ORIGINAL ARTICLE

Noninvasive mechanical ventilation in emergency services in Catalonia: the VNICat registry cohort study

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Objectives. To study how noninvasive ventilation (NIV) is used in prehospital emergency services and hospital emergency departments. To explore associations between NIV use and hospital mortality.

Methods. Prospective analysis of a consecutive multicenter cohort of patients who were treated with NIV between February and March 2015. The study was undertaken in emergency medical services in Catalonia and 8 Catalan hospital emergency departments. We collected information during the acute episode and on discharge, as well as data describing the patients' condition when stable. The dependent variable was all-cause hospital mortality.

Results. We studied 184 acute episodes requiring NIV, in the prehospital setting in 25 cases (13.6%) and in the hospital in 159 (86.4%). The most common scenario was acute heart failure (AHF) (38.0%). The second most common was chronic obstructive pulmonary disease (COPD) (34.2%). In most cases, NIV was discontinued in the emergency department. Mortality was 7.5% during prehospital care and 21.4% in the hospital. Hospital mortality was associated with limiting the use of life support. We detected no significant differences in mortality between the groups of patients with AHF vs COPD.

Conclusions. The use of NIV in prehospital and hospital emergency care follows current evidence-based recommendations and is required more often for AHF than for exacerbated COPD. Hospital mortality is high in this context and is associated with frequent limiting of life support.

Keywords: Noninvasive ventilation. Respiratory insufficiency. Emergency health services. Registers.

Estudio de cohortes de pacientes tratados con ventilación no invasiva en servicios de urgencias prehospitalarios y hospitalarios de Cataluña: registro VNICat

Objetivo. Conocer las características de la ventilación no invasiva (VNI) en los servicios de urgencias prehospitalarios y hospitalarios. Comparar los resultados obtenidos en función de la mortalidad hospitalaria.

Método. Estudio de cohortes multicéntrico, analítico, prospectivo con inclusión consecutiva de pacientes en los que se realizó VNI durante febrero y marzo de 2015 en el ámbito prehospitalario por el Sistema d'Emergències Mèdiques (SEM) y en 8 servicios de urgencias (SU) hospitalarios de Cataluña. Se recogieron las características basales, del episodio agudo y de destino, y la variable dependiente fue la mortalidad hospitalaria por todas las causas.

Resultados. Se recogieron 184 episodios de VNI, 25 episodios (13,6%) prehospitalarios y 159 (86,4%) hospitalarios. El escenario más frecuente para su uso fue la insuficiencia cardiaca aguda (ICA) (38,0%) seguido de la agudización de la enfermedad pulmonar obstructiva crónica (EPOC) (34,2%). En la mayoría de casos la VNI se retira en los SU. La mortalidad fue del 7,5% y del 21,4% en urgencias prehospitalarias y hospitalarias, respectivamente. La mortalidad hospitalaria se relacionó con más presencia de limitación del tratamiento de soporte vital (LTSV). No hubo diferencias de mortalidad entre los diferentes escenarios clínicos.

Conclusiones. La VNI en los SU prehospitalarios y hospitalarios sigue las recomendaciones de la evidencia científica actual y se realiza principalmente en la ICA y en la agudización de la EPOC. La mortalidad hospitalaria es elevada y se relaciona con la LTSV, que es muy frecuente.

Palabras clave: Ventilación no invasiva. Insuficiencia respiratoria. Servicios de urgencias. Registro.

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Introduction

Non-invasive ventilation (NIV) is part of the management of acute respiratory failure (ARF)[1]. Its use over time has been increasing, passing in some registries from 4.4% in 1998 to 11.1% in 2004 in adult patients treated in intensive care units (ICU)[2] and 11.6% in 2006 to 18.2% in 2012 in pediatrics[3]. The scientific evidence has been provided in the beginning by clinical trials and meta-analyses, performed mostly in ICU[4-12], the most scientific clinical scenarios in which NIV is the exacerbation of chronic obstructive pulmonary disease (COPD)[13], Acute heart failure (AHF)[14] and ARF in the patient with immunosuppression[15]. These are, therefore, the scenarios where NIV is most frequently performed[16] and where the success of NIV prevents intubation and decreases mortality, as long as there is a correct selection of patients and no delay in intubation if this is indicated, since this may worsen the prognosis. These acute situations are very prevalent in the emergency services (EMS) and thanks to the technological advance, together with the scientific evidence provided in this area[17-20], nowadays the NIV is performed in the US, not only in the hospital, but also in the pre-hospital setting[21,22], and even in new scenarios such as palliative use[23]. The NIV is widely accepted by the urgenciologists as a very useful technique, with a use limited only by the lack of knowledge of the technique and the availability of ventilators[24].

In our environment, there are few research works of the NIV in the Spanish EMS'. They are studies based on specific clinical scenarios (both in COPD[25] and AHF[26]) and in a single center. It is known that in Spain, in the absence of more recent data, NIV is a technique that is performed in 45.7% of EMSs[27], but we have not found multicentric records describing how the patients in which NIV are performed in emergencies, both in the prehospital and in the hospital setting. The objective of the NIVCat registry (VNICat in Spanish) was to describe the characteristics of the patients in whom NIV is performed in prehospital and hospital emergencies and to investigate if there is any clinical scenario that is related to worse survival results.

Method

The VNICat registry is a multicentre, analytical, prospective cohort study with consecutive inclusion of patients in whom NIV was performed during a period of one month, between February and March 2015, and in which NIV was carried out in the prehospital setting by the Emergències Mèdiques System (EMS) and in 8 hospital hospitals in Catalonia. The inclusion criterion was any adult patient who underwent NIV and signed informed consent. The decision to initiate the NIV depended on the physician responsible for the patient, as well as the modality, interface and respirator used, following the protocols established in each center. There were no exclusion criteria, except the refusal to participate in the registration or the inability to sign informed consent. The study was approved by the Clinical Research Ethical Committee of the Hospital Universitari de Bellvitge. All patients signed informed consent to participate.

Patient baseline characteristics (age, sex, pathological history, Charlson index), acute episode, NIV and efficacy data were collected if there was a life-sustaining treatment limitation (LSTL) according to the emergency physician's criteria that performed the NIV in a consensual way with patients and relatives, gasometry upon admission to the emergency room, clinical improvement (subjective decrease of dyspnoea), stay in emergencies and hospitalization, final destination from emergencies and hospital mortality.

For the description of the qualitative variables, absolute and relative frequencies were used and the median with interquartile range (IQR) for quantitative variables. For the comparisons, the chi-square test was used for the first (or in the 2 × 2 tables the exact Fisher test when the expected numbers were less than 5) and the Student's t-test for independent measurements for the second the main outcome-dependent variable was all-cause mortality during hospital admission. A logistic regression model was performed for mortality in the different clinical scenarios adjusted to the variables that in the bivariate study resulted in statistically significant differences. The differences were statistically significant when the p value was less than 0.05 or when the 95% CI of the OR excluded the value 1. The statistical program used was SPSS 19.0.

Results

We collected 184 episodes of NIV, 25 episodes (13.6%) prehospital collected by the EMS and 159 (86.4%) hospital. The distribution of the centres can be seen in Table 1. The characteristics of the population are described in Table 2. A high percentage of patients older than 75 years, predominantly men, high Charlson index and a high percentage of patients with LSTL. The most frequent clinical indications were AHF and COPD. Regarding the technique of NIV, the mode with support pressure and the naso-buccal interface were the most used. Regarding the efficacy of the technique, it stands

Table 1. Distribution of the patients recruited according to the center (ordered in ascending order)

	n (%)
Hospital Sant Pau i Santa Tecla (Tarragona)	8 (4.3)
Hospital Universitari Mútua de Terrassa	10 (5.4)
Fundació Althaia. Xarxa Assistencial de Manresa	10 (5.4)
Hospital de Viladecans	12 (6.5)
Hospital de Sant Joan Despí Moisès Broggi	13 (7.1)
Parc Sanitari Sant Joan de Déu (Sant Boi de Llobregat)	14 (7.6)
Hospital de Mollet	14 (7.6)
Hospital de Calella	15 (8.2)
Hospital Universitari de Bellvitge (L'Hospitalet de Llobregat)	16 (8.7)
Coorporació Sanitaria Parc Taulí (Sabadell)	21 (11.4)
Sistema d'Emergències Mèdiques (SEM)	25 (13.6)
Hospital Universitari Doctor Josep Trueta (Girona)	26 (14.1)
Total	**184 (100.0)**

Table 2. Characteristics of the total population (n = 184)

	n (%)
Demographics	
Age in years [median (BER)]	79 (67-84)
Age ≥ 75 years	109 (59.5)
Male	107 (58.2)
Baseline characteristics	
Smoking	100 (57.1)
Hypertension	143 (78.6)
Diabetes mellitus	70 (38.0)
Acute myocardial infarction	32 (17.4)
Chronic renal failure	35 (19.0)
Stroke	13 (7.1)
Dementia	17 (9.2)
Peripheral arterial disease	25 (13.6)
COPD	110 (59.8)
Previous cardiac insufficiency	92 (50)
Charlson Index [median (IQR)]	3 (1-4)
Limitation of life support treatment	76 (42.9)
Features of NIV use	
Clinical indication	
Acute cardiac insufficiency	70 (38.0)
Increased COPD	63 (34.2)
Pneumonia	18 (9.8)
Other	33 (17.9)
Support pressure mode	158 (85.9)
Nasal buccal interface	155 (84.2)
Facial interface	29 (15.8)
Specific Ventilator for NIV	169 (91.8)
Efficacy of the technique	
Clinical improvement	143 (77.7)
Failure/Intolerance	21 (11.4)
OTI	11 (6.0)
Death	9 (4.9)
Prehospital NIV#	10 (6.3)
Withdrawal NIV in the emergency room#	133 (83.1)
Data related to the times#	
Acute cardiac insufficiency	
NIV initiation time (minutes) [median (IQR)]	66.5 (10-466)
Total NIV time (hours) [median (IQR)]	7.5 (4.1-15.3)
Hospital stay (days) [median (IQR)]	8.0 (4.5-13.5)
Increased COPD	
NIV initiation time (minutes) [median (IQR)]	62.0 (10-265)
Total NIV time (hours) [median (IQR)]	23.5 (7.6-52.6)
Hospital stay (days) [median (IQR)]	10.0 (5.5-12.5)
Gasometrical data#	
Hypoxemia (pO_2 < 60 mmHg)	151 (95.0)
Hypercapnia (pCO_2 > 45 mmHg)	130 (81.8)
Acidosis (pH < 7.35)	106 (66.7)
Respiratory acidosis (acidosis with hypercapnia)	100 (62.9)
Destination from the emergency#	
Hospitalization	139 (87.4)
Internal Medicine	55 (34.6)
Pneumology	34 (21.4)
Intensive care unit	28 (17.6)
Cardiology	8 (5.0)
Others	14 (8.8)
Mortality in emergency room	12 (7.5)
Emergency discharge	8 (5.0)
Evolutionary data	
Total hospital mortality	34 (21.4)
Emergency re-visit 30 days†	23 (18.4)
Hospital readmission at 30 days†	18 (14.4)

QR: interquartile range; COPD: chronic obstructive pulmonary disease; NIV: non-invasive ventilation; OTI: orotracheal intubation; PO_2: partial pressure of oxygen; PCO_2: partial pressure of carbon dioxide.

#For the calculation, patients were excluded from the Medical Emergencies System (total n = 159).

†Residents in the hospital were excluded (n = 125) for the calculation of re-visit and readmission.

Table 3. Univariate study according to hospital mortality (for the calculation patients were excluded from the Sistema d'Emergències Mèdiques)

	Deaths N = 34 n (%)	Alive N = 125 n (%)	Value of p
Datos demográficos			
Age ≥ 75 years	25 (73,5)	71 (56,8)	0,077
Male	17 (50,0)	74 (59,2)	0,336
Personal history			
Smoking	14 (42,4)	75 (61,5)	0,050
Hypertension	26 (78,8)	95 (76,6)	0,792
Diabetes mellitus	12 (35,3)	43 (34,4)	0,923
Acute myocardial infarction	9 (26,5)	19 (15,2)	0,126
Chronic renal insufficiency	9 (26,5)	23 (18,4)	0,298
Stroke	2 (5,9)	11 (8,8)	0,582
Dementia	5 (14,7)	10 (8,0)	0,236
Peripheral arterial disease	4 (11,8)	20 (16,0)	0,541
EPOC	19 (55,9)	78 (62,4)	0,490
Previous heart failure	19 (55,9)	59 (47,2)	0,369
Features of the NIV			
Supported Pressure Modes	30 (88,2)	111 (88,8)	0,927
Pre-hospital NIV	2 (5,9)	8 (6,4)	0,912
Limitation of treatment of life support	25 (73,5)	42 (35,6)	< 0,001
Gasometric data by scenarios			
COPD exacerbation (n=57)	n = 6	n = 51	
Acidosis	5 (83,3)	38 (74,5)	0,635
Hypercapnia	6 (100,0)	50 (98,0)	0,729
Respiratory acidosis	5 (83,3)	38 (74,5)	0,635
Acute cardiac insufficiency (n = 50)	n = 12	n = 38	
Acidosis	9 (75,0)	25 (65,8)	0,551
Hypercapnia	11 (91,7)	24 (63,2)	0,060
Respiratory acidosis	9 (75)	20 (52,6)	0,171

COPD: chronic obstructive pulmonary disease; NIV: non-invasive ventilation; OTI: orotracheal intubation.
#For the calculation, the patients of the Emergències System Mediques (n = 159).

out that in more than three-quarters of cases the technique was associated with a clinical improvement. In pre-hospital use of NIV at the hospital, there was very little pre-hospital use. In most episodes, the NIV was withdrawn in the EMS itself.

The patients had hypoxemic and hypercapnic respiratory failure, with a high percentage of associated respiratory acidosis. The hospital admission was mostly in the departments of internal medicine and pulmonology. The mortality in emergencies was low, however, total hospital mortality was high. Reconstruction and re-entry at 30 days were also high.

In the comparative hospital mortality study detailed in Table 3, LSTL was the only variable that was associated with higher hospital mortality. Figure 1 shows that, due to clinical scenarios, the exacerbation of COPD presented lower mortality compared to the rest of the scenarios. However, in making the adjustment by the LSTL variable, this significance was not maintained.

Discussion

The VNICat registry is the first multicenter study carried out in Spain on the actual use of NIV in prehospital and hospital emergencies, emphasizing that its use

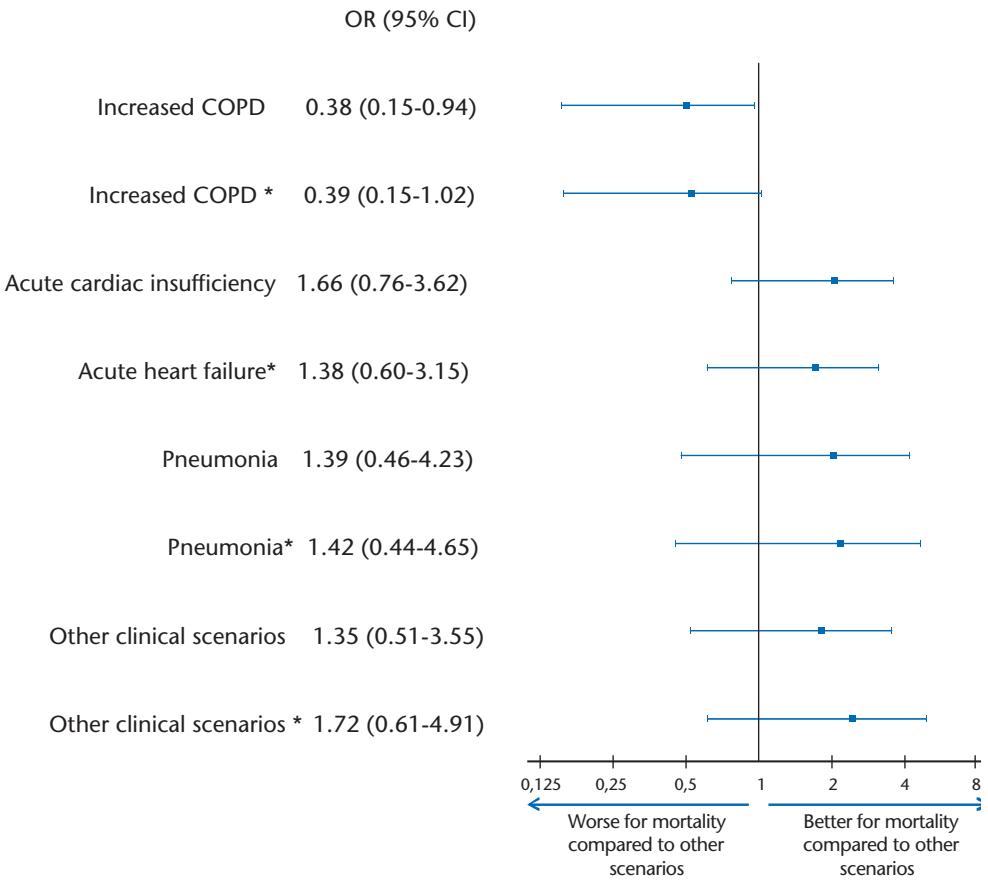

Figure 1. Odds ratio (OR) for hospital mortality in each clinical setting in which non-invasive ventilation is performed compared to the others. The OR for each scenario is presented crude and adjusted by the variable limitation of life support treatment (*). COPD: chronic obstructive pulmonary disease.

is in line with current scientific evidence, with clinical scenarios where AHF and COPD, and is less used in other scenarios with less evidence, such as pneumonia[1].

The most commonly used ventilation modality is the support pressure. This fact was already observed by Andreu-Ballester et al.[27], in our environment, although the study is a survey. Considering that AHF accounts for 38% of our patients, this fact is striking, since Continuous positive airway pressure (CPAP) would be the first choice in this scenario, because of its ease of use[28]. This discordance could be due to the high prevalence of respiratory insufficiency hypercapnia, since this data coincides with the aforementioned study, where up to 90.5% present this type of respiratory insufficiency.

The effectiveness of NIV is high. A registry performed by Cabrini et al.[29] shows 129 episodes of NIV performed outside the ICU, in a third level hospital and by a specialized team, and obtained a 77.5% overall success, a result very similar to ours. However, only 41% of the cases were EMSs and in this subgroup the response to NIV was higher, of 87% in these patients. The success of the NIV in the EMS determines its withdrawal in the service itself in more than 80% of cases. This fact seems to us logical in the AHF since the time of NIV is short. As described by Carratala et al.[26], the treatment time of NIV in AHF is 4.25 (2.54) hours. However, it is less explicable in COPD, which requires longer NIV. Iglesias Lepine et al.[25] found an average duration of NIV in this scenario of 35 (21) hours. Therefore, a lack of continuity of care resources in these patients is evident in most centres, which forces patients to stay longer to patients in the ED.

The mortality in the emergency room was 7.5%, but the hospital mortality was higher, 21.4%. This high mortality cannot be explained only by the mortality of AHF and COPD. In the AHF, EAHFE31 records a hospital mortality rate of 7.6%, which reaches 9.4% at 30 days and we know that the use of NIV in these patients identifies a higher risk profile. In COPD, in-hospital and 60-day mortality is 11% and 20%, respectively[32]. We believe that one aspect that can explain this high mortality is the high presence of patients with LSTL, which in our series reached 42.9%. LSTL, as the study by Azoulay et al.[33] shows, is associated with worse survival outcomes in NIV. This study, conducted in 54 intensive care units in France and Belgium analysed a total of 708 patients receiving NIV, identified a group of 134 (18.9%) patients who were instructed not to intubate and compared with the 574-patient group Without this limitation. Hospital mortality was 44% and 12%, res-

pectively (p <0.0001). Another study by Schettino et al.[34], which analysed 131 episodes of NIV in patients with non-intubation order and in different locations (EMS, critical unit or conventional ward), showed a total hospital mortality of 64.9% For scenarios was 39% in AHF, 37.5% in COPD, 86% in hypoxemic respiratory failure, 77% in post-intubation failure, and 68% in hypercapnic respiratory failure in patients without COPD. In this study, albumin is predicted to be a predictor of mortality ≤ 2.5 g/dl and > 35 points in the Simplified Acute Physiology Score (SAPS) II[34].

In relation to the high percentage of patients with LSTL, which is the only variable in our registry related to higher hospital mortality, it is possible to say that LSTL was assessed according to the criteria of the physician who indicated NIV, a critical aspect for emergency physicians. Studies show that the LSTL decision or non-intubation order is influenced by many aspects. On the one hand, aspects specific to the patient, and on other hand, the doctor's emotional aspects, such as a not optimistic personality or structural aspects[35,36]. There is the definition of terminal or palliative patient, in cardiac insufficiency[37] and in COPD[38], as a non-tributary patient to invasive measures, that is, non-tributary to orotracheal intubation. This is where NIV is the therapeutic ceiling. There is also evidence in scenarios such as hypercapnic respiratory insufficiency of the benefit of NIV in patients with LSTL[39]. But consensus documents are needed to define which LSTL patient will benefit most from a NIV. All patients with LSTL should be evaluated if NIV is indicated, but not all patients with LSTL have NIV. What we can say is that in our study when comparing the hospital mortality of the different scenarios and adjust the results by the LSTL variable, there were no statistically significant differences. It is essential to carry out studies in this population that provide us with evidence of the profile of the patient with LSTL who will have a real benefit of NIV.

The VNICat registry has a number of limitations. One of them is that the use of NIV is probably not homogeneous in all EMS hospitals because the indication depends primarily on the experience of the medical team, since it requires learning and training. Another limitation is that the reference population of each center may lead to greater or lesser use of NIV and the modality used, since there may be areas with a higher prevalence of COPD patients with hypercapnia, where NIV is used more with PS modality, or areas with more presence of patients with LSTL. One limitation is that high and low complexity centres participate in the registry, which may present differences in available resources and therefore condition the completion of NIV in emergency rooms or in adjacent units. Another limitation is related to the lack of gasometrical and clinical evolution parameters that could explain the evolution of these patients, but was not the objective of the present study. Finally, we know that there is a mixed decompensation percentage that is not reflected in our registry and may act as a confounding factor. However, despite these limitations, the strength of the study lies in the fact that it is multicentric, with consecutive inclusion and therefore gives real results of the NIV currently performed in emergencies.

In conclusion, the VNICat registry provides information of interest to the NIV that is performed in the prehospital and hospital emergency, highlighting previously unknown characteristics of the use of this technique in our environment and opens future research routes, especially in the field of the LSTL.

Conflicting interests

The authors declare no conflict of interest reated to this article.

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Ethical Responsibilities

The study was approved by the Comité de Ética e Investigación Clínica del Hospital Universitari de Bellvitge, Barcelona.

Informed consent was obtained from participants.

All authors have confirmed the maintenance of confidentiality and respect for patients' rights in the author's responsibilities document, publication agreement and assignment of rights to EMERGENCIAS.

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