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Survival of patients with chronic respiratory failure on long-term oxygen therapy and or non-invasive ventilation at home

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A R T I C L E   I N F O

S U M M A R Y

Background & aims: Chronic respiratory failure (CRF) is the common fate of respiratory diseases where systemic effects contribute to outcomes. In a prospective cohort of home-treated patients with CRF, we looked for predictors of long-term survival including respiratory, nutritional and inflammatory dimensions.
Methods: 637 stable outpatients with CRF, 397 men, 68 ± 11 years, on long-term oxygen therapy and/or non-invasive ventilation from 21 chest clinics were enrolled and followed over 53 ± 31 months. CRF resulted from Chronic Obstructive Pulmonary Disease (COPD) in 48.5%, restrictive disorders 32%, mixed (obstructive and restrictive patterns) respiratory failure 13.5%, bronchiectasis 6%. Demographic characteristics, smoking habits, underlying respiratory diseases, forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), arterial blood gases, 6-min walking distance (6MWD), hemoglobin, body mass index (BMI), serum albumin, transthyretin, C-reactive protein (CRP), history of respiratory assistance, antibiotic and oral corticosteroid use during the previous year were recorded.
Results: 322 deaths occurred during the follow-up. One-, five- and 8-year actuarial survival was 89%, 56% and 47%. By Cox univariate analysis, age, respiratory disease, PaO_2, $PaCO_2$, FEV_1/FVC, BMI, 6MWD, activity score, type and length of home respiratory assistance, smoking habits, oral corticosteroid and antibiotic

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uses, albumin, transthyretin, hemoglobin and CRP levels were associated with survival. Multivariate analysis identified eight independent markers of survival: age, FEV_1/FVC, PaO_2, $PaCO_2$, 6MWD, BMI, serum transthyretin, CRP $\geq$ 5 mg/l.

Conclusions: In CRF, whatever the underlying diseases, besides the levels of obstructive ventilatory defect and gas exchange failure, 6MWD, BMI, serum transthyretin and CRP $\geq$ 5 mg/l predicted long-term survival identifying potential targets for nutritional rehabilitation.

1. Introduction

Chronic respiratory diseases are set to become the third leading cause of deaths in the world [1]. In patients with end-stage respiratory diseases median survival is from two to six years after the initiation of long-term oxygen therapy (LTOT) and/or home mechanical ventilation (HMV) [2]. Regarding this public health issue related to aging and smoking, the identification of factors associated with survival may help to better shape therapeutic interventions [3]. Chronic respiratory failure (CRF) should be considered as a systemic disease that requires a systems approach for both evaluation and treatment [4–6]. In patients with CRF, the impact of malnutrition on survival is established [2,7]. Disease management of patients with CRF should take into account the multiple facets of the disease, including respiratory, inflammatory and nutritional status as recommended in chronic pulmonary diseases whatever their etiology [6].

The present prospective multi-centre study aimed to determine predictors of long-term survival in a cohort of CRF patients previously enrolled in a cross-sectional survey [5], independently of the underlying respiratory diseases, showing that CRF is an actual entity with its own determinants.

2. Methods

2.1. Subjects

Patients were consecutively recruited during the yearly outpatient examination as required for reimbursement of home treatment fees. Twenty-one outpatient clinics within the French *Association Nationale pour les Traitements A Domicile, les Innovations et la Recherche* (ANTADIR) network participated in this prospective survey [5]. Inclusion criteria were age >18 years, LTOT and/or HMV for more than 3 months and PaO_2 on room air $\leq$8 kPa at initiation of home treatment. Exclusion criteria were cystic fibrosis, neuromuscular diseases, sleep apnea syndrome, history of exacerbation during the last 3 months, and any condition likely to affect the 6-month survival. In order to assess the role of chronic systemic inflammation, recent exacerbation was considered as an exclusion criterion. Main aetiologies of CRF were: COPD defined accordingly to Global initiative on Obstructive Lung Disease (GOLD) guidelines [8], bronchiectasis defined on chest computed tomography, restrictive disorders including chest wall diseases as kyphoscoliosis, thoracoplasty sequelae, and pulmonary fibrosis defined on pulmonary function tests and chest computed tomography, and mixed respiratory failure combining restrictive and obstructive defects. Thus, 637 patients, 240 females and 397 males, 68 ± 11 years old, were included. This observational study was approved by the French *Commission Nationale Informatique et Libertés*. Patients gave their informed consent for their participation.

2.2. Methods

Baseline demographic data, smoking habits, physical activity level, respiratory disease, pulmonary function tests, hemoglobin, body mass index (BMI), serum albumin, transthyretin and C-reactive protein (CRP) as well as oral corticosteroid and antibiotic use during the previous year were collected and tested for their predictive value of survival. Outcome data were collected by phone call to physicians of the 21 centers participating in the study. Neither comorbidities nor causes of deaths were recorded since simple declarations are known to be inaccurate in terms of sensitivity and specificity.

Body weight and height were recorded at the time of enrollment Acut-off of 21 for BMI to define under-nutrition in the context of COPD was used [3,5–7,9–11]. Serum albumin, transthyretin and CRP were determined using conventional methods. Participating laboratories agreed to check the quality of their measurements by using a blinded quality control system [12]. Blood gases were measured on room air, except in 47 patients dependent on respiratory assistance. Respiratory function was assessed by forced expiratory volume in one second (FEV_1) and forced vital capacity

Table 1
Demographic data and home treatment according to lung diseases.

	n	Age Mean ± SD	Sex ratio M/F	Home treatment Months on home treatment, mean ± SD	LTOT, n	Non-invasive HMV, n	Invasive HMV, n	LTOT and non-invasive HMV, n	LTOT and invasive HMV, n
All patients	637	68 ± 11	1.7	51 ± 54	318	109	18	183	9
COPD	309	70 ± 10[b]	4.2	40 ± 45[c]	232	19	3	54	1
Bronchiectasis	40	63 ± 15[a,c,d]	0.7	51 ± 46	14	2	2	22	0
Restrictive disorders	202	68 ± 12[b]	0.7	70 ± 64[a,d]	32	72	12	79	7
Mixed respiratory failure	86	68 ± 11[b]	1.3	46 ± 49[c]	40	16	1	28	1
ANOVA or Chi², p		<0.01	<0.0001	<0.0001	<0.0001				

n: Number of patients. LTOT: long-term oxygen therapy. HMV: home mechanical ventilation, ANOVA and post-hoc test of Fisher.
[a] Significantly different with COPD patients.
[b] With bronchiectasis patients.
[c] With restrictive disease patients and,
[d] With mixed respiratory failure.