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TITLE

Pseudomonas aeruginosa in patients hospitalized for COPD exacerbation. A prospective study.

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All authors declare that they have no conflict of interest of any nature with this paper

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Abstract

Background. Risk factors for Pseudomonas aeruginosa (PA) isolation in patients hospitalized for COPD exacerbation remain controversial. The aim of our study was to determine the incidence and risk factors for PA isolation in sputum at hospital admission in a prospective cohort of patients with AECOPD.

Methods. We prospectively studied all patients with COPD exacerbation admitted to our hospital between June 2003 and September 2004. Suspected predictors of PA isolation were studied. Spirometric and 6 minute walking test were performed 1 month after discharge. High-resolution computed tomography (HRCT) was performed in a randomized manner with 1 of every 2 patients to quantify the presence and extent of bronchiectasis. Patients were followed up during the subsequent year for hospital readmissions.

Results. A total of 188 patients were included, of whom 31 (16.5%) had PA in sputum at initial admission. BODE index (OR: 2.18; CI 95%: 1.26-3.78; p=0.005), admissions in the previous year (OR: 1.65; CI 95%: 1.13-2.43; p=0.005), systemic steroid treatment (OR: 14.7; CI 95%: 2.28-94.8; p=0.01), and previous isolation of PA (OR: 23.1; CI 95%: 5.7-94.3; p<0.001) were associated with PA isolation. No relationship was seen between bronchiectasis in HRCT and antibiotic use in the previous 3 months.

Conclusions. PA in sputum at hospital admission is more frequent in patients with poorer scoring on the BODE index, previous admissions, oral corticosteroids and prior isolation of PA.

Introduction

The role of bacterial infection in COPD exacerbation remains controversial. [1,2] Recent studies have correlated COPD exacerbation with the overgrowth of the bacterial load or with the acquisition of a new strain of pathogenic bacteria.[3-5] In ambulatory patients *Haemophilus influenzae, Moraxella catarrhalis*, and *Streptococcus pneumoniae* are the three major pathogens isolated in COPD exacerbations, while *Pseudomonas aeruginosa* (PA) is uncommon and is usually associated with the greatest degree of functional impairment.[6-10] Hospitalized patients for acute exacerbation of COPD (AECOPD) usually have more advanced disease [11], and the infecting pathogens could be different.

Recent European guidelines underscore the need for specific studies on risk factors for PA in COPD exacerbated patients.[12] This is an important issue because empirical antibiotic regimens designed to cover this pathogen are different from those aimed to cover for the usual microorganisms. Nevertheless, contradictory results regarding the role of PA in sputum at admission in COPD hospitalized patients have been reported.[13-15] Our hypothesis was that there would be specific risk factors that would predict a change in flora and an increased risk for the presence of PA in sputum in this population. On this basis, the aim of the study was to determine the incidence and risk factors for PA isolation in sputum at hospital admission in a prospective cohort of patients with AECOPD.

Methods

Subjects

We prospectively studied all consecutive patients admitted to our institution for AECOPD between June 2003 and September 2004. All episodes of hospital readmissions of the cohort during the subsequent year until September 2005 were also prospectively followed up. The study was carried out in a 500-bed university hospital in the province of Barcelona, Spain. Inclusion criteria were hospitalization for AECOPD and basal forced spirometry showing $FEV_1 \leq 70\%$ of their reference value and β_2-agonist reversibility of predicted FEV_1 of < 15% and/or 200 ml. with FEV1/FVC < 70%. Exclusion criteria included a history of asthma or bronchiectasis as a predominant illness, pneumonia or pulmonary edema at admission, hospitalization for causes other than AECOPD, or patient refusal to participate in the study. COPD exacerbation was defined following Anthonisen's criteria.[16] Admission criteria were at the discretion of the emergency room physician. For the purposes of this study, patients were divided into two groups: those in whom PA was isolated in sputum at hospital admission (PA group) and those in whom PA was not isolated in sputum at hospitalization (non-PA group). Written informed consent was obtained from each subject and the study was approved by the ethics committee at our institution.

Clinical evaluation

At the initial visit, patients provided a complete clinical history and underwent physical examination. Information collected included demographic characteristics, body mass index (BMI), comorbidity (as measured by the Charlson index), previous functional dependence (Katz score) and dyspnoea measured by the modified Medical Research Council (mMRC). Information on smoking history, number of hospitalizations for COPD within last year, time to last hospital discharge, use of antibiotics within the last three months and prior admission, use of systemic or inhaled corticosteroids, and chronic home use of oxygen

therapy prior to admission were also collected. Chronic systemic corticosteroid use was considered when doses equivalent to prednisone ≥ 5mg/day had been given for at least the 3 previous months.

Microbiological studies

Spontaneous or induced sputum samples were collected at admission and at each readmission, before antibiotic administration (online supplement 1). Bacterial agents were classified into potential pathogens (PPMs) and non-PPMs, as previously described.[3] Only PPMs were evaluated. In some patients with ≥ 2 of PA in sputum in different admissions, strains were typed by pulsed-field gel electrophoresis. The presence of a mucoid phenotype on PA isolation agar plates was recorded.

HRCT evaluation

The presence of bronchiectasis was assessed at the first hospital admission. To limit radiation and costs, patients were randomised for a high-resolution computed tomography (HRCT) of the chest, in a 2:1 ratio. The diagnosis of bronchiectasis was based on standard criteria. HRCT scans were interpreted by two experienced radiologists blinded to the patients clinical grouping and microbiological status. Posterior consensus was reached in case of disagreement. Bronchiectasis score was detailed in online supplement 2.

Follow-up

A follow up visit took place approximately 1 month after discharge. At this visit, forced spirometry and bronchodilatador testing were performed according to standard techniques[17]. Six-minute walking-test was performed following the ATS recommendations[18]. BODE index was also calculated as the sum score proposed by Celli et al[19]. In case of hospital readmission within the first month after discharge, the patient was

followed up for one month after reaching clinical stability. All patients were followed up for hospital readmission during the year after discharge.

Statistical analysis

Sample size calculation was based on FEV_1 values (postbronchodilator FEV_1 40% of predicted for PA patients, and 50% for non-PA patients, with an α and β error of 0.05 and 0.1, respectively). A percentage of 10% patient loss was assumed. Accordingly, the calculated size was 234 patients. To assess factors associated with PA isolation, we compared the PA and non-PA groups. To detect significant differences between groups we used the chi-square test with continuity correction for categorical variables. Quantitative variables were analyzed using Student's t-test or their corresponding non-parametrical tests when the distribution of data, so required. The relationship between bronchiectasis score and FEV_1 was calculated with the Pearson correlation coefficient. For multivariate analysis a logistic regression model was constructed with PA isolation as a dependent variable. In this model independent variables included the most clinically relevant variables that were found to be significant in bivariate analysis.

Data analysis was performed in SPSS for Windows software package version 11 (SPSS Inc, Chicago). In all analyses, we considered P values ≤ 0.05 to be statistically significant. All reported P values are two-tailed.

Results

Patient characteristics

Over the study period, a total of 254 patients with a suspected diagnosis of AECOPD were admitted to hospital. Of these, 66 patients were excluded for the following reasons: impossibility to perform spirometry or lack of spirometric criteria (26 patients; 10.2%), pneumonia (25 patients; 9.8%), bronchiectasis as a main manifestation of disease (6 patients; 2.3%), idiopathic fibrosis (4 patients; 1.6%), and others (5 patients; 2.0%). The studied population was predominantly men (95%), with a mean age of 72.1 (±10.0 SD) years and mean length of stay of 11 (±8.7) days. Sociodemographic and functional characteristics are shown in Table 1.

Of the 188 patients included, 157 (83.5%) were in the non-PA group and 31 (16.5%) constituted the PA-group. When comparing groups, no significant differences in age or gender were observed. PA isolation in sputum was more frequent in patients with the worst values of Katz score (4.7 versus 5.6; p=0.03) and the mMRC (3.4 versus 2.7; p=0.001). The PA group had a stronger history of smoking than patients in the non-PA group (73.7 mean of pack-years of smoking versus 56.8; p= 0.02). Previous hospital admissions in the last month (32.3 % versus 14.0%; p=0.001) and number of previous episodes of admission within the last year (3.1 versus 0.9; p= 0.002) were more frequent in the PA group. Acute and chronic steroid therapy were more frequent in patients in the PA group (22.6% versus 6.6%; p= 0.012 and 12.9% vs. 2.5%; p<0.01, respectively). No relation between the use of inhaled steroids or antimicrobial use in the last three months and PA isolation was found.

Respiratory parameters significantly associated with the presence of PA in sputum at admission were: severity of disease as measured by postbronchodilator FEV_1 (38.7% mean of FEV_1 versus 45.9%; p=0.012), the poorest values for 6 minute walking test (217.5 meters versus 343.7; p<0.001) and chronic home oxygen therapy (32.3 versus 15.6; p= 0.041).

BODE index was also significantly associated with PA isolation (7.3 vs. 5.4; p= 0.0005). As a summary, data of significant variables in bivariate analysis are shown in Table 2.

HRCT scan of the chest was performed in 88 randomized patients. Patients with HRCT were similar with respect to age, previous admissions, corticosteroid use, FEV_1, FVC, and other physiological parameter measured, compared to those who did not undergo HRCT scanning. Forty-six patients (52%) had significant detectable bronchiectasis on HRCT (two or more dilated bronchi; global score in percentage ≥ 5.6%). Of those in whom bronchiectasis was detected, the median score was 25% (range 5-56) (Figure 1). No statistical relationship was seen between the total bronchiectasis score and FEV_1 measurement (r^2=0.059; p=0.058), 6 minute walking test (r^2 =0.002; p=0.784) or BODE index (r^2=0.009; p= 0.94). Similarly, no relation was found between score of bronchiectasis and positive bacterial culture (p= 0.76) or PA isolation in sputum at admission (p=0, 09; CI 95%: 0.99-1.05).

Microbiological findings

Of the 188 patients included, 119 (63.3%) had good quality sputum in the first hospital admission. Non-PPMs were isolated in 55% of these patients while PPMs were found in 45% of cases. A single bacterial species was isolated in 50 patients, two in 3, and three in 1. PA was the most frequently isolated species in patients with valid sputum (31/119 cases; 26%) followed by *S. pneumoniae* and *H. influenzae* (11 cases, each; 9.2%). The presence of other microorganisms was infrequent.

During the initial admission and the subsequent year of prospective follow-up, a total of 469 episodes of hospitalization due to COPD exacerbation were collected (134 in PA group and 335 in non-PA group), and valid sputum was collected in 220 episodes (47%). Patients with positive bacterial cultures of sputum (any microorganism) had a lower FEV_1 than patients with negative sputum cultures at admission (p=0.003).

As shown in Figure 2, the global incidence of PA isolation in the index of hospitalization and readmissions during the subsequent year was 23.18% of all episodes. *H. influenzae* (11%) and *S. pneumoniae* (10%) remained common etiologies for COPD exacerbation in patients requiring hospitalization. Patients in the PA-group were readmitted more frequently than patients in the non-PA group (p=0.001), and were more likely to present valid sputum during these readmissions than patients in the non-PA group (p<0.001). The relation between different microorganisms and FEV_1 is shown in Figure 3.

Among the 31 patients with PA in the first admission, in 12 it was isolated only once, in 11 twice, and in 8 ≥3 times, in sputum cultures performed during subsequent admissions. Previous isolation of PA was associated with a higher probability of a new PA isolation (p<0.001). Molecular typing of 41 PA strains from 10 patients obtained in different exacerbations showed that the current strain was identical to the original in 7 patients (70 %) and in 37 (90%) of samples. Of note, all persisting PA strains were non-mucoid (6 patients) with a single instance of persisting mucoid strain (1 patient) (Online supplement). Table 3 shows the antibiotic susceptibility pattern of PA isolates. Of 31 patients in the PA-group, only 4 patients received empirical antibiotic treatment with pseudomonal coverage (quinolones: 3 patients and ceftazidime: 1 patient). Twelve patients received antipseudomonal treatment when the microbiological results were known.

Factors associated with PA isolation in multivariate analysis

Table 4 summarizes the results of multivariate analysis of factors potentially associated with PA isolation. Significant variables associated independently with PA isolation were BODE index (OR: 2.18; CI 95%: 1.26-3.78; p=0.005), number of hospital admissions in the previous year (OR: 1.65; CI 95%: 1.13-2.43; p=0.005), systemic steroid treatment (OR: 14.7; CI 95%: 2.28-94.8; p=0.01), and previous isolation of PA (OR: 23.1; CI 95%: 5.7-94.3; p<0.001).

Discussion

In this prospective study we offer a comprehensive evaluation of the incidence and risk factors for PA isolation in a large prospective cohort of patients hospitalized for AECOPD. To our knowledge, the present study is the first to assess specifically, in a prospective cohort, the multidimensional risk factors of PA isolation in sputum in patients hospitalized for AECOPD. The most important finding of our study is the strong relationship between PA isolation at hospital admission and several markers of respiratory functional impairment. Additionally, our study shows that the incidence of PA in sputum in this population is high (23% of total episodes). Specifically, this incidence is higher than that reported in ambulatory patients [5,8-10].

Various studies regarding the microbiology of hospitalized patients for AECOPD have recently been published. Eller et al showed the relevance of gram-negative bacilli isolation in sputum as the most frequent species isolated in a cohort of 112 patients (48.2% of cultures positive for PPMs) [13]. More recently, Lin et al showed similar results [20]. However, both studies were retrospective, and with a likely selection bias (higher rate of sputum collection among patients with more severe disease or no antibiotic response during hospitalization). In contrast, Groenewegen et al only reported PA isolation in 15% of positive cultures (13/85) and 18% of cultures positive for PPMs (13/71)[15]. The present study also confirms previous data [2, 8, 9, 14, 15] reporting a higher incidence of bacterial isolation in sputum in patients with worse values of FEV_1.

The relationship between the type of bacteria isolated and the degree of functional impairment, as measured by FEV_1, has been a matter of debate in recent years. Eller et al reported a correlation between lower FEV_1 values and the presence of PA in patients hospitalized for AECOPD [13]. In contrast, Groenewegen et al were not able to demonstrate differences between the type of bacteria isolated and clinical characteristics or lung functional parameters [14]. A possible explanation is that Groenewegen et al performed

spirometries prior to discharge from hospital and therefore they should not be considered true baseline values.

The risk factors for PA isolation in sputum in patients with AECOPD have become a major issue. Although guidelines offer recommendations for the subset of patients in whom PA should be strongly suspected, limited data exist to identify this population, and the available data come mostly from studies involving ambulatory patients [8,10,12,21]. Up to the present time, the accepted risk factors for PA isolation in hospitalized patients were previous hospitalization, recent antibiotic therapy, disease severity measured with FEV_1 and previous infection with PA. The present study confirms some of these risk factors, and adds new prognostic variables such as functional dependence, dyspnea score, walking test, oral corticosteroid treatment and, of note, the BODE index. This multidimensional index is an excellent marker of severity in COPD and provides more reliable information about vital prognosis, risk of hospitalization and treatment response than the FEV_1 [19,22,23]. Additionally, BODE index, along with systemic steroids treatment, hospital admissions during the previous year and previous isolation of PA, are independent factors associated with the isolation of PA in sputum in AECOPD.

Our study was not able to demonstrate a relationship between antibiotic treatment in the last three months and the presence of PA in sputum. This result is concordant with previous studies [14].

One of the most important points of criticism in studies dealing with AECOPD is the inclusion of patients with bronchiectasis. Bronchiectasis is thought to be a special entity. However, recent studies based on 44 and 110 outpatients yielded evidence that moderate bronchiectasis on HRCT is common in ambulatory COPD patients, although studies dealing with the incidence of bronchiectasis in hospitalized patients with COPD were lacking [24,25]. We can confirm that the prevalence of moderate bronchiectasis is high in this population (52%). However, no relationship was seen between bronchiectasis score and spirometric

measurements or the presence of PA in the sputum. Although we cannot rule out a shortfall of statistical power, these results are similar to previous studies [24].

One of the limitations of our study was the lack of distinction between bacterial colonization of the lower airways and infection by PA, and this issue remains unsolved. Recently, Murphy and coworkers showed that isolation of a new strain of PA in ambulatory patients was associated with the occurrence of an exacerbation. In their study most new strains of PA (54%) cleared up, and in the majority of cases (67.7%) without active antibiotic therapy. Colonization understood as persistent carriage was observed in only 23% of patients.[26] Some studies would suggest that the use of quantitative cultures is useful to distinguish between infection and colonization, but no conclusive results are available [8,14]. Many studies have used semiquantitative methods to evaluate bacterial infection in AECOPD and, more importantly, recent work has shown that bacteria obtained from good quality sputum are the same as those obtained through bronchoscopy and protected specimen brush [27,28]. Another limitation of our study was the significant number of patients in the control group (non-PA) without a valid sample of sputum, and the low rate of isolation of PPMs. Nonetheless, the percentage of positive sputum samples was similar to that found in previous prospective studies [15,28], and the aim of our study was to determine the risk factors for PA isolation in patients hospitalized with AECOPD comparing them with those without PA in the sputum. Finally, the low number of women in our cohort of COPD patients is concordant with previous studies in our area and probably related with the low prevalence of tobacco use among women for many years [11,29].

Our study shows that the majority of PA isolates remain susceptible to most antipseudomonal agents, including fluoroquinolones. We would concur with recent guidelines that suggest these drugs be considered as empirical treatment for patients with the worst functional impairment [12,21], but variations in the antibiotic resistance profiles in different geographic areas should be contemplated. The present study was not designed to evaluate the utility of specific antimicrobial treatment in persistence of PA, and therefore we

cannot specify whether their use can improve the prognosis in these patients. We have commented previously that a high percentage of the PA disappears without antibiotic treatment [26], and the higher number of readmissions in the PA group seems to be more related with a greater severity of the disease than with failure of the antibiotic treatment. Future research leading to better understanding the role of the specific antimicrobial treatment in these patients is needed.

In summary, we have shown the high prevalence of PA isolation in sputum in patients hospitalized for AECOPD. PA is associated with the worst functional parameters, systemic corticosteroid treatment, previous hospital admissions, worse values of BODE index, and previous isolation of PA.

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Figure legend

Figure 1. Total bronchiectasis score: 46 of 88 patients (52%) had significant detectable bronchiectasis (two or more dilated bronchi; global score in percentage ≥ 5.6%) on HRCT.

Figure 2. Bacterial isolates (%). Valid sputum: index admission (n=119), total admissions (n=220). Non-PPM= non-potential pathogenic microorganisms, PA=*Pseudomonas aeruginosa*, EB= enterobacterias, HI= *Haemophilus influenzae*, SP *Streptococcus pneumoniae*, MC= *Moraxella catharralis*.

Figure 3. Relation between FEV_1 values and bacterial isolates (p=0.035).

Non-PPM= non-potential pathogenic microorganisms, PA=*Pseudomonas aeruginosa*, EB= enterobacterias, HI= *Haemophilus influenzae*, SP *Streptococcus pneumoniae*, MC= *Moraxella catharralis*.

Figure 1. Total bronchiectasis score in 88 patients.

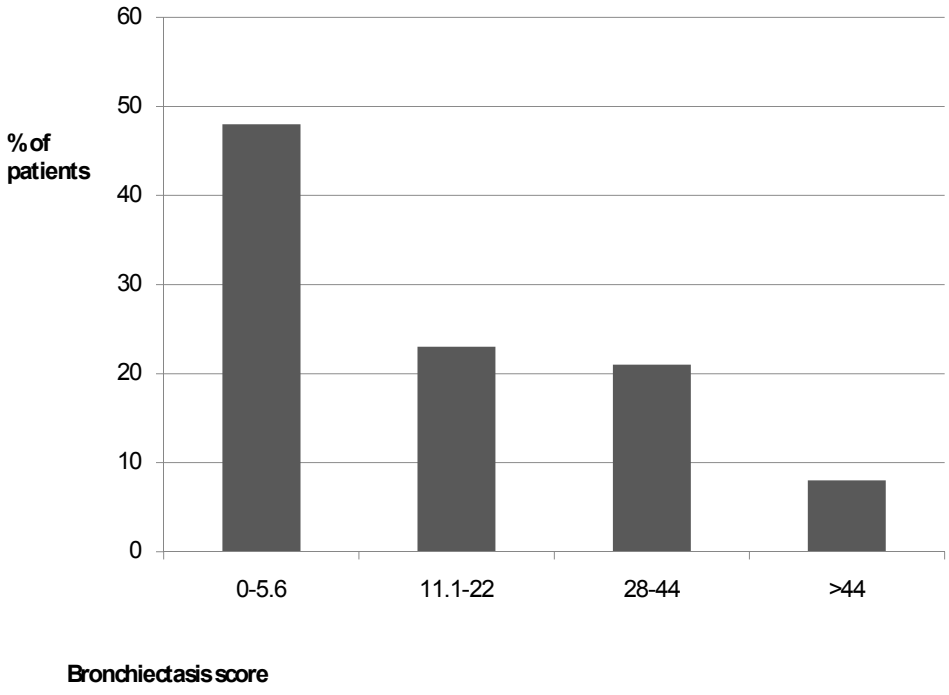

Figure 2. Bacterial isolates of patients with valid sputum.

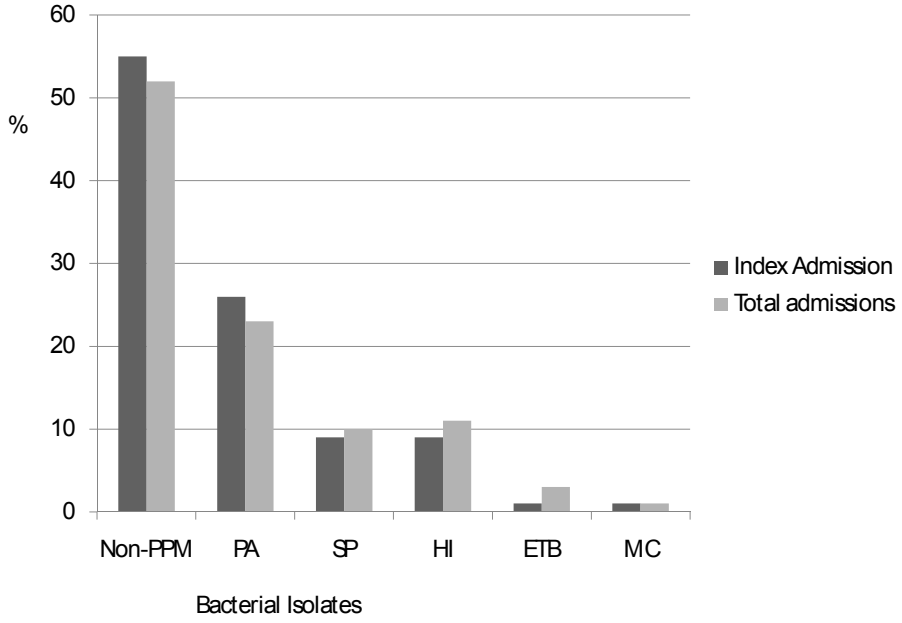

Figure 3

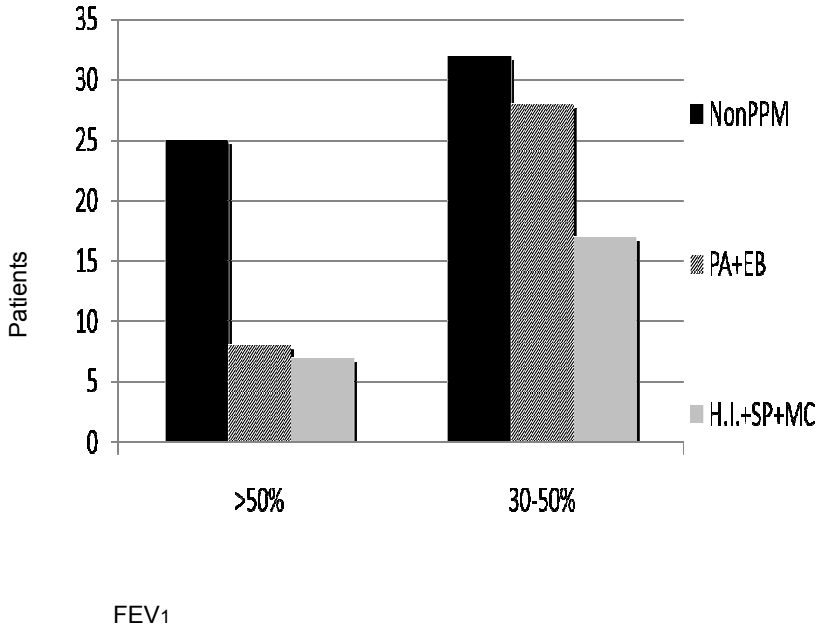

Table 1. Characteristics of 188 patients hospitalized with acute COPD exacerbation during the period of study.

Characteristics	Total (n=188)
Age, years	72.11 (10.0)
Male gender (%)	178 (94.7 %)
FEV_1, L PBD	1.04 (0.37)
FEV_1 predicted PBD	44 (14.52)
Severity according to GOLD Stage	
Stage II, moderate	65 (34.6%)
Stage III, severe	95 (50.5%)
Stage IV, very severe	28 (14.9%)
Walking test (meters)	330 (105)
Charlson index	2.17 (1.3)
Katz Score	5.46 (1.3)
Dyspnea (mMRC)	2.78 (1.2)
Pack-years of smoking	59.84 (35.4)
Number of patients with a hospital admission in the previous month	32 (17 %)
Episodes of admission in previous year	1.27 (2.0)
Days hospitalized in previous year	12.84 (25.9)
Antimicrobials in last three months (number %)	62 (33 %)
Body Mass Index	27.8 (5,2)
Inhaled steroids (%)	140 (76.5%)
Systemic steroids (%)	17 (9.3%)

All data are quoted as means and standard desviation, unless otherwise specified.

PBD= postbronchodilator test

Table 2. Characteristics of 188 patients hospitalized with acute COPD exacerbation; PA-group as compared with 157 patients in non-PA group.

	PA group (n=31)	Non-PA group (n=157)	P	O.R.	C.I: 95%
Katz index	4.74 (1.9)	5.61 (1.1)	0.03	0.67	0.51-0.90
Dyspnea (mMRC)	3.43 (0.8)	2.66 (1.2)	0.001	2.07	1.22-3.50
Smoking (p/y)	73.7 (39.7)	56.76 (33.8)	0.02	1.01	1.003-1.02
Hospital admission in last month (%)	10 (32%)	22 (14%)	0.001	2.95	1.16-7.48
Nº admissions in previous year	3.06 (3.5)	0.91 (1.3)	0.002	1.47	1.19-1.81
Days hospitalized in previous year	38.3 (51.7)	8 (12.7)	0.004	1.04	1.02-1.06
Antibiotic treatment in previous 3 months (%)	11 (35.5%)	51 (32.5%)	0.828	1.14	0.51-2.57
Systemic corticosteroids (%)	7 (22.6 %)	10 (6.6 %)	0.01	3.57	1.17-10.88
Chronic systemic corticosteroids (%)	4 (12.9%)	4 (2.5%)	0.01	5.66	1.3-24
FEV_1 % PBD	38.7 (12.2)	45.9 (14.7)	0.01	0.96	0.93-0.99
Walking test meters	217.5 (103)	343.7 (98.5)	<0.001	0.99	0.98-0.99
BODE index	7.32 (1.72)	5.42 (2.53)	<0.001	1.45	1.17-1.78
Number of Anthonisen criteria			0.735		
1	6 (19%)	40 (26%)			
2	8 (26%)	41 (26%)			
3	17 (55%)	76 (48%)			
Previous isolation PA	19 (61.3%)	12 (7.6%)	<0.001	122	25.5-590
Home oxygen therapy	10 (32.3%)	24 (15.3%)	0.04	0.48	0.19-1.1

All data are quoted as means and SD, except those expressed as percentage.

PBD= postbronchodilator test

Table 3. Antibiotic resistance profile of 31 PA isolates

Antibiotic	**Number of susceptible strains (%)**
Ciprofloxacin	24 (77.4)
Piperacillin-Tazobactam	26 (83.9)
Ceftazidime	27 (87.1)
Imipenem	27 (87.1)
Gentamicin	25 (80.6)
Amikacin	27 (87.1)

Table 4. Risk factors associated with PA isolation in sputum in 188 patients hospitalized with COPD exacerbation; multivariate analysis.

Variable	**p**	**O.R.**	**C.I. 95%**
BODE index	0.005	2.18	1.26-3.78
Hospital admissions in previous year	0.005	1.65	1.13-2.43
Systemic steroid treatment	0.01	14.7	2.28-94.8
Previous isolation of PA	<0.001	23.1	5.7-94.3

Online supplement

1.-Microbiological data:

Sputum collection and microbiological studies were performed using the usual methods. Sputum induction was performed with a 3% saline nebulizer and respiratory physiotherapy, when required. Only good quality samples (<10 squamous epithelial cells and >25 leucocytes per field) were accepted for processing. Sputum samples were processed microbiologically for semiquantitative culture following accepted laboratory methods. Using the microbiological loop, sputa were seeded in MacConkey agar under aerobic conditions, and in chocolate agar and blood agar at an atmosphere containing 5 to 7% CO_2.

2.-HRCT evaluation

Bronchiectasis was scored in each lobe: 0 if no bronchiectasis was present; 1 if less than one lung segment was affected; 2 if more than one lung segment was affected and 3 when gross cystic bronchiectasis involved the entire lobe. The lingula was graded as a separate lobe, resulting in a maximum score of 18 per patient. The overall bronchiectasis score was expressed as a percentage [(Bronchiectasis score/Bronchiectasis maximum score) x 100]. In accord with previous studies, patients with a score of 0 or 1 (less than 2 affected segments) were considered normal.

1.- Angrill J, Agusti C, de Celis R, Rano A, Gonzalez J, Sole T, Xaubet A, Rodriguez-Roisin R, Torres A. Bacterial colonisation in patients with bronchiectasis: microbiological pattern and risk factors. *Thorax* 2002;57:15-9.

2.- Patel IS, Vlahos I, Wilkinson TM, et al. Bronchiectasis, exacerbation indices, and inflammation in chronic obstructive pulmonary diseases. *Am J Respir Crit Care Med* 2004¸170:400-7.

Table 1 Online supplement

Persistent strain of PA in patients with 2 or more PA

PATIENT	PFGE	PHENOTYPE
1	A	Non-Mucoid
	A	Non-Mucoid
	A	Non-Mucoid
	A	Non-Mucoid
	A	Non-Mucoid
	A	Non-Mucoid
	A	Non-Mucoid
	A	Non-Mucoid
2	B	Mucoid
	C	Mucoid
3	D	Non-Mucoid
	D	Non-Mucoid
4	E	Non-Mucoid
	E	Non-Mucoid
	E	Non-Mucoid
	E	Non-Mucoid
	F	Non-Mucoid
5	G	Non-Mucoid
	G	Non-Mucoid
6	H	Non-Mucoid
	H	Non-Mucoid
7	I	Non-Mucoid
	I	Non-Mucoid
	I	Non-Mucoid
8	J	Non-Mucoid
	J	Non-Mucoid
9	K	Non-Mucoid
	K	Non-Mucoid
	K	Non-Mucoid
	K	Non-Mucoid
	L	Non-Mucoid
10	M	Mucoid
	M	Mucoid
	M1	Mucoid
	M1	Mucoid
	M2	Mucoid
	M	Mucoid

PFGE= Pulsed field gel electrophoresis.

Figure 1. Online supplement

HRCT in patients with PA