One-Year Follow up of Noninvasive Respiratory Support in General Wards

Francesca Moretto, Martina Fracazzini, Federico Verdina, Daniela Ferrante, Sara Baino, Francesca Grossi, Luigi Castello, Gianmaria Cammarota, Piero Balbo, Pier Paolo Sainaghi, Mauro Campanini, Mario Pirisi, Giuseppe Patti, Alberto Dal Molin, Francesco Della Corte, Paolo Navalesi, and Rosanna Vaschetto

BACKGROUND: Noninvasive respiratory support (NRS) has been used to treat acute respiratory failure outside the ICU, but existing data have left many knowledge gaps for managing NRS in general wards. The primary objective of this study was to describe indications, duration of treatment, and outcomes of subjects treated with NRS outside the ICU. The secondary objective was to compare outcomes based on age < 80 or ≥ 80 y. METHODS: This retrospective observational study was conducted at Maggiore della Carità University Hospital in Novara, Italy, and included all patients treated with noninvasive ventilation (NIV) or CPAP outside the ICU from November 2017 to October 2018, with 1 year of follow-up. RESULTS: Of the 570 treatments performed, 383 subjects were analyzed, 136 NIV and 247 CPAP. Subjects' median (interquartile range [IOR]) age was 79 (72–85) y, and the main diagnoses of respiratory failure were cardiogenic pulmonary edema in 128 subjects (33%), pneumonia in 99 (26%), and COPD exacerbation in 52 (14%), with a median (IQR) treatment duration of 38 (16-74) h. Rapid response team visits lasted a median (IQR) 3 (2-6) d. Interface-related pressure lesions occurred in 13% of the subjects, in no case leading to definitive treatment discontinuation. Compared with the subjects \geq 80 y old, the younger subjects had a median (IQR) longer hospitalization (16 [10-24] d vs 13 [9–20] d; P = .003) but slightly decreased in-hospital mortality (21% vs 30%; P = .061) and a decreased post-discharged 1-year mortality in hospital survivors (25% vs 41%; P = .002), differences observed only in the subjects treated with NIV. CONCLUSIONS: In a real-life setting outside the ICU, NIV and CPAP managed by a rapid response team with a daily visit in collaboration with ward staff highly experienced in NRS allowed us to treat the subjects without major complications. Post-discharge 1-year mortality was higher in the subjects ≥ 80 y old treated with NIV for acute hypercapnic respiratory failure. Key words: Noninvasive ventilation; intensive care; general ward; rapid response team; acute respiratory failure; frail elderly. [Respir Care 2022;67(9):1138-1146. © 2022 Daedalus Enterprises]

Introduction

Noninvasive respiratory support (NRS) has been largely used in the treatment of acute respiratory failure (ARF) in the ICU and, more recently, in general wards both under ordinary circumstances¹⁻⁵ and during the pandemic.⁶⁻⁸ Management of NRS outside the ICU requires a trained staff, and inadequate training is the main cause of its lack of use in general wards.^{2,9} Guidelines for NRS management in general wards have not been specifically defined, nevertheless, a high success rate with few collateral effects has been demonstrated in treating subjects

under the supervision of an expert rapid response team.¹ Indications for NRS have recently been updated.¹⁰ Either NIV or CPAP is recommended for patients with ARF due to cardiogenic pulmonary edema to reduce mortality and ICU transfer rates.¹⁰ In COPD exacerbation, NIV is indicated in patients with acute moderate respiratory acidosis, together with standard medical care, showing a decrease in mortality and endotracheal intubation rates; whereas, in cases of pneumonia or other causes of de novo hypoxemic ARF, the guidelines do not offer a recommendation, given the high level of the uncertainty of evidence.¹⁰

Not less important, NRS in hospital wards can also be applied for the management of ARF in elderly patients (age ≥ 80 y), more often than in younger patients, when used in the context of a do-not-intubate order.^{11,12} An association between increasing age and higher NRS failure rate was reported in observational studies and led to uncertain outcomes.^{13,14} Although NIV and CPAP have been extensively applied outside the ICU during the pandemic,⁶⁻⁸ limited data are available on the management of NIV and CPAP in the general wards,^{15,16} and the duration of the therapy and outcomes,³ particularly in elderly subjects.¹¹ The primary study objectives were to monitor the indication, duration of the treatment, and outcome of the subjects treated with NIV and CPAP outside the ICU. On a secondary analysis, the outcome was also evaluated based on subject age < 80 or ≥ 80 y.

Methods

Study Design

This was a retrospective observational monocentric study conducted at Maggiore della Carità University Hospital, a 700-bed hospital, in Novara, Italy. Data collection lasted from November 2017 to October 2018, and a 1-year follow-up was concluded in October 2019. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee (protocol CE 64/19). The ethics committee waived the requirement to obtain any informed consent for data collected retrospectively.

QUICK LOOK

Current knowledge

Noninvasive respiratory support is used to treat acute respiratory failure, including outside the ICU. Few data are available on its use in general wards, particularly for elderly patients.

What this paper contributes to our knowledge

Application of noninvasive respiratory support in the general wards for treatment of, mainly, cardiogenic pulmonary edema, pneumonia, and COPD exacerbation was feasible, with few complications, under the supervision of an expert rapid response team and appeared safe for elderly subjects.

Subject Enrollment and Data Collection

All adult subjects admitted to Maggiore della Carità University Hospital with either hypoxemic or hypercapnic ARF treated with CPAP or NIV outside the ICU were included. In the case of multiple hospitalizations for the same subject, only data from the first hospitalization were considered. Demographic characteristics; comorbidities; ARF diagnosis; clinical parameters, that is, blood cell counts and arterial blood gas values at hospital admission, hours of ventilatory support per day in the case of NIV derived from ventilator counter, and the presence of interface-related pressure lesions were recorded. For CPAP, a counter was not available, so continuous support was defined as per day because CPAP was normally discontinued for no longer than 2–3 min, only when strictly necessary for changing the interface or subjects' nursing. NIV

Supplementary material related to this paper is available at http://www.rcjournal.com.

Drs Moretto, Fracazzini, Verdina, Ferrante, Baino, Castello, Sainaghi, Pirisi, Patti, Dal Molin, Della Corte, and Vaschetto are affiliated with the Dipartimento di Medicina Traslazionale, Università del Piemonte Orientale, Novara, Italy. Dr Ferrante is affiliated with the Unit of Medical Statistics, Department of Translational Medicine, University of Eastern Piedmont and Cancer Epidemiology, CPO Piemonte, Novara, Italy. Drs Grossi, Dal Molin, Della Corte, and Vaschetto are affiliated with the Anestesia e Terapia Intensiva, Azienda Ospedaliero Universitaria "Maggiore della Carità," Novara, Italy. Dr Castello is affiliated with the Medicina D'Urgenza, Azienda Ospedaliero Universitaria "Maggiore della Carità," Novara, Italy. Dr Cammarota is affiliated with the Dipartimento di Medicina e Chirurgia, Università degli Studi di Perugia, Perugia, Italy. Dr Balbo is affiliated with the Pneumologia, Azienda Ospedaliero Universitaria "Maggiore della Carità," Novara, Italy. Drs Sainaghi, Campanini, and Pirisi are affiliated with the Medicina Interna, Azienda Ospedaliero Universitaria "Maggiore della Carità," Novara, Italy. Dr Patti is affiliated with the Cardiologia, Azienda Ospedaliero Universitaria "Maggiore della Carità," Novara, Italy. Dr Navalesi is affiliated with the Istituto di Anestesia e Rianimazione, Azienda Ospedale-Università di Padova, Dipartimento di Medicina - DIMED -Università di Padova, Padova, Italy.

Drs Moretto and Fracazzini are co-senior authors.

Dr Navalesi discloses relationships with Dräger, Intersurgical, Resmed, Philips, Novartis, MSD, and Getinge; has a patent, 102020000008305, pending to Università di Padova, and a patent, 102016000114357, with royalties paid from Intersurgical. Dr Vaschetto discloses a relationship with Intersurgical. The other authors have disclosed no conflicts of interest.

This research was conducted at Maggiore della Carità University Hospital, Novara, Italy.

This work was supported by funding from the University of Piemonte Orientale, AGING Project–Department of Excellence–DIMET.

Correspondence: Rosanna Vaschetto MD PhD, Dipartimento di Medicina Traslazionale, Università del Piemonte Orientale, via Solaroli 17, 28100, Novara, Italy. E-mail: rosanna.vaschetto@med.uniupo.it.

DOI: 10.4187/respcare.09625

and CPAP therapeutic goals, that is, full treatment, the ceiling of treatment or palliative, date of treatment discontinuation, hospital discharge, ICU transfers, re-admissions, and mortality during the hospital stay and after 1 year were also registered. An electronic case report form (on an Access database [Microsoft Office, Microsoft, Redmond, WA]), accessible only on hospital computers and password protected, was used for data collection in accordance with the policy concerning personal data management. Hospital data were also searched to assess the hospital length of stay, ICU transfers, re-admissions, mortality at hospital discharge; a regional-based database and interviews with subjects' general practitioner were used to assess 1-year mortality.

NIV and CPAP

During the study period, different ventilators for NIV were available: Vivo 30 (Breas Medical AB, Mölnlycke, Sweden), V60 (Philips Respironics, Murrysville, Pennsylvania), and Respironics Trilogy 202 (Philips, Amsterdam, Netherlands). The interfaces mainly used were oronasal and total face masks (ResMed, San Diego, California; Philips, Amsterdam, Netherlands). PEEP was initially set at 5 cm H₂O and inspiratory pressure to get a tidal volume of 6-8 mL/kg of predicted body weight and a breathing frequency in a normal range, that is, 16-20 breaths/minute. Settings were subsequently modified according to subjects' needs and tolerance. CPAP was delivered through helmets (Intersurgical, Mirandola [Modena], Italy; Dimar S.r.l., Medolla [Modena], Italy) via flow meters (typically 40-100 L/min, depending on the setting chosen) with a scale that allowed the clinician to regulate oxygen and air flow separately to set the inspiratory oxygen fraction. CPAP was set between 10 and 12 cm H₂O according to the subject's needs and tolerance. Periodically, NIV and CPAP training was offered to medical and nurse personnel.

Rapid Response Team

The rapid response team in charge was carried out by an intensivist and a senior resident in anesthesia. The decision to prescribe NIV or CPAP was reserved for the rapid response team present 24 h/d, 7 d/wk in the hospital. Sometimes NIV or CPAP was started in the emergency department, nonetheless, the rapid response team was consulted to decide whether to continue NIV or CPAP in the wards. Monitoring of the subjects on NIV and CPAP was performed by the ward staff (saturation, noninvasive blood pressure, heart rate, breathing frequency, comfort, and dyspnea). The rate of the monitoring depended on the degree of stability of the vital signs. Blood gas analyses were always obtained before starting NRS and 1–2 h after treatment. Rapid response team visits were performed at least once a day. If a subject became unstable, then further visits and the frequency of blood gas analysis and

monitoring were decided by the rapid response team. The treatment and follow-up algorithm is schematically presented in Figure 1S (see the supplementary materials at http://www.rcjournal.com).

Statistical Analysis

Descriptive statistics were used to summarize the subjects' demographic characteristics and laboratory values. Categorical variables are presented as numbers and percentages, whereas continuous variables are presented as medians (interquartile ranges [IQR]). Non-parametric Mann-Whitney U test and the Fisher exact were used to assess the difference between medians and categorical variables in the 2 independent samples, respectively. Kaplan-Meier curves and log-rank test were used to describe 1-year survival analysis. The Cox proportional regression model was used to evaluate which factors had the greatest impact on survival and the logistic regression method to evaluate the influencing factors on different outcomes. All the hypothesis tests were 2-tailed, and a P value of .05 was considered significant. Descriptive and inferential statistics evaluations were conducted by using Stata v. 15 (StataCorp, College Station, Texas).

Results

From November 2017 to October 2018, 570 noninvasive respiratory support treatments outside the ICU were performed at Maggiore della Carità University Hospital. We analyzed 383 treatments, 136 NIVs (36%), and 247 CPAPs (64%) (Fig. 1). Out of the 383 subjects treated with NRS, 74 (19%) started the treatment in the emergency department and continued it in the general wards, 45 with NIV and 29 with CPAP. The treatment duration in the emergency department lasted a median (IQR) time of 3.0 (2.0–4.5) h before being hospitalized in the general ward. Most of the treatments, 167 (44%), were conducted in internal medicine

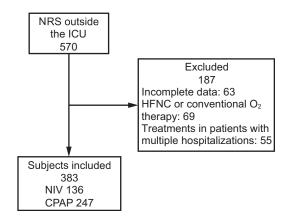


Fig. 1. Flow chart. NRS = noninvasive respiratory support; HFNC = high-flow nasal cannula; NIV = noninvasive ventilation.

Admission Wards Treatments	Subjects Treated, n (%) ($N = 383$)
Cardiac surgery	3 (1)
Cardiology	34 (9)
General surgery	25 (6)
Thoracic surgery	3 (1)
Vascular surgery	4 (1)
Hematology	21 (5)
Gastroenterology	11 (3)
Infectious diseases	6 (2)
Subintensive care unit	16 (4)
Internal medicine	167 (44)
Nephrology	7 (2)
Neurosurgery	5 (1)
Neurology	17 (4)
Orthopedics	6 (2)
Pulmonology	11 (3)
Coronary unit	42 (11)
Urology	5 (1)

wards, as shown in Table 1. The main demographic and clinical characteristics of subjects overall and stratified by age are summarized in Table 2. The subjects had a median (IQR) age of 79 (72–85) y and 57% were men. The main cause of ARF was cardiogenic pulmonary edema in 128 subjects (33%), pneumonia in 99 (26%), and COPD exacerbation in 52 (14%). The subjects with a do-not-intubate order were 31% of the total, being significantly higher among those age \geq 80 y versus younger subjects, that is, 44% versus 19%, *P* < .001. Consistent with the existing literature, NIV was mainly used in COPD exacerbation (35%), whereas CPAP was mainly used in cardiogenic pulmonary edema (42%), as shown in Table 1S (see the supplementary materials at http://www.rcjournal.com).

The laboratory values on hospital entrance are presented in Table 3. No major differences were present, only creatinine was slightly higher in the elderly subjects. In Tables 2S and 3S (see the supplementary materials at http://www. rcjournal.com), laboratory values are presented stratified by ARF diagnosis and etiology, that is, hypoxemic and hypercapnic. As shown in Table 4, median (IQR) NIV effective treatment duration was 38 (16-74) h, with a presence of interface-related pressure lesions in 13% of the subjects. Superficial or lower-grade lesions were reported and in no case led to definitive treatment discontinuation. The median (IQR) rapid response team visits lasted 3 (2-6) d. The median (IQR) overall hospital stay was 15 (10-22) d, significantly longer in the subjects < 80 y old (median [IQR], 16 [10-24] d vs 13 [9-20] d]; P = .003). Intubation was performed in 9% of the subjects included in the study; when excluding the subjects with a do-not-intubate order, the

intubation rate reached 12.5%. In-hospital mortality was 25% overall, which reached 49% at 1 year.

When considering only hospital survivors, the post-discharged 1-year mortality was 32% (Fig. 2A), which was significantly higher in the elderly subjects versus the subjects < 80 y old, 41% versus 25%; P = .002 (Fig. 2B). When analyzing the possible risk factors for mortality at 1 year, age and the do-not-intubate order status were the only independent predictors, as shown in Tables 4S (see the supplementary materials at http://www.rcjournal.com). When stratifying subjects according to NRS treatment (ie, NIV or CPAP) and age, mortality at 1 year was significantly higher in older subjects treated with NIV (62% in elderly subjects vs 38% in the subjects < 80 y old; P = .001) (Fig. 3A) but not in those treated with CPAP (28% in subjects \geq 80 y old vs 20% in the younger ones; P = .13) (Fig. 3B). Mortality at 1 year according to the ARF diagnosis is depicted in Figure 2S (see the supplementary materials at http://www. rcjournal.com). Forty-one subjects (11%), mainly in the younger group (29 [15%]; P = .008), required ICU admission after starting NRS in the general wards, whereas 38 (10%) needed another NRS treatment during the same or a new hospitalization, with no difference between the groups. Risk factors associated with ICU transfer and with NRS re-treatment are shown in Table 5S A and B, respectively (see the supplementary materials at http://www.rcjournal. com).

Discussion

To our knowledge, this was the largest monocentric study conducted on NRS outside the ICU, including data of 383 subjects in 1 year in the general wards of a university hospital. NRS outside the ICU setting was started by the rapid response team, which also carried out daily visits, treatment adjustment, and monitoring. We considered a population affected by several causes of ARF, including both hypoxemic and hypercapnic ARF, with cardiogenic pulmonary edema as the most frequent cause, followed by pneumonia and COPD, in line with indications in the literature.^{1,2} Anecdotally, there seems to have been an increase in patients treated with NRS outside the ICU over the past 10 years. Cabrini et al¹ reported, in a single-center study in 2008, of 129 subjects treated in a 1,100-bed hospital in 6 months. In our hospital of 700 beds, \sim 500 treatments were performed in 1 year, when also considering the re-treatments. The wards other than the ICU where NRS is delivered for ARF treatment seem to have changed. Whereas Cabrini et al,¹ in 2008, had the emergency department treating 41% of the cases and the internal medicine department treating only 27% of the cases, almost 10 years later, the same group highlighted that 37% of the cases were started in the medical ward and only 6.8% of the treatments were started in the emergency department and then continued in

NRS IN GENERAL CARE WARDS

Clinical and Demographic Characteristics	Total Subjects $(N = 383)$	Subjects < 80 y $(n = 194)$	Subjects $\ge 80 \text{ y}$ ($n = 189$)	Р
Age, median (IQR) y	79 (72–85)	72 (65–77)	86 (82–88)	<.001
Sex				
Men	218 (57)	122 (63)	96 (51)	.02
Women	165 (43)	72 (37)	93 (49)	.02
Noninvasive respiratory support				
NIV	136 (36)	69 (36)	67 (35)	>.99
CPAP	247 (64)	125 (64)	122 (65)	>.99
ARF diagnosis				
Cardiogenic pulmonary edema	128 (33)	59 (31)	69 (37)	.23
Pneumonia	99 (26)	49 (25)	50 (26)	.82
COPD	52 (14)	25 (13)	27 (14)	.77
Other	104 (27)	61 (31)	43 (23)	.066
Comorbidities				
Cardiomyopathy	186 (49)	73 (38)	113 (60)	<.001
Hypertension	165 (43)	74 (38)	91 (48)	.051
Diabetes	85 (22)	50 (26)	35 (19)	.11
Obesity	48 (13)	34 (18)	14 (7)	.003
Chronic renal failure	65 (17)	31 (16)	34 (18)	.68
Smoking	45 (12)	33 (17)	12 (6)	.001
Hematologic malignancy	27 (7)	18 (9)	9 (5)	.11
Long-term home NIV	9 (2)	7 (4)	2(1)	.17
Others	75 (20)	51 (26)	24 (13)	<.001
Do-not-intubate order status	120 (31)	36 (19)	84 (44)	<.001

Table 2. Demographic and Clinical Characteristics of the Subjects Treated with Noninvasive Respiratory Support Based on Age

IQR = interquartile range

NIV = noninvasive ventilation

ARF = acute respiratory failure

Table 3. Laboratory Values at the Baseline Presented Overall and Stratified By Age

Baseline Laboratory Values	Total Subjects ($N = 383$)	Subjects < 80 y ($n = 194$)	Subjects ≥ 80 y ($n = 189$)	Р
pH	7.39 (7.32–7.45)	7.40 (7.33–7.45)	7.38 (7.30–7.44)	.15
P _{aCO2} , mm Hg	41.6 (36.0–55.3)	40.6 (36.1–54.0)	42.4 (35.7–56.0)	.55
P _{aO2} , mm Hg	60.0 (49.2–73.4)	59.3 (48.3-73.0)	60.1 (49.5–75.4)	.47
HCO ₃ ⁻ , mEq/L	25.9 (22.6-31.1)	26.3 (22.4–31.4)	25.8 (22.6-31.0)	.81
Lactate, mMol/L	1.3 (0.9–2.3)	1.3 (1.0–2.0)	1.5 (1.0–2.5)	.20
White blood cells, $\times 10^3/\mu L$	11.0 (8.0–16.0)	11.0 (8.0–16.0)	12.0 (8.0–16.8)	.29
Neutrophils, $\times 10^3/\mu$ L,	9.0 (6.0–12.0)	9.0 (6.0–12.0)	9.0 (6.0–13.0)	.23
Creatinine, mg/dL	1.00 (1.00-2.00)	1.00 (0.86–1.71)	1.00 (1.00-2.00)	.037
Alanine aminotransferase, U/L	22 (16–37)	23 (17-40)	20 (15–34)	.068

the general wards.³ Our data were in line with this change, with most of our subjects treated on internal medicine wards (44%). It is also noteworthy that, in both studies, as well as in our center, the staff is highly experienced in NRS application, which is necessary for treatment success.^{1,3}

Major indications for NRS outside the ICU remain cardiogenic pulmonary edema, pneumonia, and COPD, as in our setting,^{1,3} whereas the subjects treated NRS seem to be older (ie, median [IQR], 79 [72–85] y) compared with an average age of 71 y in other studies conducted in similar

Outcomes of the Subjects Treated	
Clinical 6	

	Clinical			Total Subjects $(N = 383)$				V 2	Subjects < 80 y ($n = 194$)	~			SI	Subjects $\ge 80 \text{ y}$ ($n = 189$)			Ρ
38 (16-74) 38 (12-91) 41 (20-78) 38 (17-71) 33 (12-60) 36 (15-71) 32 (12-61) 36 (15-71) 36 (15-71) 36 (15-71) 36 (15-71) 36 (15-71) 36 (15-71) 36 (15-71) 36 (12-71) 48 (20-68) 30 (13) 8 (10) 10 (20) 13 (25) 9 (38) 28 (14) 5 (18) 4 (14) 6 (21) 14 (12) 21 (12) 7 (13) 6 (27) 3 (1-3) 3 (1-6) 13 (1-6) 14 (1-7) 3 (1-6) 3 (1-7) 3 (1-6) 4 (1-7) 4 (1-7) 4 (1-7) 4 (1-7) 3 (1-3)	Outcomes	Total	CPE	Pneumonia	COPD	Other	Total	CPE	Pneumonia	COPD	Other	Total	CPE	Pneumonia	COPD	Other	
90(13) 8(10) 10(20) 13(20) 13(20) 13(20) 13(20) 13(20) 13(20) 13(20) 13(20) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12) 6(27) 7(12)	NIV treatment duration h*	38 (16–74)			41 (20–78)	36 (12–68)	38 (17–77)	33 (26–61)	68 (27–153)		33 (12–66)	36 (15–71)				48 (20–68)	.91
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Interface- related pres- sure lesions, n(%)	50 (13)	8 (16)	10 (20)	13 (26)	19 (38)	28 (14)	5 (18)	4 (14)	6 (21)	13 (47)	22 (12)	3 (14)	6 (27)	7 (32)	6 (27)	.45
	Treatment du- ration as rapid response team visits, d	3 (2-6)	3 (2-5)	3 (1-6)	4 (3–7)	3 (2–5)	3 (2-6)	3 (2–5)	3 (1-6)	4 (2-7)	4 (2–5)	4 (2–5)	4 (2–5)	4 (2–5)	4 (3–7)	3 (2-5)	.26
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Hospital LOS, d	15 (10–22)	16 (10–21)	16 (10–23)	11 (7–16)	14 (10–26)	16 (10–24)	17 (10–23)	19 (12–24)	11 (5–16)	15 (11–29)	13 (9–20)	14 (10–20)	13 (9–20)	11 (8–16)	13 (7–23)	.003
189 (49) 58 (31) 55 (29) 25 (13) 51 (27) 79 (41) 21 (26) 25 (32) 6 (8) 27 (34) 110 (58) 37 (34) 30 (27) 19 (17) 24 (22) < 81 (21) 18 (22) 20 (25) 10 (12) 33 (41) 59 (30) 14 (24) 15 (25) 6 (10) 24 (41) 22 (12) 4 (18) 5 (23) 4 (18) 9 (41) 41 (11) 12 (29) 15 (37) 4 (10) 10 (24) 29 (15) 10 (33) 2 (7) 6 (21) 12 (6) 2 (17) 4 (13) 2 (17) 4 (13) 2 (17) 4 (13) 3 (31) 33 (9) 11 (33) 10 (30) 3 (10) 9 (27) 24 (12) 9 (33) 7 (29) 2 (17) 4 (13) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33)	Hospital mor- tality, n (%)	97 (25)	28 (29)	32 (33)	6) 6	28 (29)	41 (21)	8 (20)	14 (34)	4 (10)	15 (36)	56 (30)	20 (36)	18 (32)	5 (9)	13 (23)	.061
81 (21) 18 (22) 20 (23) 14 (24) 15 (25) 6 (10) 24 (41) 22 (12) 4 (18) 5 (23) 4 (18) 9 (41) > NRS 41 11 12 (29) 15 37 4 (10) 10 (24) 13 2 (7) 6 (21) 12 (6) 2 17 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 6 (21) 12 (6) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2 (17) 4 (33) 2	One-year mor- tality, n (%) ICU admission, n (%)	189 (49)	58 (31)	55 (29)	25 (13)	51 (27)	79 (41)	21 (26)	25 (32)	6 (8)	27 (34)	110 (58)	37 (34)	30 (27)	19 (17)	24 (22)	<.001
41 (11) 12 (29) 15 (37) 4 (10) 10 (24) 29 (15) 10 (34) 11 (38) 2 (7) 6 (21) 12 (6) 2 (17) 4 (33) 2 (17) 4 (33) t 33 (9) 11 (33) 10 (30) 3 (10) 9 (27) 24 (12) 9 (38) 7 (29) 2 (8) 6 (25) 9 (5) 2 (23) 3 (33) 1 (11) 3 (33) and 38 (10) 13 (34) 7 (19) 10 (26) 8 (21) 24 (12) 8 (33) 4 (17) 6 (25) 6 (25) 14 (7) 5 (36) 3 (21) 4 (29) 2 (14)	Fotal	81 (21)	18 (22)	20 (25)	10 (12)	33 (41)	59 (30)	14 (24)	15 (25)	6 (10)	24 (41)	22 (12)	4 (18)	5 (23)	4 (18)	9 (41)	<.001
33 (9) 11 (33) 10 (30) 3 (10) 9 (27) 24 (12) 9 (38) 7 (29) 2 (8) 6 (25) 9 (5) 2 (23) 3 (33) 1 (11) 3 (33) snt 38 (10) 13 (34) 7 (19) 10 (26) 8 (21) 24 (12) 8 (33) 4 (17) 6 (25) 6 (25) 14 (7) 5 (36) 3 (21) 4 (29) 2 (14)	After NRS treatment	41 (11)	12 (29)	15 (37)	4 (10)	10 (24)	29 (15)	10 (34)	11 (38)	2(7)	6 (21)	12 (6)	2 (17)	4 (33)	2 (17)	4 (33)	.008
	Intubation Re-treatment		11 (33) 13 (34)	10 (30) 7 (19)	3 (10) 10 (26)	9 (27) 8 (21)	24 (12) 24 (12)	9 (38) 8 (33)	7 (29) 4 (17)	2 (8) 6 (25)	6 (25) 6 (25)	9 (5) 14 (7)	2 (23) 5 (36)	3 (33) 3 (21)	1 (11) 4 (29)	3 (33) 2 (14)	.01 .12

NRS IN GENERAL CARE WARDS

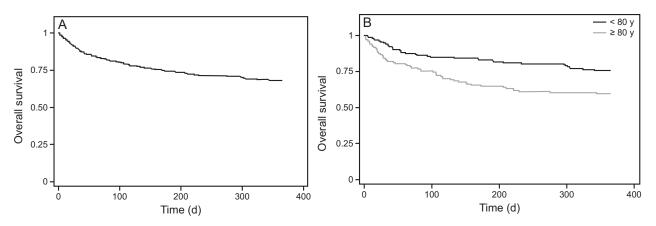


Fig. 2. One-year overall (A) and based on ages < 80 y or ≥ 80 y (B) survival after hospital discharge of the subjects treated with noninvasive respiratory (NRS) support outside the ICU.

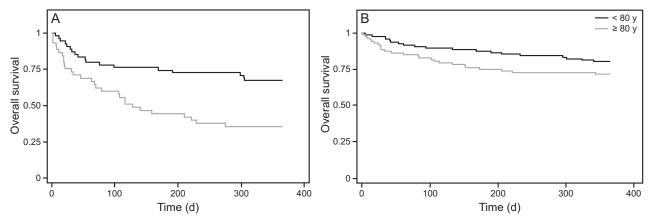


Fig. 3. One-year overall survival of noninvasive ventilation (NIV) (A) and CPAP (B) treatments based on age < 80 y or ≥ 80 y.

settings but some time ago.^{1,3} Although ideally the best place to start NRS is in a monitored setting with a good nurse-to-patient ratio,¹⁷ in some hospitals, patients on the general wards can be started on noninvasive respiratory support during rapid response team evaluation. General wards are characterized by reduced house staff availability, especially during the night shift; therefore, the possibility of detecting NRS-related adverse events, such as air leaks, accidental disconnection, oxygen desaturation, aspiration, and mask intolerance, might be lower than in the ICU.^{4,18} Despite these potential pitfalls, NRS has been proved safe, especially for subjects who are hypercaphic and in general wards.^{1,19,20} The guidelines suggest, in the presence of contraindications that would increase the risk of NRS failure, to rapidly consider the placement in high-dependence unit or ICU.21

Three studies showed that NRS started by the rapid response team in a wide variety of settings outside the ICU had a high success rate^{1,19,22} and few complications.^{1,19}

However, in another study, by Schneider et al,²³ 60% of the subjects placed on NRS were ultimately transferred to an ICU or a high-dependence unit, which suggests against this practice. In our study, few subjects required ICU admission after NRS in the general ward and few complications, for example, skin pressure lesions, were detected, which suggests that having clinicians knowledgeable in NIV and CPAP with daily rapid response team visits was successful in our setting.

The 1-year mortality found in our population, that is, 49%, seemed higher compared with that found by Cabrini et al³ in a similar setting, 34%, but the subjects included were younger and with fewer comorbidities. A French group highlighted outcomes of elderly subjects (age >80 y) treated with NRS for several ARF origins in the ICU.²⁴ In the ICU setting, mortality rates, both in the hospital (40%) and after 1 year of follow-up (69%), was much higher compared with those found in our subjects.²⁴ In our setting, the subjects treated with NIV has a significantly lower survival at 1 year

compared with those treated with CPAP. This difference might mainly be related to the etiology of respiratory failure, with hypercapnic ARF treated predominantly with NIV and hypoxemic ARF treated with CPAP, although we could not exclude that interfaces²⁵ and settings²⁶ might have a role, as shown in some subsets of hypoxemic ARF. In our study, the subjects age ≥ 80 y had a shorter hospital stay compared with the younger subjects. This finding was related to the higher in-hospital mortality in the oldest group.

Our study had limitations. Despite prospectively documented data, the study was retrospective, with bias related to the study design. Our data on the NRS duration have been reported only for NIV by monitoring the ventilator counter. Because a counter integrated in the flow meter was not available, precise data on CPAP treatment duration are not available. Our report supports the use of the rapid response team, with a background of more than 10 years of management of NRS outside the ICU,⁵ where nurses and physicians from the general wards constantly follow courses and refreshes on NRS topics. Because the efficacy and safety of NRS outside the ICU are strongly dependent on the clinical knowledge of the hospital staff, as well as the organization, a generalized adoption of the rapid response team for treatment with NRS outside the ICU cannot be recommended.

Conclusions

In our hospital, the application of NRS outside the ICU for mainly cardiogenic pulmonary edema, pneumonia, and COPD exacerbation has been extensively used with success and few complications, also in elderly subjects. Post-discharged 1-year mortality was higher in the subjects age ≥ 80 y treated with NIV for hypercapnic ARF.

REFERENCES

- Cabrini L, Idone C, Colombo S, Monti G, Bergonzi PC, Landoni G, et al. Medical emergency team and non-invasive ventilation outside ICU for acute respiratory failure. Intensive Care Med 2009;35(2):339-343.
- Cabrini L, Moizo E, Nicelli E, Licini G, Turi S, Landoni G, et al. Noninvasive ventilation outside the intensive care unit from the patient point of view: a pilot study. Respir Care 2012;57(5):704-709.
- Cabrini L, Landoni G, Bocchino S, Lembo R, Monti G, Greco M, et al. Long-term survival rate in subjects with acute respiratory failure treated with noninvasive ventilation in ordinary wards. Crit Care Med 2016;44(12):2139-2144.
- Mehta S, Hill NS. Noninvasive ventilation. Am J Respir Crit Care Med 2001;163(2):540-577.
- Sainaghi PP, Colombo D, Re A, Bellan M, Sola D, Balbo PE, et al. Natural history and risk stratification of subjects undergoing non-invasive ventilation in a non-ICU setting for severe COPD exacerbations. Intern Emerg Med 2016;11(7):969-975.

- Aliberti S, Radovanovic D, Billi F, Sotgiu G, Costanzo M, Pilocane T, et al. Helmet CPAP treatment in subjects with COVID-19 pneumonia: a multicentre cohort study. Eur Respir J 2020;56(4):2001935.
- Franco C, Facciolongo N, Tonelli R, Dongilli R, Vianello A, Pisani L, et al. Feasibility and clinical impact of out-of-ICU noninvasive respiratory support in subjects with COVID-19-related pneumonia. Eur Respir J 2020;56(5):2002130.
- Vaschetto R, Barone-Adesi F, Racca F, Pissaia C, Maestrone C, Colombo D, et al. Outcomes of COVID-19 subjects treated with continuous positive airway pressure outside the intensive care unit. ERJ Open Res 2021;7(1):00541-2020.
- Cabrini L, Esquinas A, Pasin L, Nardelli P, Frati E, Pintaudi M, et al. An international survey on noninvasive ventilation use for acute respiratory failure in general non-monitored wards. Respir Care 2015;60 (4):586-592.
- Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al; Suhail Raoof Members of the Task Force. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J 2017;50(2):1602426.
- Ugurlu AO, Sidhom SS, Khodabandeh A, Ieong M, Mohr C, Lin DY, et al. Use and outcomes of noninvasive ventilation for acute respiratory failure in different age groups. Respir Care 2016;61(1):36-43.
- 12. Curtis JR, Cook DJ, Sinuff T, White DB, Hill N, Keenan SP, et al; Society of Critical Care Medicine Palliative Noninvasive Positive Ventilation Task Force. Noninvasive positive pressure ventilation in critical and palliative care settings: understanding the goals of therapy. Crit Care Med 2007;35(3):932-939.
- Bellani G, Grasselli G, Cecconi M, Antolini L, Borelli M, De Giacomi F, et al. Noninvasive ventilatory support of patients with COVID-19 outside the intensive care units (WARd-COVID). Ann Am Thorac Soc 2021;18(6):1020-1026.
- Avdeev SN, Yaroshetskiy AI, Tsareva NA, Merzhoeva ZM, Trushenko NV, Nekludova GV, Chikina SY. Noninvasive ventilation for acute hypoxemic respiratory failure in patients with COVID-19. Am J Emerg Med 2021;39:154-157.
- Brambilla AM, Prina E, Ferrari G, Bozzano V, Ferrari R, Groff P, et al; 3P study group. Non-invasive positive pressure ventilation in pneumonia outside intensive care unit: an Italian multicenter observational study. Eur J Intern Med 2019;59:21-26.
- Ugurlu AO, Sidhom SS, Khodabandeh A, Ieong M, Mohr C, Lin DY, et al. Where is noninvasive ventilation actually delivered for acute respiratory failure? Lung 2015;193(5):779-788.
- Elliott MW, Confalonieri M, Nava S. Where to perform noninvasive ventilation? Eur Respir J 2002;19(6):1159-1166.
- Ambrosino N. Should we perform noninvasive ventilation anywhere? Expert Rev Respir Med 2012;6(2):131-133.
- Olivieri C, Carenzo L, Vignazia GL, Campanini M, Pirisi M, Corte FD, Navalesi P. Does noninvasive ventilation delivery in the ward provide early effective ventilation? Respir Care 2015;60(1):6-11.
- Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. Lancet 2000;355(9219):1931-1935.
- 21. Davidson AC, Banham S, Elliott M, Kennedy D, Gelder C, Glossop A, et al; BTS Standards of Care Committee Member, British Thoracic Society/Intensive Care Society Acute Hypercapnic Respiratory Failure Guideline Development Group, On behalf of the British Thoracic Society Standards of Care Committee. BTS/ICS guideline for the ventilatory management of acute hypercapnic respiratory failure in adults. Thorax 2016;71 (Suppl 2):ii1-ii35.
- 22. Khalid I, Hamad WJ, Khalid TJ. Outcome of patients treated with noninvasive ventilation by a medical emergency team on the wards: scarce and probably secure and resourceful monitoring in select subjects– reply. Respir Care 2014;59(5):e89-e90.

- Schneider AG, Calzavacca P, Mercer I, Hart G, Jones D, Bellomo R. The epidemiology and outcome of medical emergency team call subjects treated with non-invasive ventilation. Resuscitation 2011;82(9):1218-1223.
- Schortgen F, Follin A, Piccari L, Roche-Campo F, Carteaux G, Taillandier-Heriche E, et al. Results of noninvasive ventilation in very old subjects. Ann Intensive Care 2012;2(1):5.
- 25. Ferreyro BL, Angriman F, Munshi L, Del Sorbol L, Ferguson ND, Rochwerg B, et al. Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. JAMA 2020;324(1):57-67.
- Brochard L, Slutsky A, Pesenti A. Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. Am J Respir Crit Care Med 2017;195(4):438-442.