



## The new face of non-small-cell lung cancer in men: Results of two French prospective epidemiological studies conducted 10 years apart



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### ABSTRACT

**Objectives:** To evaluate the impact of epidemiological changes observed in 10 years in men with NSCLC on 1-year mortality; to compare prognosis factors of 1-year mortality according to gender.

**Material and methods:** The French College of General Hospital Respiratory Physicians conducted two prospective epidemiological multicentre studies at a 10-year interval (KBP-2000-CPHG and KBP-2010-CPHG). These studies included all adult patients with primary lung cancer histologically or cytologically diagnosed between 1<sup>st</sup> January and 31<sup>st</sup> December for the years 2000 and 2010, managed in the pneumology department of the participating hospitals. A standardised form was completed for each patient. A steering committee checked recruitment exhaustiveness. Vital status 1 year after diagnosis was collected. **Results:** In 2000 and 2010 respectively, 137 and 104 centres included 3921 and 4597 men and 748 and 1486 women with NSCLC. In 2010 compared to 2000, male patients were older but had better performance status (PS); they were less frequently ever-smokers and heavy smokers; their cancer (usually diagnosed at advanced stage) was more often adenocarcinoma ( $p < 0.0001$ ). In 10 years, 1-year mortality has significantly decreased in men (from 61.2% to 56.6%,  $p < 0.0001$ ) and in women (from 58.1% to 50.9%,  $p < 0.0001$ ), but remained higher in men than in women leading to increased difference between men and women. Decreased 1-year mortality remained statistically significant after adjustment on age, PS, smoking, and histology (men: OR = 0.81, 95% CI = 0.73–0.90,  $p < 0.0001$ ; women: 0.71, 0.57–0.88,  $p < 0.002$ ). Active smoking was not a prognosis factor in men (OR = 1.04, CI = 0.79–1.37,  $p = 0.78$ ); age (>75 years) had less impact on mortality in men than in women (men: OR = 1.43, CI = 1.22–1.67,  $p \leq 0.0001$ ; women: OR = 2.32, CI = 1.71–3.15;  $p < 0.0001$ ).

**Conclusions:** The improved 1-year survival in 2010 as compared with 2000 was independent of age, smoking, PS, and histology, suggesting that it reflected new treatment and strategy efficacy. One-year mortality remains higher in men than in women.

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**Abbreviations:** ANOVA, analysis of variance; CCTIRS, French advisory committee on research information processing in the health field; CNIL, French data protection commission; CPHG, French College of General Hospital Respiratory Physicians; InVS, French health-watch institute; NSCLC, non-small-cell lung cancer; OR, odds ratio; PS, performance status; PM, particulate matter; PS, performance status; SD, standard deviation; TNM, tumour-node-metastasis.

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## 1. Introduction

In 2012, with an estimated number of 39,500 new cases and 29,900 deaths, lung cancer was the 4<sup>th</sup> form of cancer by frequency and the prime cause of death from cancer in France. In men, lung cancer represented 14% of all cancers in 2012 and was responsible for 25% of all cancer deaths. Whereas, between 2005 and 2012, standardised lung cancer incidence and mortality increased in women (+5.4% and +3.7% per year, respectively), they slightly decreased in men (−0.3% and −2.2% per year, respectively) [1]. This difference in pattern between men and women is reported in most Western countries. It is largely explained by gender differences in smoking habits, as lung cancer incidence and mortality trends closely reflect patterns in smoking prevalence several years earlier [2]. In France, smoking increased in men until the 1980s and decreased after the 1990s, whereas in women it increased until the 1990s and started to fall in 2005, leading to a 10-year lag in smoking decrease between men and women [3].

In 2000 and 2010, the French College of General Hospital Respiratory Physicians (CPHG) conducted two prospective multicentre epidemiological studies, KBP-2000-CPHG and KBP-2010-CPHG, to compare patient and lung cancer characteristics at a 10-year interval [4–7]. These studies showed that lung cancer characteristics have changed in France in 10 years: more women, more never-smokers, and more adenocarcinomas [6]. They also showed that although main gender differences at diagnosis persisted, they faded in part with the increased proportion of non-smokers and adenocarcinomas in men [7]. The present article, which focuses on men, evaluates the impact of epidemiological changes observed in 10 years in men with NSCLC on 1-year mortality and compare prognosis factors according to gender.

## 2. Material and methods

Material and methods were previously described in detail [4–7].

The study protocols were approved by French data protection commission (CNIL) on 2 August 2000 (900019) and 11 January 2010 (909479). The KBP-2010-CPHG protocol was also approved by the advisory committee on research information processing in the health field (CCTIRS) on 19 November 2009 and by the French Society of Pneumology review board on 23 April 2010 (N° 2010-008). All patients were duly informed of the study objectives and requirements and gave oral consent before inclusion.

Lung specialists in the pneumology departments of all French general hospitals (overseas *Départements* and Territories included) were contacted in 1999 and 2009 to participate in KBP-2000-CPHG and KBP-2010-CPHG. Participation in one study was independent of participation in the other.

Participants included all patients aged over 18 years managed in their centres for primary lung cancer diagnosed histologically or cytologically between 1<sup>st</sup> January and 31<sup>st</sup> December for 2000 (KBP-2000-CPHG) or for 2010 (KBP-2010-CPHG). Data on patients and lung cancer characteristics were collected on anonymous standardised forms specifically drawn up for each study. A steering committee assessed study completeness by checking regularity of inclusion throughout the year for all centres individually and taken together, and coherence of data between 2000 and 2010 for centres that participated in both studies.

Vital status and date of death were obtained from the investigator or town council of the patient's birth place at least 1 year after the date of diagnosis.

Standard SAS® procedures (SAS Institute, Cary, NC, USA) were used for univariate and multivariate analysis. The population was described in terms of the questionnaire variables. Results were expressed as mean ± standard deviation (SD) or percentage. Uni-

variate analysis used the Chi<sup>2</sup> test to assess association between categorical variables, and the Student *t* test or analysis of variance (ANOVA) (for normal distributions) or non-parametric tests (for non-normal distributions) to analyse quantitative variables. All fatal cases were considered, regardless of cause of death. Patients who were alive 1 year after the date of diagnosis were censored at that date. Mortality rate was calculated using Kaplan–Meier method. One year mortality risk was assessed on multivariate analysis using a logistic regression model. Adjustments were made for age, smoking status, PS, and cancer histology. Statistical test results were considered significant at  $p < 0.05$  (two-sided).

## 3. Results

In 2000 and 2010 respectively, 137 and 104 centres included 4670 and 6083 patients with NSCLC: 3921 and 4597 men and 748 and 1486 women, respectively (1 missing value on gender in 2000).

Compared to 2000, male patients in 2010 were significantly older (65.7 versus 64.4 years;  $p < 0.0001$ ), more frequently never-smokers (4.7% versus 2.5%;  $p < 0.0001$ ), and more frequently had better PS at diagnosis (PS0 to PS1: 69.4% versus 65.9%;  $p < 0.0001$ ). In 2010, active and former smokers were less commonly heavy consumers than in 2000 (43.7 versus 45.1 pack-years;  $p = 0.003$ ), and former-smokers' smoking duration was shorter (34.8 versus 35.8 years;  $p = 0.007$ ) and cessation duration longer (15.3 versus 11.4 years;  $p < 0.0001$ ) (Table 1).

The most frequently reported form of NSCLC was adenocarcinoma in 2010 but squamous-cell carcinoma in 2000 (48.7% and 34.9% of all NSCLCs in 2010 versus 31.5% and 50.3% in 2000,  $p < 0.0001$ ). In 2010, NSCLCs were still diagnosed at advanced stages: 56.9% diagnosed at stage IV, versus 41.6% in 2000 ( $p < 0.0001$ ) (Table 2).

Vital status at 1 year was known for 3767 male patients in 2000 (95.1%) and 4549 in 2010 (99.0%). In 2010, 1-year survival, although low, was greater than in 2000 (43.4% versus 38.8%;  $p < 0.0001$ ). Multivariate analysis (Table 3) showed that, in 10 years, in men, 1-year mortality had significantly decreased independently of other factors (odds ratio (OR) = 0.81, 95% confidence interval (95% CI): 0.73–0.90;  $p < 0.0001$ ). Other independent risk factors were age (>75 years), histology (adenocarcinoma or large-cell carcinoma), and high PS at diagnosis. PS was the most relevant risk factor. Smoking was not a significant independent risk factor of 1-year mortality in men (OR = 0.91, 95% CI: 0.69–1.19;  $p = 0.48$  for former smokers and OR = 1.04, 95% CI: 0.79–1.37;  $p = 0.78$  for active smokers).

Vital status at 1 year was known for 712 female patients (95.2%) in 2000 and 1471 (99.0%) in 2010. In 2010, 1-year survival was greater than in 2000 (49.1% versus 41.9%,  $p < 0.0001$ ). Multivariate analysis (Table 4) showed that, in 10 years, in women, 1-year mortality had significantly decreased independently of other factors (OR = 0.71, 95% CI: 0.57–0.88;  $p = 0.002$ ). Other independent risk factors were age (>75 years), histology (large-cell carcinoma: OR = 1.12, 95% CI: 0.86–1.46;  $p = 0.39$ ), and high PS at diagnosis. PS was the most relevant risk factor. Active smoking was also a significant independent risk factor of 1-year mortality in women (never-smokers versus active smokers: OR = 1.65, 95% CI: 1.28–2.13;  $p = 0.0001$ ).

## 4. Discussion

In the last decade, much was said or written about the changes in lung cancer patterns in women, although lung cancer remains a predominantly male disease. The present article therefore focuses on changes in lung cancer in men.

The KBP-CPHG studies demonstrate that, in 10 years, behind the apparent epidemiological stability of lung cancer in men reported

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