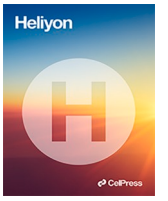
Heliyon 10 (2024) e26437

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Does $PaCO_2$ correction have an impact on survival of patients with chronic respiratory failure and long-term non-invasive ventilation?

Audrey Thomas [a,*], Sandrine Jaffré [a], Vianney Guardiolle [b], Tanguy Perennec [c], Frédéric Gagnadoux [d], François Goupil [e], Cédric Bretonnière [a], Vivien Danielo [a], Jean Morin [a], François-Xavier Blanc [a]

[a] Nantes Université, CHU Nantes, Department of Respiratory Medicine, l'institut du thorax, Nantes, France
[b] Nantes Université, CHU Nantes, Data Clinic, INSERM CIC 1413, Nantes, France
[c] Radiotherapy Department, West Cancer Institute, Saint Herblain, France
[d] Department of Respiratory and Sleep Medicine, Angers University Hospital, Angers, France
[e] Department of Respiratory Diseases, Le Mans General Hospital, Le Mans, France

ARTICLE INFO

Keywords:
Chronic obstructive pulmonary disease
Chronic respiratory failure
Non-invasive ventilation
Obesity-hypoventilation syndrome
Hypercapnia
Survival

ABSTRACT

Background and objective: Non-invasive ventilation (NIV) improves survival of patients with chronic respiratory failure (CRF). Most often, pressure settings are made to normalize arterial blood gases. However, this objective is not always achieved due to intolerance to increased pressure or poor compliance. Few studies have assessed the effect of persistent hypercapnia on ventilated patients' survival. Data from the Pays de la Loire Respiratory Health Research Institute cohort were analyzed to answer this question.

Study design and methods: NIV-treated adults enrolled between 2009 and 2019 were divided into 5 subgroups: obesity-hypoventilation syndrome (OHS), COPD, obese COPD, neuromuscular disease (NMD) and chest wall disease (CWD). $PaCO_2$ correction was defined as the achievement of a $PaCO_2 < 6$ kPa or a 20% decrease in baseline $PaCO_2$ in COPD patients. The endpoint was all-cause mortality. Follow-up was censored in case of NIV discontinuation.

Results: Data from 431 patients were analyzed. Median survival was 103 months and 148 patients died. Overall, $PaCO_2$ correction was achieved in 74% of patients. Bivariate analysis did not show any survival difference between patients who achieved$PaCO_2$ correction and those who remained hypercapnic: overall population: $p = 0.74$; COPD: $p = 0.97$; obese COPD: $p = 0.28$; OHS: $p = 0.93$; NMD: $p = 0.84$; CWD: $p = 0.28$.

Conclusion: Moderate residual hypercapnia under NIV does not negatively impact survival in CRF patients. In individuals with poor tolerance of pressure increases, residual hypercapnia can therefore be tolerated under long-term NIV. Larger studies, especially with a higher number of patients with residual $PaCO_2 > 7$ kPa, are needed to confirm these results.

* Corresponding author. CHU Nantes, Service de Pneumologie, Hôpital G. et R Laënnec, Bd J. Monod, 44093 Nantes cedex 1, France.
E-mail address: audrey.thomas@ght85.fr (A. Thomas).

https://doi.org/10.1016/j.heliyon.2024.e26437
Received 18 May 2023; Received in revised form 11 February 2024; Accepted 13 February 2024
Available online 18 February 2024

1. Introduction

Long-term non-invasive ventilation (NIV) is a cornerstone in the treatment of chronic respiratory failure (CRF). NIV improves the quality of life, increases survival and decreases the number of hospitalizations in these patients [1–7]. It is used in patients with chronic obstructive pulmonary disease (COPD) in case of chronic hypercapnia or repeated hospitalizations for hypercapnic exacerbations [1,2,8]. The other approved indications are obesity-hypoventilation syndrome (OHS), kyphoscoliosis and neuromuscular diseases (NMD) [9,10].

Upon NIV initiation, one of the objectives of NIV is to normalize the partial pressure of carbon dioxide ($PaCO_2$) or, for COPD patients, to achieve a 20% decrease in $PaCO_2$ [1,11]. However, in practice, such a correction is not always achieved because of, poor compliance, increased leaks or poor tolerance of NIV. The current literature is contradictory about a potential effect of residual hypercapnia on survival under NIV.

Therefore, the aim of this study was to compare the survival of long-term ventilated patients depending on whether or not $PaCO_2$ correction was achieved.

2. Materials and methods

2.1. Patients and study design

This was a multicenter prospective cohort study. All included patients were from the French Pays de la Loire Respiratory Health Research Institute cohort study group (IRSR-PL). Inclusion criteria were: adult patients with CRF for whom long-term NIV was indicated and who had given their written consent.

Patients were included in three hospitals: Angers University Hospital, Nantes University Hospital, and Le Mans General Hospital, France, between September 2009 and February 2019.

They were divided into five subgroups according to the type of CRF: OHS (obesity [Body Mass Index (BMI) $\geq$ 30 kg/m^2] associated with diurnal hypercapnia [$PaCO_2 \geq 6$ kPa]), chest wall disease (CWD, kyphosis or scoliosis), NMD, COPD (presence of an incompletely reversible obstructive ventilatory defect [FEV1/FVC ratio $<$ 70%]), and obese COPD (incompletely reversible obstructive ventilatory defect associated with obesity [BMI $\geq$ 30 kg/m^2]). Patients with amyotrophic lateral sclerosis were not included in the study.

2.2. NIV initiation

NIV was initiated during a scheduled hospitalization, or after a stay in intensive care unit for respiratory decompensation.

Ventilation settings were adjusted according to the machine data, awakening arterial blood gases values, nocturnal oximetry, transcutaneous capnography, ventilatory polygraphy.

The initial objective was to achieve a $PaCO_2 < 6$ kPa. Inspiratory positive airway pressure was increased in increments of 2 cmH_2O, depending on the patient's tolerance, until achieving $PaCO_2$ correction. Expiratory positive airway pressure was increased in increments of 1 cmH_2O to correct obstructive events. The safety breathing rate was set by subtracting 2 from the patient's spontaneous breathing rate. When ventilation was not sufficient to correct hypoxemia, oxygen was added to NIV.

The various NIV devices used in this cohort were from Philips Respironics® (mainly Synchrony II, Trilogy 100, BIPAP A30 and A40) and ResMed® (mainly VPAP III ST, Stellar 150 and Lumis 150 ST). Different interfaces were used: nasal, nostril or oronasal mask, depending on patient's tolerance.

2.3. Follow-up

A follow-up visit was scheduled 6 months after NIV initiation. Pulmonary function tests and arterial blood gases (at rest, during the day, remotely from ventilation) were performed. In case of long-term oxygen therapy (LTOT), arterial blood gases were measured under usual oxygen flow. During that visit, compliance was assessed and averaged over the last month before the visit.

Patients were divided into subgroups depending on the $PaCO_2$ measured during the follow-up visit after NIV initiation. In OHS, obese COPD patients and patients with a restrictive pattern (NMD and CWD), a $PaCO_2 < 6$ kPa was considered as corrected. In COPD patients, $PaCO_2$ was considered as corrected if it was < 6 kPa or if it decreased by at least 20% compared to its pre-NIV value.

2.4. Ethical aspects

The IRSR-PL cohort study group was authorized by the National Commission on Computer Technology and Freedom (CNIL) on 07/04/2008 (no. 908 157). A positive advice was received from the Advisory Committee on Information Processing in Material Research (CCTIRS) on December 17, 2009.

The database was anonymous and coded, and was approved by the Ethics Committee of Angers University.

2.5. Data collected and statistical analyzes

Upon NIV initiation, the following data were collected: patients' age, gender, BMI, smoking status, use of LTOT, diabetes, dyslipidemia, cardiovascular comorbidities (arterial hypertension, rhythm disorders, coronary artery disease), the context in which NIV

was initiated, the settings, and arterial blood gases measured before initiating ventilation.

The endpoint was all-cause mortality. Follow-up was censored in case of NIV discontinuation. Data on mortality and NIV discontinuation were collected from the cohort provider (ASTEN SANTE), with a cut-off date of May 31, 2021.

The primary endpoint was the overall survival of patients, depending on whether or not $PaCO_2$ correction was achieved under NIV. The secondary endpoint was the survival according to CRF etiology (five subgroups), depending on $PaCO_2$ correction under NIV.

Statistical analyzes were performed using R software (version 3.6.1).

Data for quantitative variables were presented as a median [first quartile-third quartile]. Data for categorical variables were presented as a percentage.

Survival curves were estimated using the Kaplan-Meier method. The log-rank test was used to compare bivariate survival data.

The Cox model was used to calculate hazard ratios (HR); the variables were selected using the backward elimination method.

3. Results

3.1. Baseline patients' characteristics

Between 2009 and 2019, 656 patients were included in the IRSR-PL cohort. A total of 225 patients were excluded (no arterial blood gas measurement during follow-up, death or NIV discontinuation before the first follow-up visit, amyotrophic lateral sclerosis, cystic fibrosis, sequelae of tuberculosis, sequelae of thoracic surgery, bronchiectasis). Thus, data of 431 patients were analyzed.

Baseline patients' characteristics are presented in Table 1.

The largest group was the OHS group (39% of patients), followed by the obese COPD group (27% of patients), the NMD group (15% of patients), the COPD group (14% of patients) and the CWD group (6% of patients).

Patients with NMD were younger ($p = 0.001$). BMI was significantly higher in the OHS group ($p < 0.001$).

FEV1 was significantly lower in COPD and obese COPD patients ($p < 0.001$).

pH was significantly higher and $PaCO_2$ lower in the NMD subgroup ($p < 0.001$). $PaCO_2$ was significantly higher in obese COPD patients ($p < 0.001$). Proportion of patients with dyslipidemia, diabetes, or cardiovascular disease was higher in the OHS group (45%, 51%, and 82% of patients, respectively).

3.2. Settings, compliance, tolerance

NIV was initiated during a scheduled hospitalization in 54% of cases, after a stay in intensive care without invasive ventilation in 34% of cases and with invasive ventilation in 12% of cases. In the NMD group, NIV was initiated during a scheduled hospitalization in 72% of cases.

Table 1
Baseline patients' characteristics according to the type of chronic respiratory failure.

	COPD	Obese COPD	OHS	NMD	CWD	Total
	(n = 59)	(n = 117)	(n = 167)	(n = 64)	(n = 24)	(n = 431)
Age (years)	64 [59–68]	64 [62–66]	65 [61–67]	57 [51–64]**	66 [62–73]	64 [62–65]
Male gender (%)	71	65	53	52	46	58
BMI (kg/m^2)	24 [22–26]	37 [35–39]**	43 [42–44]**	29 [26–31]	22 [20–28]	37 [35–38]
Current or past smoking (%)	95	82	47	32	33	60
LTOT (%)	34	20	14	5	13	17
VC (% of predicted value)	67 [59–71]	75 [71–80]	84 [79–87]	53 [50–64]	51 [41–68]	73 [70–76]
FEV1 (% of predicted value)	34 [30–41]**	55 [51–59]**	80 [75–84]**	52 [47–64]	50 [38–61]	63 [58–66]
FEV1/VC ratio (%)	41 [35–48]**	59 [56–61]**	76 [75–77]	82 [77–85]	73 [70–82]	70 [67–71]
TLC (% of predicted value)	111 [98–122]	96 [90–99]	87 [83–90]	69 [62–75]	56 [44–69]	89 [86–91]
pH	7.35 [7.33–7.37]	7.35 [7.33–7.37]	7.37 [7.35–7.38]	7.40 [7.37–7.41]**	7.37 [7.33–7.40]	7.37 [7.36–7.37]
$PaCO_2$ (kPa)	8.00 [7.30–8.90]	8.13 [7.70–8.67]	7.44 [7.10–7.87]	6.60 [6.10–6.94]**	7.15 [6.50–8.54]	7.47 [7.30–7.80]
PaO_2 (kPa)	8.20 [7.47–8.90]	8.75 [8.40–8.94]	8.65 [8.39–9.00]	9.87 [9.40–10.67]	9.87 [8.14–12.40]	8.80 [8.60–9.00]

BMI: body mass index.
COPD: chronic obstructive pulmonary disease.
CWD: chest wall disease.
FEV1: forced expiratory volume in 1 s.
FEV1/VC: forced expiratory volume in 1 s relative to vital capacity.
LTOT: long-term oxygen therapy.
NMD: neuromuscular disease.
OHS: obesity-hypoventilation syndrome.
$PaCO_2$: partial pressure of carbon dioxide in the arterial blood at baseline.
PaO_2: partial pressure of dioxygen in the arterial blood at baseline.
TLC: total lung capacity.
VC: vital capacity.
*$p < 0.05$; **$p < 0.01$ (as compared with the overall population).

The ST (Spontaneous-Timed) mode was chosen in 99% of cases and the AVAPS (Average Volume-Assured Pressure Support) mode in 1% of cases. Facial masks were the most commonly used interface.

Median daily compliance was 7.1 h.

In our cohort, NIV was discontinued in 20% of patients who were classified as being at the end of follow-up. The proportion of NIV discontinuation was higher in the OHS group.

Median time between NIV initiation and the first follow-up visit was 5 months.

The ventilation settings and their tolerance are detailed in Table 2.

3.3. $PaCO_2$ correction

There was a significant decrease in $PaCO_2$ under NIV in each subgroup at the follow-up visit (Fig. 1).

$PaCO_2$ correction was achieved under NIV in 74% of cases (320 patients). In the remaining cases, $PaCO_2$ ranged between 6.21 kPa and 6.94 kPa (Table 3).

3.4. Overall survival

The median survival was 103 months (corrected $PaCO_2$: 96 months, 95% CI [77- not reached]; uncorrected $PaCO_2$: 128 months, 95% CI [70-not reached]; upper confidence limit not reached due to low number of events). The mortality rate was 34% (corrected $PaCO_2$: 111/320 patients; uncorrected $PaCO_2$:37/111 patients).

Bivariate analysis did not show any statistically significant difference in survival in the overall population between patients who achieved $PaCO_2$ correction under NIV and those who remained hypercapnic ($p = 0.74$) (Fig. 2).

In the overall population, multivariate analysis of factors associated with mortality showed that age (in years) was a poor prognostic factor (HR 1.05; 95% CI [1.03–1.06]) and that the absence of decline in vital capacity was a protective factor (HR 0.99; 95% CI [0.98–0.99]) (Table 4). The presence of hypercapnia under NIV did not significantly influence the survival, nor the delta of $PaCO_2$ change (difference between before and after NIV initiation).

3.5. Subgroups' survival

Bivariate analysis did not show any statistically significant difference in survival in each etiological subgroup between patients who achieved $PaCO_2$ correction under NIV and those who remained hypercapnic after NIV discontinuation (Table 5).

4. Discussion

In this 10-year multicenter cohort study of CRF patients, we showed no difference in survival depending on whether or not $PaCO_2$ correction was achieved after NIV initiation. No predictive factor of mortality other than age was identified.

Our cohort was large, with a predominance of patients in the OHS subgroup, as in the cohorts of Janssens et al. and Laub et al. [12, 13]. Other similarities were found compared to other CRF cohorts. In particular, patients in the OHS and obese COPD subgroups had a higher number of comorbidities (dyslipidemia, diabetes, cardiovascular comorbidities), patients in the NMD subgroup were younger,

Table 2
Settings, compliance and tolerance.

	COPD (n = 59)	Obese COPD (n = 117)	OHS (n = 167)	NMD (n = 64)	CWD (n = 24)	Total (n = 431)
Facial mask (%)	93	85	77	74	71	81
Nostril mask (%)	0	1	1	0	8	1
Nasal mask (%)	7	14	22	26	21	18
IPAP (cmH_2O)	20 [18–20]	22 [20–22]	22 [21–22]	19 [18–20]	19 [17–20]	20 [20–21]
EPAP (cmH_2O)	6 [5–6]	8 [8–9]	9 [8–10]	7 [5–7]	5 [5–8]	8 [8–8]
Frequency (cycles/min)	16 [15–16]	16 [15–16]	16 [16–16]	16 [16–16]	16 [16–16]	16 [16–16]
Compliance (hours/day)	7.5 [6.7–8.4]	7.1 [6.8–7.7]	7.0 [6.7–7.5]	6.9 [5.9–8.1]	7.9 [5.8–8.5]	7.1 [7.0–7.5]
NIV discontinuation (%)	19	14	25	19	20	20
- due to poor tolerance (%)	0	0	2	0	4	1
- due to poor compliance (%)	2	3	5	6	8	5
- due to improvement* (%)	7	6	10	5	4	7
- for another reason (%)	10	5	8	8	4	7

COPD: chronic obstructive pulmonary disease.
CWD: chest wall disease.
NMD: neuromuscular disease.
OHS: obesity-hypoventilation syndrome.
IPAP: inspiratory positive airway pressure.
EPAP: expiratory positive airway pressure.
[a]Includes patients on continuous positive airway pressure (CPAP) and those in whom NIV was discontinued due to lung transplantation.

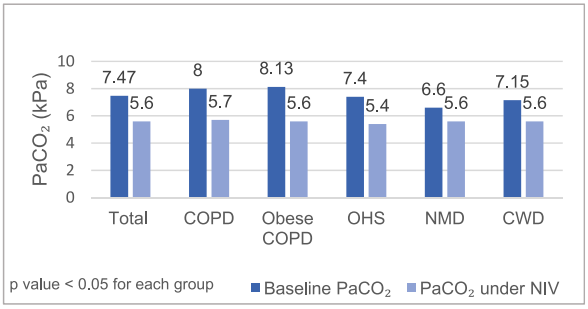


Fig. 1. Changes in $PaCO_2$ under NIV in the whole population and in each subgroup (comparison of values at baseline and at the follow-up visit). COPD: chronic obstructive pulmonary disease; CWD: chest wall disease; NMD: neuromuscular disease; NIV: non-invasive ventilation; OHS: obesity-hypoventilation syndrome; $PaCO_2$: partial pressure of carbon dioxide in the arterial blood.

Table 3
Proportion of patients achieving $PaCO_2$ correction under NIV at the follow-up visit, in the total population and in each subgroup. Corresponding median $PaCO_2$ values.

	COPD (n = 59)	Obese COPD (n = 117)	OHS (n = 167)	NMD (n = 64)	CWD (n = 24)	Total (n = 431)
Patients achieving $PaCO_2$ correction	50	77	132	44	17	320
$PaCO_2$ (kPa)	5.60 [5.40–5.85]	5.47 [5.30–5.50]	5.20 [5.10–5.30]	5.37 [5.20–5.50]	5.58 [5.40–5.60]	5.37 [5.30–5.47]
Patients not achieving $PaCO_2$ correction	9	40	35	20	7	111
$PaCO_2$ (kPa)	6.40 [6.08–7.60]	6.40 [6.27–6.54]	6.36 [6.20–6.54]	6.21 [6.10–6.54]	6.94 [6.10–7.87]	6.40 [6.27–6.40]

COPD: chronic obstructive pulmonary disease.
CWD: chest wall disease.
NMD: neuromuscular disease.
OHS: obesity-hypoventilation syndrome.
$PaCO_2$: partial pressure of carbon dioxide in the arterial blood.

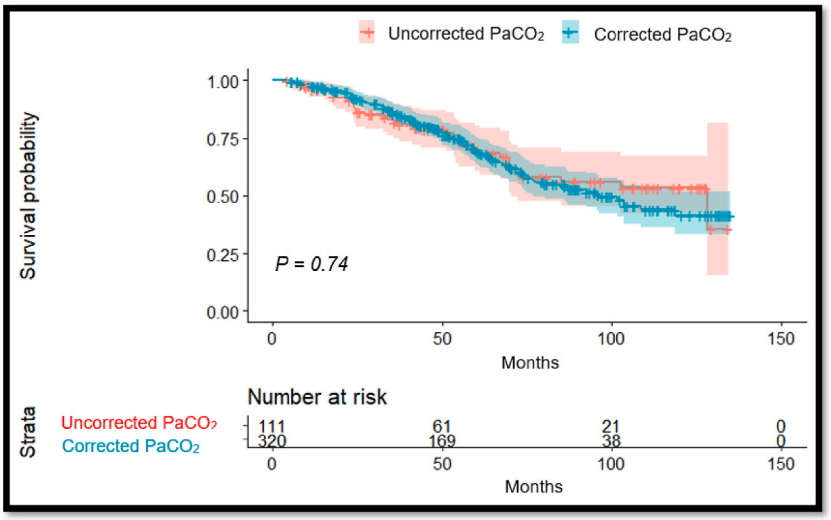


Fig. 2. Kaplan-Meier survival curves for all NIV patients according to $PaCO_2$ correction.

and there was a female predominance in the CWD subgroup.

One of the specificities of our study was to separate COPD patients into two subgroups. In their studies, Borel et al. and Budweiser et al. have shown a survival difference in ventilated COPD patients depending on their BMI: an increase in BMI was associated with an increase in survival [14,15]. Since our study focused on survival, we considered that it was important to take that factor into account.

Table 4
Analysis of factors associated with mortality in our cohort (Cox model).

	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Corrected $PaCO_2$	1.16	[0.74–1.84]	0.51			
HCO3 upon initiation	1.01	[0.97–1.05]	0.70			
Age	1.05	[1.03–1.07]	1.07^{-7}	1.05	[1.03–1.06]	1.01^{-9}
Male gender	0.87	[0.57–1.31]	0.50			
BMI	1.00	[0.98–1.02]	0.64			
Active or past smoking	1.61	[1.02–2.54]	0.04	1.40	[0.98–2.00]	0.06
FEV1	1.00	[0.99–1.02]	0.98			
VC	0.99	[0.98–1.01]	0.23	0.99	[0.98–0.99]	0.01
Absence of LTOT	1.10	[0.67–1.82]	0.70			
Diabetes	1.34	[0.87–2.05]	0.19			
Dyslipidemia	0.38	[0.04–3.31]	0.38			
Cardiovascular disease[1]	0.89	[0.53–1.48]	0.64			
NIV scheduled	0.93	[0.52–1.65]	0.80			

BMI: body mass index.
CI: confidence interval.
FEV1: forced expiratory volume in 1 s.
HCO3: arterial bicarbonates.
HR: hazard ratio.
LTOT: long-term oxygen therapy.
$p < 0.05$ was considered significant.
$PaCO_2$: partial pressure of carbon dioxide in the arterial blood.
VC: vital capacity.
[a]Presence of diabetes or dyslipidemia or cardiovascular disease (rhythm disorder, coronary artery disease, arterial hypertension).

Table 5
Subgroups' survival data.

	COPD	Obese COPD	OHS	NMD	CWD
	(n = 59)	(n = 117)	(n = 167)	(n = 64)	(n = 24)
Patients achieving $PaCO_2$ correction	50	77	132	44	17
Events (death)	20	35	40	13	3
Median survival (months)	86	75	104	96	not reached
95% IC	55-not reached	60-not reached	80-not reached	61-not reached	74-not reached
Patients not achieving $PaCO_2$ correction	9	40	35	20	7
Events (death)	4	13	11	6	3
Median survival (months)	55	128	not reached	not reached	not reached
95% IC	41-not reached	72-not reached	70-not reached	67-not reached	18-not reached
p value	0.97	0,28	0,93	0,84	0,28

Patients in the NMD subgroup accounted for 15% of the whole cohort. This proportion was low compared to other studies, including that by Geak Poh Tan et al., and could be explained by the exclusion of amyotrophic lateral sclerosis patients [16]. Indeed, for these patients, the objective of NIV is to improve the quality of life and comfort, but with no strict objective of capnia normalization. Furthermore, it has been clearly demonstrated that the survival of these patients was shorter than that of other patients with NMD [13,16].

In our study, ventilation was set with the aim of normalizing $PaCO_2$, as in the cohorts of Léger et al., Janssens et al., and Windisch et al. [12,17,18]. The ventilation settings applied in our patients were higher than those used in the cohorts of Janssens et al., Casanova et al. and Borel et al. [12,19,20]. In the more recent study from Jolly et al. who investigated predictive factors of NIV success, pressure levels were identical to ours for COPD and OHS patients [21]. However, in our study, pressure levels were higher in patients with NMD and CWD. These high-pressure levels had no effect on NIV discontinuation nor compliance. In our study, the median compliance was 7.1 h per day, i.e., better than reported in the studies of Janssens et al. and Jolly et al. (6.9 and 5.86 h per day, respectively) [12,21]. Similarly, the rate of NIV discontinuation due to a poor compliance was 5% in our study, compared to 6.6% in the cohort of Janssens et al. and 14% in the cohort of Borel et al. [12,20].

Finally, our objective of $PaCO_2$ normalization was achieved in 74% of cases. This result, as well as the high compliance and low rate of NIV discontinuation, were markers of efficacy and good tolerance of our NIV setting method. This result was close to the percentages of correction achieved in the studies of Jolly et al. (77%) and Janssens et al. (correction in 80% of cases in OHS patients, 84% in patients with CWD, 85% in patients with NMD), except for COPD patients [12,21]. Only 32% of COPD patients achieved $PaCO_2$ correction under NIV in the study of Janssens et al. compared to 85% in our study [12]. Such a difference could be explained by the higher pressure levels applied in our cohort and by the choice to use a 20% decrease as a target for $PaCO_2$ reduction, in line with the study of Köhnlein et al., which was not the case in the cohort of Janssens et al. [1,12].

We did not show a survival difference between normocapnic and hypercapnic patients under NIV but that does not mean that one does not exist. The main explanation was the low $PaCO_2$ level in patients who remained hypercapnic under NIV. Indeed, in our study, median $PaCO_2$ ranged from 6.21 to 6.94 kPa in this group. It cannot be excluded that above 7 kPa, hypercapnia has a negative impact on prognosis. However, in our study, the number of patients with a $PaCO_2 > 7$ kPa under NIV was very low and the groups were too unbalanced to answer this question.

Very few studies have investigated the survival of long-term ventilated CRF patients according to their $PaCO_2$. Our findings support those of Raveling et al., who have not shown any difference in survival in ventilated hypercapnic COPD patients, depending on whether or not they achieved a 20% decrease in $PaCO_2$ one year after NIV initiation [22]. In most cases, the effect of the baseline $PaCO_2$ was investigated, but not residual hypercapnia under NIV. Thus, Budweiser et al. and Duiverman et al. did not find any association between survival and baseline $PaCO_2$ in ventilated COPD patients and in patients with a restrictive pattern, respectively [15, 23].

Our results were unexpected compared to the study of Köhnlein et al. [1]. This study highlighted the importance of $PaCO_2$ correction in the survival of ventilated COPD patients. The study of Köhnlein et al. has been conducted over a shorter period of time; the importance of hypercapnia correction could be lessened over time. Moreover, FEV1 of their patients was 26%, compared to 34% in our study, and it could be assumed that $PaCO_2$ correction is a challenge in the most severe patients.

Bivariate analysis did not show any statistically significant difference in survival between normocapnic and hypercapnic patients under NIV in each subgroup. However p value was lower in the obese COPD and CWD subgroups than in the other subgroups.

Another consideration is the choice of the $PaCO_2$ to assess residual hypoventilation under NIV. The diurnal value could be lower than the nocturnal one, with changes in $PaCO_2$ in the short term. In the cohort of Budweiser et al. including 126 ventilated OHS patients, a >23% decrease in nocturnal $PaCO_2$ under NIV (compared to baseline nocturnal $PaCO_2$) was associated with a better prognosis [4].

Our study has some limitations. First, 26% of patients did not achieve $PaCO_2$ correction under NIV, and survival data were compared between two unbalanced groups. Second, since the mortality rate was low, this could have reduced the statistical power for identifying prognostic factors. Thurd, our study focused only on survival. It would be interesting to look for a difference in functional or cognitive status depending on whether or not $PaCO_2$ correction was achieved after NIV initiation. Finally, the study sample was too small to confirm the lack of effect of residual hypercapnia when it exceeded 7 kPa.

Sharing cohorts will allow a meta-analysis to be carried out with sufficient power on this topic.

5. Conclusion

Based on the findings from our multicenter cohort, moderate residual hypercapnia under NIV does not negatively impact survival in CRF patients. In patients with poor tolerance of pressure increases, residual hypercapnia can therefore be tolerated under NIV. Larger studies, in particular with a higher number of patients with residual $PaCO_2 > 7$ kPa, are needed to confirm these results.

Ethics declarations

This study was reviewed and approved by Ethics Committee of Angers University. All patients provided informed consent to participate in the study.

Priori presentation

This work was presented in part at the French-speaking annual congress of respiratory medicine (CPLF) which took place at Lille, France (January 22, 2022).

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

We make available an anonymous synthetic version of our database, that is provided as supplementary data.

CRediT authorship contribution statement

Audrey Thomas: Writing – review & editing, Writing – original draft, Methodology, Data curation. **Sandrine Jaffré:** Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Vianney Guardiolle:** Software, Methodology. **Tanguy Perennec:** Methodology. **Frédéric Gagnadoux:** Funding acquisition, Data curation. **François Goupil:** Funding acquisition, Data curation. **Cédric Bretonnière:** Writing – original draft. **Vivien Danielo:** Supervision. **Jean Morin:** Writing – original draft, Resources, Investigation, Data curation. **François-Xavier Blanc:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to

influence the work reported in this paper.

Acknowledgements

The authors thank the IRSR-PL, the clinical research team of the Institut du thorax, CHU Nantes, and the Lung Innovation ($LungO_2$) cluster for their support.

Abbreviation

BMI	body mass index
COPD	chronic obstructive pulmonary disease
CRF	chronic respiratory failure
CWD	chest wall disease
FEV1	forced expiratory volume in 1 s
IRSR-PL:	Pays de la Loire Respiratory Health Research Institute
LTOT	long-term oxygen therapy
NMD	neuromuscular disease
NIV	non-invasive ventilation
OHS	obesity-hypoventilation syndrome
$PaCO_2$	partial pressure of carbon dioxide

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e26437.

References

[1] T. Köhnlein, W. Windisch, D. Köhler, A. Drabik, J. Geiseler, S. Hartl, et al., Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial, Lancet Respir. Med. 2 (2014) 698–705, https://doi.org/10.1016/S2213-2600(14)70153-5.

[2] P. Murphy, S. Rehal, G. Arbane, S. Bourke, P. Calverley, A.M. Crook, et al., Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation: a randomized clinical trial, JAMA 317 (2017) 2177–2186, https://doi.org/10.1001/jama.2017.4451.

[3] D. Annane, D. Orlikowski, S. Chevret, Nocturnal mechanical ventilation for chronic hypoventilation in patients with neuromuscular and chest wall disorders, Cochrane Database Syst. Rev. (2014), https://doi.org/10.1002/14651858.CD001941.pub3. CD001941.

[4] S. Budweiser, S.G. Riedl, R.A. Jörres, F. Heinemann, M. Pfeifer, Mortality and prognostic factors in patients with obesity-hypoventilation syndrome undergoing noninvasive ventilation, J. Intern. Med. 261 (2007) 375–383, https://doi.org/10.1111/j.1365-2796.2007.01765.x.

[5] G. Boussaïd, H. Prigent, P. Laforet, J.C. Raphaël, D. Annane, D. Orlikowski, et al., Effect and impact of mechanical ventilation in myotonic dystrophy type 1: a prospective cohort study, Thorax 73 (2018) 1075–1078, https://doi.org/10.1136/thoraxjnl-2017-210610.

[6] S. Nowbar, K.M. Burkart, R. Gonzales, A. Fedorowicz, W.S. Gozansky, J.C. Gaudio, et al., Obesity-associated hypoventilation in hospitalized patients: prevalence, effects, and outcome, Am. J. Med. 116 (2004) 1–7, https://doi.org/10.1016/j.amjmed.2003.08.022.

[7] C. Gonzalez, G. Ferris, J. Diaz, I. Fontana, J. Nunez, J. Marin, Kyphoscoliotic ventilatory insufficiency. Effects of long-term intermittent positive-pressure ventilation, Chest 124 (2003) 857–862, https://doi.org/10.1378/chest.124.3.857.

[8] B. Ergan, S. Oczkowski, B. Rochwerg, A. Carlucci, M. Chatwin, E. Clini, et al., European respiratory society guideline on long-term home non-invasive ventilation for management of chronic obstructive pulmonary disease, Eur. Respir. J. 54 (2019) 1901003, https://doi.org/10.1183/13993003.01003-2019.

[9] J.F. Masa, B. Mokhlesi, I. Benítez, F.J. Gomez de Terreros, M.A. Sánchez-Quiroga, A. Romero, et al., Long-term clinical effectiveness of continuous positive airway pressure therapy versus non-invasive ventilation therapy in patients with obesity hypoventilation syndrome: a multicentre, open-label, randomised controlled trial, Lancet 393 (2019) 1721–1732, https://doi.org/10.1016/S0140-6736(18)32978-7.

[10] Clinical indications for noninvasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD, and nocturnal hypoventilation - a consensus conference report, Chest 116 (1999) 521–534, https://doi.org/10.1378/chest.116.2.521.

[11] D. Orlikowski, H. Prigent, J. Gonzalez, T. Sharshar, J.C. Raphael, Long term domiciliary mechanical ventilation in patients with neuromuscular disease (indications, establishment and follow up), Rev. Mal. Respir. 22 (2005) 1021–1030, https://doi.org/10.1016/s0761-8425(05)85732-8.

[12] J.P. Janssens, S. Derivaz, E. Breitenstein, B. De Murat, J.W. Fitting, J.C. Chevrolet, et al., Changing patterns in long-term noninvasive ventilation. A 7-year prospective study in the Geneva Lake Area, Chest 123 (2003) 67–79, https://doi.org/10.1378/chest.123.1.67.

[13] M. Laub, B. Midgren, Survival of patients on home mechanical ventilation: a nationwide prospective study, Respir. Med. 101 (2007) 1074–1078, https://doi.org/10.1016/j.rmed.2006.10.007.

[14] J.C. Borel, J.L. Pépin, C. Pison, A. Vesin, J. Gonzalez-Bermejo, I. Court-Fortune, et al., Long-term adherence with non-invasive ventilation improves prognosis in obese COPD patients, Respirology 19 (2014) 857–865, https://doi.org/10.1111/resp.12327.

[15] S. Budweiser, R.A. Jörres, T. Riedl, F. Heinemann, A.P. Hitzl, W. Windisch, et al., Predictors of survival in COPD patients with chronic hypercapnic respiratory failure receiving noninvasive home ventilation, Chest 131 (2007) 1650–1658, https://doi.org/10.1378/chest.06-2124.

[16] G. Poh Tan, N. McArdle, S. Singh Dhaliwal, J. Douglas, C. Siobhan Rea, B. Singh, Patterns of use, survival and prognostic factors in patients receiving home mechanical ventilation in western Australia: a single centre historical cohort study, Chron. Respir. Dis. 15 (2018) 356–364, https://doi.org/10.1177/1479972318755572.

[17] W. Windisch, Quality of life in home mechanical ventilation study group. Impact of home mechanical ventilation on health-related quality of life, Eur. Respir. J. 32 (2018) 1328–1336, https://doi.org/10.1183/09031936.00066407.

[18] P. Leger, J.M. Bedicam, A. Cornette, O. Reybet-Degat, B. Langevin, J.M. Polu, et al., Nasal intermittent positive pressure ventilation. Long-term follow-up in patients with severe chronic respiratory insufficiency, Chest 105 (1994) 100–105, https://doi.org/10.1378/chest.105.1.100.

[19] C. Casanova, B.R. Celli, L. Tost, E. Soriano, J. Abreu, V. Velasco, et al., Long-term controlled trial of nocturnal nasal positive pressure ventilation in patients with severe COPD, Chest 118 (2000) 1582–1590, https://doi.org/10.1378/chest.118.6.1582.
[20] J.C. Borel, B. Burel, R. Tamisier, S. Dias-Domingos, J.P. Baguet, P. Levy, J.L. Pepin, et al., Comorbidities and mortality in hypercapnic obese under domiciliary noninvasive ventilation, PLoS One 8 (2013) e52006, https://doi.org/10.1371/journal.pone.0052006.
[21] G. Jolly, L. Razakamanantsoa, E. Fresnel, Z. Gharsallaoui, A. Cuvelier, M. Patout, Defining successful non-invasive ventilation initiation: data from a real-life cohort, Respirology 26 (2021) 1067–1075, https://doi.org/10.1111/resp.14118.
[22] T. Raveling, G. Bladder, J.M. Vonk, J.A. Nieuwenhuis, F.M. Verdonk-Struik, P.J. Wijkstra, et al., Improvement in hypercapnia does not predict survival in COPD patients on chronic noninvasive ventilation, Int. J. Chronic Obstr. Pulm. Dis. 13 (2018) 3625–3634, https://doi.org/10.2147/COPD.S169951.
[23] M.L. Duiverman, G. Bladder, A.F. Meinesz, P.J. Wijkstra, Home mechanical ventilatory support in patients with restrictive ventilatory disorders: a 48-year experience, Respir. Med. 100 (2006) 56–65, https://doi.org/10.1016/j.rmed.2005.04.015.