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Long-term follow-up and mortality of patients with chest wall diseases on noninvasive ventilation

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TO THE EDITOR:

Chest wall diseases (CWDs) are characterized by decreased compliance of the chest wall and impaired ventilatory mechanics,[1,2] leading to chronic hypercapnic respiratory failure (CHRF). Patients with kyphoscoliosis and post-tuberculosis sequelae (TbS) have a higher risk of CHRF, depending on the degree of deformity and the age of onset.[3] The clinical presentation of CWDs is usually nonspecific, with a restrictive lung pattern, and sleep-disordered breathing frequently occurs with sleep hypoventilation preceding diurnal respiratory failure.[4]

Noninvasive ventilation (NIV) is commonly used to treat CWDs that result in CHRF combined with hypoventilation symptoms (fatigue, morning headache, hypersomnolence, tiredness, or dyspnea) or with the development of related complications. NIV improves hypoventilation symptoms, arterial blood gases (ABG), and pulmonary function test (PFT) results, and it prolongs survival.[5-8] Data on the benefits of short-term NIV are mostly available from uncontrolled trials or studies with larger and more consistent samples of patients with neuromuscular disorders. In a meta-analysis, no significant difference between volume- and pressure-cycled NIV was found in terms of survival.[2] Long-term oxygen therapy (LTOT) alone was associated with worse survival of CWD patients when compared with NIV.[7,8]

The expected survival for patients with CHRF due to kyphoscoliosis and TbS are 8 and 3 years, respectively. Factors such as female sex, younger age, higher BMI, higher Pao_2, and lower $Paco_2$ appear to be favorable independent prognostic factors in CWD patients treated with NIV or LTOT.[9]

The present study aimed to characterize and evaluate the survival of patients with CWD under follow-up after starting NIV. The primary outcome was survival time since NIV treatment initiation.

The authors conducted a retrospective descriptive analysis involving adult patients with CWD on home NIV who were followed up at a pulmonology outpatient clinic between January of 2010 and January of 2022.

Clinical data with information about treatment and mortality were collected from the medical records of the patients. PFT and polysomnography results (at baseline) and ABG analysis (at baseline and during NIV treatment) were also obtained. Comorbidities were classified using the Charlson Comorbidity Index (CCI), which predicts mortality using a score that assigns weights (1, 2, 3, or 6) to each condition that a patient has.[10]

Statistical analysis was performed using the IBM SPSS Statistics software package, version 28 (IBM Corporation, Armonk, NY, USA). Statistical significance was set at $p < 0.05$. Categorical and quantitative variables were described as absolute and relative frequencies or as means ± standard deviations. Comparisons between survivors and nonsurvivors were performed with t-tests for independent samples for continuous variables and with chi-squared tests for categorical variables. To analyze the overall sample and to compare survivors according to their diagnosis we used the Mantel-Cox, Breslow, and Tarone-Ware tests. The Cox proportional hazards model was employed to adjust the variables. The selection of independent variables for the multivariate Cox model was based on statistical significance and on curves that presented proportional risks in the univariate analysis.

During the 12-year study period, 39 CWD patients on NIV were followed. The mean age was 60.2 ± 16.4 years, and there was a predominance of females (51.3%) and nonsmokers (82.1%). In this cohort of patients with CWD and CHRF, idiopathic kyphoscoliosis (66.7%) and acquired abnormalities of the thoracic cage, mainly TbS (33.3%), were diagnosed. The mean CCI was 2.1 ± 1.1, considering that CWD is a chronic pulmonary disease. Descriptive summary statistics and comparisons between survivors and nonsurvivors are displayed in Table 1.

A restrictive lung pattern and a simultaneous diagnosis of obstructive sleep apnea were found in 51.3% and in 23.1% of the overall sample, respectively. At baseline (prior to NIV treatment), ABG analysis revealed CHRF (Pao_2 = 61.1 ± 9.7 mmHg; and $Paco_2$ = 59.5 ± 13.0 mmHg). After NIV initiation, both Pao_2 (an increase of 14.8 ± 14.5 mmHg) and $Paco_2$ (a decrease of 15.1 ± 11.7 mmHg) improved.

NIV was initiated in the presence of hypoventilation symptoms plus CHRF and in that of acute hypercapnic respiratory failure in 53.8% and in 46.2% of the sample, respectively. Patients with hypoventilation due to other respiratory diseases were excluded from the study. Most of the patients underwent pressure-targeted mode of NIV (87.2%) and wore facial masks (79.5%). LTOT was simultaneously used with NIV in 66.7% of the patients, with a mean flow rate of 1.8 ± 0.8 L/min.

In our sample, the 12-year and 5-year mortality rates were 46% and 15%, respectively. Mortality rates were higher in patients with TbS than in those with kyphoscoliosis (54% vs. 42%). The median survival time since NIV initiation was 146.0 ± 19.4 months, and no differences were found between the groups of diagnosis.

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Table 1. Descriptive statistics and comparison between survivors and nonsurvivors.[a]

Variable	Group		p	Total
	Survivor (n = 21)	Nonsurvivor (n = 18)		(N = 39)
Demographics				
Female sex	9 (42.9)	11 (61.1)	0.26	20 (51.3)
Age at follow-up initiation, years	58.3 ± 15.2	62.4 ± 17.8	0.22	60.2 ± 16.4
Smoking status				
Current smoker	1 (4.8)	0 (0.0)	0.64	1 (2.6)
Former smoker	3 (14.3)	3 (16.7)		6 (15.4)
Never smoker	17 (81.0)	15 (83.3)		32 (82.1)
BMI, kg/m^2	25.4 ± 5.3	24.7 ± 6.1	0.35	25.1 ± 5.6
Diagnosis				
Kyphoscoliosis	15 (71.4)	11 (61.1)	0.46	26 (66.7)
Tuberculosis sequelae	6 (28.6)	7 (38.9)		13 (33.3)
Comorbidity				
CCI	1.8 ± 0.9	2.5 ± 1.2	0.03	2.1 ± 1.1
PFT at baseline				
Normal pattern	3 (14.3)	0 (0.0)	0.20	3 (7.7)
Restrictive pattern	11 (52.4)	9 (50.0)		20 (51.3)
Mixed pattern	7 (33.3)	9 (50.0)		16 (41.0)
FVC, % predicted	49.6 ± 18.1	38.0 ± 11.6	0.01	43.9 ± 16.2
FEV_1, % predicted	43.4 ± 15.5	34.2 ± 10.9	0.02	38.9 ± 14.1
TLC, % predicted	62.0 ± 18.1	63.4 ± 9.2	0.43	62.6 ± 14.4
MIP, % predicted	42.5 ± 16.5	39.0 ± 18.4	0.35	41.2 ± 16.7
Polysomnography at baseline				
Respiratory disturbance index	19.9 ± 10.6	6.6 ± 1.6	0.01	16.9 ± 10.9
Minimum saturation, %	81.1 ± 6.8	81.2 ± 14.5	0.50	81.2 ± 9.8
Arterial blood gases				
Pao_2 at baseline, mmHg,	61.4 ± 10.6	60.7 ± 9.0	0.41	61.1 ± 9.7
Pao_2 after NIV initiation, mmHg	73.6 ± 12.7	69.9 ± 10.6	0.18	71.9 ± 11.7
$Paco_2$ at baseline, mmHg	54.9 ± 6.0	74.1 ± 11.5	0.01	64.0 ± 13.2
$Paco_2$ after NIV initiation, mmHg	46.2 ± 8.6	50.2 ± 8.5	0.08	48.1 ± 8.7
NIV				
Age at initiation, years	62.5 ± 10.8	65.4 ± 17.5	0.27	63.8 ± 14.2
Symptoms at initiation				
Hypoventilation and chronic hypercapnia	10 (47.6)	11 (61.1)	0.40	21 (53.8)
AHRF	11 (52.4)	7 (38.9)		18 (46.2)
Pressure-targeted mode	19 (90.5)	15 (83.3)	0.65	34 (87.2)
Facial mask	16 (76.2)	15 (83.3)	0.70	31 (79.5)
Nasal mask	5 (23.8)	3 (16.7)		8 (20.5)
LTOT + NIV				
LTOT	12 (57.1)	14 (77.8)	0.17	26 (66.7)
Flow rate, L/min	1.8 ± 0.6	1.7 ± 0.9	0.35	1.8 ± 0.8

CCI: Charlson Comorbidity Index; PFT: pulmonary function test; NIV: noninvasive ventilation; AHRF: acute hypercapnic respiratory failure; and LTOT: long-term oxygen therapy. [a]Values expressed as n (%) or mean ± SD.

Nonsurvivors presented with more comorbidities, lower FVC and FEV_1 in % of predicted values, lower respiratory disturbance index, and higher $Paco_2$ at baseline than did survivors. Older and female patients using LTOT showed a trend toward higher mortality, but the difference was not statistically significant.

Univariate Cox analysis identified the following variables as significant predictors of mortality: CCI (hazard ratio [HR] = 1.70; p = 0.02), Pao_2 after NIV initiation (HR = 0.95; p = 0.05) and $Paco_2$ at baseline (HR = 1.03; p = 0.01). No significant differences were found regarding demographic variables, diagnosis, PFT results, polysomnography results, NIV mode, mask use, and LTOT use. In the multivariate Cox analysis, lower Pao_2 after NIV initiation (HR = 0.93; p = 0.01) and higher $Paco_2$ at baseline (HR = 1.07; p = 0.01) were associated with mortality.

This retrospective study helps support the benefits of long-term NIV on morbidity and mortality in patients with CWD. This study showed a median survival time

of 12 and 13 years, respectively, for patients with kyphoscoliosis and TbS who were treated with NIV; therefore, survival was extended in 4 and 10 years, respectively, when compared with previous evidence.[9]

Some of the potential strengths of the design of this study were the homogeneity of the cohort and the long follow-up period. To the best of our knowledge, this is the largest cohort of CWD patients on NIV reported by a Portuguese center. This study has limitations, such as the small sample size, and the effects of NIV on quality of life and lung function were not evaluated. The data presented herein reflect the clinical expertise of a single institution and may not be fully representative of practices elsewhere.

In conclusion, the findings of the present study suggest that patients with CWD on NIV may have their risk of mortality reduced, which can be predicted based on $Paco_2$ at diagnosis and on Pao_2 after NIV initiation.

AUTHOR CONTRIBUTIONS

JAB: study conception and design; data collection; statistical analysis; and drafting and review of the manuscript. CR and FF: critical review of the manuscript. All of the authors approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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