Journal Pre-proof

Association of sleep-related hypoxemia with survival in patients with non-small cell lung cancer – the NEOSAS-GFPC study group

Grégoire Justeau, M.D, PhD, Laurent Greillier, M.D, PhD, Florent Vinas, M.D, Lionel Falchero, M.D, Olivier Bylicki, M.D, Marie Bernardi, M.D, Francis Martin, M.D, Isabelle Simon, M.D, Didier Debieuvre, M.D, Chrystèle Locher, Acya Bizieux-Thaminy, M.D, Virginie Levrat, M.D, Stéphanie Fry, M.D, Camille Guguen, M.D, Frédéric Goutorbe, M.D, Philippe Masson, M.D, Franck Soyez, M.D, Christos Chouaid, M.D, PhD, Patrick Saulnier, M.D, PhD, Frédéric Gagnadoux, M.D, PhD

PII: S0012-3692(26)00279-5

DOI: https://doi.org/10.1016/j.chest.2025.12.060

Reference: CHEST 7400

To appear in: *Chest*

Received Date: 12 June 2025

Revised Date: 23 December 2025

Accepted Date: 30 December 2025

Please cite this article as: Justeau G, Greillier L, Vinas F, Falchero L, Bylicki O, Bernardi M, Martin F, Simon I, Debieuvre D, Locher C, Bizieux-Thaminy A, Levrat V, Fry S, Guguen C, Goutorbe F, Masson P, Soyez F, Chouaid C, Saulnier P, Gagnadoux F, Association of sleep-related hypoxemia with survival in patients with non-small cell lung cancer – the NEOSAS-GFPC study group, *Chest* (2026), doi: https://doi.org/10.1016/j.chest.2025.12.060.

Association of sleep-related hypoxemia with survival in patients with non-small cell lung cancer – the NEOSAS-GFPC study group

Authors : Grégoire Justeau, M.D, PhD,[a] Laurent Greillier, M.D, PhD,[b] Florent Vinas, M.D,[C] Lionel Falchero, M.D,[d] Olivier Bylicki, M.D,[e] Marie Bernardi, M.D,[f] Francis Martin, M.D,[g] Isabelle Simon, M.D,[g] Didier Debieuvre, M.D,[h] Chrystèle Locher,[i] Acya Bizieux-Thaminy, M.D,[J] Virginie Levrat, M.D,[k] Stéphanie Fry, M.D,[l] Camille Guguen, M.D,[n] Frédéric Goutorbe, M.D,[m] Philippe Masson, M.D,[o] Franck Soyez, M.D,[p] Christos Chouaid, M.D, PhD,[c] Patrick Saulnier, M.D, PhD,[q,r] Frédéric Gagnadoux M.D, PhD,[a].

[a] Pneumology Department, CHU d'Angers, Angers, France.

[b] Multidisciplinary Oncology and Therapeutic Innovations, Aix-Marseille University, APHM, INSERM, CNRS, CRCM, Hôpital Nord, Marseille, France.

[c] Pneumology Department, Centre Hospitalier Intercommunal de Créteil, Créteil, France.

[d] Pneumology Department, CH Villefranche-Sur-Saône, France.

[e] Pneumology Department, Hôpital d'Instruction des Armées Sainte-Anne Toulon, France

[f] Pneumology Department, CHI Aix-En-Provence, France.

[g] Sleep Unit, Centre Hospitalier de Compiègne-Noyon, 60200 Compiègne, France.

[h] Pneumology Department, Groupe Hospitalier de la Région Mulhouse Sud-Alsace, Hôpital Emile Muller, GHRMSA - Mulhouse, Mulhouse, France.

[i] Pneumology Department, Grand Hôpital de l'Est Francilien (Meaux), Meaux, France.

[j] Pneumology Department, CH Départemental Vendée, La Roche-sur-Yon, France.

[k] Pneumology Department, Groupe Hospitalier De La Rochelle-Ré-Aunis, La Rochelle, France.

[l] Pneumology, Immunology and Allergology Department, CHU de Lille, Lille, France.

[n] Pneumology Department, Centre Hospitalier Le Mans, Le Mans, France.

[m] Pneumology Department, CH Béziers, Béziers, France.

[o] Pneumology Department, Cholet General Hospital, Cholet, France.

[p] Pneumology Department, Centre d'étude du sommeil Antony, France

[q] MINT, INSERM U1066, CNRS 6021, University of Angers, SFR-ICAT 4208, Angers, France.

[r] Pharmacy department, CHU Angers, Angers, France.

Corresponding Author: Grégoire Justeau, MD, PhD

CHU d'Angers, 4 rue Larrey, 4 rue Larrey | 49933 Angers CEDEX 09

Email: gregoire.justeau@chu-angers.fr

Abstract word count: 264

Manuscript word count: 3138

Number of Tables: 3

Number of figures: 4

Number of references: 49

Short title:

Sleep-related hypoxemia and survival in non-small cell lung cancer

Statement of conflicts of interest

GJ, CL, IS, FS, DD, LF, ABT, FV, PM, LG, MB, FM, VL, SF, CG, FGo and PS declare no conflicts of interest, OB declares consulting fees, honoraria and travel accommodation from TAKEDA, MSD, ASTRA-ZENECA, CC declares grants, consulting fees, travel accommodation and honoraria from Boehringer Ingelheim, Hoffman-Roche, Takeda, BMS, MSD, Astra Zeneca, Amgen, Janssen and Pfizer, FG declares consulting fees from RESMED and SEFAM, honoraria from CIDELEC and travel accommodation from ASTEN Santé

Contributors

FG, PS and CC wrote the protocol. FG, LG, and CC participated in the implementation of the study. GJ, FG, and PS collected study data. FG and CC acquired study funding. FG, GJ and PS managed the data.

GJ, FG, LG and CC wrote the manuscript. GJ, FG and PS did the statistical analysis. GJ, FG, CC and PS had access to and verified all data. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors validated the final version of the manuscript

The GFPC 05-2015 NEOSAS investigators

F Gagnadoux (Le Centre Hospitalier et Universitaire Angers, France), F Vinas (Le Centre Hospitalier Intercommunal de Créteil, France), G Oliviero (Le Centre Hospitalier Longjumeau, France), O Bylicki (Hôpital d'Instruction des Armées Sainte-Anne Toulon, France), A Bizieux (Le Centre Hospitalier Départemental Les Oudairies La Roche sur Yon, France), L Falchero (Centre Hospitalier Villefranche, France), C Locher (Centre Hospitalier de Meaux, France), C Guguen (Le Centre Hospitalier du Mans, France), P Thomas (Centre hospitalier intercommunal des Alpes du Sud, Gap, France), S Martinez (Centre Hospitalier du Pays d'Aix, Aix en Provence, France), D Debieuvre (Hopital Emile Muller, Mulhouse, France), I Simon (Centre Hospitalier Intercommunal de du sommeil Compiègne-Noyon), C Rotomondo-Monroux (Centre Hospitalier d'Antibes, France), C Launois (Centre Hospitalier et Universitaire de Reims, France), V Levrat (Centre Hospitalier de la Rochelle, France), F Vergne (Hopital d'instruction des armées de Brest, France), F Soyez (Hopital Privé d'Anthony, France), J Nardi (Polyclinique Les Bleuets, Reims, France), L Portel (Centre Hospitalier de Libourne, France), H Le Floch (Hopital d'instruction des armées de Percy, France), MP d'Ortho (Hopital Bichat Claude Bernard, France), S Fry (Centre Hospitalier Universitaire de Lille, France), F Goutorbe (Centre Hospitalier de Béziers, France), C El Khouri (Centre Catherine de Sienne, Nantes, France), E Antone (Centre Hospitalier Universitaire de Poitiers, France), A Tiotu (Centre Hospitalier Universitaire de Nancy, France), P Masson (Centre Hospitalier de Cholet, France), H Pegliasco (Hopital Européen Marseille, France)

Acknowledgments

The study was supported by research grants from the Institut Recherche en Santé Respiratoire des Pays de la Loire and from ResMed Inc.

The funding sources had no role in the design, conduct, or analysis of the study or in the decision to submit the manuscript for publication.

The study was supported by the Centre Hospitalier Universitaire de Angers and the Groupe Français de Peumo Cancérologie.

Abstract

Background: Obstructive sleep apnea (OSA) and its hypoxia-related consequences are associated with an increased lung cancer risk.

Research Question: Is there an association of OSA and sleep-related hypoxemia with increased mortality in patients with non-small cell lung cancer (NSCLC).

Study Design and Methods: Patients with newly-diagnosed NSCLC and Eastern Cooperative Oncology Group performance status (ECOG-PS) 0–2 enrolled in this multi-center study (27 study sites) underwent questionnaires, home sleep-study, and were followed for 18 months. OSA was defined as a 3% oxygen desaturation index (ODI)≥16 events/h. Cox proportional hazards models were used to evaluate the association of OSA and terciles of indices of sleep-related hypoxemia (ODI, mean oxygen saturation [SpO_2], % time with SpO≤90% [T90]) with mortality.

Results: Of 1,201 patients with newly diagnosed NSCLC enrolled between February 2016 and December 2020, 1001 with valid sleep study were analyzed (71% males, mean [Standard deviation], age 63.6 [9.7], 11% of stage I or II), and 383 (38%) had OSA. Compared to non-OSA patients, those with OSA had no difference in sleep quality, quality of life, ECOG-PS, cancer stage at diagnosis and survival. However, patients with severe sustained sleep-related hypoxemia were at higher risk of death (Hazard ratio [95% confidence interval] 1.35 [1.05-1.74] for T90 ≥35 vs <4%; 1.48 [1.16-1.98] for mean SpO_2<91 vs ≥93%) after adjustment for confounders including ECOG-PS, cancer stage, and SpO_2 on room air, and surgical treatment.

Interpretation: In patients with newly diagnosed NSCLC, severe nocturnal hypoxemia is associated with lower overall survival. The impact of oxygen therapy on survival deserves to be evaluated in patients with NSCLC and marked nocturnal hypoxemia.

Clinical Trial Registration: ClinicalTrial.gov, number NCT02648087.

Key words: obstructive sleep apnea, non-small cell lung cancer, nocturnal hypoxemia, cancer prognosis

Abbreviations

AHI: apnea-hypopnea index

BMI: body mass index

CI: confidence interval

COPD: Chronic Obstructive Pulmonary Disease

ECOG-PS: Eastern Cooperative Oncology Group performance status

EQ-5D: EuroQol five-dimensions

ESS: Epworth Sleepiness Scale

GFPC: Groupe Français de Pneumo-Cancérologie

HIF-1α: hypoxia inducible factor-1α

HR: hazard ratio

IH: intermittent hypoxia

NSCLC: Non-small cell lung cancer

ODI: oxygen desaturation index

OSA: Obstructive sleep apnea

PSQI: Pittsburgh Sleep Quality Index

QD2A: Questionnaire of Depression 2nd version, Abridged

SpO2: arterial oxygen saturation

T90 percentage of recording time with oxygen saturation ≤90%

VEGF; vascular endothelial growth factor

Non-small cell lung cancer (NSCLC) constitutes a significant global health challenge and represents the leading cause of cancer-related mortality in developed countries [1]. Its elevated mortality rate can be explained by the late-stage diagnosis and the aggressive nature of the disease. While tobacco smoking is the primary risk factor for lung cancer, exploration into other factors such as exposure to air pollution, occupational carcinogens, and genetic predispositions is steadily advancing.

Obstructive sleep apnea (OSA) is a prevalent disorder characterized by repetitive episodes of partial (hypopnea) or complete (apnea) obstruction of the upper airways during sleep, resulting in intermittent hypoxia (IH), increased intrathoracic pressure swings, and sleep fragmentation [2, 3]. Expanding literature demonstrates an association between OSA and cancer risk. Growing evidence from population- and clinic-based cohort studies reveals that the severity of OSA and sleep-related hypoxemia may adversely affect both overall cancer risk and incidence of certain cancers [4–10]. Many of the intimate molecular mechanisms that may associate OSA with greater cancer incidence and progression or incidence of lung cancer are linked to IH-induced overexpression of the hypoxia inducible factor (HIF)-1α and which in turn increases the concentration of molecules associated with greater tumor neovascularization, especially vascular endothelial growth factor (VEGF), and thus the probability of tumor growth and aggressiveness [11, 12]. Among studies that have evaluated the links between specific cancer sites and OSA, cutaneous malignant melanoma has received particular attention [13]. Aggressiveness markers such as Breslow index, presence of ulceration and mitotic index were associated with traditional metrics of OSA severity such as the apnea-hypopnea index (AHI) and the 3% oxygen desaturation index 3% (ODI) in a large prospective cohort of patients diagnosed with cutaneous malignant melanoma [14]. There is also growing interest in the association of OSA and nocturnal hypoxemia with lung cancer incidence and progression. Subgroup analyses from the two largest sleep-clinic cohort studies showed a higher incidence of lung cancer for the patients presenting severe OSA and nocturnal hypoxemia [7, 10]. In a meta-analysis of 4 885 518 patients from four observational studies, patients with OSA had an approximately 30% higher risk of lung cancer compared with those without OSA [15]. A recent study has demonstrated that moderate-to-severe

OSA is associated with increased expression of serum biomarkers of immune evasion, lymphangiogenesis and tumor cell aggressiveness in patients with lung cancer [16]. Data from retrospective studies have suggested an association of OSA severity and nocturnal hypoxemia with increased cancer mortality [17, 18]. These findings deserve to be confirmed prospectively with proper adjustment for confounders. This prospective multicenter study aimed to determine *1*-the prevalence and clinical correlates of OSA in patients with newly diagnosed NSCLC and *2*-the association of OSA and sleep-related hypoxemia with the overall survival.

Study Design and Methods

The *NEOSAS* prospective multicenter study was conducted within the Groupe Français de Pneumo-Cancérologie (GFPC) research network. Patients eligible for this study met the following criteria: histologically or cytologically confirmed NSCLC; aged≥18 years; Eastern Cooperative Oncology Group performance status (ECOG-PS) 0–2; be willing to participate in the research and have given written informed consent. Exclusion criteria were as follows: history of treated OSA in the previous 12 months; previous history or newly diagnosed severe Chronic Obstructive Pulmonary Disease (COPD) (forced expiratory volume in 1 second <50%) or other severe chronic lung disease; long term oxygen therapy; pregnancy. The study was conducted in accordance with the Declaration of Helsinki, approved by the local independent ethics committee (Comité de Protection des Personnes [CPPP] Ouest N°2; case 2015/14; date of approval: June 9th 2015), and registered with ClinicalTrial.gov, number NCT02648087.

Procedures

Patients who fulfilled the inclusion criteria and none of the exclusion criteria were enrolled consecutively and assessed for OSA with the use of the same home sleep-study screening device (ApneaLink, ResMed) for all participants. As described previously, this device determines airflow through nasal pressure and includes oxygen saturation measurements [19, 20]. The recording was considered valid if at least 180 minutes of pulse-oximetry signal were successfully recorded. Each patient enrolled in the study completed surveys including anthropometric data, smoking habits and

medical history. Functional status was evaluated with the ECOG-PS. Patients were invited to complete questionnaires including the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), the Pichot Questionnaire of Depression 2nd version, Abridged (QD2A) and the The EuroQol five-dimensions (EQ-5D) quality of life questionnaire. The PSQI is a self-administered questionnaire that assesses sleep quality and quantity during the previous month [21]. The PSQI contains 19 items that produce a global sleep quality score from 0 to 21. A higher global PSQI score indicates a poorer sleep quality. A PSQI score <5 is considered good sleep quality. Assessment of daytime sleepiness was performed using the ESS, a reliable and validated questionnaire for measuring daytime sleepiness in adults [22]. Depressive mood was measured with the QD2A, a French 13-item questionnaire specifically designed for depression screening in community studies with a high internal consistency [23]. A total score ≥7 indicates a high probability of major depression. Follow-up visits were programmed at 3, 6, 12 and 18 months.

Outcomes

The primary outcome was the prevalence of OSA among individuals newly diagnosed NSCLC. In line with previous reports [19], OSA was defined by an overnight 3% oxygen desaturation index (ODI) of at least 16 events per hour of recording.

Secondary outcomes included the association between OSA with functional status, cancer stage sleep and quality of life questionnaires at diagnosis. We also explored the association of mortality at 18 months with OSA, AHI categories and oximetry-derived indices of sleep-related hypoxemia including ODI, the percentage of recording time with oxygen saturation (SpO_2) ≤90% (T90) and, mean SpO_2. Each of these parameters (ODI, T90, and mean SpO_2) were divided into terciles of the variable.

Statistical analysis

All analyses were conducted using the latest version of R-Studio (Version 2023.12.1+402). Variables were described using means and standard deviations (SD) for continuous variables, and number and percentage for qualitative variables. Comparison between groups were performed using Student's t-test for continuous variables and Chi-squared test (or Ficher exact test when the conditions were not

satisfied) for qualitative variables. Kaplan-Meier overall survival curves were reported and compared using the Log-Rank test. Survival data correspond to the time between the date of inclusion and the date of death (expressed in months). Censored data correspond to the time between the date of last observation and the date of inclusion. Cox proportional hazards models were used to evaluate the association of OSA and terciles of indices of sleep-related hypoxemia (ODI, T90, and mean SpO_2) with mortality. Associations were evaluated unadjusted (Model 1) and adjusted for covariates including Age (years), gender, body mass index (BMI, kg/m^2), smoking status (ever vs never smoker), cancer stage at diagnosis (1-2 vs 3-4), PS ECOG at diagnosis (0-1 vs 2), history of hypertension (yes vs no), stroke (yes vs no), cardiac disease (yes vs no), diabetes mellitus (yes vs no), COPD (yes vs no) (Model 2). An additional adjustment for SpO_2 at rest on room air and the use of thoracic surgery as a first-line treatment for NSCLC (Model 3) The results were expressed as hazard ratios (HR) and 95% confidence intervals (CI). Associations were considered statistically significant for a P value<0.05.

Results

Population

Of 1,201 patients with newly diagnosed NSCLC across 27 study sites from the GFPC between February 2016 and December 2020, 41 had exclusion criteria and 155 had invalid screening sleep study. A total of 1,005 patients with valid home sleep-study were analyzed (Figure 1). The mean age at inclusion was of 63,6 years (SD 9.75) and 71% were men. The mean body mass index (BMI) was of 24.24 kg/m2 (SD 4.85). Regarding the characteristics of cancer 25% of patients presented a squamous NSCLC and the remaining corresponded to non-squamous NSCLC. Only 11% of patients presented a localized NSCLC (stage I or II) whereas 89% presented a locally advanced or metastatic lung cancer (stage III or IV). Patients' functional status was relatively preserved with 86% of patients with ECOG-PS 0-1.

Prevalence and clinical correlates of OSA

As Shown in Table 1, OSA, was diagnosed in 386 patients (38%). Compared to non-OSA patients, those with OSA were older (p<0,0001), more often male (p<0,0001), had higher BMI (p<0,0001) and more frequent comorbidities including hypertension (p<0,0001), cardiac diseases (p=0,021) and diabetes (p=0,006). OSA was associated with a higher proportion of squamous NSCLC (p=0,003) and there was a trend toward a lower proportion of localized NSCLC (stage I and II) in patients with OSA (p=0.067). The first-line treatment of NSCLC was not significantly different between OSA and non-OSA patients. However, patients with severe sleep-related hypoxemia at diagnosis were less likely to undergo surgery and more likely to receive immunotherapy than patients with less severe hypoxemia (see e-Table 1). As expected, the patients with OSA had more pronounced nocturnal hypoxemia with higher values of ODI (p<0,0001) and T90 (p<0,0001) and lower mean SpO_2) (p=0,004).

The comparison of quality of life and sleep questionnaires between OSA and non-OSA patients showed higher ESS among patients with OSA (p=0.036), but no significant differences in quality of life, perceived sleep quality and depressive symptoms (Table 2). Among patients with OSA, only 38 patients received continuous positive airway pressure.

A shown in Figure 2 there was no association between intermittent hypoxemia measured by ODI and cancer stage at diagnosis. No association either was found with severe sleep-related sustained hypoxemia (higher T90 and lower mean SpO_2).

OSA, sleep-related hypoxemia and mortality.

As shown in Figures 2 and 3 and table 3, OSA, AHI categories and terciles of ODI were not associated with mortality. Conversely, we found a significant association between indices of sustained sleep-related hypoxemia and mortality (Figure 4). Patients with the highest levels of T90 (>35%) and those with the lowest mean nocturnal SpO_2 (<91%) were at higher risk of death (HR 1.54 [95%CI 1.21-1.95] and 1.68 [95%CI 1.34-2.11] respectively). The association remained significant after adjustment for anthropomorphic data, cancer stage and ECOG-PS at diagnosis, and comorbidities according to model 2 (HR 1.40 [95%CI 1.09-1.80] and HR 1.50 [95%CI 1.18-1.91] respectively). Further adjustment for SpO_2

at rest on room air and the use of thoracic surgery as a first-line treatment for NSCLC (Model 3) did not change the magnitude of the associations of T90 and mean SpO_2 with mortality (HR 1.35 [95%CI 1.05-1.74] and HR 1.48 [95%CI 1.16-1.98] respectively) (Table 3).

Discussion

In this large multicenter prospective study, we found a prevalence of 38% of OSA defined by an ODI> 15 events/h in patients with newly diagnosed NSCLC and ECOG-PS 0–2. Compared to non-OSA patients, those with OSA did not present any significant difference in terms of sleep quality, quality of life, ECOG-PS, cancer stage at diagnosis and survival. However, patients with severe sustained sleep-related hypoxemia, as assessed by T90 and mean SpO_2, were at higher risk of death after adjustment for major confounders including ECOG-PS, cancer stage at diagnosis and SpO_2 at rest on room air and first-line surgical treatment.

The relatively high prevalence of OSA in our study is consistent with previous reports in smaller populations of patients with lung cancer [24–26]. Although the ESS was significantly higher in OSA patients, the majority of them did not have excessive daytime sleepiness in the present report, as in previous studies on comorbid OSA in patients with lung cancer [27, 28]. Likewise, the lack of difference between patients with and without OSA in terms of quality of life, perceived sleep quality, and depressive symptoms, suggests that the indication for sleep recording cannot be based on the finding of more severe diurnal functional impairment in patients with NSCLC. Although not linked to OSA, our study confirms data from recent systematic review and meta-analysis with up to 60% of patients having a PSQI score greater than 5 indicating impaired sleep quality sleep disturbances and the risk of lung cancer: a meta-epidemiological study [29]. Significant associations were found between sleep disturbances and various factors, including age, education level, fatigue, pain, cancer stage, anxiety, and depression, the latter being the most significant [30]. Furthermore, common sleep disturbances, namely extreme sleep duration, symptoms of insomnia, and an evening chronotype, were associated with an increased risk of lung cancer [30]. Future research should concentrate on identifying high-risk individuals and implementing tailored interdisciplinary interventions.

In a recent study, Cubillos-Zapata et al. found that moderate-to-severe OSA was associated with increased expression of serum biomarkers of immune evasion, lymphangiogenesis and tumour cell aggressiveness in high-risk individuals participating in a lung cancer screening cohort (SAILS study) and those with established lung cancer (SAIL study) [16]. However, previous prognostic clinic-based studies addressing concurrent OSA and lung cancer included small samples of patients and reported conflicting results [24]. With a prospective multicenter design and a large sample size of unselected patients with newly diagnosed NSCLC and objective assessment of sleep-disordered breathing, our study overcomes the main limitations of previous prognostic reports in the field. In line with a recent meta-analysis [31], we found no association of OSA and its severity assessed by common metrics including AHI and ODI, with the overall survival of patients with NSCLC.

Our key finding that marked sleep-related hypoxemia is associated with increased mortality in patients with NSCLC is consistent with the concept that hypoxia might promote malignant behavior of cancer cells through different mechanisms [32]. Firstly, hypoxia stabilizes hypoxia-inducible factors (HIFs), mainly HIF-1α and HIF-2α [33–35]. These proteins act as transcription factor allowing cancer cells to adapt to low oxygen conditions by promoting angiogenesis, metabolic reprogramming, and resistance to apoptosis, all of which contribute to tumor survival and aggressiveness [35]. Secondly hypoxia stimulates the production of vascular endothelial growth factor and other pro-angiogenic factors [36]. Other canonical features of cancer progression such as Epithelial-Mesenchymal Transition, metabolic adaptations (Warburg Effect), genomic instability and autophagy have been shown to be influenced by hypoxia [37–39]. Furthermore, hypoxia induces an immunosuppressive tumor microenvironment by recruiting regulatory T cells, myeloid-derived suppressor cells, and polarizing macrophages into an M2 pro-tumor phenotype [40, 41].

Our finding that T90 but not ODI predicts mortality in NSCLC is consistent with previous studies evaluating the association of sleep-disordered breathing with cancer incidence [7, 42]. A significant proportion of respiratory events considered in the calculation of ODI are accompanied by small drops in oxygen saturation resulting in low T90 and preserved mean SpO_2. While the ODI is considered a

measure of intermittent hypoxemia, it does not provide information on the actual depth or duration of oxygen desaturations. The nocturnal hypoxic burden is not fully captured by frequency-based metrics such as ODI and AHI that use a single minimum oxygen nadir to identify events, potentially limiting their use as predictive markers [43, 44]. In community-dwelling older men, Baumert et al. have demonstrated that T90 is not only a consequence of acute desaturations, but also reflects non-specific drifts in oxygen saturation, these two components being significantly associated with CV death [44]. Smoking-related lung disease, obesity, and heart failure, when severe, cause sustained oxygen desaturations below 90%, and could also worsen the prognosis in patients with NSCLC through other non-hypoxia mechanisms. COPD is considered to be one of the important comorbid diseases in NSCLC patients, with a prevalence of 50%-70% [45]. The presence of COPD and emphysema is associated lower survival in patients with NSCLC [45, 46]. Patients with severe COPD or other severe chronic lung disease as well as those receiving long term oxygen therapy were excluded from the present study. Furthermore, to assess the independent impact of sleep-related hypoxemia on mortality, we co-varied the Cox models for BMI, medical history of mild-to-moderate COPD, cardiac diseases and risk factors, and SpO_2 at rest on room air. However, as pulmonary function tests and arterial blood gases were not available in our database, the contribution of underlying smoking-related respiratory disorders to sleep-related hypoxemia and increased mortality cannot be excluded.

There is a growing awareness of the need to consider comorbidities and their prognostic impact in patients with newly diagnosed lung cancer, particularly in localized or locally advanced stages [47]. Our study suggests that systematic screening for sleep-related hypoxemia by pulse oximetry could be part of the workup for comorbidities in patients with NSCLC. Further prospective studies including blood gas measurement and pulmonary function tests are required to determine the relative contribution of OSA and comorbid smoking-related lung diseases to sleep-related hypoxemia and NSCLC prognosis. The impact of oxygen therapy in patients with NSCLC and marked sleep-related hypoxemia should also be studied.

Some limitations of our study are acknowledged. For practical reasons and to ensure efficient recruitment and consistency of data across multiple sites, we used a simple screening device (ApneaLink) that was based on oximetry and nasal pressure recordings and used automated algorithms to analyze signals, rather than the conventional standard test for OSA in which polysomnographic data from an overnight stay in a hospital or clinic are scored manually. The delays in carrying out in-lab polysomnography risked delaying the implementation of cancer treatment. The screening device that was used in the present study has been shown to be a reliable method for diagnosing moderate-to-severe OSA [19, 20]. However, our screening device did not allow for an accurate identification central apneas and hypopneas, potentially favored by higher age, male predominance, cardiac co-morbidities and exposure to opioids. In our cohort, only a minority of patients with OSA have initiated CPAP therapy which precluded any meaningful statistical comparisons of survival between treated and untreated patients. This very low proportion of subjects treated with CPAP can be explained by the fact that medical management was primarily focused on newly diagnosed NSCLC treatment, and that patients with OSA had few symptoms, notably excessive daytime sleepiness. We acknowledge that a longer follow-up would have been preferable, as 18 months approximately corresponded to the median survival of our population. The median survival values of NSCLC in real-life conditions being between 17 and 24 months [48, 49], a substantial proportion of events occur within the first 18 months. Furthermore, the 18-month follow-up of our cohort was sufficient to demonstrate a significant association of sleep-related hypoxemia with overall survival in patients with NSCLC, after adjustment for major confounders. We also acknowledge that in the absence of spirometry and arterial blood gases data in our study, residual confounding from undiagnosed COPD or unmeasured pulmonary function remains. Furthermore, we did not have precise data on the specific causes of death. However, the low median survival of participants and the association of marked sleep-related hypoxemia with cancer stage at diagnosis are in favor of deaths mainly linked to cancer and difference in survival between groups was maintained even after adjusting for SpO_2 at rest on room air.

Interpretation

In conclusion, OSA is highly prevalent in patients with newly diagnosed NSCLC. Sustained nocturnal hypoxemia is associated with lower overall survival. The impact of oxygen therapy on survival deserves to be evaluated in patients with NSCLC and marked nocturnal hypoxemia.

References

1 Siegel RL, Miller KD, Fuchs HE, *et al.* Cancer statistics, 2022. *CA Cancer J Clin* 2022; 72: 7–33.

2 Benjafield AV, Ayas NT, Eastwood PR, *et al.* Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med* 2019; 7: 687–698.

3 Heinzer R, Vat S, Marques-Vidal P, *et al.* Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir Med* 2015; 3: 310–318.

4 Almendros I, Martinez-Garcia MA, Farré R, *et al.* Obesity, sleep apnea, and cancer. *Int J Obes (Lond)* 2020; 44: 1653–1667.

5 Gagnadoux F, Bailly S, Schwab RJ. CPAP recall and cancer risk: should we be concerned? *Eur Respir J* 2024; 64: 2401591.

6 Justeau G, Gagnadoux F. Sleep apnoea and cancer risk: Where are we now? *Respir Med Res* 2022; 81: 100905.

7 Justeau G, Gervès-Pinquié C, Le Vaillant M, *et al.* Association Between Nocturnal Hypoxemia and Cancer Incidence in Patients Investigated for OSA: Data From a Large Multicenter French Cohort. *Chest* 2020; 158: 2610–2620.

8 Martínez-García MA, Campos-Rodriguez F, Durán-Cantolla J, *et al.* Obstructive sleep apnea is associated with cancer mortality in younger patients. *Sleep Med* 2014; 15: 742–748.

9 Nieto FJ, Peppard PE, Young T, *et al.* Sleep-disordered breathing and cancer mortality: results from the Wisconsin Sleep Cohort Study. *Am J Respir Crit Care Med* 2012; 186: 190–194.

10 Kendzerska T, Povitz M, Leung RS, *et al.* Obstructive Sleep Apnea and Incident Cancer: A Large Retrospective Multicenter Clinical Cohort Study. *Cancer Epidemiol Biomarkers Prev* 2021; 30: 295–304.

11 Martínez-García MÁ, Oscullo G, Gómez-Olivas JD, *et al.* Is obstructive sleep apnea a risk factor for lung cancer?-from pathophysiological mechanisms to clinical data. *Ann Transl Med* 2023; 11: 422.

12 Sánchez-de-la-Torre M, Cubillos C, Veatch OJ, *et al.* Potential Pathophysiological Pathways in the Complex Relationships between OSA and Cancer. *Cancers (Basel)* 2023; 15: 1061.

13 Martinez-Garcia MA, Campos-Rodriguez F, Almendros I, *et al.* Cancer and Sleep Apnea:

Cutaneous Melanoma as a Case Study. *Am J Respir Crit Care Med* 2019; 200: 1345–1353.

14 Martinez-Garcia MA, Campos-Rodriguez F, Nagore E, *et al.* Sleep-Disordered Breathing Is Independently Associated With Increased Aggressiveness of Cutaneous Melanoma: A Multicenter Observational Study in 443 Patients. *Chest* 2018; 154: 1348–1358.

15 Cheong AJY, Tan BKJ, Teo YH, *et al.* Obstructive Sleep Apnea and Lung Cancer: A Systematic Review and Meta-Analysis. *Ann Am Thorac Soc* 2022; 19: 469–475.

16 Cubillos-Zapata C, Troncoso-Acevedo F, Díaz-García E, *et al.* Sleep apnoea increases biomarkers of immune evasion, lymphangiogenesis and tumour cell aggressiveness in high-risk patients and those with established lung cancer. *ERJ Open Res* 2024; 10: 00777–02023.

17 Li L, Lu J, Xue W, *et al.* Target of obstructive sleep apnea syndrome merge lung cancer: based on big data platform. *Oncotarget* 2017; 8: 21567–21578.

18 Ferreira PM, Carvalho I, Redondo M, *et al.* The role of obstructive sleep apnea and nocturnal hypoxia as predictors of mortality in cancer patients. *Sleep Med* 2024; 121: 258–265.

19 Chai-Coetzer CL, Antic NA, Rowland LS, *et al.* Primary care vs specialist sleep center management of obstructive sleep apnea and daytime sleepiness and quality of life: a randomized trial. *JAMA* 2013; 309: 997–1004.

20 McEvoy RD, Antic NA, Heeley E, *et al.* CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea. *N Engl J Med* 2016; 375: 919–931.

21 Le Guen Y, Gagnadoux F, Hureaux J, *et al.* Sleep disturbances and impaired daytime functioning in outpatients with newly diagnosed lung cancer. *Lung Cancer* 2007; 58: 139–143.

22 Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991; 14: 540–545.

23 Gagnadoux F, Le Vaillant M, Goupil F, *et al.* Depressive symptoms before and after long-term CPAP therapy in patients with sleep apnea. *Chest* 2014; 145: 1025–1031.

24 Yuan F, Hu Y, Xu F, *et al.* A review of obstructive sleep apnea and lung cancer: epidemiology, pathogenesis, and therapeutic options. *Front Immunol* 2024; 15: 1374236.

25 Cabezas E, Pérez-Warnisher MT, Troncoso MF, *et al.* Sleep Disordered Breathing Is Highly Prevalent in Patients with Lung Cancer: Results of the Sleep Apnea in Lung Cancer Study. *Respiration* 2019; 97: 119–124.

26 Liu W, Zhou L, Zhao D, *et al.* Development and Validation of a Prognostic Nomogram in Lung Cancer With Obstructive Sleep Apnea Syndrome. *Front Med (Lausanne)* 2022; 9: 810907.

27 Lee H, Kim HH, Kim KY, *et al.* Associations among sleep-disordered breathing, sleep quality, and lung cancer in Korean patients. *Sleep Breath* 2023; 27: 1619–1628.

28 Seijo LM, Pérez-Warnisher MT, Giraldo-Cadavid LF, *et al.* Obstructive sleep apnea and nocturnal hypoxemia are associated with an increased risk of lung cancer. *Sleep Med* 2019; 63: 41–45.

29 Hu Y, Xiao LD, Tang C, *et al.* Prevalence and risk factors of sleep disturbances among patients with lung cancer: systematic review and meta-analysis. *Support Care Cancer* 2024; 32: 619.

30 Zhou T, Wang Z, Qiao C, *et al.* Sleep disturbances and the risk of lung cancer: a meta-epidemiological study. *BMC Cancer* 2023; 23: 884.

31 Li J, Cao D, Huang Y, *et al.* Sleep duration and health outcomes: an umbrella review. *Sleep Breath* 2022; 26: 1479–1501.

32 Chen Z, Han F, Du Y, *et al.* Hypoxic microenvironment in cancer: molecular mechanisms and therapeutic interventions. *Signal Transduct Target Ther* 2023; 8: 70.

33 Huang H-Y, Lin S-W, Chuang L-P, *et al.* Severe OSA associated with higher risk of mortality in stage III and IV lung cancer. *J Clin Sleep Med* 2020; 16: 1091–1098.

34 Huang T, Mariani S, Redline S. Sleep Irregularity and Risk of Cardiovascular Events: The Multi-Ethnic Study of Atherosclerosis. *J Am Coll Cardiol* 2020; 75: 991–999.

35 Tirpe AA, Gulei D, Ciortea SM, *et al.* Hypoxia: Overview on Hypoxia-Mediated Mechanisms with a Focus on the Role of HIF Genes. *Int J Mol Sci* 2019; 20: 6140.

36 Shibuya M. Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies. *Genes Cancer* 2011; 2: 1097–1105.

37 Bartrons R, Caro J. Hypoxia, glucose metabolism and the Warburg's effect. *J Bioenerg Biomembr* 2007; 39: 223–229.

38 Daskalaki I, Gkikas I, Tavernarakis N. Hypoxia and Selective Autophagy in Cancer Development and Therapy. *Front Cell Dev Biol* 2018; 6: 104.

39 Tam SY, Wu VWC, Law HKW. Hypoxia-Induced Epithelial-Mesenchymal Transition in Cancers: HIF-1α and Beyond. *Front Oncol* 2020; 10: 486.

40 Ke X, Chen C, Song Y, *et al.* Hypoxia modifies the polarization of macrophages and their inflammatory microenvironment, and inhibits malignant behavior in cancer cells. *Oncol Lett* 2019; 18: 5871–5878.

41 Kumar V, Gabrilovich DI. Hypoxia-inducible factors in regulation of immune responses in tumour microenvironment. *Immunology* 2014; 143: 512–519.

42 Campos-Rodriguez F, Martinez-Garcia MA, Martinez M, *et al.* Association between obstructive sleep apnea and cancer incidence in a large multicenter Spanish cohort. *Am J Respir Crit Care Med* 2013; 187: 99–105.

43 Khoshkish S, Hohl M, Linz B, *et al.* The association between different features of sleep-disordered breathing and blood pressure: A cross-sectional study. *J Clin Hypertens (Greenwich)* 2018; 20: 575–581.

44 Baumert M, Immanuel SA, Stone KL, *et al.* Composition of nocturnal hypoxaemic burden and its prognostic value for cardiovascular mortality in older community-dwelling men. *Eur Heart J* 2020; 41: 533–541.

45 Wu K, Wang J, Zhao L, *et al.* The prognosis of non-small cell lung cancer combined with chronic obstructive pulmonary disease: A systematic review and meta-analysis. *Clin Respir J* 2020; 14: 389–396.

46 Gao Y-H, Guan W-J, Liu Q, *et al.* Impact of COPD and emphysema on survival of patients with lung cancer: A meta-analysis of observational studies. *Respirology* 2016; 21: 269–279.

47 Islam KMM, Jiang X, Anggondowati T, *et al.* Comorbidity and Survival in Lung Cancer Patients.

Cancer Epidemiol Biomarkers Prev 2015; 24: 1079–1085.

48 Li F, Li F, Lu H, *et al.* Analysis of age-related survival differences in advanced non-small cell lung cancer patients based on real-world data. *BMC Cancer* 2025; 25: 1244.

49 Nyen JE, Booth AØ, Husby Ø, *et al.* Targeted treatment and survival in advanced non-squamous non-small cell lung cancer patients - a nationwide and longitudinal study. *Front Oncol* 2025; 15: 1506041.

Figure Legends

Figure 1: Study workflow

Abbreviations: NSCLC: Non-small cell lung cancer; GFPC, Groupe Français de Pneumo-Cancérologie

Figure 2: Cancer stage at diagnosis according to sleep-related hypoxemia severity.

Abbreviations: ODI, 3% oxygen desaturation; T90, % of sleep recording time with oxygen saturation (SpO2) ≤90%; Mean SpO_2, mean arterial oxygen saturation

Comparisons were performed using Chi square test.

Figure 3: Kaplan-Meier survival curves according to the presence or absence of obstructive sleep apnea (OSA).

The log-rank test was used to compare the survival distribution across categories.

Figure 4: Kaplan-Meier survival curves according indices of sleep-related hypoxemia (terciles of percentage of recording-time with oxygen saturation [SpO_2] ≤90% [Figure 3A], terciles of mean SpO_2 [Figure 3B])

The log-rank test was used to compare the survival distribution across categories.

Table 1: Characteristics of study population according to the presence or absence of obstructive sleep apnea (OSA)

	All	No OSA	OSA	P values
n	1,005	619	386	
Men, n (%)	709 (71)	405 (66)	304 (79)	**< 0.001**
Age, years	63.67 (9.75)	62.32 (9.64)	65.58 (9.52)	**< 0.001**
BMI, kg/m^2	24.24 (4.85)	23.58 (4.67)	25.64 (4.81)	**< 0.001**
Comorbidities				
Hypertension, n (%)	338 (34)	175 (28)	163 (42)	**< 0.001**
Stroke, n (%)	36 (4)	21 (3)	15 (4)	0.670
Cardiac disease, n (%)	138 (14)	73 (12)	65 (17)	**0.021**
Diabetes, n (%)	144 (14)	74 (12)	70 (18)	**0.006**
COPD, n (%)	168 (17)	110 (18)	58 (15)	0.275
Ever-smoker, n (%)	896 (90)	554 (89)	342 (88)	0.861
Daily Alcohol intake, n (%)	447 (45)	277 (45)	170 (44)	0.893
Cancer characteristics				
Squamous NSCLC, n (%)	257 (26)	139 (22)	118 (30)	**0.003**
Stage I-II, n (%)	109 (11)	87 (14)	22 (6)	0.067
ECOG-PS 0-1, n (%)	860 (86)	532 (86)	328 (84)	0.873
Cancer 1st line treatment				
Surgery, n (%)	183 (18)	109 (17)	74 (19)	0.545
Chemoradiation, n (%)	78 (8)	52 (8)	26 (7)	0.289
Chemotherapy, n (%)	566 (56)	339 (55)	227 (59)	0.079
Immunotherapy, n (%)	88 (9)	56 (9)	32 (8)	0.361
Targeted therapy, n (%)	36 (4)	25 (4)	11 (3)	0.552
Clinical trial, n (%)	54 (5)	38 (6)	16 (4)	0.080
Sleep study characteristics				
AHI, events/h	**11.4 (13.9)**	**4.27 (4.22)**	**22.9 (16.1)**	**<0.001**
ODI, events/h	16.11 (15.53)	7.02 (3.93)	30.67 (15.50)	**< 0.001**
T90, %	30.1 (33.9)	23.9 (31.9)	40.1 (34.6)	**< 0.001**
Mean SpO_2, %	91.3 (5.68)	91.7 (6.9)	90.8 (2.69)	**0.004**

Abbreviations: BMI, body mass index; SpO_2, oxygen saturation; COPD, chronic obstructive pulmonary disease; NSCLC; non-small cell lung cancer; ECOG-PS: Eastern Cooperative Oncology Group performance status; ODI, 3% oxygen desaturation; T90, % of sleep recording time with SpO_2<90%.
Data are expressed as mean (standard deviation) or number (%).
Comparisons between OSA and no-OSA patients were performed using Student's t-test for quantitative variables or Chi square test for qualitative variables.

Table 2: Quality of life and sleep questionnaires according to the presence or absence of obstructive sleep apnea (OSA)

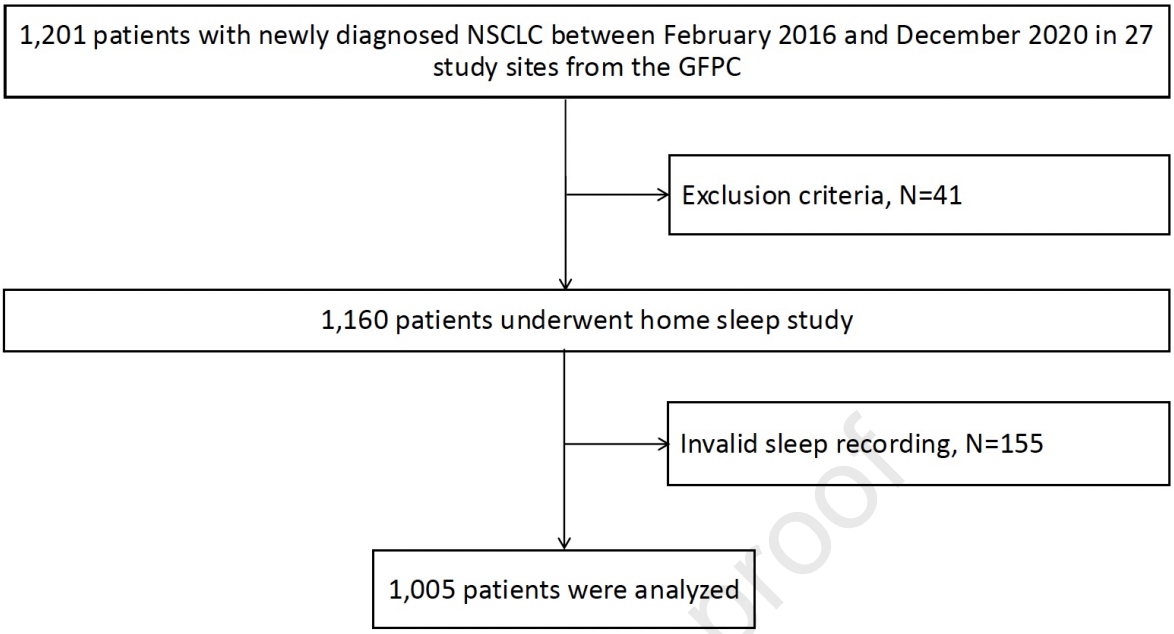
	All	No OSA	OSA	P values	Missing data
Quality of life					
EQ-5D Mobility	1.30 (0.49)	1.29 (0.50)	1.32 (0.50)	0.445	74
EQ-5D Selfcare	1.11 (0.37)	1.11 (0.36)	1.12 (0.37)	0.624	74
EQ-5D Usual activities	1.37 (0.57)	1.36 (0.57)	1.37 (0.57)	0.750	75
EQ-5D Pain/Discomfort	1.78 (0.62)	1.75 (0.58)	1.79 (0.63)	0.367	76
EQ-5D Anxiety/Depression	1.58 (0.62)	1.56 (0.61)	1.58 (0.61)	0.758	77
Sleep quality					
PSQI	6.87 (3.99)	6.69 (3.92)	6.88 (4.04)	0.523	88
PSQI≥5, %	67	68	66	0.893	
Depressive symptoms					
QD2A	3.08 (3.19)	2.81 (2.93)	3.14 (3.25)	0.154	80
QD2A≥7, %	15.1	15.9	12.5	0.221	
Excessive daytime sleepiness					
ESS	5.12 (3.77)	4.68 (3.53)	5.26 (3.85)	0.036	75
ESS≥11, %	8.8	5.1	9.8	**0.028**	

Abbreviations: EQ-5D, EuroQol five-dimensions; PSQI, Pittsburgh Sleep Quality Index; QD2A, Pichot Questionnaire of Depression 2nd version, Abridged; ESS, Epworth Sleepiness Score,
Data are expressed as mean (standard deviation) or percentage,
Comparisons between OSA and no-OSA patients were performed using Student's t-test for quantitative variables or Chi square test for qualitative variables,

Table 3: Cox proportional hazard models assessing the association of mortality with indices of nocturnal hypoxemia

	Median survival, months	Mortality rate, %	Model 1 HR [95%CI]	Model 2 HR [95%CI]	Model 3 HR [95%CI]
AHI, events/h					
<15	19.33	41.7	Reference	Reference	Reference
15 to <30	18.60	44.2	0.99 [0.76-1.30]	1.06 [0.81-1.39]	1.06 [0.80]
≥30 (152)	18.16	44.6	1.01 [0.74-1.38]	1.07 [0.78-1.48]	1.06 [0.77-1.48]
ODI, events/h					
<7.2	18.4	43.2	Reference	Reference	Reference
7.2 to <17.1	19.7	41.6	0.89 [0.70-1.13]	0.92 [0.72-1.18]	0.93 [0.72-1.18]
≥17.1	19.3	43.8	0.93 [0.74-1.17]	0.91 [0.71-1.17]	0.91 [0.71-1.18]
T90, %					
<4	NA	37.8	Reference	Reference	Reference
4 to <35	19.3	42.9	1.15 [0.90-1.47]	1.17 [0.91-1.51]	1.16 [0.90- 1.50]
≥35	16.8	47.6	**1.54** [**1.21-1.95**]	**1.40** [**1.09-1.80**]	**1.41** [**1.12-1.82**]
Mean SpO_2, %					
≥93%	NA	38.1	Reference	Reference	Reference
91 to <93%	19.3	42.8	1.22 [0.96-1.54]	1.17 [0.91-1.49]	1.16 [0.91-1.48]
<91%	16	49.7	**1.68** [**1.34-2.11**]	**1.50** [**1.18-1.91**]	**1.47** [**1.15-1.87**]

Abbreviations: HR, hazard ratio; CI, confidence interval, ODI, 3% oxygen desaturation; T90, % of sleep recording time with oxygen saturation (SpO_2) <90%.
Model 1: unadjusted
Model 2: adjusted for age, gender body mass index, smoking habits, cancer stage at diagnosis (I-II *vs* III-IV), Eastern Cooperative Oncology Group performance status (0-1 *vs* 2), history of hypertension (yes vs no), stroke (yes vs no), cardiac disease (yes vs no), diabetes mellitus (yes vs no), chronic obstructive pulmonary disease (yes vs no).
Model 3: adjusted for model 2 + SpO2 at rest on room



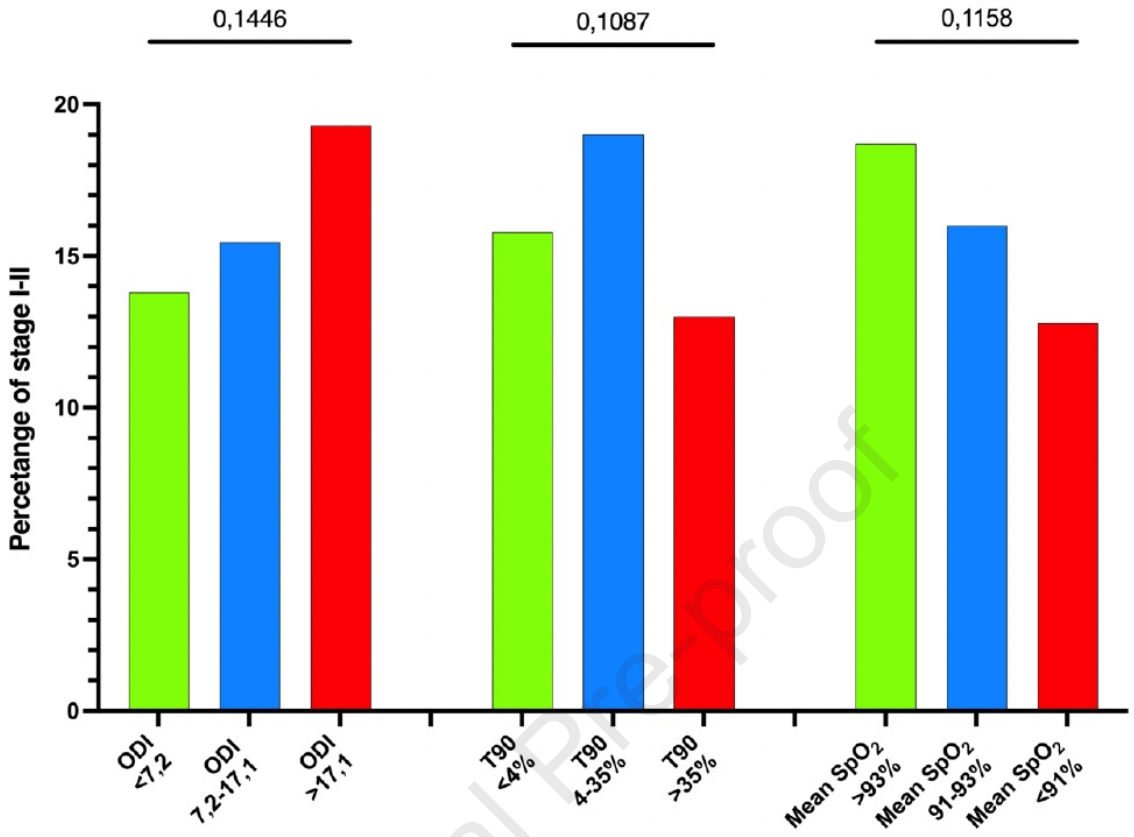


Figure 3

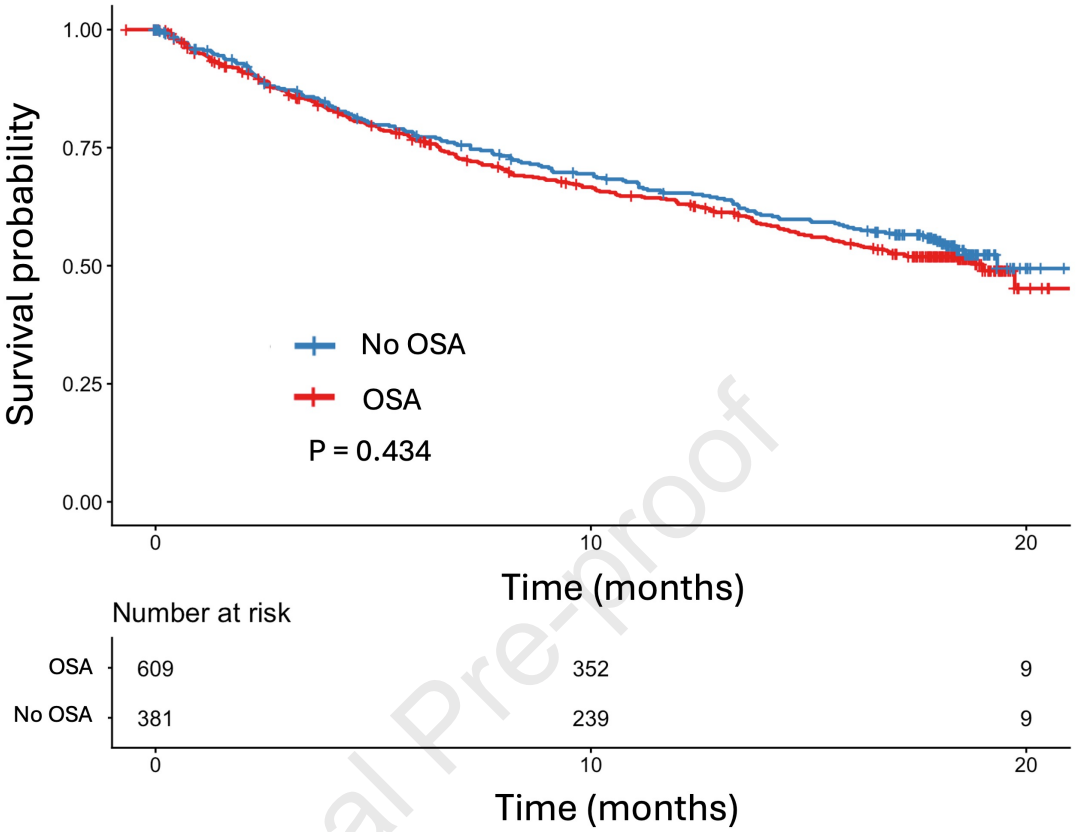


Figure 4 A

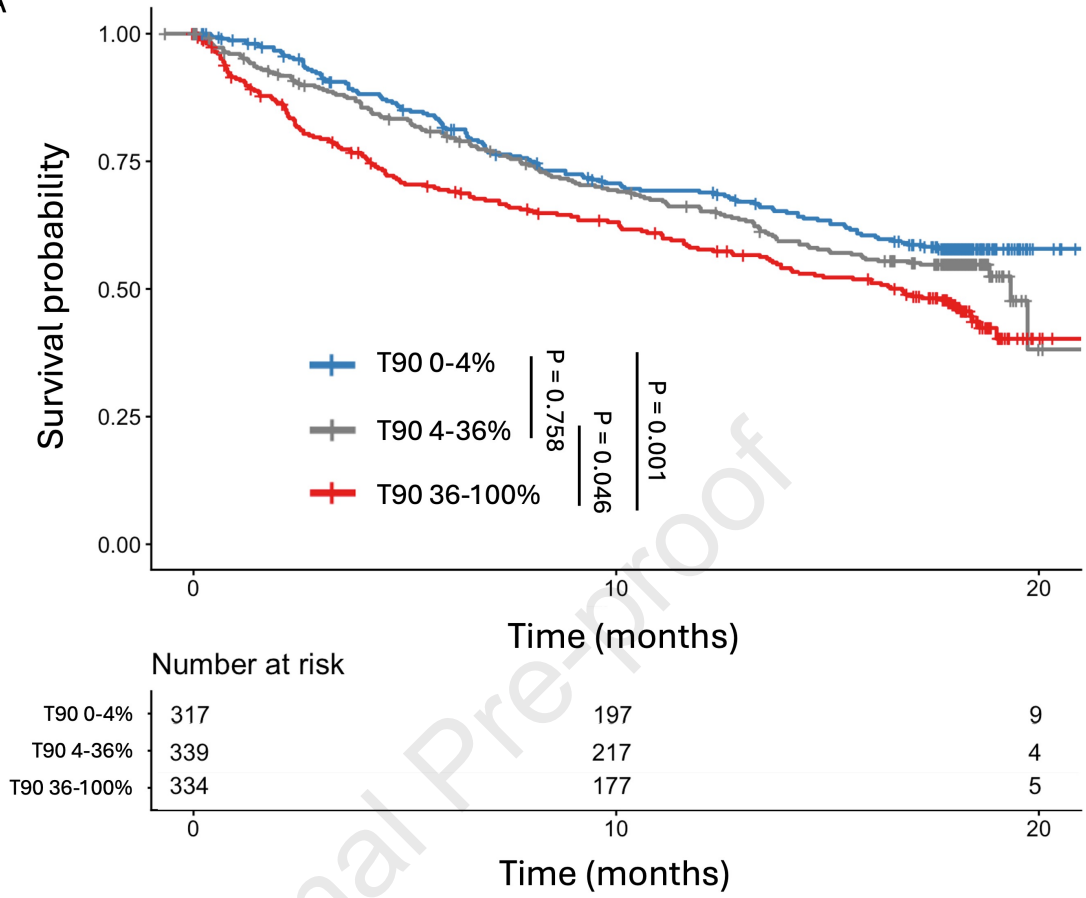
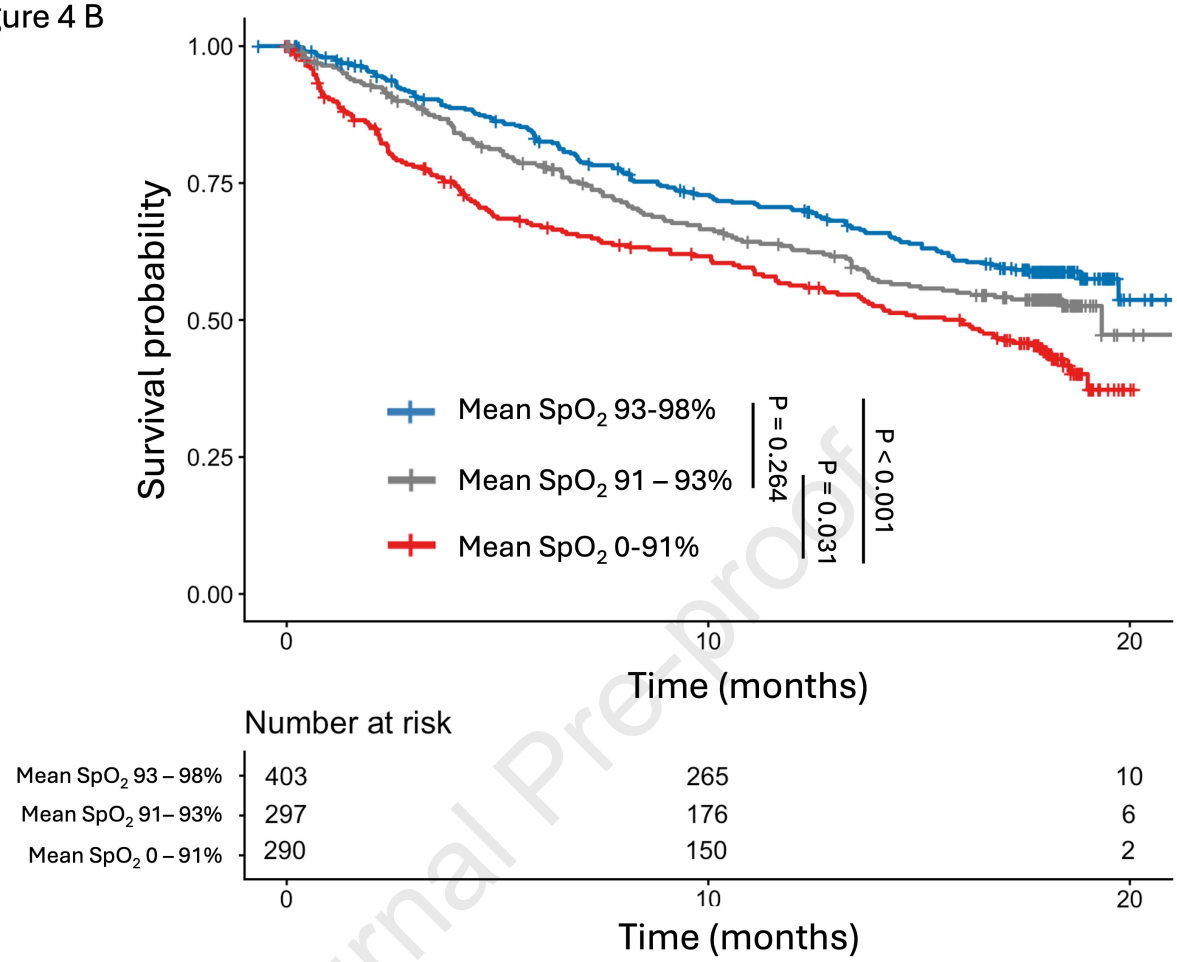


Figure 4 B



Take-Home Points

Study Question: Is obstructive sleep apnea (OSA) and sleep-related hypoxemia associated with survival in patients with newly diagnosed non-small cell lung cancer (NSCLC).

Results: OSA was prevalent (38%) in patients with NSCLC, but was not associated with survival. However, patients with severe sustained nocturnal hypoxemia had lower overall survival.

Interpretation: The unfavorable prognostic value of nocturnal hypoxemia in patients with NSCLC, justifies further investigation in clinical trials.

Supplemental Material

Association of sleep-related hypoxemia with survival in patients with non-small cell lung cancer – the NEOSAS-GFPC study group

Authors : Grégoire Justeau, M.D, PhD,[a] Laurent Greillier, M.D, PhD,[b] Florent Vinas, M.D,[C] Lionel Falchero, M.D,[d] Olivier Bylicki, M.D,[e] Marie Bernardi, M.D,[f] Francis Martin, M.D,[g] Isabelle Simon, M.D,[g] Didier Debieuvre, M.D,[h] Chrystèle Locher,[i] Acya Bizieux-Thaminy, M.D,[J] Virginie Levrat, M.D,[k] Stéphanie Fry, M.D,[l] Camille Guguen, M.D,[n] Frédéric Goutorbe, M.D,[m] Philippe Masson, M.D,[o] Franck Soyez, M.D,[p] Christos Chouaid, M.D, PhD,[c] Patrick Saulnier, M.D, PhD,[q,r] Frédéric Gagnadoux M.D, PhD,[a].

[a] Pneumology Department, CHU d'Angers, Angers, France.

[b] Multidisciplinary Oncology and Therapeutic Innovations, Aix-Marseille University, APHM, INSERM, CNRS, CRCM, Hôpital Nord, Marseille, France.

[c] Pneumology Department, Centre Hospitalier Intercommunal de Créteil, Créteil, France.

[d] Pneumology Department, CH Villefranche-Sur-Saône, France.

[e] Pneumology Department, Hôpital d'Instruction des Armées Sainte-Anne Toulon, France

[f] Pneumology Department, CHI Aix-En-Provence, France.

[g] Sleep Unit, Centre Hospitalier de Compiègne-Noyon, 60200 Compiègne, France.

[h] Pneumology Department, Groupe Hospitalier de la Région Mulhouse Sud-Alsace, Hôpital Emile Muller, GHRMSA - Mulhouse, Mulhouse, France.

[i] Pneumology Department, Grand Hôpital de l'Est Francilien (Meaux), Meaux, France.

[j] Pneumology Department, CH Départemental Vendée, La Roche-sur-Yon, France.

[k] Pneumology Department, Groupe Hospitalier De La Rochelle-Ré-Aunis, La Rochelle, France.

[l] Pneumology, Immunology and Allergology Department, CHU de Lille, Lille, France.

[n] Pneumology Department, Centre Hospitalier Le Mans, Le Mans, France.

[m] Pneumology Department, CH Béziers, Béziers, France.

[o] Pneumology Department, Cholet General Hospital, Cholet, France.

[p] Pneumology Department, Centre d'étude du sommeil Antony, France

[q] MINT, INSERM U1066, CNRS 6021, University of Angers, SFR-ICAT 4208, Angers, France.

[r] Pharmacy department, CHU Angers, Angers, France.

e-Table 1: Cancer first-line treatment modalities according to the severity of sleep-related nocturnal hypoxemia at diagnosis.

Cancer 1st line treatment	All	T90 <4%	T90 4-35%	T90>35%	P values
Surgery, n (%)	183 (18.2)	79 (22.7)	64 (19.2)	40 (12.3)	**< 0.001**
Chemo radiation, n (%)	78 (7.8)	27 (7.8)	23 (6.9)	28 (8.6)	0.694
Chemotherapy, n (%)	566 (56.3)	182 (52.3)	198 (59.5)	186 (57.4)	0.540
Immunotherapy, n (%)	88 (8.8)	26 (7.5)	20 (6.0)	42 (13.0)	**0.012**
Targeted therapy, n (%)	36 (3.6)	15 (4.3)	12 (3.6)	9 (2.8)	0.361
Clinical trial, n (%)	54 (5.4)	19 (5.5)	16 (4.8)	19 (5.9)	0.248

Abbreviations: T90, % of sleep recording time with $SpO_2 \leq 90\%$.