Bronchial colonisation in patients with lung cancer: a prospective study

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ABSTRACT Bronchial colonisation is frequently reported in patients with lung cancer, and has a potential impact on therapeutic management and prognosis. We aimed to prospectively define the prevalence and nature of bronchial colonisation in patients at the time of diagnosing lung cancer.

210 consecutive patients with lung cancer underwent a flexible bronchoscopy for lung cancer. The type and frequency of bacterial, mycobacterial and fungal colonisation were analysed and correlated with the patients' and tumours' characteristics.

Potential pathogens were found in 48.1% of samples: mainly the Gram-negative bacilli *Escherichia coli* (8.1%), *Haemophilus influenzae* (4.3%) and *Enterobacter* spp. (2.4%); Gram-positive cocci, *Staphylococcus* spp. (12.9%) and *Streptococcus pneumoniae* (3.3%); atypical mycobacteria (2.9%); *Candida albicans* (42.9%); and *Aspergillus fumigatus* (6.2%). Aged patients (p=0.02) with chronic obstructive pulmonary disease (p=0.008) were significantly more frequently colonised; however, tumour stage, atelectasis, bronchial stenosis and abnormalities of chest radiography were not associated with a higher rate of colonisation. Squamous cell carcinoma tended to be more frequently colonised than other histological subtypes. Airway colonisation was reported in almost half of patients presenting with lung cancer, mainly in fragile patients, and was significantly associated with worse survival (p=0.005).

Analysing colonisation status of patients at the time of diagnosis may help improve the management of lung cancer.

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Introduction

Lung cancer remains a major public health problem worldwide for both sexes, and its incidence and mortality are increasing [1]. Despite substantial improvements in the diagnosis and therapeutic management of the different histological types of lung cancer, morbidity and mortality are still high, notably due to pulmonary infectious complications, which account for 35–70% of cases [2–4]. Radio-clinical presentations range from bronchitis to septicaemia, including pneumonia and empyema. These complications often occur post-therapeutically but pulmonary infection may also be present at the initial diagnosis of cancer [2, 3, 5].

It has been suggested that bronchial colonisation plays a key role in the establishment of pulmonary infections in patients with lung cancer, and thus clearly influences the therapeutic management and probably the prognosis of cancer [3, 4, 6, 7]. In such patients, colonisation may arise following local bronchial impairment, *e.g.* stenosis or impaired mucociliary clearance, or be caused by more general abnormalities, including immunosuppression, malnutrition, smoking, chronic obstructive pulmonary disease (COPD) and chemotherapy [5, 8–11]. Studies indicate that bronchial colonisation can be demonstrated in 10–83% of patients with lung cancer and may be caused by potential pathogenic microorganisms (PPMs), mainly *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Staphylococcus aureus* [2–8, 11, 12]. Other potential microbial agents, such as mycobacteria and fungi, have not been investigated systematically.

A review of the literature highlights important differences in the methodologies used to detect bronchial colonisation [7]. Microorganisms have been isolated from bronchoalveolar fluid, sputum, protected specimen brush and bronchoscopic aspirations. In some cases, colonisation has not been clearly distinguished from infection because of the absence of specific colonisation thresholds: $\geqslant 10^2$ cfu·mL^{-1} for protected specimen brush or $\geqslant 10^4$ cfu·mL^{-1} for bronchial aspirates, irrespective of the species of microorganism [5, 11, 12]. Moreover, these studies do not discriminate between bronchial samples used for cancer diagnosis and those obtained during neoplastic evolution, except in our retrospective study of 388 patients [11]. Overall, although the importance of infection in lung cancer patients has been previously demonstrated, a clear picture of the prevalence of bronchial colonisation in lung cancer patients cannot be obtained from the literature because of the patient selection criteria used, the mix of pre- and post-diagnosis analyses, the variety of procedures used and the discrepancies between defining infection and colonisation.

In our study, we aimed to prospectively determine the prevalence and nature of bronchial colonisation in per-endoscopic aspirations from patients presenting with lung cancer at the time of diagnosis and before any specific treatment. We also assessed the potential relationships between colonisation and the histological and radio-clinical presentation of the cancer as well as its potential impact on patient survival.

Methods

Ethical considerations

This study was performed with the approval of our institutional ethical committees (CPP region Midi-Pyrénées, CCTIRS, CNIL, CHU de Toulouse) under reference 0803203. Written informed consent was obtained from each patient before inclusion.

Patients and study design

This prospective study included a cohort of patients with lung cancer, who had undergone flexible bronchoscopy and bronchial aspiration at the time of diagnosis of cancer to evaluate the prevalence and nature of their bronchial colonisations. Patients (n=210) were consecutively enrolled in our Pulmonary Diseases Dept, Hôpital Larrey, CHU de Toulouse, Toulouse, France, between August 2008 and January 2010.

Clinical and paraclinical data were collected from each patient at the time of the initial bronchoscopy for diagnosis of cancer, and during follow-up. Relevant characteristics of patients included were: clinical signs of fever; cough; sputum samples; biological markers of infection, such as blood leukocyte and neutrophil counts and C-reactive protein-serum concentration; chest radiography for signs of infection or atelectasis; and endoscopic evidence of stenosis, ulceration and sub-epithelial infiltration. Medical history of smoking (pack-years), diabetes, alcoholism, immunosuppression and COPD (according to the Global Initiative for chronic Obstructive Lung Disease (GOLD) score) were also collected from each patient. Cancer was staged according to the 1997 TNM (tumour, node, metastasis) classification (as the new 2009 classification was not available at the beginning of the study). All these data were recorded in a Microsoft Access database for further statistical analyses.

TABLE 1 Histological types, disease staging and TNM (tumour, node, metastasis) classification of lung cancer diagnosed in the studied population

Characteristic	Patients n (%)
Histological types	
Adenocarcinoma	107 (51.2)
Squamous cell carcinoma	62 (29.7)
Small cell carcinoma	21 (10.0)
Large cell carcinoma	7 (3.3)
Other	12 (5.7)
Staging	
0	0 (0.0)
I or II	38 (11.9)
III	49 (24.4)
IV	114 (56.7)
ND	9 (4.7)
T descriptor	
T0	0 (0.0)
T1	25 (11.9)
T2	59 (28.1)
T3	33 (17.6)
T4	69 (32.9)
TX	5 (2.4)
ND	15 (7.1)
N descriptor	
N0	48 (22.9)
N1	15 (7.1)
N2	61 (29.0)
N3	59 (28.1)
NX	12 (5.7)
ND	15 (7.1)
M descriptor	
M0	85 (40.5)
M1	112 (53.3)
ND	13 (6.2)

ND: not done.

Bronchoscopic procedures

Following local anaesthesia of the airways by spraying xylocaine (1%, 10 mL) without epinephrine, all patients underwent per-endoscopic lung aspirates at the distal part of the bronchi close to the tumour site. For this, we used standard video-bronchoscopes (PENTAX EB 1570 K; PENTAX Medical Company, Montvale, NJ, USA), 5.1-mm external diameter, equipped with a 2-mm-operator canal. In some cases, we used an interventional video-bronchoscope, 6.2-mm external diameter, equipped with a 2.8-mm operator canal.

Microbiological analyses

Lung aspirates (10–20 mL) were processed within 2 h for bacterial, mycobacterial and mycological analysis using routine procedures. Possible upper airway contaminations were ruled out according to the Bartlett–Murray–Washington classification. Only grade IV or V samples were processed (grade IV: 10–25 squamous epithelial cells and >25 leukocytes; grade V: <10 epithelial cells and >25 leukocytes per field using a low-magnification lens ($\times 100$)) [13].

Bacterial colonisation was defined as the isolation of microorganisms in bronchoscopic aspirates at a threshold of $\geqslant 10^2$ cfu·mL^{-1}, whereas infection was considered at $>10^5$ cfu·mL^{-1} [11, 14]. Regardless of the amount, isolation of mycobacteria and non-commensal fungi were considered as colonisation or an infection depending on the species isolated [11].

Data analyses

Baseline characteristics at the time of diagnosis were recorded (per cent for qualitative variables, mean $\pm$ SD for quantitative variables). The prevalence of colonised patients at both thresholds ($\geqslant 10^2$ and $\geqslant 10^5$ cfu·mL^{-1}) at the time of diagnosis was computed with a 95% confidence interval. We compared

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TABLE 2 Characteristics of colonised patients with lung cancer

Microorganism	n (%) $\geqslant 10^2$ cfu·mL^{-1}	% $\geqslant 10^2$–$<10^5$ cfu·mL^{-1}	% $\geqslant 10^5$ cfu·mL^{-1}
PPM			
Staphylococcus aureus	27 (12.9)	3.3	9.5
Escherichia coli	17 (8.1)	6.2	1.9
Proteus mirabilis	14 (6.7)	4.3	2.4
Haemophilus influenzae	9 (4.3)	2.4	1.9
Klebsiella oxytoca	8 (3.8)	1.4	2.4
Streptococcus pneumoniae	7 (3.3)	0.5	2.8
Serratia spp.	6 (2.9)	2.9	0.0
Enterobacter spp.	5 (2.4)	1.0	1.4
Pseudomonas aeruginosa	5 (2.4)	1.4	1.0
Morganella morganii	1 (0.5)	0	0.5
Stenotrophomonas maltophilia	1 (0.5)	0	0.5
Non-PPM			
Streptococcus viridans	188 (89.5)		
Neisseria spp.	95 (45.2)		
Haemophilus parainfluenzae	91 (43.3)		
Rothia spp.	18 (8.6)		
Corynebacterium spp.	13 (6.2)		
Coagulase-negative *Staphylococcus*	10 (4.8)		
Atypical *Mycobacterium*	6 (2.9)		
Aspergillus fumigatus	13 (6.2)		
Candida albicans	90 (42.9)		
No microorganism	8 (3.8)		

PPM: potential pathogenic microorganisms.

baseline characteristics between colonised and non-colonised patients using the appropriate tests (t-test, Wilcoxon's test, Chi-squared or Fisher's exact test). We estimated the association between baseline characteristics and the probability of being colonised using a multivariate logistic regression. The first multivariate model included characteristics that tended to be associated with colonisation in bivariate analysis ($p<0.20$): sex, age, leukocytes, COPD and histological type. Survival curves were estimated using the Kaplan–Meier method according to colonisation status, and were compared by a log-rank test. Survival was then studied according to colonisation status using a multivariate Cox model adjusted for potential confounders. These were associated with survival at a p-value of <0.20 in bivariate analyses (sex, age, histological type, disease stage, diabetes, alcohol use and performance status).

The number of further bronchopulmonary infections per patient was then assessed using bivariate analyses (assuming Poisson distributions). Next, the number of bronchopulmonary infections per patient, according to colonisation, was assessed by multivariate regression analysis adjusted for sex, disease stage and alcohol use: all of which had been associated with bronchopulmonary infection in bivariate analyses at a p-value of <0.20. We used negative binomial regression to take into account the over-dispersion phenomenon. Statistical analyses were computed using Stata SE 11.1 (StataCorp LP, College Station, TX, USA).

Results

Population characteristics

The population consisted of 161 males (76.7%) and 49 females (23.3%), mean age 61.9 years; 63.6% were still working. Patients were mainly performance status 1 (53.5%) and 84.5% were active smokers. Medical history indicated COPD in 45.5% of patients with GOLD stage 1 in 69.0%. Diabetes was recorded in 13.0%, immunosuppression in 22.3% (86.4% of which was due to cancer) and a history of systemic corticotherapy in 8.6%. Frequent alcohol consumption (*i.e.* >30 g of alcohol per day) was found in 16.4%.

Anatomopathology and staging

Histological types, disease staging and TNM descriptions of lung cancers diagnosed in the 210 patients are reported in table 1. Adenocarcinoma predominated (51.2%) over other histological types, including squamous-cell carcinoma (29.7%), small-cell lung carcinoma (10.0%) and large-cell lung carcinoma (3.3%). According to the 1997 TNM classification, T4 was found in 32.9%, N2 in 29.0% and M1 in 53.3% of patients.

TABLE 3 Univariate analysis of the association between the patients' characteristics and bacterial colonisation

Characteristic	Not colonised	Colonised	p-value
Age years	60.4	63.5	0.02
Sex			
Male	79 (72.5)	82 (81.2)	0.14
Female	30 (27.5)	19 (18.8)	
Leukocytes mean per mm^3	9608 (n=95)	10166 (n=87)	0.24
COPD			
No	66 (63.5)	44 (44.9)	0.008
Yes	38 (36.5)	54 (55.1)	
COPD			
Stage I	23 (23.2)	26 (31.7)	0.75
Stage II	6 (6.1)	9 (11.0)	
Stages III/IV	4 (4.0)	3 (3.7)	
Diabetes			
No	94 (86.2)	87 (87.9)	0.73
Yes	15 (13.8)	12 (12.1)	
Corticotherapy			
No	95 (92.2)	85 (90.4)	0.65
Yes	8 (7.8)	9 (9.6)	
Performance status			
0	31 (29.2)	28 (29.2)	0.41
1	61 (57.5)	47 (49.0)	
2	11 (10.4)	17 (17.7)	
3–4	3 (2.8)	4 (4.2)	
Smoking			
No	7 (6.5)	5 (5.0)	0.39
Yes	87 (81.3)	88 (88.0)	
Ex-smoker	13 (12.1)	7 (7.0)	
Histological type			
Squamous cell carcinoma	24 (22.2)	38 (37.6)	0.14
Adenocarcinoma	59 (54.6)	48 (47.5)	
Large cell carcinoma	5 (4.6)	2 (2.0)	
Small cell carcinoma	13 (12.0)	8 (7.9)	
Other	7 (6.5)	5 (5.0)	
Stage			
0	0.0	0.0	0.58
I or II	17 (16.3)	21 (21.6)	
III	25 (24.0)	24 (24.7)	
IV	62 (59.6)	52 (53.6)	

Data are presented as n (%), unless otherwise stated. n=210. COPD: chronic obstructive pulmonary disease.

Colonisation characteristics

Colonisation by PPMs was recorded in 101 of the 210 patients at the threshold $>10^2$ cfu·mL^{-1} (48.1%, 95% CI 41.2–55.1) (table 2).

A high proportion of PPMs were detected at between 10^2 and 10^5 cfu·mL^{-1}: at the latter threshold only 44 of the 210 patients were colonised (20.9%, 95% CI 15.7–27.1). Overall the predominant species were *S. aureus* (12.9%) ahead of *Escherichia coli* (8.1%) and *Proteus mirabilis* (6.7%). Mycological colonisation was recorded in 105 of the 210 patients (50.0%, 95% CI 43.0–57.0) with *Candida albicans* found in 42.9% and *Aspergillus fumigatus* in 6.2% of patients. Six patients harboured an atypical *Mycobacterium* (2.9%, 95% CI 1.05–6.11). Banal flora mainly consisted of *Streptococcus viridans* (89.5%), *Neisseria* spp. (45.2%) and *Haemophilus parainfluenzae* (43.3%).

Univariate analyses highlighted that age was significantly associated with bacterial colonisation (63.5 *versus* 60.4 years old, p=0.02), and males were colonised more than females (p=0.14) (table 3). Moreover, patients with COPD were at higher risk of colonisation (p=0.008) (table 3). Interestingly, there was a trend for more colonisation in patients with squamous cell carcinoma (37.6% *versus* 22.2%) (p=0.14) (table 3).

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TABLE 4 Multivariate analysis of the association between patient characteristics and bacterial colonisation

	OR (95% CI)	p-value[#]
Sex		
Male	1.00	0.49
Female	0.76 (0.34–1.67)	
Age years		
38.0–55.2	1.00	0.19
55.3–60.1	1.59 (0.65–3.89)	
61.1–69.73	2.68 (1.08–6.61)	
69.75–87.0	1.89 (0.76–4.67)	
Leukocytes per mm^3		
3600–7900	1.00	0.15
8000–9000	2.10 (0.82–5.40)	
9100–11 500	1.21 (0.547–3.08)	
11 560–21 700	2.53 (1.00–6.41)	
COPD		
No	1.00	0.09
Yes	1.78 (0.90–3.53)	
Histological type		
Adenocarcinoma	1.00	0.53
Squamous cell carcinoma	1.64 (0.76–3.52)	
Large cell carcinoma	0.46 (0.08–2.70)	
Small cell carcinoma	1.05 (0.33–3.26)	
Other	0.75 (0.16–3.39)	

COPD: chronic obstructive lung disease; [#]: likelihood ratio test. n=175.

Associations between patient characteristics and colonisation were investigated using multivariate analysis (table 4). Interestingly, females had a diminished risk of colonisation (OR 0.76; p=0.49). The multivariate analysis confirmed that the oldest patients tended to have a higher risk of colonisation compared to those aged 38–55 years (p=0.19); the odds of being colonised increased by a factor of 2.68–1.89 for those aged 61–69 and 69–87 years (table 4). Also, COPD patients and those with >8000 leukocytes per mm^3 had a higher probability of colonisation (OR 1.8 and 2.1; p=0.14 and 0.08, respectively). The multivariate analysis did not find any association between colonisation and any of the other patient characteristics, including the histological type of cancer. Squamous cell carcinoma tended to be more frequently colonised compared to other histological subtypes, though this did not reach significance (p=0.53; OR 1.64, 95% CI 0.76–3.52) (table 4).

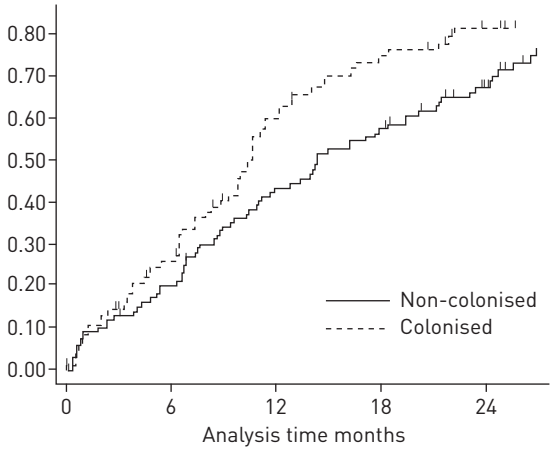

FIGURE 1 Survival curves of patients with lung cancer who were non-colonised or colonised (Kaplan–Meier failure estimate) (n=210).

TABLE 5 Multivariate analysis of the association between patient survival and bacterial colonisation

	Hazard ratio (95% CI)	p-value[#]
Bacterial colonisation		
No	1.00	
Yes	1.75 (1.19–2.58)	0.005
Sex		
Male	1.00	
Female	0.46 (0.28–0.75)	0.002
Age years		
38.0–55.2	1.00	
55.3–60.1	0.95 (0.56–1.59)	0.84
61.1–69.73	0.77 (0.44–1.32)	0.34
69.75–87.0	1.09 (0.62–1.92)	0.77
Histological type		
Squamous cell carcinoma	1.00	
Adenocarcinoma	1.08 (0.67–1.73)	0.76
Large cell carcinoma	1.84 (0.70–4.83)	0.21
Small cell carcinoma	1.24 (0.60–2.57)	0.57
Other	2.47 (1.07–5.73)	0.04
Stage		
I or II	1.00	
III	4.91 (2.20–10.94)	<0.0001
IV	10.73 (5.05–22.79)	<0.0001
Diabetes		
No	1.00	
Yes	1.55 (0.86–2.80)	0.15
Alcohol		
No	1.00	
Yes	1.62 (0.98–2.66)	0.06
Performance status		
0	1.00	
1	1.47 (0.94–2.29)	0.09
2	1.75 (0.88–3.48)	
3–4	5.23 (1.94–14.10)	

[#]: Hazard ratio test. n=190.

Survival analyses and further bronchopulmonary infections

Figure 1 shows the survival curves for colonised and non-colonised patients. The survival analyses indicate that non-colonised patients survived longer than those who were colonised: 50% of colonised patients died at 10.7 months, whereas 50% of non-colonised patients died at 14.3 months (log-rank test: p=0.04). After adjustment for sex, age, histological type, disease stage, diabetes, alcohol use and performance status, the rate of dying was 1.75 (CI 95% 1.19–2.58) higher for patients who were colonised (table 5).

In the study population, infectious complications arose in 71 of 210 patients (33.8%) (table 6). In bivariate analysis, the average incidence of further bronchopulmonary infections was 4.4 per 100 patients per month. In bivariate analyses, the number of further bronchopulmonary infections per patient was 1.31 times higher in patients who were colonised (p=0.16). The number of bronchopulmonary infections per patient was 2.01 times higher in those who frequently consumed alcohol (p=0.002). The risk of bronchopulmonary infection was also slightly increased for males (p=0.06) and for higher disease stage (p=0.20). In multivariate analysis, colonisation was associated with 1.61 times (95% CI 0.93–2.82; p=0.09) more bronchopulmonary infections per patient compared to those who were not colonised (table 7).

Figure 2 shows the survival curves for infected and non-infected patients. The survival analyses indicate that non-infected patients tended to survive better than those who were infected: *i.e.* 50% of infected patients died at 9.8 months compared to 50% of non-infected patients who died at 12.8 months (log-rank test: p=0.08).

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TABLE 6 Infectious complications reported during patient follow-up

	Complications n	Patients with at least one complication n (%)[#]
Bronchial infections (per patient)		
1	39	39 (18.6)
2	12	6 (2.9)
3	24	8 (3.8)
5	5	1 (0.5)
Pleural effusion (per patient)		
1	1	1 (0.5)
2	2	1 (0.5)
Septicaemia	12	12 (5.7)
Septic shock	3	3 (1.4)
Febrile aplasia	8	8 (3.8)
Bronchopulmonary tuberculosis	0	0 (0.0)
Bronchopulmonary aspergillosis	3	3 (1.4)
Overall total	109	71 (33.8)
Total infectious complications per patient		
0	139	139 (66.2)
1	47	47 (22.4)
2	28	14 (6.7)
3	21	7 (3.3)
4	8	2 (0.9)
5	5	1 (0.5)

[#]: out of 210 patients.

Discussion

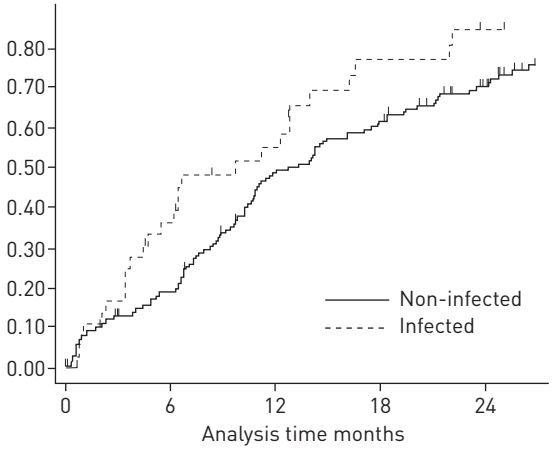
In this study, we prospectively investigated the tracheal–bronchial tree for microbial colonisation, which is the primary site of infection in patients with lung cancer [2]. One study reports that pulmonary infection may impact negatively on the survival of lung cancer patients [3]. A thorough review of the literature indicated that bronchial colonisation has been often evaluated in patients undergoing a cancer resection, as this population has a high risk of severe pulmonary infectious complications and mortality following thoracic surgery [6, 7, 15–18].

In our study, we have clearly demonstrated a high incidence of colonisation by PPMs in nearly 50% of patients presenting with lung cancer at the time of diagnosis and before any antitumour treatment. The incidence and nature of bacterial colonisation were similar to those reported in other large prospective or retrospective studies, which highlight the high frequency of the potentially pathogenic Gram-negative bacilli

TABLE 7 Multivariate analysis of the association between patient characteristics and infectious complications

	IRR (95% CI)	p-value
Bacterial colonisation		
No	1.00	0.09
Yes	1.61 (0.93–2.82)	
Sex		
Male	1.00	0.25
Female	0.67 (0.33–1.33)	
Disease stage		
I or II	1.00	0.15
III	1.23 (0.56–2.69)	
IV	1.91 (0.93–3.94)	
Alcohol use		
No	1.00	
Yes	2.06 (1.02–4.14)	0.04

IRR: incidence rate ratio. n=198.



Number at risk					
Non-infected	166	116	71	53	31
Infected	44	22	13	6	3

FIGURE 2 Survival curves of patients with lung cancer who were non-infected or infected (Kaplan–Meier failure estimates) (n=210).

(*H. influenzae*, *E. coli*, *Klebsiella spp.*, *Pseudomonas aeruginosa*) and Gram-positive cocci (*S. aureus* and *Streptococcus pneumoniae*) [2, 5, 6, 11, 12]. These bacteria are responsible for the main pulmonary complications observed during the course of bronchial cancers [2, 3, 8]. In particular, *S. aureus, P. aeruginosa* and *Klebsiella spp.* may harm patients about to undergo surgery or chemotherapy. Moreover, the increasing use of broad-spectrum antibiotics, associated with invasive chemotherapy, seems to contribute to the emergence of *S. pneumoniae* in particular. Anti-pneumococcal and anti-*H. influenzae* vaccination of patients with lung cancer may help prevent these infectious complications [19–21].

In contrast, airway colonisation by mycobacteria and potential pathogenic fungi in patients with lung cancer has not been systematically assessed in the literature. Here, we provide interesting insights into their bronchial prevalence in these patients. Remarkably, the yeast *C. albicans* was frequently isolated in per-endoscopic aspirations (90 out of 210 patients). In our previous study, the prevalence of *C. albicans* was lower (13.9%) [11]. Results from our studies and others indicate that fungal colonisation, particularly when caused by *C. albicans*, is more common in patients with lung cancer because of immunosuppressive cofactors [22]. Moreover, atypical mycobacteria were found in six immunosuppressed patients after corticotherapy.

Attempts to identify risk factors for colonisation revealed that colonised patients were significantly older than non-colonised patients, a risk factor we reported recently in a large retrospective survey [11]. In particular, males seem to be at more risk for colonisation because of a greater incidence of smoking and environmental factors [11]. Airway colonisation can also arise because of local and general abnormalities [2, 20]. For instance, corticotherapy can contribute to colonisation by mycobacteria and fungi in patients with bronchial cancer [23, 24]. Clearly, such microorganisms are now emerging in patients with lung cancer [8, 11, 25], especially in patients with a medical history of corticotherapy or undergoing heavy immunosuppressive chemotherapy or radiotherapy [21, 24–26]. Therefore, airway colonisation needs to be taken into account for the therapeutic management of patients with lung cancer depending on their immunosuppressive status. Moreover, patients with COPD were significantly more often colonised by PPMs, as described elsewhere [5, 9, 10]. In COPD, inflammation and oxidative stress that occur in the bronchial endothelium could help microorganisms adhere to the epithelium, thus promoting colonisation, leading to epithelial restructuring and emphysema [9, 27].

Although adenocarcinoma or squamous cell carcinoma were recorded in nearly 80% of patients, no significant association was found between any histological type of cancer and colonisation, as has been reported previously [4, 11], although squamous cell carcinoma patients tended to be colonised more often than others.

In conclusion, our prospective study shows that bronchial colonisation by PPMs was found in nearly 50% of patients with lung cancer. In particular, the following patients may be at higher risk of colonisation: smokers, males and those with COPD. In these patients, survival is lower in colonised patients over a given period ($p=0.04$), and tends to be linked to infectious complications in patients with bronchopulmonary colonisation detected at recruitment. We believe that prospective evaluation of the prevalence and nature of colonisation in patients at the time of cancer diagnosis may offer valuable information for the subsequent management of therapies, including surgery and chemotherapy.

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