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ORIGINAL RESEARCH

Long-Term Home Non-Invasive Ventilation in Patients with Severe COPD with Hypercapnic Respiratory Failure: Impact on Long-Term Survival, Exacerbations and Mortality Related Factors

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Background: Non-invasive ventilation (NIV) improves outcomes in acute life-threatening hypercapnic respiratory failure due to exacerbations of COPD (ECOPD), but the benefits of long-term home NIV (LTH-NIV) for managing hypercapnic chronic respiratory failure (CRF) in COPD remain unclear.

Purpose: 1) To assess the long-term survival of severe COPD patients with hypercapnic CRF started on LTH-NIV and mortality related factors; 2) To evaluate the impact of LTH-NIV on ECOPD and hospital admissions at follow-up.

Patients and Methods: COPD patients who started LTH-NIV between January 2009 and December 2018 were included. Medical records and clinical outcomes were retrospectively reviewed.

Results: Forty-four COPD patients (mean [SD] age 66.5 [10.4] years, 81.8% men) with severe airflow obstruction (mean [SD] FEV_1 36 [16] % of predicted), hypercapnic CRF (mean [SD] $PaCO_2$ 60.8 [9.2] mmHg) and exacerbator phenotype (mean [IQR] moderate-severe ECOPD 3 [3] in previous year) were included. Median survival from LTH-NIV was 100.3 months. Survival at one, three and five years was 86.4%, 72.7% and 68.2%, respectively. In a multivariate Cox regression model, patients with a significantly increased risk of death were those with older age, lower absolute FVC, more hospitalisations and especially those adapted to LTH-NIV in the acute phase (HR 3.67 (IC 1.04–13), $p<0.05$). LTH-NIV allowed an estimated mean reduction in ECOPD of 39.7% (65.2% in hospitalisations) at 12 months and 57.4% (81% in hospitalisations) at 24 months.

Conclusion: The survival rate of COPD patients with hypercapnic CRF on LTH-NIV is currently high (>50% at 5 years). Adaptation to LTH-NIV in the stable phase is the most important prognostic determinant and should be considered especially in patients with more hospitalisations and lower FVC values. Initiation of LTH-NIV reduces moderate to severe ECOPD at follow-up.

Keywords: long-term home non-invasive ventilation, COPD, chronic respiratory failure, exacerbations, survival, mortality

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic progressive lung disease characterised by non-reversible airflow obstruction and intermittent exacerbations.[1] While the role of acute non-invasive ventilation (NIV) has been shown to improve outcomes in acute life-threatening hypercapnic respiratory failure due to COPD exacerbations,[2,3] the evidence for the clinical effectiveness of long-term home NIV (LTH-NIV) for the management of COPD with hypercapnic chronic respiratory failure (CRF) is less clear.[3] The ERS Task Force recommends LTH-NIV in two different clinical situations: 1.- patients with chronic stable hypercapnic COPD and 2.- patients with COPD following a life-threatening episode of acute hypercapnic respiratory failure requiring acute NIV, if hypercapnia persists after the acute

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episode.[3] However, currently there is a low level of evidence on the impact of LTH-NIV on survival or the number of exacerbations in patients with COPD and hypercapnic CRF, mainly due to the heterogeneity of the trials conducted to date.[4,5] For this reason, the optimal time to start LTH-NIV, the ventilating strategies and the device settings used also need to be refined.[5] Furthermore, there are few data reporting long-term survival of COPD patients using LTH-NIV[6–9]

In view of the above, the main objective of the present study is to assess the long-term survival of a cohort of patients with severe COPD and hypercapnic CRF started on LTH-NIV and the factors associated with this mortality. Among these factors, the clinical situation in which LTH-NIV is initiated (stable versus acute) may have an impact on outcomes. A secondary objective is to evaluate the impact of LTH-NIV initiation on the number of exacerbations and hospital admissions over the following 2 years.

Materials and Methods

Study Design and Participants

COPD patients (FEV1/FVC ratio <0.7) with optimized medical therapy as stated by Global Initiative for Chronic Obstructive Lung Disease (GOLD),[1] who initiated LTH-NIV between January 2009 and December 2018 were included. Patients were routinely controlled at the Respiratory Day Care Unit of Sabadell Hospital.[10] Decision to initiate LTH-NIV was based on a comprehensive clinical and physiological assessment by the same team of pulmonologists and a physiotherapist with experience in home ventilation based on patient symptoms, arterial blood gas and lung function test results. Medical data and clinical outcomes were prospectively recorded and retrospectively analyzed. This study complied with all applicable laws regarding the protection of human subjects, in accordance with the Declaration of Helsinki.

Outcomes

The primary outcome was to assess overall survival since initiation of LTH-NIV and factors associated with mortality. Moderate-to-severe COPD exacerbations (ECOPD), respiratory hospitalisations and length of hospital stay in the 12 months before LTH-NIV and 2 years after initiation of LTH-NIV were assessed as secondary outcomes.

Home NIV Initiation and Titration

Patient selection was in line with published guidelines.[3] LTH-NIV could be initiated following a life-threatening ECOPD with acute hypercapnic respiratory failure (AHRF) requiring acute NIV and hospitalisation, if hypercapnia persisted following the acute episode. For chronic stable hypercapnic COPD, LTH-NIV was initiated at the Respiratory Day Care Unit as outpatients during daytime as published elsewhere.[11] NIV settings were titrated to normalise or at least cause a significant reduction of $PaCO_2$ (−20%). Interface selection (either oro-nasal or nasal) was based on patient comfort and air leak control. Ventilation was delivered using pressure support mode and supplementary oxygen was applied through the ventilator whenever necessary. NIV settings and oxygen flow rate were titrated to control hypoventilation and hypoxemia aiming to ideally maintain SpO_2 above 90% and to normalize CO_2. Patients and their care providers were trained in order to be able to put on, adjust and take off the interface and manage the ventilator main functions. LTH-NIV efficacy and adherence after titration were monitored by the review of the ventilator records and with a nocturnal pulse oximetry.

Clinical, Ventilator Data and Follow-Up

All patients underwent the same scheduled clinical assessments at the Respiratory Day Care Unit by the same team of pulmonologists prior to and following LTH-NIV. COPD treatment, pulmonary function test results, arterial blood gases and use of home oxygen therapy were recorded prior to initiate LTH-NIV. A short-term follow-up visit 1 month after LTH-NIV initiation was performed in order to assess adherence, potential difficulties and adverse events related to therapy. Afterwards monitoring visits were conducted every 3 to 4 months throughout the follow-up in the Respiratory Day Care Unit with a Medical call center for unscheduled visits due to exacerbations or problems with the ventilator.[10] In each visit arterial blood gases or capnography under LTH-NIV were evaluated alternately. In all visits efficacy and

adherence were monitored by the regular review of the ventilator records and interface and ventilator settings were re-adjusted if needed. The number of ECOPD, hospitalisations for respiratory disease and length of hospital stay were recorded 12 months before and 2 years after the start of LTH-NIV.

Definition and Treatment of Exacerbations

ECOPD was defined as a sustained worsening of the patient's condition from the stable state and beyond normal day-to-day variations, of acute onset, and requiring a change in regular treatment (antibiotics with or without corticosteroids, with or without hospital admission) in a patient with underlying COPD.[12] ECOPD were attended from Monday to Friday (8:00 AM to 5:00 PM) at the Respiratory Day Care Unit, always by the same team of pulmonologists.[10] Outside these hours, ECOPD were attended at the emergency department or by the general practitioner. Decisions regarding hospital admission were made in accordance with clinical practice guidelines.[1]

Statistical Analysis

Mean ± SD or median (interquartile range [IQR]) was used to summarise continuous variables where appropriate, and percentages and frequencies were used for categorical variables. The number of exacerbations, hospitalisations and days in hospital were corrected for the length of follow-up. Repeated measures ANOVA was used to estimate the population mean of exacerbations, number of hospitalisations and length of hospital stay at different time points. Univariate analysis was performed using the $\chi 2$ test for categorical variables and the comparison of means test for quantitative parameters to determine variables associated with mortality at the end of the study. The Kaplan-Meier method was used to estimate survival times and functions, and the Log rank test was used to compare survival curves. Finally, to determine the factors associated with survival in multivariate analysis, a Cox regression model was constructed, selecting the variables that were statistically significant in univariate survival analysis and that improved the model fit. Variables were chosen based on biological plausibility and clinical relevance to ensure meaningful interpretation. To minimize the risk of overfitting, we applied L2 regularization and internally validated the model performance using 5-fold cross-validation.

Results

Patients

A total of 44 patients (mean [SD] age of 66.5 [10.4] years, 81.8% men) who initiated LTH-NIV were included. The cohort had severe COPD as evidenced by severe airflow obstruction (mean [SD] FEV_1 of 36 [16] % of predicted) and hypercapnic respiratory failure (mean [SD] $PaCO_2$ of 60.8 [9.2] mmHg with an exacerbator phenotype (mean [IQR] moderate-severe ECOPD were of 3 [3] and hospitalisations requiring acute NIV the year prior to LTH-NIV were 1 [1] respectively). Thirty-one patients (70.4%) received long-term oxygen therapy (LTOT) and 20 patients (45.5%) were transitioned from continuous positive airway pressure (CPAP) therapy to LTH-NIV. Clinical and functional baseline variables appear in Table 1.

Ventilation Data, Adjusting of Parameters, and Compliance

Of the total cohort, 30 patients (68.2%) were adapted to LTH-NIV in acute phase following an ECOPD (100% hospitalized). The remaining 14 patients (31.8%) were adapted in stable phase (86% outpatient, in the Respiratory Day Care Unit). Ventilatory support was delivered in spontaneous-timed mode in all cases. The most commonly used interface was oro-nasal, employed in 75% of patients during the adaptation phase, increasing to 86% by the end of follow-up. The remaining patients used nasal interfaces. The initial mean (IQR) inspiratory positive airway pressure (IPAP) was 19 (4) cmH_2O, and expiratory positive airway pressure (EPAP) was 6 (3) cmH_2O. At the end of follow-up, IPAP and EPAP values were 20 (3.5) and 7 (3) cmH_2O, respectively. The mean back-up respiratory rate remained constant at 12 breaths per minute throughout the study. Additionally, 35 patients (79.5%) required oxygen supplementation through the ventilator. All patients completed the scheduled clinical assessments at the Respiratory Day Care Unit, with the exception of one patient who discontinued follow-up after undergoing lung transplantation. Compliance with LTH-NIV was high: 95.5% of patients were adherent, as confirmed by systematic review of ventilator data showing

Table 1 Baseline Variables COPD Patients Who Started LTH-NIV and Their Odds Ratio for Mortality

	Total N=44	OR for Mortality	95% IC	*p value*
Age initiation LTH-NIV, mean ± SD, years	66.6 ± 10.4	1.04	1.01–1.08	*<0.05*
Acute phase adaptation to LTH-NIV n(%)	30 (68.2)	2.60	1.08–6.28	*<0.05*
LTOT prior LTH-NIV	31 (70.4)	2.27	0.95–5.18	*0.06*
MRC dyspnoea score, mean	2.7	1.09	0.67.1.76	*ns*
BMI, kg/m^2	32 ± 7.5	0.927	0.88–0.97	*<0.01*
ADO index[13]	5.3 ± 1.2	1.97	1.30–2.97	*<0.01*
Active smokers n (%)	8 (18.2)	1.74	0.20–13.30	*ns*
Pack-years	57.7 ± (27.2)	1	0.98–1.01	*ns*
Lung function, mean ± SD				
FVC, absolute value, L	2.14 ± 0.7	0.446	0.22–0.88	*<0.05*
FVC, % predicted	55.3 ± 16.6	0.975	0.95–1.00	*0.055*
FEV_1, absolute value, L	0.9 ± 0.4	0.278	0.09–0.79	*<0.05*
FEV_1, % predicted	36.2 ± 16.5	0.976	0.95–1.01	*ns*
FEV_1/ FVC	46.6 ± 13.3	0.98	0.94–1.01	*ns*
Respiratory exacerbations 12-month prior LTH-NIV, median (IQR)				
Total excerbations	3 (3)	1.26	1.04–1.54	*<0.05*
Hospitalisations	2 (2)	1.29	1.03–1.60	*<0.05*
Hospitalisations requiring acute NIV	1 (1)	1.26	0.86–1.84	*ns*
Hospital stay, days	22 (32)	1.01	1.00–1.02	*<0.05*
Gas exchange in stability prior LTH-NIV, mean ± SD				
pH	7.38± 0.05	0.98	0.87–1.11	*ns*
PaO_2, mmHg	56.1 ±7.9	1.02	0.99–1.04	*ns*
$PaCO_2$, mmHg	60.8 ±9.2	1.02	0.99–1.07	*ns*
$HCO3^-$, mmol/L	34 ±4.5	1.06	0.97–1.15	*ns*
Gas exchange after LTH-NIV titatrion, mean ± SD				
pH	7.39 ± 6.9	0.96	0.86–1.09	*ns*
PaO_2, mmHg	57.6 ± 7.6	0.98	0.94–1.03	*ns*
$PaCO_2$, mmHg	49.2 ±6.8	1.02	0.96–1.08	*ns*
$HCO3^-$, mmol/L	29.5 ±3.2	1.02	0.9–1.06	*ns*

Notes: Continuous variables are presented as mean ± standard deviation and categorical variables as No (%) unless otherwise indicated.

Abbreviations: LTH-NIV, long-term home non-invasive ventilation; LTOT, long-term oxygen therapy; MRC Medical Research Council dyspnoea score; BMI, Body Mass Index; ADO index[13] (age, dyspnoea, airflow obstruction); FEV_1, forced-expiratory volume in 1 second; FVC, forced vital capacity; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen.

a mean daily usage of ≥ 4 hours. Only two patients (4.5%) failed to meet the minimum compliance threshold at all scheduled assessments.

Survival

The median survival time since the adaptation of the LTH-NIV was 100.3 months (95% confidence interval [CI], 73.9–126.7). Survival at first, third and fifth years was 86.4%, 72.7% and 68.2% respectively. The follow-up period ranged from 3 to 14 years. Fourteen patients (31.8%) remained alive at the end of the follow-up. Of the 30 patients who died during follow-up, 20 (66.7%) died in the hospital and 10 (33.3%) at home. The main cause of death was respiratory in 16 (53.3%) patients followed by oncological disease in 3 (10%). In 7 (23.3%) cases the cause was unknown as they were home deaths.

Table 2 Effect of LTH-NIV on Mortality in Multivariate Cox Regression Analysis

	Multivariate Analysis	
	HR (95% CI)	***p value***
Age initiation LTH-NIV	1.05 (1.015–1.09)	*<0.01*
Hospitalisations	1.383 (1.035–1.849)	*<0.05*
Baseline FVC, absolute value, L	0.173 (0.06–0.49)	*<0.01*
Adaptation to LTH-NIV, acute versus stable phase	3.673 (1.04–13)	*<0.05*

Abbreviations: HR, Hazard ratio; IC, confidence interval; LTH-NIV, long-term home non-invasive ventilation; FVC, forced vital capacity.

Clinical and functional variables and their odds ratios for mortality are shown in Table 1. The variables that were associated with higher mortality rates were: older age, lower Body Mass Index (BMI), higher ADO multi-component index (age, dyspnoea, airflow obstruction),[13] worse lung function (FVC and FEV_1), previous moderate-severe ECOPD and adaptation to LTH-NIV in the acute phase. Blood gas values before and after initiation of LTH-NIV were not associated with mortality.

In the multivariate Cox regression model, patients with significantly increased risk of death after initiation of LTH-NIV were those with older age, lower absolute FVC values, more hospitalisations in the previous year, and especially those adapted to LTH-NIV in the acute phase HR 3.67 (IC 1.04–13), p<0.05. See Table 2. Model performance was stable across different penalization strengths, with concordance index (C-index) values ranging from 0.59 to 0.62 in 5-fold cross-validation, indicating consistent predictive ability and minimal risk of overfitting.

Figures 1–3 show the Kaplan–Meier curves for survival according adaptation to LTH-NIV in the acute versus stable phase (Figure 1), FVC (> or ≤ 50%) (Figure 2) and number of hospitalisations in the previous year (< or ≥ 2) (Figure 3).

Exacerbations

The 44 study participants had a total of 126 ECOPD in the 12 months prior to starting LTH-NIV; 95 (75.4%) were severe and required hospitalisation, of which 28 (29.5%) required NIV in the acute phase with a total of 1126 days of

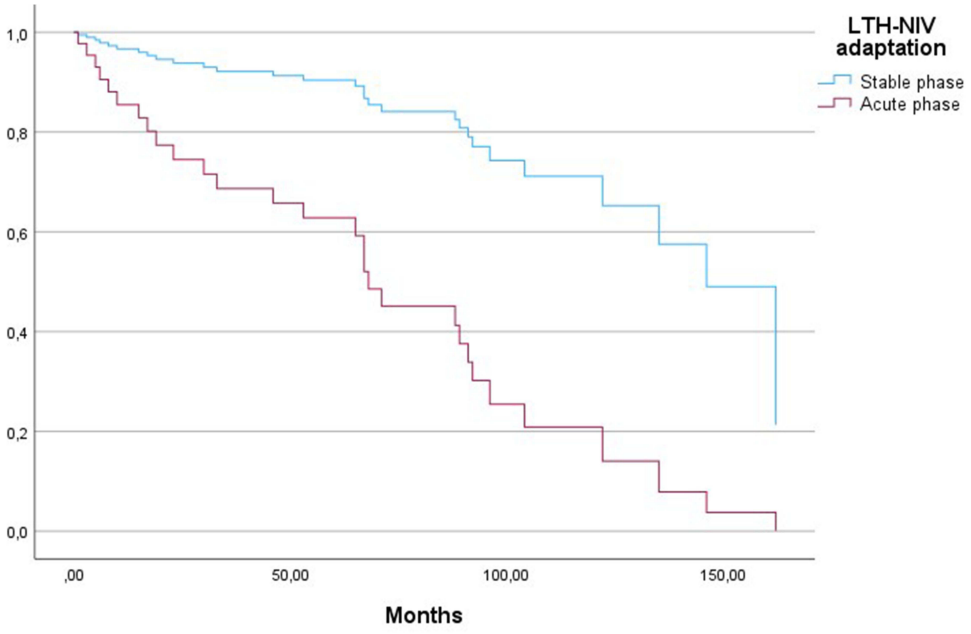

Figure 1 Kaplan-Meier curves for survival according to LTH-NIV adjustment during an acute exacerbation versus disease stability.

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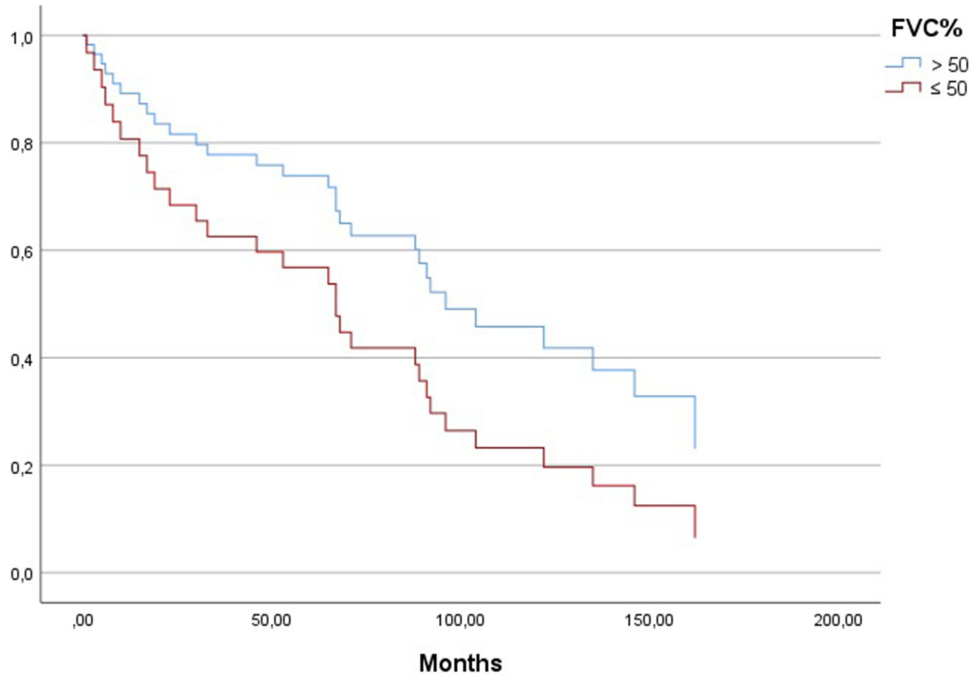

Figure 2 Kaplan–Meier curves for survival by forced vital capacity (> or ≤ 50).

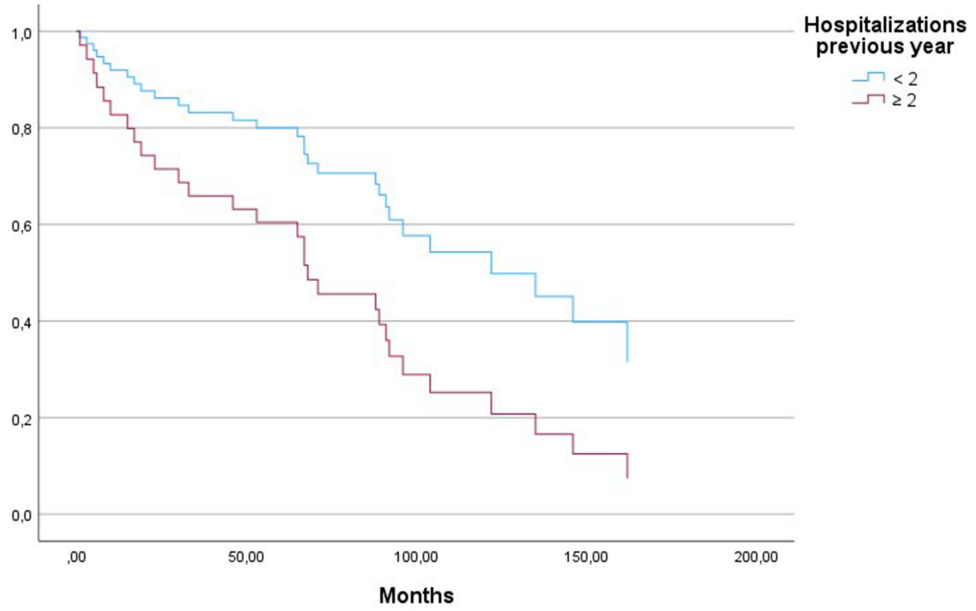

Figure 3 Kaplan-Meier curves for survival according to number of hospitalisations in the previous year (< or ≥ 2 hospitalisations).

hospitalisation (Table 3). LTH-NIV allowed an estimated mean reduction in ECOPD of 39.7% at 12 months and 57.4% at 24 months compared to baseline. Greater reductions were observed in hospitalisations, which decreased by 65.2% at 12 months and 81% at 24 months (Figure 4), and in mean respiratory hospital days, which decreased by 53.3% and 80.9% at these two time points.

Patients adapted to LTH-NIV in the stable phase had a significantly longer time to first ECOPD than those adapted in the acute phase ($p<0.05$) (Figure 5).

Table 3 Moderate to Severe exacerbations of COPD in the 12 months Prior to LTH-NIV and in the 2 years After Starting LTH-NIV

	No LTH-NIV	LTH-NIV		
	Prior 12 Months (n=44)	**0-12 Months (n=44)**	**12-24 Months (n=38)**	***p value***
ECOPD moderate-to-severe				
Total Median (IQR) per year Median (IQR) per month	126 3 (3) 0.25 (0.25)	76 1.50 (3) 0.125 (0.23)	53 1(2) 0.08 (0.19)	*p<0.01*
Hospital admissions				
Total Median (IQR) per year Median (IQR) per month	95 2 (2) 0.16 (0.17)	33 0 (2) 0 (0.17)	18 0 (1) 0 (0.08)	*p<0.01*
Hospital stay, days				
Total Median (IQR) per year Median (IQR) per month	1126 22.50 (32) 1.88 (2.96)	525 0 (15) 0 (1.23)	215 0 (10) 0 (0.83)	*p<0.01*

Discussion

The main finding of this study is that adaptation to LTH-NIV at a stage of clinical stability is associated with a lower risk of mortality in COPD patients with hypercapnic CRF compared with those adapted after life-threatening ECOPD requiring acute NIV. To a lesser extent, a lower number of hospitalisations in the previous year and higher absolute FVC at baseline were also associated with a lower risk of death.

The median survival observed in our study population on LTH-NIV was 100 months, or 8.3 years, with 1-year and 5-year survival rates of 86% and 68%, respectively. The observed survival is prolonged and exceeds the results of previous observational studies. Although the cohorts studied are almost contemporary, the fact that our cohort is the most recent is likely to play a role in the higher survival observed. Survival data are mainly derived from cohort studies of patients with LTH-NIV and hypercapnic CRF secondary to various diseases. A European study conducted between 2008

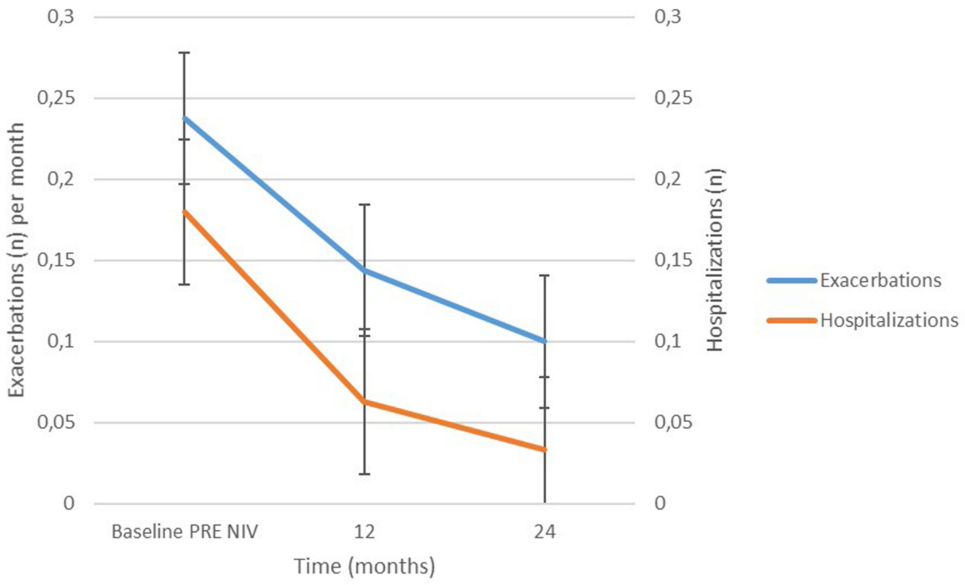

Figure 4 Moderate-to-severe exacerbations and hospitalisations in the year before starting LTH-NIV compared with the first two years after adaptation.

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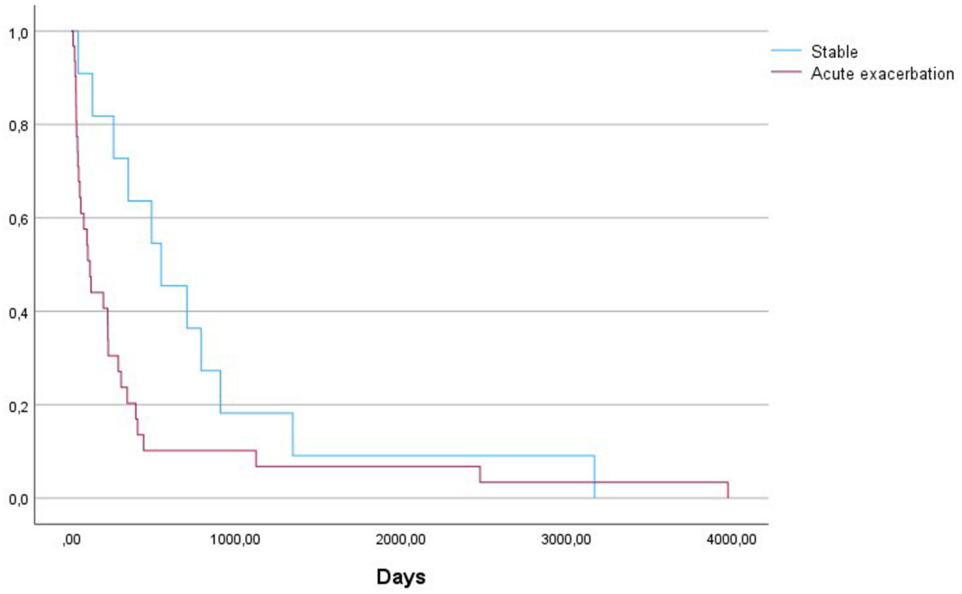

Figure 5 Time to first exacerbation after adaptation to LTH-NIV according to adaptation in the stable phase compared with the acute phase during the hospital stay.

and 2014 in two European centres in France and the UK reported a median survival of 2.7 years in patients with obstructive airways disease (6.6 years in patients with COPD-obstructive sleep apnoea overlap) on LTH-NIV therapy.[6] A Finnish study of patients who started LTH-NIV between 2012 and 2015 documented a median survival of 4.4 years in people with COPD.[7] The 5-year survival rate of COPD patients enrolled in a home mechanical ventilation programme in Chile between 2008 and 2017 was reported to be 52%.[9] The only study conducted specifically in COPD patients evaluated a cohort of 72 COPD patients who started LTH-NIV between 2010 and 2017 in a Portuguese centre, with a median survival time of 79 months (6.6 years).[8] The most common cause of death was respiratory, as we had previously observed in a cohort of patients with severe COPD.[14] The main risk factor associated with a significant reduction in survival in the COPD patients studied was acute phase LTH-NIV adaptation after life-threatening ECOPD during hospitalisation, highlighting the importance of stable phase adaptation for prognosis. The only randomised clinical trial (RCT) to show a mortality benefit of adapting LTH-NIV in stable COPD patients with hypercapnic CRF is the study by Köhnlein et al.[15] This trial randomised 195 patients with stable severe COPD and hypercapnic CRF to LTH-NIV plus LTOT versus LTOT alone and found a 1-year mortality of 12% in the LTH-NIV-LTOT group versus 33% in the LTOT alone group.[15] The 1-year mortality rate in our study (14%) is very similar to that reported in this study. Conversely, LTH-NIV could be adapted after a life-threatening ECOPD requiring acute NIV to avoid re-admission to hospital and potentially reduce morbidity and mortality. To date, two larger RCTs have examined the impact of LTH-NIV on mortality reduction as a bridging treatment from hospital to home, with different results due to different designs and timing of adaptation. Initially the RESCUE trial[16] included 201 COPD patients admitted to hospital with a life-threatening episode of acute hypercapnic ECOPD and prolonged hypercapnia (mean PaCO2 ~48 mmHg) more than 48 h after cessation of acute NIV and were randomised to receive LTH-NIV plus LTOT or LTOT alone. At 1 year, there was no difference between the two groups in the primary outcome of time to readmission or death. The early in-hospital assessment and mild hypercapnia after the acute event may have led to the inclusion of a subset of patients with likely spontaneously reversible hypercapnia and may explain the lack of improvement in mortality in the LTH-NIV plus LTOT group. Later, the HOT-HMV trial[17] studied 116 COPD patients with persistent hypercapnia ($PaCO_2$ >53 mmHg) at 2–4 weeks after a life-threatening ECOPD with acute CRF treated with acute NIV and were randomised to receive LTH-NIV plus LTOT or LTOT alone. The LTH-NIV plus LTOT group resulted in an increased time to readmission or death within 12 months. Over the 12 months of the study there was no significant effect on mortality although the trend favoured the LTH-NIV plus LTOT group. The higher level of $PaCO_2$ at enrolment and the timing selection of patients with persistent hypercapnia at 2–4 weeks following a life-threatening ECOPD were major determinants of the enhanced outcome in

the HOT-HMV trial versus de RESCUE trial.[16,17] Unlike these major COPD clinical trials, which excluded patients with morbid obesity and obstructive sleep apnea, our real-life study included all COPD patients starting LTH-NIV.[15–17] In relation to the results observed in the present study, and reinforcing the impact on survival when comparing adaptation to LTH-NIV in the stable phase with the acute phase, other observational studies have shown similar results.[6,8] In a cohort study of COPD patients with hypercapnic CRF and the need for LTH-NIV therapy, patients who started LTH-NIV during an acute exacerbation showed reduced survival compared with those who started LTH-NIV during disease stability (median survival 37 months versus 100 months).[8] Therefore, early and stable initiation of LTH-NIV can be considered to achieve a survival benefit in patients with severe COPD and hypercapnic CRF.

In addition, other risk factors associated with mortality were identified: age, previous hospitalisations and a lower absolute FVC at baseline were also associated with significantly worse survival. Age has been associated with mortality in previous cohort studies, both in patients with severe COPD[14] and in patients on LTH-NIV therapy for hypercapnic CRF secondary to multiple diseases.[6] Notably, the number of hospitalisations in the year before to the onset of LTH-NIV is the second most important factor influencing prognosis. Hospitalisation is known to have a negative impact on the prognosis of COPD and has been associated with an increase in mortality.[18] Furthermore, in a multicentre cohort study of severe COPD patients following a respiratory day-care programme, persistent hospitalisations (>2) were also associated with increased mortality.[10] Finally, a lower absolute FVC at baseline without a correlation with higher BMI values was also associated with higher mortality rates, which is considered a more stringent parameter of air trapping in these severe COPD patients with higher mortality rates. Blood gas values before and after initiation of LTH-NIV were not associated with mortality. Therefore, we cannot say that a ventilation strategy focused on greater $PaCO_2$ reductions is associated with a better prognosis. In this regard, European clinical guidelines reflect the very low certainty of the available evidence and provide only conditional recommendations for $PaCO_2$ reduction and ventilation strategies.[3] We would also like to highlight the impact of LTH-NIV in reducing the number of moderate to severe ECOPD, admissions and days spent in hospital in the first 2 years after its introduction. In the second year, the impact on reducing hospital admissions and length of stay was even greater than in the first year, reaching a significant 80% compared with the year before LTH-NIV was introduced. Patients adapted to LTH-NIV in the stable phase had a significantly longer time to first ECOPD than those adapted in the acute phase, highlighting the importance of adapting to LTH-NIV in the stable phase. This finding is consistent with some of the previous RCTs with 1-year follow-up. In the study by Kohnlein et al,[15] a reduction in emergency hospital admissions was observed in the NIV group compared with the control group (2.2 vs 3.1 ECOPD per patient per year). Murphy et al also found a reduction in the annual frequency of ECOPD in the NIV group compared with the control group (3.4 vs 5.1 exacerbations per patient per year).[17] An observational study with 2 years of follow-up also found a significant reduction in the number of acute ECOPD and hospitalisations after the introduction of LTH-NIV.[8]

This study has some limitations related to its design. Due to the retrospective nature of the study, there are some data that could not be analysed, such as the 6-minute walk test, which was available in very few patients and which is part of the BODE prognostic index and was an independent predictor of survival in another cohort of COPD patients on LTH-NIV therapy.[8] In addition, the single-centre design reflects our local practice and it must be taken into account that the decision to start LTH-NIV therapy and the device settings depend on the clinical decisions of the attending pulmonologists. However, the strength of the study is its real-life design, including an unselected sample of patients with severe COPD and LTH-NIV therapy, providing practical information for clinicians caring for similar patients.

Conclusion

The survival rate of patients with COPD and hypercapnic CRF on LTH-NIV is currently high, over 50% at 5 years. Adaptation to LTH-NIV in the stable phase is the most important prognostic determinant and should be considered especially in those with two or more hospitalisations in the previous year and with lower FVC values (≤50%). This strategy may increase survival and reduce moderate to severe ECOPD.

Artificial Intelligence Involvement

The author did not use any artificial intelligence language models for generating the text.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of Sabadell Hospital, Institut d'Investigació e Innovació I3PT 2023/5053. Informed consent was obtained from all living patients. For deceased patients, the Institutional Review Board waived consent for the use of anonymised medical data in this retrospective study, in accordance with ethical and legal guidelines.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare not to have any conflicts of interest that may be considered to influence directly or indirectly the content of the manuscript.

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