic pulmonary edema in the aged, together with an equal distribution of these in the middle-aged (Fig. 2) ($P < .001$). Among subjects receiving NIV, pneumonia and other acute lung diseases predominated in the younger, acute-on-chronic lung disease in the middle-aged, and elderly and cardiogenic pulmonary edema in the aged groups (Fig. 3) ($P < .001$).

NIV Success and Mortality Rates and Other Outcomes

Overall NIV success and mortality rates were similar between age groups regardless of do-not-intubate status (Table 3, $P = .08$ and .12, respectively). As anticipated, overall in-hospital mortality was significantly lower for NIV than invasive mechanical ventilation subjects (18% vs 32%, respectively, $P < .001$), but mortality rates were similar between the NIV and invasive mechanical ventilation groups for younger subjects (18% vs 14%, respectively, $P = .61$). Among subjects receiving NIV, aged subjects (≥80 y) had significantly higher NIV success and mortality rates than the

Table 1. Baseline Characteristics of Subjects at Enrollment

	Younger (18–44 y) (n = 129)			Middle-Aged (45–64 y) (n = 394)			Elderly (65–79 y) (n = 414)			Aged (≥80 y) (n = 288)			P (Comparison of NIV Groups Among All Age Groups)
	Invasive Mechanical Ventilation (n = 101)	NIV (n = 28)	P	Invasive Mechanical Ventilation (n = 259)	NIV (n = 135)	P	Invasive Mechanical Ventilation (n = 213)	NIV (n = 201)	P	Invasive Mechanical Ventilation (n = 153)	NIV (n = 135)	P	
Age, y (range)	36 (30–40)	37 (28–41)	.99	56 (50–61)	57 (53–62)	.02	73 (68–77)	72 (68–76)	.27	84 (82–88)	85 (82–88)	.55	<.001
BMI, kg/m^2 (range)	25 (21–30)	28 (21–38)	.16	27 (23–32)	29 (23–37)	.01	26 (23–31)	27 (23–33)	.17	24 (21–27)	25 (22–30)	.01	.004
Female, n (%)	39 (39)	10 (36)	.78	107 (41)	67 (50)	.12	104 (49)	90 (45)	.41	88 (58)	76 (56)	.84	.10
DNI, n (%)	0 (0)	2 (7)	.046	2 (1)	16 (12)	<.001	1 (1)	37 (18)	<.001	2 (1)	42 (31)	<.001	<.001
Heart rate, beats/min (range)	112 (99–132)	109 (94–124)	.38	104 (85–123)	98 (86–119)	.16	98 (76–118)	96 (83–115)	.85	98 (79–116)	92 (78–108)	.22	.002
Systolic BP, mm Hg (range)	130 (110–157)	116 (106–144)	.18	119 (89–149)	131 (109–150)	.02	110 (88–145)	132 (107–154)	<.001	117 (90–153)	124 (104–144)	.10	.53
Diastolic BP, mm Hg (range)	75 (60–95)	71 (59–83)	.16	65 (50–87)	70 (57–86)	.18	61 (49–78)	67 (55–83)	.002	59 (41–76)	61 (55–79)	.02	.31
Breathing frequency, breaths/min (range)	20 (14–28)	28 (20–34)	<.001	20 (14–28)	24 (20–30)	<.001	21 (15–28)	26 (22–32)	<.001	22 (15–31)	26 (21–32)	.003	.07
pH (range)	7.31 (7.19–7.40)	7.39 (7.29–7.43)	.037	7.32 (7.18–7.41)	7.31 (7.25–7.39)	.28	7.28 (7.18–7.38)	7.29 (7.22–7.37)	.29	7.27 (7.15–7.38)	7.30 (7.22–7.38)	.32	.005
P_{CO_2}, mm Hg (range)	39 (34–47)	41 (35–59)	.32	42 (33–58)	60 (45–81)	<.001	43 (35–72)	64 (48–81)	<.001	46 (37–60)	60 (47–71)	<.001	.01
HCO_3 (range)	21 (16–25)	26 (21–32)	.002	22 (18–26)	29 (24–36)	<.001	23 (17–29)	29 (23–36)	<.001	23 (18–26)	27 (23–34)	<.001	.23
P_{aO_2}/F_{IO_2} (range)	236 (142–397)	180 (93–286)	.45	152 (114–256)	170 (107–240)	.90	148 (101–218)	175 (125–240)	.29	97 (56–203)	149 (110–250)	.06	.98
SAPS II (range)	33 (23–44)	24 (15–34)	.003	42 (31–56)	27 (23–35)	<.001	52 (39–60)	37 (31–44)	<.001	53 (45–63)	39 (33–49)	<.001	<.001
Modified SAPS II (range)	30 (21–40)	24 (15–28)	.003	33 (23–46)	19 (14–24)	<.001	36 (25–45)	22 (16–29)	<.001	35 (27–45)	21 (15–31)	<.001	.02

NIV = noninvasive ventilation
BMI = body mass index
DNI = do-not-intubate
BP = blood pressure
SAPS = Simplified Acute Physiology Score

Table 2. Location of Admittance From and Noninvasive Ventilation (NIV) Initiation for All NIV Subjects and NIV Subjects With Do-Not-Intubate Order

	18–44 y (All/DNI n = 28/2)	45–64 y (All/DNI n = 135/16)	65–79 y (All/DNI n = 201/37)	≥80 y (All/DNI n = 135/42)
Admitted from*				
Home	20 (74)/2 (100)	106 (78)/10 (63)	167 (83)/27 (73)	78 (58)/16 (38)
NH/group home/AL	2 (7)/0	22 (16)/6 (37)	16 (8)/8 (22)	51 (38)/26 (62)
Other acute care hospitals	5 (19)/0	4 (3)/0	7 (4)/0	3 (2)/0
Rehabilitation centers	0/0	1 (1)/0	7 (4)/2 (5)	2 (2)/0
Other	0/0	2 (2)/0	1 (1)/0	0/0
Location of initiation†				
ED	8 (29)/2 (100)	54 (40)/9 (56)	63 (31)/13 (35)	60 (44)/20 (48)
ICU	15 (53)/0	49 (37)/3 (19)	94 (47)/16 (43)	51 (38)/12 (28)
Wards	5 (18)/0	26 (19)/3 (19)	39 (19)/8 (22)	21 (16)/10 (24)
Other	0/0	6 (4)/1 (6)	5 (3)/0	3 (2)/0

Categorical variables are provided as number of subjects and percentage of subjects within that age group in parentheses for all noninvasive ventilation subjects and subjects with a do-not-intubate order, respectively.
* $P < .001$; data were available for 27, 135, 198, and 134 subjects for each age group, respectively.
† $P = .26$.
DNI = do-not-intubate
NH = nursing home
AL = assisted living
ED = emergency department

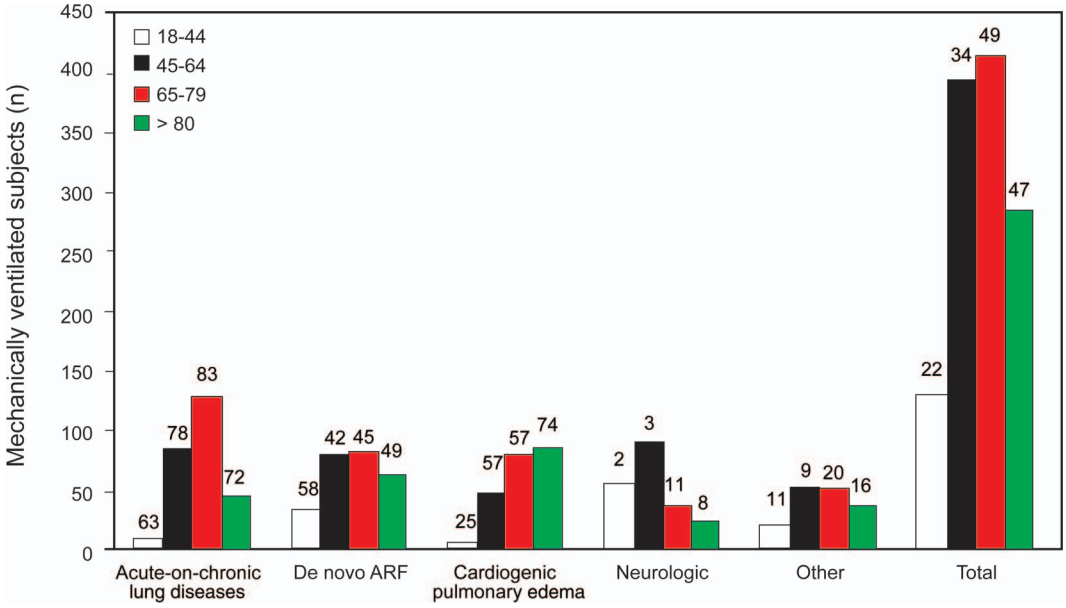

Fig. 2. Number of ventilator starts (including both noninvasive ventilation [NIV] and invasive mechanical ventilation subjects) based on age and etiology of ARF. Numbers above bars are NIV utilization rates (ie, NIV starts/total ventilator starts for acute respiratory failure). ARF = acute respiratory failure.

combined younger groups (<80 y) (76% vs 66% and 25% vs 16%, $P = .040$ and .02, respectively).

Mean length of stay and total duration of mechanical ventilation were similar between NIV and invasive mechanical ventilation groups for different age groups (data not shown), except for total duration of mechanical ventilation being significantly longer for invasive mechanical ventilation than NIV in aged subjects (4.7 vs 2.6 d, $P = .001$). Withdrawal of support rates, hospital length of stay for NIV subjects, and duration of NIV use did not differ between age groups (Table 3). Complications (such as pneumonia, gastric distention, pneumothorax, and vomiting into mask) were similarly infrequent in the different age groups.

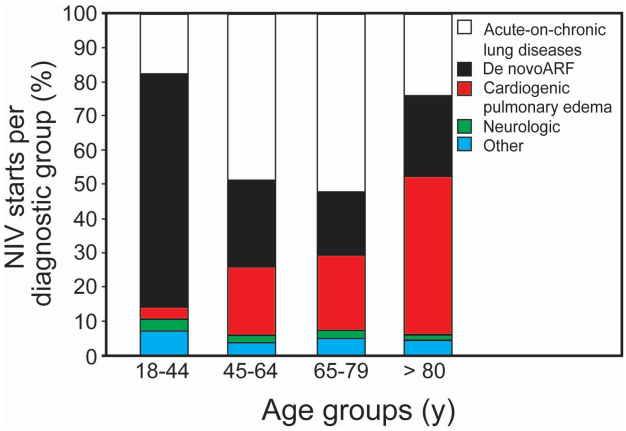

Fig. 3. Distribution of causes of acute respiratory failure (ARF) in subjects using noninvasive ventilation (NIV) according to age groups.

Discussion

In this prospective cohort study, we found that NIV utilization for ARF as a percentage of all ventilator starts was highest for subjects >65 y old and lowest for subjects 18–44 y old, which is probably explained by the greater prevalence of chronic lung or heart disorders in the older and neurologic/toxic conditions (mainly drug and alcohol overdose) in the younger age groups. Additionally, do-not-intubate status was observed more frequently with aging, also contributing to greater use of NIV in the elderly and aged. NIV success and in-hospital mortality rates were similar in the different age groups.

A number of previous studies support the use of NIV in older age groups.[4-7,15] Benhamou et al[15] reported more frequent use of NIV in elderly subjects with ARF admitted to an ICU (64%) than in younger subjects (47%), with higher mortality in the elderly group (21% vs 9%, respectively) reflecting outcomes in the general ICU population. In a randomized, controlled trial of elderly subjects with hypercapnic ARF admitted to a respiratory care unit, NIV decreased the rate of meeting intubation criteria (7.3 vs 63.4%, $P < .001$) and mortality (odds ratio = .40, $P < .05$) compared with standard medical treatment.[7]

Consistent with the above results, our study shows greater utilization of NIV with advancing age. Stefan et al[2] also reported increasing use of NIV with age for 1,364,624 medical subjects hospitalized with an ARF diagnosis (12, 21, 28, and 34% in subjects age 18–44, 45–64, 65–84, and ≥85 y old, respectively). The lower rates of NIV use compared with our study could be due to their reliance on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD9-CM) coding[16]; differences in prevalence of etiologies of ARF (pneumonia being the most common diagnosis); or different practices between our hospitals and those in the sample of Stefan et al.[2] In addition, they observed that older subjects received less invasive mechanical ventilation and less expensive care overall, consistent with earlier studies[3,17,18] and with the idea that intensity of care decreases with aging as more patients and their proxies choose to limit treatment. In a 2-y prospective cohort study on subjects with ARF admitted to a medical ICU, Schortgen et al[6] also reported NIV use in 60% of elderly subjects (≥80 y old) requiring ventilator support compared with only 32% of younger subjects. Our NIV utilization rate in aged subjects was 47%, but this lower rate was in a population with a lower prevalence of do-not-intubate status than in the study by Schortgen et al[6] (31% vs 40%).

With regard to subject characteristics, our older NIV subjects had lower body mass indexes and heart rates with more frequent acidosis, hypercapnia, and do-not-intubate statuses than younger subjects, similar to Schortgen et al.[6] These differences from younger age groups most likely reflect the greater prevalence of acute-on-chronic lung disease and other chronic illnesses among older patients. Also in our study, the severity of illness increased with age, but after adjustment for age, SAPS II scores were actually higher in the younger age group, due to their greater prevalence of neurologic/toxic and de novo ARF. Reflecting the greater burden of chronic illness, aged subjects were also more likely to be admitted from chronic care facilities compared with other groups.

Contrary to our expectations, age alone did not determine the location of care in our study, but subjects with a do-not-intubate status were more often treated outside of the ICU than those without a do-not-intubate order. In a previous survey, subjects with cancer and their caretakers considered the ICU "a bad place to die."[19] Our study found that slightly more than a quarter of elderly do-not-intubate subjects using NIV were treated in the ICU; considerations like need for nursing care and monitoring, bed availability, and patient and/or family preference may override ethical considerations so that a significant minority of such patients still receive ICU care. On the other hand, 10 of 21 (48%) aged subjects treated on regular wards had a do-not-intubate status as opposed to 11 of 70 (16%) of those < 80 y ($P = .001$).

Palliative use of NIV in patients with a do-not-intubate order or when endotracheal intubation is deemed inappropriate has become increasingly common.[20,21] In our study, a do-not-intubate status imparted a worse prognosis among subjects treated with NIV compared with those without one, undoubtedly related to a higher prevalence of diseases with worse prognoses. However, there was no significant impact of age on outcomes of NIV subjects with a do-not-intubate status.

Prior studies have reported conflicting results on the effect of age and the presence of a do-not-intubate order on NIV failure rate. Scarpazza et al[4] found that older age

Table 3. Outcomes of Noninvasive Ventilation (NIV) Based on Age for All NIV Subjects and NIV Subjects With Do-Not-Intubate Orders

	18–44 y (All/DNI n = 28/2)	45–64 y (All/DNI n = 135/16)	65–79 y (All/DNI n = 201/37)	≥80 y (All/DNI n = 135/42)	Overall (All/DNI n = 499/97)	P
Success rates, %						
All NIV subjects	54	65	68	76	69	.08
NIV subjects with DNI	50	56	68	79	70	.27
NIV subjects without DNI	54	66	68	74	68	.25
Mortality rates, %						
All NIV subjects	18	13	17	24	18	.11
NIV subjects with DNI	50	38	35	33	35	.98
NIV subjects without DNI	15	10	13	20	14	.17
Withdrawal of support, %						
All NIV subjects	14	10	10	19	13	.12
NIV subjects with DNI	50	38	16	26	25	.29
Hospital LOS, d	11 (6–22)	7 (4–14)	7 (4–13)	7 (4–11)	7 (4–13)	.02
Duration of NIV, d	0.7 (0.1–3.3)	0.7 (0.1–2.5)	1.0 (0.3–3.2)	0.6 (0.2–1.7)	0.8 (0.2–1.7)	.02*
Duration of mechanical ventilation, d	4.8 (0.9–9.6)	2.7 (0.4–6.3)	2.2 (0.5–6.1)	0.9 (0.2–6.1)	1.8 (0.4–5.5)	<.001

* Covers duration of NIV as first iteration.
DNI = do-not-intubate
NIV = noninvasive ventilation
LOS = length of stay

was associated with a higher NIV failure rate. In contrast, in a recent multi-center French database study including 3,163 subjects with ARF requiring ventilator support (but excluding do-not-intubate patients) younger age was found to be one of the independent risk factors for NIV failure ($P < .001$).[22] In the study by Schortgen et al,[6] NIV failure rates were similar across age groups (40% vs 42% in subjects <80 y and ≥80 y, respectively), and mortality rates were shown to be higher in the older subjects (25% vs 40%, $P < .01$). Our study found no association between the different age groups with regard to success or mortality rates. This may reflect the counterbalancing effects of a higher rate of NIV failure and mortality associated with de novo respiratory failure in the younger age group and the higher rate of withdrawal of support in the aged. On the other hand, when we combined all subjects younger than 80 y and compared them with subjects > 80 y, the aged had higher NIV success and mortality rates, probably due to the higher prevalence of chronic disorders and do-not-intubate orders, respectively.

Limitations of our study include its observational design and lack of controls, precluding conclusions about the effectiveness of NIV in different age groups. In addition, the data were accrued from selected hospitals in a region of the United States and may not be generalizable to other centers elsewhere. Furthermore, although the number of subjects enrolled is higher than in most of the prior epidemiologic studies, we are limited by small numbers of subjects in some of our subgroups (especially the younger). Our study also has important strengths, including our acquisition of data by prospective identification of subjects and on-site data gathering that offers greater reliability compared with off-site survey studies. We have also selected a group of hospitals representing a mix of academic and community settings, providing a real-life snapshot of actual NIV use.

Conclusions

We conclude that NIV is used more frequently in subjects older than 65 y than in younger subjects, approaching 50% of ventilator starts for ARF, reflecting the higher prevalence of acute-on-chronic lung disease and cardiogenic pulmonary edema as causes of ARF in the older age groups. NIV is used least often in adults < 45 y, reflecting the higher prevalence of neurologic and de novo causes of ARF than in the older age groups, etiologies for which NIV is used infrequently. NIV success and in-hospital mortality rates are similar between age groups. Having a do-not-intubate status is associated with a higher mortality in NIV subjects than in those without one, but age does not affect outcome in do-not-intubate subjects treated with NIV. These data support the routine use of NIV to treat elderly and aged patients with ARF when they have appropriate diagnoses, with the expectation of achieving outcomes at least as good as or even better than those in younger patients.

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