Survival in a Cohort of Patients With Chronic Obstructive Pulmonary Disease: Comparison Between Primary and Tertiary Levels of Care

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OBJECTIVE: To compare the cumulative probability of survival in a cohort of patients with chronic obstructive pulmonary disease (COPD) attended at primary and tertiary levels of health care.

PATIENTS AND METHOD: A cohort study was carried out at the Department of Pneumology of the Centro Médico Nacional La Raza (Mexico DF) on 87 of the 114 patients with confirmed diagnosis of COPD.

All patients followed a 6-month physical activity and educational program. Patients underwent the COPD diagnostic tests recommended by the American Thoracic Society and were randomized and distributed in 2 groups: Group A had 44 patients who received tertiary care, and Group B had 43 who received primary care. Follow up lasted from 1993 to 2001. Exacerbations, hospital admissions, exercise duration, hospital stay, and death or study abandonment were recorded for all patients. Respiratory function tests were performed annually. Annual and total mortality, distribution by sex, loss in life expectancy, mean age at death, and cumulative probability of survival were analyzed.

RESULTS: No differences were found between the groups in population or initial characteristics. Respiratory function declined in both groups, although the decline was smaller in Group A: mean (SD) forced expired volume in 1 second, 8.93% (8.72%) compared with 17.71% (2.51%) and annual drop in blood pressure of 1.39 mm Hg compared with 1.95 mm Hg. Annual exacerbations were 0.23 in Group A compared with 2.07 in Group B; hospitalizations, 0.06 compared with 0.92, and length of stay, 15.76 days compared with 17.32 days. Mean age at death was 66.12 compared with 60.6; loss of life expectancy was 13.88 years lost compared with 19.4, and the cumulative probability of survival was 0 compared with 0.224.

CONCLUSIONS: There are many reasons for the differences found: better medical management, health education, and family involvement at the tertiary level. These factors, included in international COPD guidelines, must be incorporated into primary health care.

Key words: *COPD. Survival. Mortality.*

Supervivencia en una cohorte con EPOC. Análisis comparativo entre el primer y tercer niveles de atención

OBJETIVO: Comparar la probabilidad de supervivencia acumulada en una cohorte de pacientes con enfermedad pulmonar obstructiva crónica (EPOC) atendidos en primer y tercer niveles.

PACIENTES Y MÉTODO: En el Departamento de Neumología del Centro Médico Nacional La Raza (México DF) se efectuó un estudio de cohortes en 87 enfermos de 114 con diagnóstico confirmado de EPOC. Todos entraron en un programa de actividad física y educacional de 6 meses; se les efectuaron pruebas diagnósticas recomendadas por la American Thoracic Society para la EPOC y se formaron 2 grupos: grupo A, formado por 44 pacientes atendidos en el tercer nivel, y grupo B, compuesto por 43 pacientes atendidos en el primer nivel. El seguimiento se llevó de 1993 a 2001. En todos se contabilizaron las exacerbaciones, los ingresos hospitalarios, el tiempo de ejercicio, la estancia hospitalaria y las defunciones o abandono del estudio. Anualmente se realizaron pruebas de la función respiratoria. Se analizaron la mortalidad anual y total, la distribución por sexos, los años potenciales de vida perdidos, la edad media de fallecimiento y la probabilidad acumulada de supervivencia.

RESULTADOS: No hubo diferencia entre las características poblacionales ni iniciales. Ambos grupos mostraron un declive de la función respiratoria, aunque fue menor en el grupo A (volumen espiratorio forzado en el primer segundo del 8,93 ± 8,72 frente al 17,71 ± 2,51%; caída anual de la presión arterial de oxígeno de 1,39 frente a 1,95 mmHg). Las exacerbaciones anuales fueron 0,23 frente a 2,07; las hospitalizaciones, 0,06 frente a 0,92, y los días de estancia, 15,76 frente a 17,32. La edad media de fallecimiento fue de 66,12 frente a 60,6; los años de vida perdidos de 13,88 frente a 19,4, y la probabilidad acumulada de supervivencia de 0 frente a 0,224.

CONCLUSIONES: Las razones de las diferencias encontradas son múltiples: mejor control médico, educación para la salud y corresponsabilidad familiar. Estos factores, incluidos en las guías internacionales de la EPOC, deben difundirse al primer nivel de atención.

Palabras claves: *EPOC. Supervivencia. Mortalidad.*

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Introduction

Chronic obstructive pulmonary disease (COPD) is a serious public health problem, exceeding other degenerative and neoplastic chronic diseases in high health care costs, which involve *a)* increased health care demand at outpatient and hospital levels; *b)* use of drugs and oxygen therapy, and *c)* indirect costs from disability in terms of loss of work time and life years. It has been estimated that by 2020 COPD will become the third most frequent cause of death and the fifth of disability. Several measures have been taken to improve management of this problem—such as lifestyle changes, new medications, and improved diagnosis and treatment protocols.[1-3] Results to date have been unsatisfactory, as incidence, prevalence, and mortality are increasing. Preventative approaches have therefore been proposed—such as large scale formal and informal educational campaigns to increase understanding of the disease and encourage better decision making on the part of patients, their families, and health care personnel.[4]

The objective of this study was to compare the treatment of COPD patients under specialist care with those under primary care, as rational treatment and good health education for these patients is associated with improvements in the cumulative probability of survival and reduction in the number of exacerbations, hospitalizations, duration of hospital stay, and functional decline. These factors and their impact on several measures such as functional impairment and potential loss of life years were studied.

Patients and Methods

The study was carried out at the pneumology department of the Hospital General del Centro Médico Nacional La Raza, a referral centre for respiratory diseases that are difficult to control. The department has a changing patient population due to the process of referral and counter referral between it and the primary and secondary level care units it supports.

Patients

During the last 3 months of 1991, 146 patients with suspected COPD were attended. All patients were treated by pneumologists at the outpatients department of the unit. COPD diagnosis was made in accordance with the American Thoracic Society diagnostic and treatment criteria.[5] Of the examined population, diagnosis was confirmed in 114 patients who were invited to participate in the study; 87 accepted.

The study protocol was approved by the hospital ethics and research committees. Before patients signed their informed consent on the first visit, they were given a thorough explanation of what COPD was, the risk factors involved, its history and treatment, the length and objectives of the study, and the reason for performing it.

The instructive phase was carried out in 3 sessions and was divided into 3 parts. The first was informative, enabling the patients and their family to understand the disease and the various causative factors, preventative measures, and therapies. Written information clearly explaining the disease process was also provided. The second part concerned the administration of both oral and inhaled medication; correct inhalation was taught, including coordination and use of spacers. The third part emphasized the importance of low impact exercise (walking), how and when exercise could be increased, and the need to combine it with exercises that improved gas exchange and provoked feelings of relaxation (diaphragmatic breathing) before and after taking exercise.

Treatment recommendations emphasized the importance of taking the medication prescribed by the doctor, avoiding self medication, and keeping in close contact with the research staff to resolve any doubts. To this end patients were given the telephone number of the COPD unit and of a pager. Patients were also assured they could withdraw from the study at any stage of the investigation without their medical care being affected. Once all doubts had been resolved, treatment was determined by the specialist and was based on bronchodilators, oxygen therapy, breathing exercises, and at least 30 minutes of physical exercise a day (low impact walking) limited only by the symptoms which presented. Patients were seen every 2 months during 6 months accompanied by the family member who had attended the information sessions. The objective of involving a family member was to encourage activities to be carried out correctly and to have someone to supervise and check compliance with both medication and physical exercise.

During the 6 months, patients who presented any exacerbation immediately consulted the researcher who attended every case. Once the patients were stable, the tests were repeated and patients were randomly distributed to 2 treatment groups.[6]

Measurements

During the study period, all patients underwent annual spirometry to measure forced vital capacity, forced expiratory volume in 1 second (FEV_1), PaO_2, and $PaCO_2$. Time walking, the number of exacerbations and hospitalizations, and the number of days in hospital were also determined. Patients who failed to keep an appointment were called by telephone or visited at home to determine the reason.

Initially a Vitalograph (Lenexa, Kansas, USA) spirometer was used to measure functional status but from 1995 a previously calibrated Flow Mate (Marsh-McBirney, Frederick, MD, USA) was used. Results were correlated with the reference values proposed by the American Thoracic Society[7] in 1991, by Goldman and Beclake[8] in 1959, and by Cotes and Hall[9] in 1970. Blood gases were measured with a 120 L unit.

The following variables were examined to assess the impact that differences between levels of care had on the COPD patients: annual and total mortality, distribution by sexes, working-age mortality rate, postnatal mortality rate, years of potential life lost, mean age at death, and cumulative probability of survival.

Intervention

Group A consisted of 44 patients of both sexes who continued to be attended by the specialized COPD clinic, at tertiary level of care, with 3-monthly visits to ensure compliance. If problems presented, patients could telephone

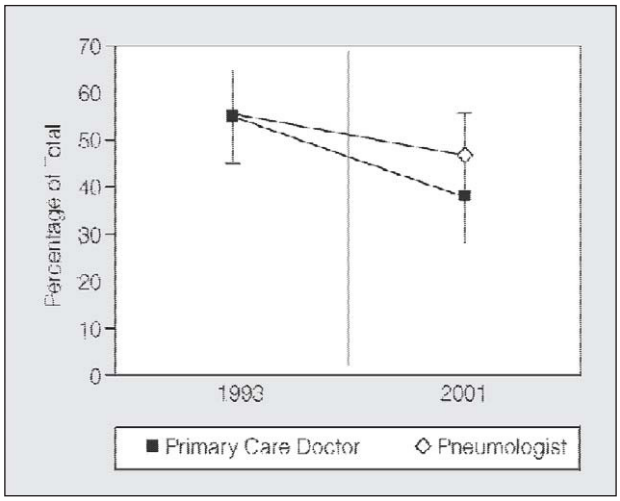

Figure 1. Decline of forced expiratory volume in 1 second.

or go to the emergency department. Clinical and functional status was assessed annually. Patients in Group B (n=43) were told they would continue treatment at their primary care center, visiting according to the indications of the doctor treating them, and that they would be examined annually at the department to assess progress and, if necessary, to adjust medication. These patients were told to contact their family doctor or the second level of care hospital when symptoms increased or there were clinical signs of deterioration.

TABLE 1
Demographic and Clinical Characteristics*

	Group A (n=44)	Group B (n=43)	*P*
Mean (SD) age, years	56.9 (12.1)	57.8 (7.99)	NS
Men/women	23/21	27/16	NS
Years of diagnosis, mean (SD)	11.27 (3.44)	9.04 (3.56)	NS
Previous smoking	34 (77%)	31 (72%)	NS
Supplementary oxygen	5 (11.36%)	8 (18.6%)	NS
GOLD classification			
IIb	30 (68%)	29 (67%)	NS
III	14 (32%)	14 (33%)	NS

*GOLD indicates Global Initiative for Chronic Obstructive Pulmonary Disease; NS, not significant.

TABLE 2
Spirometric and Clinical Characteristics After Stabilization*

	Group A	Group B	*P*
FEV_1	55 (8.72)	54.97 (9.16)	NS
PaO_2	54.95 (5.02)	53.69 (4.61)	NS
$PaCO_2$	31.72 (5.29)	32.53 (6.84)	NS
Walking, min	33.75 (9.89)	23.6 (5.9)	<.05
Exacerbations	4.38 (0.92)	4.23 (0.92)	NS
Hospitalizations	2.22 (0.56)	2.39 (0.65)	NS
Hospital stay, days	28.34 (7.32)	32.09 (6.79)	<.05

*Data are expressed as means (SD). FEV_1 indicates forced expiratory volume in 1 second; NS, not significant.

Follow up

Follow up was performed annually from 1993 to 1998 and thereafter biennially until 2001 when the study was concluded due to the considerable decrease in the study population.

During the first 6 months, all patients followed a physical training program which consisted of a daily 30-minute walk, limited by the symptoms which presented. Participants engaged freely in progressively increasing activity during the study period.[10]

Statistical Analysis

To describe the study population and compare the groups, the Student *t* test was used for normally distributed (Gaussian) variables and the χ^2 test for non-normally distributed (non Gaussian) variables. Kaplan-Meier life tables were used to analyze the conditional probability of death, survival, and cumulative survival. *P* values less than .05 were considered significant.[11]

Results

Characteristics of the study population are shown in Tables 1 and 2. There were no significant differences between the groups at the beginning of the study. Patients presented a moderate to severe airflow obstruction, between II and III on the Global Initiative for Chronic Obstructive Pulmonary Disease classification.[12]

Respiratory Function Status and Gas Exchange

Over the study period, a sustained decrease in FEV_1 was observed in both groups but less in Group A which showed a mean (SD) decrease of 8.93% (8.72%) compared with 17.71% (2.51%) for Group B. The corresponding annual loss was 41.25 mL for Group A compared with 76.25 mL for Group B ($P<.05$) (Figure 1). A similar pattern was observed for PaO_2, with an annual decrease of 1.39 mm Hg in Group A compared with 1.95 mm Hg in Group B ($P<.05$) (Figure 2), representing an increase in exercise tolerance of 28.3 minutes compared with 20 minutes (Figure 3).

Changes in Medical Attention

There was a decrease in the number of exacerbations, –2.07 in Group A compared with –0.23 in Group B (Figure 4), in hospitalizations, –0.92 compared with –0.06, (Figure 4), and in mean number of days of hospital stay, –17.34 compared with –15.76.

Vital Statistics

Assessment over time showed the highest mortality rates to be in patients under primary level care 3 years after separating the groups. Mean age at death was 60.6 years compared with 66.12 years for the group attended at the pneumology department. Men were in the majority (ratio men to women was 1.35:1). Death

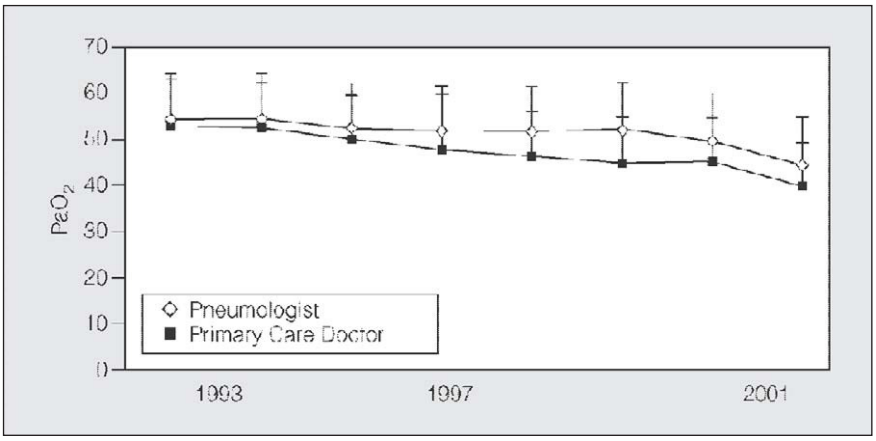

Figure 2. $PaCO_2$ results.

occurred above all after retirement from work (post-productivity), and the mean number of expected life years lost for both groups overall was 17.83. Patients under primary care lost more life years (19.4) than did patients under hospital care (13.88): the latter survived 5.52 years longer. The most common causes of death included acute respiratory infection, exacerbated chronic respiratory insufficiency, and exacerbated chronic cor pulmonale, cardiorespiratory complications frequently encountered at this unit.

The total number of years lost was 499, although Group B under tertiary care lost far fewer, the difference between the 2 groups being 277 years (Table 3). The same pattern was seen for cumulative probability of survival, with the difference between the 2 groups starting in the second year and increasing over time, the maximum level being reached at the end of the study (P<.001) (Figure 6).

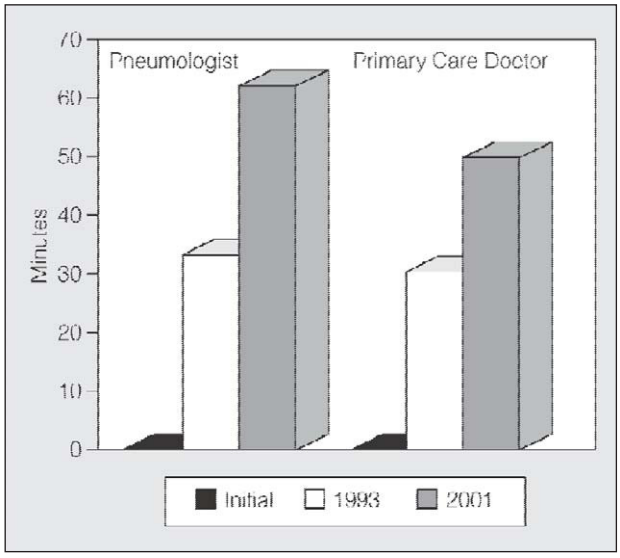

Figure 3. Increase in exercise tolerance.

Discussion

The changes in epidemiology that have occurred in Mexico have been brought about by the reduction in infant mortality and infectious diseases. This has resulted in an increase in life expectancy at birth and in patients with chronic degenerative diseases, in particular heart disease, cancers associated with smoking, and COPD, all of which have considerable impact world wide and all of which are preventable.

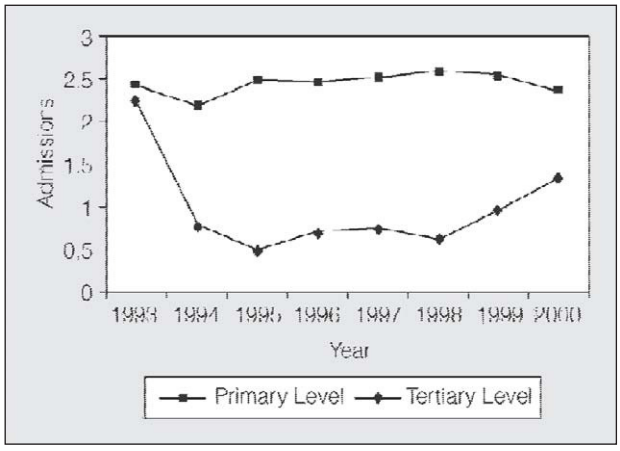

Figure 4. Mean number of hospitalizations by level of care.

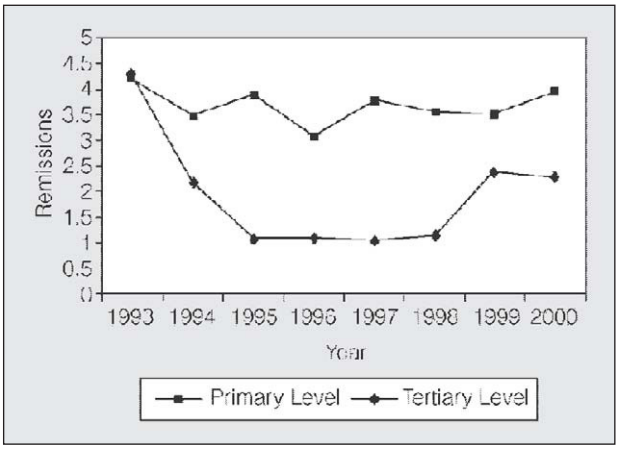

Figure 5. Mean number of exacerbations by level of care.

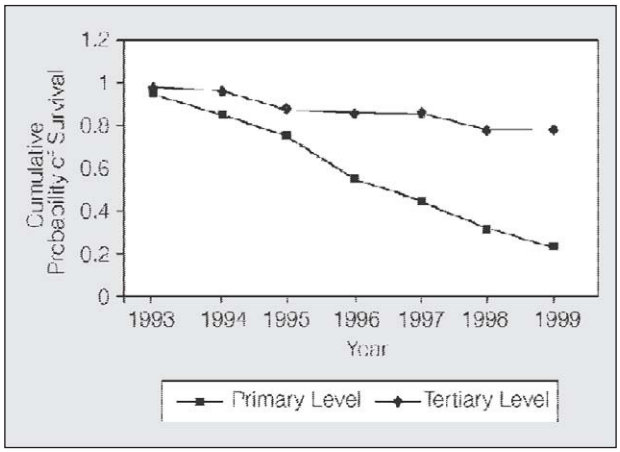

Figure 6. Cumulative probability of survival.

TABLE 3
Vital Statistics*

	Specialist	Primary Care	Total
Deaths	8	20	28
Sex			
Men	5	13	18
Women	3	7	10
Mi	185	166	180
YPLL	111	388	499
MAED	66.12	60.6	62.17
MYPLL	13.88	19.4	17.83
PR	250	800	461
PRR	142	363	390

*Mi indicates masculinity index; YPLL, years of potential life lost; MAED, mean age of early death; MYPLL, mean years of potential life lost; PR, productivity rate ×1000; PPR, post productivity rate ×1000.

The sustained rising trend in the relevance of COPD is reflected in the following figures: in 1994 there were almost 14 million patients diagnosed with chronic bronchitis and 2208 million diagnosed with emphysema; 1 year later, COPD was the cause of 16 million medical visits (9.3 million more than in 1985), caused 553 000 hospitalizations and was the fourth cause of death in the United States of America with a rate of 54.7 per 100 000 white males, 42.5 per 100 000 for black males, 31.4 per 100 000 for white females, and 15.6 per 100 000 black females.[13]

According to the American National Heart, Lung, and Blood Institute, between 4% and 6% of the adult population present signs of COPD and it is estimated that within 20 years lung disease will be one of the greatest economic burdens worldwide, with a growing rate of hospitalizations and medical visits, and a cost of over US$14 000 million.[14]

In this study we observed a loss of FEV_1 of 41.25 mL per year among patients under specialist care, an amount which can be considered "almost normal." However, the amount is almost double (76.25 mL per year) among patients under primary health care. Smoking cessation, control of symptoms, and decrease in exacerbations and hospitalizations were the factors which ameliorated decline, a finding which agrees with the longitudinal study by Rijcken and Britoon[15] in which the mean loss was 7 to 33 mL per year. The loss is not only due to smoking but also to the accumulation of lower respiratory tract infections as studies carried out in the United Kingdom by the Medical Research Council[16] in 1996 showed. These studies demonstrated that clinical signs, particularly productive cough, had a marked influence on lung function.

The clinical characteristics of COPD exacerbations have been documented.[17] Their control is important and benefits not only the patient but also hospitals and the society as well: reduction in the frequency of exacerbations considerably improves patients' quality of life and reduces the cost of medical care. COPD tends to generate a considerable demand for hospital care and 60% of these visits are produced by a small number of patients (12.2%) classified as large consumers of health resources and characterized by advanced age and a high degree of obstruction and hypoxemia; this group needs a mean of 4.1 (2.2) medical visits a year, with an average 2 hospitalizations and 7 days' duration, representing 10% of all hospital admissions, a hospitalization rate of 216 per 100 000 population per year, and 450 visits to the emergency department per 100 000 population.[18]

In a study by Miravitlles et al[19] the mean number of medical visits per year was 5.1, mean number of visits to a specialist was 0.85, and exacerbations, 1.9, in patients with mild to moderate obstruction. Mean length of hospital stay was 8.9 days. In 1988, in the city of Valencia, the mean length of hospital stay was 8.1 days for 350 COPD patients.[20]

Disease progression is determined by the cause of exacerbation and the degree of respiratory failure, classified in our study as moderate to severe—a situation which produced a large number of hospitalizations, consistent with observations in a study by Connors et al[21] of 1016 patients in whom the mean PaO_2 was 50 mm Hg. These factors were the main causes of death, among other variables, described by Zielinski et al[22] in 1997 in a cross sectional study of 215 patients. Exacerbations and respiratory failure, then, are the key factors to control in order to reduce COPD mortality.

Another study of 135 patients, admitted to hospital with COPD exacerbation and followed for 3 years, described a majority of men (96%), a mean age of 72 years, and mean duration of first hospital stay of 13 days. At the end of the study, 47.4% of patients had died and mortality was 13.4 at 1 year, 22 at 2 years, and 35 at 3 years.[23] The 3-year mortality rate is similar to the mortality of patients attended at primary care centers in our study (46.51%). The rate observed by Fernández Pérez et al[24] at 7 years was 38%, a higher rate than that of patients attended by pneumologists in our study (18.18% at 10 years due to strict control of the disease).

In our study we found that the mean age of early death was similar for both groups. There was, however, a substantial difference in the total number of years of potential life lost (up to 300% more) for patients under primary care, as well as in the rate of cumulative survival (3 times longer in those under the care of pneumologists). These figures are important in the light of the international situation: in Italy, in 1990, a total of 38 000 million days were lost and an increase of 81% by 2002 was expected (to 69 000 million). Noncommunicable diseases were expected to increase by 18.8% (from 40.9% to 59.7%).

The prevalence of COPD is estimated to increase by 300% between 1990 and 2020, meaning that the 4400 million cases will become 14 700 million. This spectacular increase is largely due to smoking, which is expected to lead to 346% more work days lost.[25,26]

Although it is true that when we started the study respiratory rehabilitation was not understood as it is today, we assumed that training could improve the muscle oxidative capacity and exercise tolerance of COPD patients, thereby improving their situation biologically, psychologically, and socially as well as permitting an early return to work. Results of the walking exercise were satisfactory as patients from both treatment groups managed to increase their exercise tolerance to almost double their initial capacity. Our approach has been recommended in guidelines published by a working group of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR).[27] Those guidelines state that assessment of improvement for chronic lung patients must go beyond lung function test parameters to include an evaluation of patients' social integration. Current results show more effective control over exacerbations and symptoms and effective improvement of exercise tolerance.

Another procedure that produces satisfactory results and contributes to reduction in COPD costs is education of health care staff and the general population on the basis that greater understanding of the disease leads to greater discipline and treatment compliance on the part of the patient. While education alone will not change FEV_1 dynamics, reduction in the number of exacerbations and hospitalizations improve quality of life and help reduce the decline in airflow.

The results obtained in this study are positive with regard to the intervention carried out by the department of pneumology and are principally a result of the introduction of specialized clinics for the treatment of the several respiratory conditions that affect our population. This study reflects the effectiveness of our COPD clinic which has been in operation now for 15 years. The results of a similar earlier program related to the treatment of asthma, published in 1990,[28] came to the conclusion that clinics specialized in the treatment of COPD were necessary to reduce hospital readmissions and that the basis of the programs was the knowledge that both the doctor and the patient had of the disease, the close relationship between the two, and complete confidence in the treatment. The advantages of that approach were confirmed in a study by Sans-Torres et al[29] published a decade later, in 2001. After a 3-year follow up of 124 patients with a mean age of 69 (7) years, FEV_1 of 35% (12%), PaO_2 of 54.6 (8) mm Hg, and $PaCO_2$ of 49 (6) mm Hg, hospital stay decreased from 14.2 days per patient to 8.1 and the numbers of visits to emergency departments fell from 2.06 to 1.5. The authors concluded that treating patients in a specialized clinic was effective in reducing the number of hospitalizations, length of hospital stay, and the number of visits to the emergency department irrespective of the severity of the patient's disease.

The problems observed with the primary care centers were that they did not meet these standards and this adversely affected outcomes. Despite published evidence and current consensus guidelines, it is only possible to have an impact on a national level by going much farther to reach primary care doctors with ample information and knowledge of the disease. In this way it will be possible to achieve better quality of life and increased survival. Fewer years will be lost and medical costs will decline.

Our department, through the COPD clinic, is implementing a home health care program for high risk COPD patients with severe functional impairment. This kind of treatment is already implemented in Spain and consists of home care by expert health care professionals with the aim of reducing mean length of hospital stay and the number of hospital readmissions, as well as improving patients' quality of life and satisfaction.[30]

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