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Mini Review

Obstructive Sleep Apnea and Lung Cancer: Epidemiological Insights and Pathophysiological Mechanisms

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Abstract

Obstructive sleep apnea (OSA) is a prevalent sleep disorder characterized by intermittent hypoxia and sleep fragmentation, which may contribute to lung cancer development and progression. This review synthesizes epidemiological evidence on the association between OSA and lung cancer incidence and mortality, highlighting inconsistencies due to study design, population differences, and confounding factors such as smoking and obesity. While some studies report an increased lung cancer risk, particularly with severe nocturnal hypoxemia, others suggest no significant association or a potential protective effect. Pathophysiologically, OSA promotes oncogenesis through hypoxia-inducible factor activation, tumor immune microenvironment remodeling, exosome-mediated signaling, nuclear factor κB pathway activation, and enhanced cancer stem cell properties. Continuous positive airway pressure therapy may mitigate these effects, with evidence suggesting reduced lung cancer incidence and improved prognosis in adherent patients. This review underscores the need for standardized studies using objective diagnostics and robust confounder adjustment to clarify the OSA–lung cancer link and optimize clinical management.

Introduction

Obstructive sleep apnea (OSA) is a prevalent sleep disorder characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to intermittent hypoxia (IH) and sleep fragmentation (SF).[1] These physiological disturbances have been increasingly recognized for their potential role in various systemic diseases, including cardiovascular disorders, metabolic dysfunction, and, more recently, oncogenesis. Among the malignancies potentially linked to OSA, lung cancer has garnered significant attention due to its high global incidence and mortality rates. Lung cancer remains one of the leading causes of cancer-related deaths worldwide, with complex etiological factors including smoking, environmental exposures, and emerging evidence suggesting a role for chronic physiological stressors such as those induced by OSA.[2]

The relationship between OSA and lung cancer is hypothesized to stem from the pathophysiological consequences of IH and SF, which may promote tumor initiation, progression, and metastasis through mechanisms such as hypoxia-inducible factor (HIF) activation, tumor immune microenvironment (TIME) remodeling, exosome-mediated signaling, and enhanced cancer stem cell (CSC) properties. Epidemiological studies exploring this association have yielded conflicting results.[3–7] These discrepancies may arise from variations in study design, population characteristics, follow-up duration, and adjustment for confounders such as smoking and obesity.

This review aims to synthesize current epidemiological evidence on the association between OSA and lung cancer incidence and mortality, while also exploring the underlying pathophysiological mechanisms driving this relationship. Additionally, it evaluates the potential impact of continuous positive airway pressure (CPAP) therapy on lung cancer risk and prognosis, highlighting its role in mitigating OSA-related oncogenic effects. By addressing these aspects, this review seeks to provide a comprehensive understanding of the interplay between OSA and lung cancer, informing future research and clinical management strategies.

Epidemiology

OSA and lung cancer prevalence and incidence

A recent cross-sectional study combining the SAIL (Sleep Apnea in Lung Cancer) and SAILS (Sleep Apnea in Lung Cancer Screening) cohorts (n = 302; NCT02764866) provided further evidence

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supporting the predominant role of nocturnal hypoxemia. Using home sleep apnea testing, moderate-to-severe OSA (apnea-hypopnea index (AHI) > 15) was associated with an 8% higher prevalence of lung cancer compared to AHI < 15, with statistical significance maintained after propensity score matching (P = 0.015) and nearest-neighbor matching (P = 0.041). Adjusted binary logistic regression revealed associations of nocturnal hypoxemia indices—T90% (P = 0.005) and ODI3% (P = 0.02)—with lung cancer presence.[8] The prospective SAILS study (NCT02764866) investigated OSA prevalence in 236 high-risk smokers (mean age 63.6 years, 45 pack-years) undergoing lung cancer screening with low-dose computed tomography. Moderate-to-severe OSA (AHI ≥ 15) was highly prevalent, and nocturnal hypoxemia (T90), reduced diffusing capacity of the lungs for carbon monoxide, greater tobacco exposure, and chronic obstructive pulmonary disease were significantly associated with OSA severity. After multivariate adjustment, nocturnal hypoxemia emerged as an independent predictor of positive screening findings (lung nodules ≥ 6 mm; odds ratio 2.6, 95% confidence interval (CI) 1.12–6.09, P = 0.027).[9]

Previous studies have identified a significant association between nocturnal oxygen desaturation (a hallmark of OSA) and increased incidence of smoking-related cancers, including lung cancer.[10] Regarding the association between OSA and lung cancer incidence, epidemiological evidence exhibits considerable inconsistency. This review synthesizes findings from eight relevant studies, encompassing diverse populations, study designs, and time spans, to elucidate the relationship between OSA, its severity (measured by the AHI, nocturnal hypoxemia indicators [T90%], or mean oxygen saturation [SaO_2]), and lung cancer incidence. These studies include retrospective cohort, prospective cohort, and matched-control designs, involving populations such as veterans, Asian cohorts, female nurses, and the general population. Lung cancer risk was evaluated using Cox proportional hazards models or standardized incidence ratios (SIR).

Gozal *et al*.,[6] utilizing a large U.S. health insurance database of approximately 5.6 million individuals, found no statistically significant association between OSA and lung cancer incidence (hazard ratio (HR) 1.02, 95% CI 0.99–1.06), nor was OSA linked to lung cancer progression or mortality. However, OSA was associated with a significantly increased risk of pancreatic, kidney, and melanoma cancers, while risks for colorectal, breast, and prostate cancers were lower. This suggests that OSA may have a limited overall impact on lung cancer but exerts a more pronounced effect on other cancer types. Similarly, Marriott *et al*.[11] conducted a study on a cohort of 20,289 patients from a sleep clinic in Western Australia (median follow-up of 11.2 years) and found no significant association between AHI (AHI > 30 vs. AHI < 5, HR 0.80, 95% CI 0.51–1.26) or T90% (T90% ≥ 2.2 vs. T90% < 0.1, HR 0.96, 95% CI 0.67–1.38) and lung cancer incidence. Although nocturnal hypoxemia was independently associated with baseline cancer prevalence, after adjusting for confounders such as age, sex, body mass index, and smoking, OSA severity showed no independent association with cancer incidence, including lung cancer, suggesting that OSA may not be a direct driver of lung cancer.

In contrast, Jara *et al*.[12] conducted a study on 1,377,285 patients within the Veterans Health Care System (median follow-up of 7.4 years) and reported a significant increase in overall cancer risk associated with OSA (HR 1.97, 95% CI 1.94–2.00), with a 32% increased incidence of lung cancer (HR 1.32, 95% CI 1.27–1.38). After adjusting for confounders such as age, sex, smoking, and obesity, OSA remained an independent risk factor for cancer development, particularly in the predominantly male veteran population, suggesting that OSA may influence lung cancer risk through specific carcinogenic mechanisms. Similarly, Kendzerska *et al*.,[4] in a multicenter retrospective study in Canada (N = 33,711, median follow-up of 7 years), found that severe OSA was associated with an increased risk of lung cancer (HR 1.34, 95% CI 1.00–1.80), whereas mild-to-moderate OSA showed no such association. Nocturnal hypoxemia (mean SaO_2 < 93.4%) was also identified as an independent risk factor for lung cancer, indicating a significant contribution of severe hypoxemia to lung cancer risk.[4] Justeau *et al*.[13] further underscored the role of nocturnal hypoxemia in a multicenter cohort study (N = 8,748, median follow-up of 5.8 years). They found no direct association between AHI and lung cancer incidence, but T90% (percentage of sleep time with oxygen saturation < 90%) was an independent risk factor for lung cancer development (T90% ≥ 13% vs. T90% < 0.01, HR 2.14, 95% CI 1.01–4.54), suggesting that chronic IH may be a critical carcinogenic mechanism. A prospective study in 2021 (Nurses' Health Study, N = 65,330, women, mean age 73.3 years, follow-up of 8 years) also found a significant association between OSA and lung cancer risk (HR 1.52, 95% CI 1.07–2.17).[14] Among non-smokers, OSA patients had approximately three times the lung cancer incidence compared to non-OSA patients (HR 2.96, 95% CI 1.42–6.18). However, this study relied on self-reported OSA diagnoses via questionnaires rather than polysomnography, potentially introducing diagnostic bias. Nevertheless, the stronger association in non-smokers suggests that hypoxemia may amplify lung cancer risk in the absence of smoking exposure.

However, some studies have reported contrasting findings. Sillah *et al*.[5] investigated 34,402 OSA patients (mean follow-up of 5.3 years) and observed an elevated overall cancer incidence (SIR 1.26, 95% CI 1.20–1.32), but lung cancer incidence was lower than expected (SIR 0.66, 95% CI 0.54–0.79, with 115 observed cases compared to 175 expected cases), suggesting a potential protective effect of OSA against lung cancer. Similarly, a 2023 study based on a 12-year follow-up from the Korea National Health Insurance Service found a significantly reduced lung cancer incidence among OSA patients (HR 0.87, 95% CI 0.82–0.93), particularly in male patients (HR 0.84, 95% CI 0.78–0.90), while no significant association was observed in female patients (HR 1.05, 95% CI 0.91–1.21).[15] This gender-specific protective effect may be related to genetic or environmental factors specific to Asian populations.

The observed discrepancies in study findings may stem from several underlying factors. Firstly, studies reporting an elevated lung cancer risk associated with OSA often involve follow-up periods exceeding seven years.[12–14] Given the chronic nature of both OSA and lung cancer, with their prolonged latency periods, the interval between disease onset and clinical diagnosis can span several years. Establishing a causal link between OSA's physiological effects and cancer progression requires OSA to persist for an extended period before cancer detection, even if undiagnosed. For instance, research suggests that squamous cell lung carcinoma typically requires approximately eight years to reach a radiologically detectable size. Secondly, many epidemiological studies rely on national health insurance databases to identify patients with OSA.[12,13] While these datasets offer valuable large-scale insights, they are prone to inherent biases. Key confounding variables, such as obesity and smoking status, are often inadequately documented or challenging to assess accurately in such registries. Insufficient adjustment for these factors can significantly skew study outcomes, leading to inconsistent findings across investigations due to variations in risk factor prevalence. Moreover, identifying OSA patients through administrative databases introduces risks of selection bias and exposure misclassification. Control groups la-

Table 1. Summary of major epidemiological studies on obstructive sleep apnea (OSA), nocturnal hypoxemia, and lung cancer incidence

First author, Year	Country/ Region	Study design	N	Follow-up (median)	OSA diagnosis	Key notes
Gozal, 2016[6]	USA	cohort	5.6 million	3.2 y	ICD codes	No association with lung cancer
Kendzerska, 2021[4]	Canada	Multicenter retrospective	33,711	7 y	PSG	The severity of OSA and nocturnal hypoxemia was independently associated with incident cancer
Jara, 2020[12]	USA (Veterans)	Retrospective cohort	1,377,285	7.4 y	ICD codes	Association with lung cancer
Justeau, 2020[13]	France	multicenter cohort	8,748	5.8 y	PSG	Nocturnal hypoxemia was associated with lung malignancies
Sillah, 2018[5]	USA	Community cohort	34,402	5.3 y	ICD codes	Paradoxical lower incidence
Huang, 2020[14]	USA	Sleep clinic cohort	65,330	8 y	Self report	OSA was associated with significantly increased risk of lung cancer
Marriott, 2023[11]	Australia	Sleep clinic cohort	20,289	11.2 y	PSG	No association
Park, 2023[15]	Korea	NHIS national cohort	267,849	12 y	operational code	Protective in Asian males

ICD, International Classification of Diseases; NHIS, National Health Insurance Service; PSG, polysomnography.

beled as "unexposed" (lacking an OSA diagnosis) may inadvertently include undiagnosed OSA cases, particularly in clinical cohorts with prevalent OSA-related risk factors, such as obesity. Conversely, diagnosed OSA patients may not fully represent the broader OSA population, as they often exhibit more severe symptoms or comorbidities. To address these limitations, community-based studies employing objective diagnostic tools, such as polysomnography, could yield more accurate estimates of OSA prevalence. However, such studies are resource-intensive, often resulting in smaller sample sizes that constrain statistical power. Another critical factor is the variability in adjusting for confounders, such as smoking, body mass index, and comorbidities. Inconsistent control for these variables may obscure or exaggerate the true association between OSA and lung cancer risk. Notably, several studies (e.g., Justeau, Kendzerska) indicate that nocturnal hypoxemia—measured by metrics like T90% (time spent with oxygen saturation below 90%) or low SaO_2—is a stronger predictor of lung cancer risk than the AHI.[4,14] This suggests that chronic IH may be a primary oncogenic mechanism in OSA-related carcinogenesis. Although AHI is a widely used diagnostic metric, it primarily quantifies the frequency of respiratory disturbances and does not fully capture OSA's pathophysiological complexity. The clinical impact of OSA extends beyond apnea and hypopnea events, encompassing the severity and cumulative duration of oxygen desaturation. As a standalone measure, AHI may fail to account for systemic effects, such as chronic inflammation, oxidative stress, and activation of the HIF pathway, all of which are critical in cancer initiation and progression (Table 1).[4–6,11–15]

OSA and mortality of lung cancer

A retrospective case series analysis of a sleep cohort with suspected OSA (2009–2014), comprising 8,261 patients, reported a lung cancer incidence rate of 242.1 per 100,000 individuals—significantly higher than that of the general adult population in Taiwan (51.5 per 100,000, $P < 0.01$).[16] Notably, cancer-related mortality at three years increased progressively with OSA severity: 25% for AHI < 15, 50% for AHI 15–29, and 80% for AHI ≥ 30 (chi-squared test for trend, $P = 0.03$). Kaplan–Meier survival analysis further demonstrated that stage III–IV lung cancer patients with AHI < 30 had significantly improved overall survival and progression-free survival compared to those with severe OSA ($P = 0.02$).

Another study conducted at the Third Affiliated Hospital of Kunming Medical University (2017) evaluated 45 patients with surgically resectable lung cancer alongside a control group. After one year of follow-up, the OSA subgroup exhibited a significantly higher overall deterioration rate (encompassing death, recurrence, and metastasis) compared to the non-OSA subgroup ($P < 0.05$). However, individual outcomes—mortality, recurrence, and metastasis rates—did not reach statistical significance (OSA subgroup: 3 deaths, 5 recurrences, 4 metastases; non-OSA subgroup: 1 death, 4 recurrences, 2 metastases).[17]

Current epidemiological findings underscore a strong association between severe OSA and elevated mortality risk in lung cancer patients, with evidence suggesting that OSA may accelerate disease progression through mechanisms such as chronic nocturnal hypoxemia. These observations highlight the need for greater clinical consideration of OSA in lung cancer management and further research into its pathophysiological role (Table 2).[16,17]

Pathogenesis

The primary pathophysiological mechanisms of OSA involve recurrent IH and SF caused by apneic episodes. Chronic intermittent hypoxia induces dysfunction across multiple physiological systems, including cardiovascular diseases, endocrine-metabolic disorders, urogenital dysfunction, and cognitive impairments. In the context of OSA, IH and SF may promote alterations in multiple signaling pathways, which not only initiate malignant transformation but also modify the tumor microenvironment, impair immune surveillance, and thereby accelerate tumor dissemination and proliferation, enhancing local and metastatic invasion. Current research primarily focuses on the impact of IH on tumor biology, with mechanisms generally attributed to changes in oxygen-sensitive pathways, oxidative stress, inflammation, invasion and metastasis, and immune responses (Fig. 1).

Table 2. Summary of major epidemiological studies on obstructive sleep apnea (OSA), nocturnal hypoxemia, and lung cancer mortality

First author, Year	Country/ Region	Study design	N	Follow-up (median)	OSA diagnosis	Key notes
Huang, 2020[16]	Taiwan	Sleep cohort	8,261	5 y	PSG	OSA is associated with an increased risk of cancer mortality
Liu, 2019[17]	China	Prospective SAILS screening	45	1 y	HSAT	The mortality, recurrence rate, and metastasis rate increased in lung cancer patients with OSA during the one-year follow-up period

HSAT, home sleep apnea testing; PSG, polysomnography; SAILS, sleep apnea in lung cancer screening.

Activation and role of HIF

IH, a hallmark feature of OSA, significantly activates HIFs, particularly HIF-1α and HIF-2α. Under hypoxic conditions, HIFs stabilize and regulate the transcription of multiple genes that promote tumor-adaptive changes. For instance, HIF-1α upregulates vascular endothelial growth factor, facilitating tumor angiogenesis and enhancing oxygen and nutrient supply to tumor cells.[18] HIF-2α supports tumor stem cell self-renewal, increasing metastatic potential. Additionally, HIFs activate matrix metalloproteinases and epithelial–mesenchymal transition-related genes, promoting tumor invasion and distant metastasis. Studies have shown that HIF-1α expression is significantly elevated in lung cancer nodules under IH conditions.[19]

Remodeling of the TIME

IH promotes tumor immune evasion and progression by reshaping the TIME. Research indicates that IH induces the recruitment of M2-type macrophages, myeloid-derived suppressor cells, and regulatory T cells, which secrete immunosuppressive factors such as interleukin (IL)-10 and transforming growth factor-beta, thereby attenuating anti-tumor immunity.[20] Concurrently, IH upregulates programmed death-ligand 1 expression through HIF and other signaling pathways, suppressing $CD8^+$ T cell activity and further facilitating immune evasion.[21,22] Moreover, IH promotes the release of pro-inflammatory cytokines (e.g., IL-6, tumor necrosis factor-alpha), amplifying the inflammatory state of the tumor microenvironment and indirectly supporting tumor proliferation and metastasis.[23]

Mediating role of exosomes

Exosomes play a critical role in OSA-induced lung cancer progression. IH stimulates tumor cells and immune cells to release exosomes carrying microRNAs (e.g., miR-21, miR-210) and proteins (e.g., vascular endothelial growth factor, HIF-1α), which modulate the TIME, promote angiogenesis, and induce immunosuppression.[24,25] Studies demonstrate that exosomes released under IH conditions enhance the malignant characteristics of lung cancer cells, such as proliferation, migration, and metastasis.[26] Exosomes can also influence distant organs via systemic circulation, forming a pre-metastatic niche that promotes tumor metastasis.[27] Furthermore, exosomes may transfer drug resistance-related molecules (e.g., P-glycoprotein), conferring chemoresistance to tumor cells.[28]

Nuclear factor κB (NF-κB) signaling pathway

NF-κB is a pivotal transcription factor in IH-induced inflammation and tumor progression. Research shows that IH activates the NF-κB pathway, inducing the expression of pro-inflammatory cytokines (e.g., IL-6, tumor necrosis factor-alpha, cyclooxygenase-2), which creates a pro-tumorigenic microenvironment.[29,30] NF-κB also upregulates anti-apoptotic genes (e.g., *BCL-2*) and cell cycle genes (e.g., Cyclin D1), enhancing tumor cell survival and proliferation.[30] Additionally, NF-κB activates matrix metalloproteinases and adhesion molecules, promoting tumor cell invasion and metastasis.[31] Notably, NF-κB interacts synergistically with HIF, amplifying pro-tumorigenic signaling.

Enhancement of CSCs

IH enhances CSC properties through multiple mechanisms, promoting lung cancer progression. Studies have found that IH upregulates CSC markers (e.g., Oct4, Sox2, Nanog) via HIF and NF-κB pathways, sustaining CSC self-renewal.[32] Furthermore, the IH-induced TIME, characterized by M2 macrophages and myeloid-derived suppressor cells, secretes transforming growth factor-beta and IL-6, which further promote CSC proliferation and differentiation.[33,34] CSCs exhibit inherent resistance to chemotherapy and radiotherapy, and IH further enhances this resistance through HIF and NF-κB, contributing to treatment failure.[35]

Treatment

Research indicates that when patients adherent to CPAP therapy are excluded from analysis, the association between OSA and lung cancer risk becomes more pronounced.[13] Conversely, among patients receiving adequate CPAP treatment, the relationship between nocturnal hypoxemia and cancer risk is no longer evident, suggesting that CPAP therapy may positively influence lung cancer incidence and prognosis by improving oxygenation status.

A recently published prospective multicenter clinical study provides further evidence supporting this hypothesis. The study examined the relationship between untreated severe OSA and melanoma prognosis, finding that untreated severe OSA significantly increased the risk of poor melanoma outcomes (HR 2.96, 95% confidence interval [CI] 1.36–6.42).[36] However, following CPAP treatment, this risk was reduced by approximately half (HR 1.66, 95% CI 0.71–3.90), indicating that CPAP therapy may mitigate cancer-related outcomes by alleviating OSA-induced hypoxemia. This finding offers preliminary support for the potential protective role of OSA treatment in cancer management, although the wide CI suggests the need for larger sample size studies to further validate these results.

Another multicenter study, through a secondary analysis of specific cancer types, further explored the impact of CPAP treatment on lung cancer incidence.[37] It found that patients receiving adequate CPAP therapy exhibited an approximately 50% reduction in lung cancer incidence compared to non-adherent patients (subdistribution HR 0.49, 95% CI 0.22–1.09). Although the CI crosses 1, indicating that statistical significance requires further confirmation, this result suggests that CPAP treatment may confer a protective effect against lung cancer development.

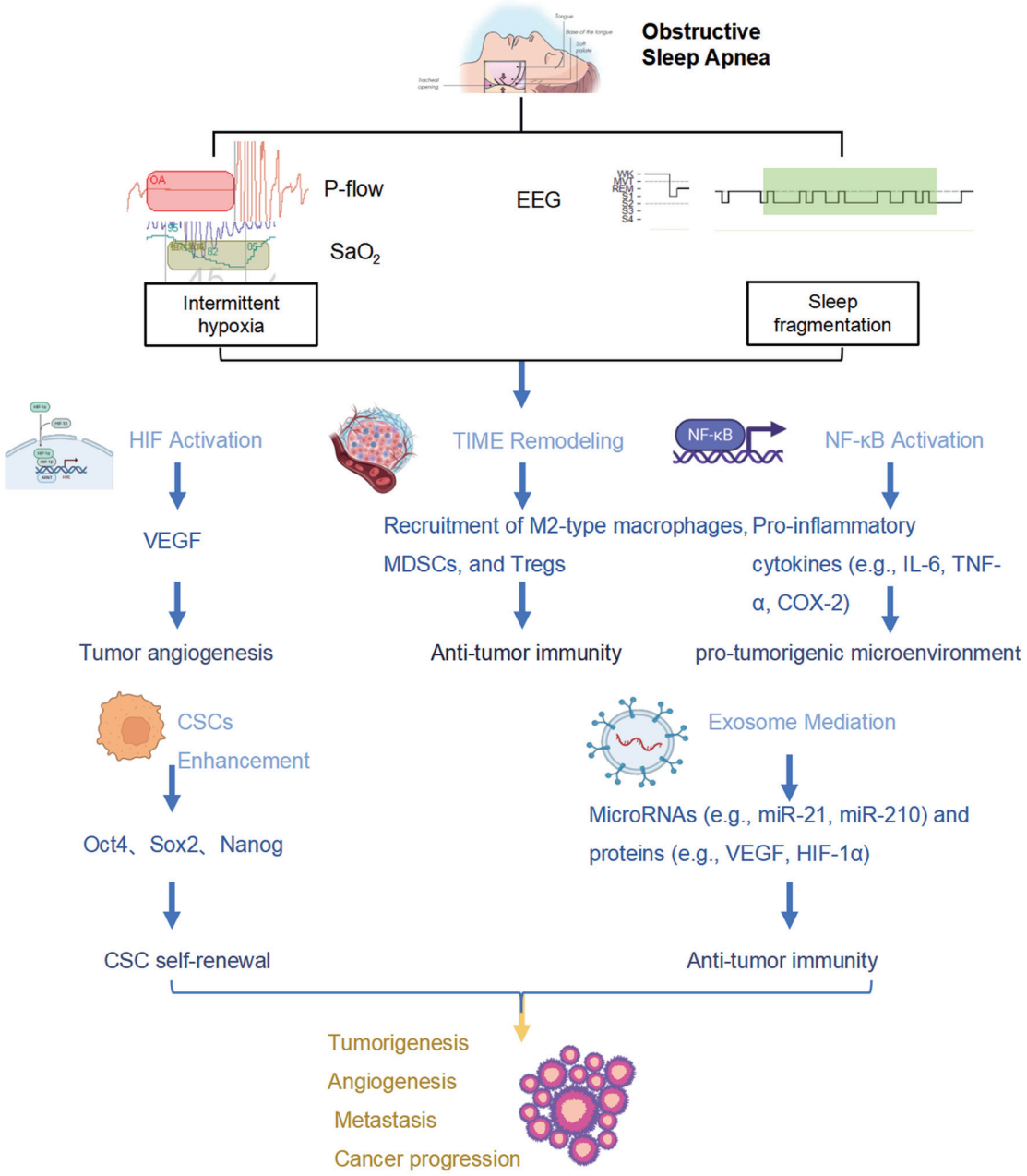

Fig. 1. Proposed mechanisms linking obstructive sleep apnea (OSA) to cancer progression. Intermittent hypoxia (IH) and sleep fragmentation in OSA lead to repeated cycles of hypoxia–reoxygenation and cortical arousals (shown by EEG and SaO_2 traces). These stressors activate hypoxia-inducible factor-1α (HIF-1α) and nuclear factor-κB (NF-κB) pathways, which drive: (1) secretion of vascular endothelial growth factor (VEGF) and subsequent tumor angiogenesis; (2) remodeling of the tumor immune microenvironment (TIME) through recruitment of M2-type macrophages, myeloid-derived suppressor cells (MDSCs), and regulatory T cells (Tregs), along with increased production of pro-inflammatory and pro-tumorigenic cytokines (IL-6, TNF-α, COX-2); (3) enhanced cancer stem cell (CSC) self-renewal via upregulation of Oct4, Sox2, and Nanog; (4) release of tumor-derived exosomes carrying oncogenic microRNAs (e.g., miR-21, miR-210) and proteins (VEGF, HIF-1α) that further promote angiogenesis, immune evasion, and metastasis. Ultimately, these molecular and cellular alterations accelerate tumorigenesis, angiogenesis, metastasis, and overall cancer progression. COX-2, cyclooxygenase-2; EEG, electroencephalogram; IH, intermittent hypoxia; IL-6, interleukin-6; Nanog, homeobox protein Nanog; NF-κB, nuclear factor kappa B; Oct4, octamer-binding transcription factor 4; SaO_2, arterial oxygen saturation; Sox2, SRY-box transcription factor 2; TNF-α, tumor necrosis factor-alpha; Tregs, regulatory T cells.

Discussion

Several narrative and systematic reviews have previously explored the relationship between OSA and cancer risk in general[38]; however, most have either addressed cancer as a whole or focused on other malignancies (e.g., breast, colorectal, or melanoma). To our knowledge, only two English-language reviews published before 2025 have specifically targeted the association between OSA and lung cancer.[39,40]

Compared with these prior works, the present review offers several novel and distinguishing features:

Inclusion of the most recent large-scale epidemiological evidence (2023–2025), including the Western Australian sleep clinic cohort (N = 20,289), the Korean NHIS 12-year follow-up study showing a paradoxical protective effect in males, and updated analyses of CPAP's impact on site-specific cancer incidence.

Comprehensive integration of emerging pathophysiological mechanisms (exosome-mediated intercellular communication, CSC enhancement, and NF-κB/HIF crosstalk) that were only briefly mentioned or absent in previous lung cancer-focused reviews.

Specific emphasis on the potential modifying effect of long-term adherent CPAP therapy on lung cancer incidence and prognosis—an area still underexplored in prior reviews.

The clinical significance of this work lies in raising awareness that severe nocturnal hypoxemia in OSA patients may represent an independent, modifiable risk factor for lung cancer, particularly in never-smokers and in populations with high OSA prevalence. This has direct implications for risk stratification, cancer screening strategies, and the urgency of treating OSA in patients with or at risk of lung cancer.

Limitations

Nevertheless, several limitations of this review must be acknowledged. First, although we performed a systematic literature search, formal meta-analysis was not feasible due to substantial heterogeneity in study design, OSA diagnostic criteria (administrative codes vs. polysomnography), hypoxemia metrics, follow-up duration, and confounder adjustment. Second, most included epidemiological studies originate from North America, Europe, and East Asia; data from Africa, South America, and South Asia remain scarce, limiting global generalizability. Third, publication bias and selective reporting of positive associations cannot be fully excluded. Finally, the majority of mechanistic evidence derives from preclinical models of chronic IH; translational studies confirming these pathways in human lung cancer tissue from OSA patients are still limited.

Future directions

Despite substantial progress, several critical knowledge gaps must be addressed to definitively establish the causal relationship between OSA and lung cancer and to translate these insights into clinical practice:

- Large-scale, prospective, polysomnography-based cohort studies with long-term (>10 years) follow-up, standardized assessment of both AHI and objective hypoxemia burden (T90%, cumulative hypoxic burden, oxygen desaturation index), and rigorous adjustment for smoking, obesity, chronic obstructive pulmonary disease, and socioeconomic factors in diverse global populations.
- Randomized controlled trials or well-designed pragmatic trials evaluating whether early, adherent CPAP therapy (or alternative therapies such as mandibular advancement devices or hypoglossal nerve stimulation) reduces lung cancer incidence and improves prognosis in patients with severe OSA and nocturnal hypoxemia.
- Integration of OSA screening into lung cancer screening programs using low-dose computed tomography, particularly in never-smokers and in regions with high OSA prevalence, to determine whether co-existing severe hypoxemia modifies screening yield, false-positive rates, and downstream cancer detection.
- Investigation of sex-specific and ethnicity-specific effects, especially the mechanisms underlying the paradoxical protective association observed in East Asian males, including genetic, hormonal, and environmental interactions.

Addressing these priorities will clarify whether OSA and nocturnal hypoxemia represent modifiable risk factors for lung cancer and help establish evidence-based recommendations for OSA diagnosis and treatment in the context of lung cancer prevention and management.

Conclusions

Accumulating evidence indicates that severe OSA, particularly when accompanied by marked nocturnal hypoxemia, is associated with increased lung cancer incidence and worse prognosis in multiple cohorts, although results remain inconsistent across populations and study designs. Nocturnal hypoxemia burden consistently emerges as a stronger and more reproducible risk predictor than the apnea–hypopnea index alone, highlighting IH as the primary oncogenic driver. Mechanistically, OSA promotes lung cancer progression through HIF activation, TIME remodeling, exosome-mediated signaling, NF-κB-driven inflammation, and enhancement of CSC properties. Long-term adherent CPAP therapy shows promising potential to mitigate these risks and improve outcomes. These findings underscore the clinical importance of recognizing and treating severe OSA and nocturnal hypoxemia in patients at risk of or diagnosed with lung cancer.

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Conflict of interest

The authors declare that they have no conflict of interest related to this publication.

Author contributions

Study concept and design (JL), literature search, data interpretation, results discussion, manuscript drafting, preparation of tables and figures (JL, TF, QZ), critical revision of the manuscript (JL), project supervision, final approval of the manuscript, and journal correspondence (JL). All authors contributed equally to this work.

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