

Baseline inflammatory markers, CPAP adherence, impacts on cardiovascular events, and mortality in obstructive sleep apnea: retrospective naturalistic study

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Background. Obstructive sleep apnea (OSA) is a known risk factor for cardiovascular (CV) morbidity and mortality. Chronic low-grade inflammation has been identified as a pathophysiological link. Continuous positive airway pressure (CPAP) therapy successfully treats OSA and has positive effects beyond improving breathing patterns during sleep. However, its potential impact on CV morbidity and mortality remains unclear.

Objectives. To determine the association between CV risk, the risk of incident malignancies, and the probability of patient death based on inflammatory parameters, anthropometry and OSA severity parameters, as well as the effectiveness of CPAP therapy.

Methods. We retrospectively analyzed data from 245 patients diagnosed with moderate-to-severe OSA, identified as having an apnea-hypopnea index ≥ 15 /h. Adherence was defined as CPAP use ≥ 4 h/night for $\geq 70\%$ of days. We assessed CV history, mortality, polysomnographic data and inflammatory parameters (C-reactive protein, leukocyte count, neutrophil-to-lymphocyte ratio [NLR], monocyte-to-lymphocyte ratio, and platelet-to-white blood cell ratio). Univariate and multivariate logistic regressions were used to identify independent predictors of CV outcomes, malignancy incidence and death within 10 years.

Results. Patients poorly adhering to CPAP therapy (39.2%) had significantly higher rates of CV complications (32.8% vs. 15.1%, $P = 0.003$), malignancies (19.7% vs. 8.3%, $P = 0.018$), and mortality (14.6% vs. 4.0%, $P = 0.003$). Non-adherence was a strong independent predictor of CV complications (odds ratio [OR] = 2.75, $P = 0.004$) and death (OR = 4.07, $P = 0.006$). In univariate analysis, age, non-adherence, and NLR were significantly associated with the risk of incident malignancy ($P = 0.022$ – 0.008); NLR was also significant in multivariate analysis ($P = 0.008$). The t90 index (time spent below 90% oxygen saturation) was an independent predictor of mortality (OR = 1.03, $P = 0.003$).

Conclusions. Non-adherence to CPAP therapy is associated with an increased risk of CV complications, malignancies and death in OSA patients. Inflammatory markers and desaturation parameters (particularly t90) are valuable predictors that should be monitored in routine practice to identify high-risk patients. Implementing strategies to improve CPAP adherence may reduce long-term systemic inflammation and clinical risks.

Baseline Inflammatory Markers, CPAP Adherence And Its Impacts On Cardiovascular Events, And Mortality In Obstructive Sleep Apnea: Retrospective Naturalistic Study

BACKGROUND: Obstructive sleep apnea (OSA) is a known risk factor for cardiovascular (CV) morbidity and mortality. Chronic inflammation has been identified as the pathophysiological link. Continuous positive airway pressure (CPAP) therapy is an effective treatment for OSA with positive effects beyond improving breathing patterns during sleep; however, its potential impact on CV morbidity and mortality remains unclear.

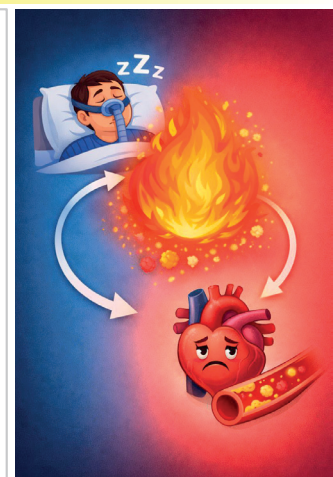
OBJECTIVES: To determine the association between CV risk, risk of malignancies or death based on inflammatory parameters, anthropometry, OSA severity, and the effectiveness of CPAP.

METHODS: Retrospectively analysis of data from OSA patients. We assessed CV history, mortality, polysomnographic and inflammatory parameters. Univariate and multivariate logistic regressions were used to identify independent predictors of CV outcomes, the incidence of malignancies, and death.

RESULTS: Patients with poor CPAP therapy had significantly higher rates of cardiovascular complications, malignancies, and mortality. Nonadherence was a strong independent predictor of CV complications and death. Age, nonadherence, and neutrophil-to-lymphocyte ratio were significantly associated with the risk of incident malignancy. The t90 index was an independent predictor of mortality.

Non-adherence to CPAP is associated with an increased risk of CV complications, malignancies, and death in OSA patients. Inflammatory and desaturation parameters should be monitored to identify high-risk patients.

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Graphical Abstract

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Key words: obstructive sleep apnea, CPAP, adherence, cardiovascular risk, systemic inflammation, mortality, inflammatory biomarkers, t90, malignancies

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INTRODUCTION

Obstructive sleep apnea (OSA) is a highly prevalent chronic condition characterized by recurrent upper airway obstruction during sleep. These episodes lead to intermittent hypoxemia, sleep fragmentation, sympathetic hyperactivation, and increased oxidative stress, which together contribute to multisystem organ burden^{1,2}.

OSA is a significant risk factor for cardiovascular (CV) conditions including arterial hypertension, ischemic heart disease, heart failure, atrial fibrillation, and stroke^{1,3}. Recent reviews have confirmed that even in individuals without manifest comorbidities, a high risk of OSA can be associated with increased levels of systemic inflammatory markers, independent of age, body weight, or hypertension⁴. Low-grade systemic inflammation is often observed in OSA. This is manifested by increased levels of C-reactive protein (CRP), higher leukocyte counts, and altered values of white blood cell subpopulations, especially neutrophils, monocytes and lymphocytes. Chronic inflammation associated with OSA is linked to atherosclerosis progression and structural changes in the myocardium⁵. Elevated CRP levels, leukocytosis, and changes in leukocyte subpopulation ratios (e.g. increased neutrophil-to-lymphocyte ratio – NLR) are significant indicators of systemic inflammation^{4,5}.

The “gold standard” treatment for moderate-to-severe OSA without indications for surgical treatment remains continuous positive airway pressure (CPAP), which maintains upper airway patency⁶. Good adherence to this therapy reduces daytime sleepiness and improves quality of life; however, it also induces positive changes in cardiac mechanics and systemic inflammation^{7,8}.

CPAP therapy also reduces the risk of major CV events and death; the risk of CV and total mortality is reduced by ~55% and ~37%, respectively, compared to untreated patients^{10,11}. The ability to predict CV complications and mortality in patients with insufficient adherence based on inflammatory markers (e.g. CRP and neutrophils) remains a subject of research. Sleep apnea is also a known risk factor for the development and progression of malignancy^{12,13}. CPAP appears to be beneficial along with

oncological treatment, and one study showed a possible trend toward reducing incident malignancies^{14,15}.

Despite the proven benefits, low adherence significantly limits the effectiveness of CPAP, as a significant proportion of patients regularly fail to comply with the recommended duration of nighttime therapy (≥ 4 hours)^{8,16}. Identifying the prognostic markers and consequences of non-adherence, including inflammatory biomarkers, may be crucial for targeted interventions.

This study aimed to evaluate the relationship between adherence to CPAP therapy, selected markers of systemic inflammation, the incidence of CV disease, and overall mortality in patients with OSA.

OBJECTIVES AND HYPOTHESES

OSA is a chronic condition with clinical consequences that extend far beyond those of sleep disturbance. Previous studies have shown that poor adherence to CPAP therapy can lead to the progression of inflammatory processes and an increased incidence of CV complications^{5,7}. In the context of these findings, our study aimed to broaden the scope and identify the relationships among adherence to CPAP therapy, parameters of chronic inflammation, and the incidence of CV complications and mortality.

Primary study objective

The main objective of this study was to determine whether non-adherence to CPAP therapy is associated with higher rates of CV complications (such as coronary heart disease, stroke, heart failure, and arrhythmia) and higher overall mortality.

Secondary objectives

The secondary aims were:

- (1) To determine if there is an association between the levels of selected inflammatory markers and the incidence of CV complications and mortality in patients with moderate-to-severe OSA.
- (2) To evaluate the influence of other clinical and laboratory factors, namely body mass index (BMI), smoking,

sleepiness according to the Epworth Sleepiness Scale (ESS), apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and time spent below 90% saturation (t90), on the occurrence of CV complications and mortality.

- (3) To evaluate whether non-adherence increases the probability of incident malignancies.
- (4) To compare the adherent and non-adherent study groups in terms of clinical and laboratory factors (age, BMI, comorbid diseases, sleep apnea severity parameters, and chronic inflammation parameters).

Hypotheses

Based on the above findings, we formulated the following hypotheses: *Patients non-adherent to CPAP therapy have*

- (1) *a higher incidence of CV complications.*
- (2) *higher mortality.*
- (3) *a higher incidence of incident malignancies.*
- (4) *(a) AHI, (b) ODI, and (c) t90 values positively correlate with the incidence of CV complications.*
- (5) *Parameters of chronic inflammation positively correlate with the incidence of CV complications.*

METHODS

Study design and patient population

This naturalistic retrospective observational study included 245 patients diagnosed with OSA who were examined in the sleep laboratory at the Department of Respiratory Diseases and Tuberculosis, University Hospital Olomouc, from 1 January 2008 to 1 January 2015. The diagnosis of OSA was established based on standard polysomnographic examinations using diagnostic criteria according to the latest American Academy of Sleep Medicine recommendations. Individuals with an AHI ≥ 15 /h (i.e. moderate-to-severe OSA) were indicated for CPAP therapy. The follow-up period was 10 years, with evaluation of the patient data in January 2025. Each check-up during the follow-up consisted of retrieval of therapy data from the CPAP machine and proper documentation of the patient's history. For the non-adherent group, data regarding complications were extracted from documentation or with the aid of general practitioners.

Inclusion criteria:

- indication to CPAP therapy, that is, AHI ≥ 15 /h (i.e. moderate-to-severe OSA);
- age 18–80 years.

Exclusion criteria:

- inability to give informed consent;
- individuals with intermediate adherence (i.e. 0.1–3.9 hours of mean CPAP use per night);
- individuals with other therapy modes (e.g. upper airway surgery, bilevel positive airway pressure, or dental surgery procedure);
- incomplete patient documentation.

Patients were divided into two groups according to their adherence to CPAP:

- adherent group – defined by an average use of CPAP ≥ 4 h per night for $\geq 70\%$ of days;
- non-adherent group – defined by complete non-adherence to therapy, CPAP rejection at the beginning of the study, or CPAP withdrawal shortly (within 3 months) after treatment initiation.

Monitored variables

The following data were obtained from medical documentation (data before therapy initiation):

- (a) Demographic and anthropometric indicators
age, sex, BMI, height, weight, neck circumference, waist circumference, hip circumference, and waist-to-hip ratio.
- (b) OSA symptomatology
ESS score, daytime sleepiness, microsleep, and insomnia.
- (c) CV and other comorbidities
hypertension, ischemic heart disease, stroke, diabetes mellitus, atrial fibrillation, asthma, pulmonary fibrosis, other interstitial lung diseases, neuromuscular diseases, chronic obstructive pulmonary disease, and several other comorbidities.
- (d) Polysomnographic indicators
AHI, ODI, t90, and average saturation.
- (e) Inflammatory and hematological parameters – before the CPAP therapy
 - CRP level, leukocyte count (total neutrophils, monocytes, eosinophils, and lymphocytes), and platelet count.
 - NLR, monocyte-to-lymphocyte ratio (MLR), and platelet-to-white blood cell ratio (PWR).
- (f) Drug therapy
use of statins, fibrates and other lipid-lowering drugs.
- (g) Nicotine dependence
 - smoking: coded as 0 = non-smoker, 1 = current smoker, and 2 = former smoker.
 - Moreover, data on CV complications and mortality were collected from all patients.
- (h) presence of CV complications (acute coronary syndrome, stroke, acute heart failure), incident malignancies, other significant diagnoses, and incidence of death.

Statistical analysis

Data were analyzed using the R software (version 4.3.1) or SPSS (version 28). Descriptive statistics were used to summarise the data (mean $\pm$ standard deviation [SD] for continuous variables, and frequencies and percentages for categorical variables). Comparisons between groups (adherent vs. non-adherent) were made using the Student t-test or a Mann–Whitney U test for continuous variables, or a chi-square test for categorical variables. We also applied a correlation analysis for inflammation measures (e.g. CRP and leukocytes), AHI/ODI/t90, and the occurrence of CV complications. Logistic regression models were constructed to predict CV complications and

Table 1. Basic characteristics of patients according to CPAP adherence.

PARAMETER	GOOD ADHERENCE	NON-ADHERENCE	<i>P</i> (t-test)
Number of patients	149	96	–
Age (mean ± SD)	56.4 ± 10.3	59.9 ± 12.2	0.004
BMI (mean ± SD)	34.8 ± 6.1	33.9 ± 6.9	0.144
ESS score (mean ± SD)	9.0 ± 4.8	6.9 ± 3.8	0.001
AHI (mean ± SD)	53.2 ± 23.5	39.5 ± 18.7	0.001
ODI (mean ± SD)	57.8 ± 25.4	48.7 ± 30.6	0.001
t90 (mean ± SD)	28.8 ± 26.5	21.1 ± 23.3	0.005
Average saturation (mean ± SD)	89.7 ± 5.0	90.8 ± 6.6	0.009
Sum of comorbidities (mean ± SD)	1.2 ± 0.9	1.6 ± 1.2	0.008
CV complications (%)	15.1	32.8	0.003
Malignity (%)	8.3	19.7	0.018
Death (%)	4.0	14.6	0.003

BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; t90, percentage of sleep with peripheral oxygen saturation < 90%; CV, cardiovascular.

mortality. The explanatory variables included adherence to CPAP, CRP, BMI, AHI, age, sex, smoking, and comorbidities. Statistical significance was set at *P*-value < 0.05.

Ethical aspects

The study was conducted in accordance with the latest Declaration of Helsinki. Local ethics committee approval was obtained under identification numbers 76/08 and 60/24 (an update and elaboration of the previous approval dated 13 June 2024). All patients signed an informed consent form for anonymized data processing.

RESULTS

Population characteristics and adherence to CPAP

The study included 245 patients with OSA, of whom 149 (60.8%) exhibited good CPAP adherence, while 96 (39.2%) were non-adherent. The non-adherent group had

a significantly higher mean age, included more females, and showed lower AHI, ODI, ESS score and t90 values, but higher mean saturation and incidence of CV complications, malignancies, and death. Non-adherent patients had a significantly higher number of comorbidities. The characteristics of the study groups are shown in Table 1.

Correlation of inflammatory markers with OSA severity and other factors

A moderate correlation was found between CRP levels and BMI, a weak positive correlation between CRP levels and ODI and t90, and a negative correlation between CRP and average saturation. These results suggest that CRP levels tend to be higher in more severe disease. Leukocyte levels were weakly correlated with BMI, AHI, and t90. PWR correlated weakly with t90 and negatively with average saturation. No significant correlations were found between NLR or MLR and BMI, AHI, ODI, t90 or average saturation (Table 2).

Table 2. Spearman's correlations between inflammatory parameters and BMI, AHI, ODI, t90, and average saturation.

INFLAMMATORY PARAMETER	BMI	AHI	ODI	t90	AVERAGE SATURATION
CRP	<i>r</i> = 0.50 (<i>P</i> < 0.001)	<i>r</i> = 0.18 (<i>P</i> = 0.006)	<i>r</i> = 0.32 (<i>P</i> < 0.0001)	<i>r</i> = 0.39 (<i>P</i> < 0.0001)	<i>r</i> = -0.36 (<i>P</i> < 0.001)
Leukocytes	<i>r</i> = 0.29 (<i>P</i> < 0.001)	<i>r</i> = 0.19 (<i>P</i> = 0.004)	<i>r</i> = 0.15 (<i>P</i> = 0.021)	<i>r</i> = 0.20 (<i>P</i> = 0.003)	<i>r</i> = -0.22 (<i>P</i> = 0.001)
PWR	<i>r</i> = 0.22 (<i>P</i> = 0.001)	<i>r</i> = 0.15 (<i>P</i> = 0.027)	<i>r</i> = 0.10 (<i>P</i> = 0.131)	<i>r</i> = 0.21 (<i>P</i> = 0.001)	<i>r</i> = -0.25 (<i>P</i> = 0.001)
NLR	<i>r</i> = 0.08 (<i>P</i> = 0.357)	<i>r</i> = -0.07 (<i>P</i> = 0.436)	<i>r</i> = 0.02 (<i>P</i> = 0.797)	<i>r</i> = 0.12 (<i>P</i> = 0.163)	<i>r</i> = -0.13 (<i>P</i> = 0.118)
MLR	<i>r</i> = -0.05 (<i>P</i> = 0.533)	<i>r</i> = -0.06 (<i>P</i> = 0.501)	<i>r</i> = 0.01 (<i>P</i> = 0.886)	<i>r</i> = 0.07 (<i>P</i> = 0.403)	<i>r</i> = -0.05 (<i>P</i> = 0.595)

BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; t90, percentage of sleep with peripheral oxygen saturation below 90%; CRP, C-reactive protein; PWR, platelet-to-white blood cell ratio; NLR, neutrophil-to-lymphocytes-ratio; MLR, monocyte-to-lymphocyte ratio.

Table 3. Predictors of CV complications – univariate and multivariate logistic regression.

VARIABLE	OR (UNIV.)	95% CI (LOWER-UPPER)	P	OR (MULTIV.)	95% CI (LOWER-UPPER)	P
Age (years)	1.06	1.02–1.10	0.001	1.09	1.04–1.13	0.001
Sum of comorbidities	1.72	1.24–2.39	0.001	–	–	–
Leukocytes (10 ⁹ /L)	1.28	1.06–1.54	0.009	1.47	1.18–1.82	0.001
PWR × 100	1.58	1.15–2.18	0.005	–	–	–
Adherence (poor and good)	2.75	1.38–5.50	0.004	–	–	–
BMI	1.05	1.00–1.10	0.055	–	–	–
Gender (female vs. male)	1.06	0.49–2.28	0.889	–	–	–
ESS	0.97	0.90–1.05	0.468	–	–	–
AHI	1.00	0.98–1.01	0.683	–	–	–
ODI	1.00	0.98–1.01	0.501	–	–	–
t90	1.01	0.99–1.02	0.321	–	–	–
Average saturation (%)	0.95	0.90–1.00	0.091	–	–	–
CRP	1.03	0.96–1.10	0.446	–	–	–
NLR	1.47	0.83–2.59	0.184	–	–	–

OR, odds ratio; CI, confidence interval; univ., univariate model; multiv., multivariate model; *P*-value < 0.05, statistically significant; BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; t90, percentage of sleep with peripheral oxygen saturation below 90%; CRP, C-reactive protein; PWR, platelet-to-white blood cell ratio; NLR, neutrophil-to-lymphocytes ratio. Age, leukocyte count, CPAP adherence, PWR, and number of comorbidities were included in the multivariate model, but only age and leukocyte count were significant.

Predictors of CV complications, malignancies, and death CV complications

Univariate logistic regression showed that older age, a greater number of comorbidities, higher leukocyte levels, and non-adherence to CPAP therapy were significant predictors of CV complications. However, the effect sizes of the number of comorbidities and the PWR × 100 parameter were small; the other odds ratios were statistically significant but negligible in size. The same was true for the multivariate model results, which confirmed age and leukocyte count as independent but negligible predictors. Other inflammatory markers (i.e. CRP and NLR) were not significant predictors of CV complications. BMI, gender, ESS score, and polysomnographic parameters,

including AHI, ODI, t90 and average saturation, also did not predict CV complications in our cohort (Table 3).

Malignancies

The predictors of malignancy included age, NLR, and non-adherence. In univariate regression, adherence and NLR were medium-sized predictors, while age was negligible. Multivariate analysis confirmed NLR as the only independent predictor. This result suggests that systemic inflammation is a potential link between OSA and malignancy onset. Gender, BMI, and polysomnographic parameters were not predictors of malignancy incidence (Table 4).

Table 4. Predictors of malignancy incidence – univariate and multivariate logistic regression.

VARIABLE	OR (univ.)	95% CI (LOWER-UPPER)	P	OR (multiv.)	95% CI (LOWER-UPPER)	P
Age (years)	1.07	1.02–1.12	0.003	–	–	–
Sum of comorbidities	1.43	0.96–2.13	0.076	–	–	–
Adherence (poor and good)	2.70	1.16–6.29	0.022	–	–	–
NLR	2.70	1.30–5.56	0.008	2.69	1.30–5.56	0.008
Gender (female vs. male)	1.11	0.44–2.82	0.827	–	–	–
BMI	1.00	0.93–1.07	0.919	–	–	–
ESS	1.00	0.97–1.10	0.961	–	–	–
AHI	0.99	0.98–1.01	0.543	–	–	–
ODI	1.00	0.99–1.02	0.787	–	–	–
t90	1.01	0.99–1.03	0.229	–	–	–
Average saturation	0.95	0.89–1.02	0.178	–	–	–
CRP	0.96	0.84–1.09	0.499	–	–	–
Leukocytes	1.16	0.94–1.44	0.159	–	–	–
PWR × 100	1.19	0.89–1.58	0.238	–	–	–
MLR	1.29	0.29–5.65	0.736	–	–	–

OR, odds ratio; CI, confidence interval; univ., univariate model; multiv., multivariate model; BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; t90, percentage of sleep with peripheral oxygen saturation below 90%; CRP, C-reactive protein; PWR, platelet-to-white blood cell ratio; NLR, neutrophil-to-lymphocytes ratio; MLR, monocyte-to-lymphocyte ratio.

Table 5. Predictors of death – univariate and multivariate logistic regression.

VARIABLE	OR (univ.)	95% CI (LOWER-UPPER)	<i>P</i>	OR (multiv.)	95% CI (LOWER-UPPER)	<i>P</i>
Age (years)	1.12	1.05–1.19	0.003	1.11	1.04–1.19	0.002
Sum of comorbidities	1.91	1.27–2.87	0.002	–	–	–
t90	1.02	1.01–1.04	0.003	1.03	1.01–1.05	0.003
Average saturation	0.94	0.89–0.99	0.030	–	–	–
Adherence (poor and good)	4.07	1.51–11.0	0.006	4.42	1.38–14.13	0.012
PWR × 100	1.35	1.01–1.81	0.042	–	–	–
NLR	1.96	0.93–4.12	0.076	–	–	–
Gender (female vs. male)	1.23	0.45–3.36	0.681	–	–	–
BMI	1.03	0.96–1.10	0.438	–	–	–
ESS	0.99	0.89–1.10	0.868	–	–	–
AHI	1.00	0.98–1.02	0.977	–	–	–
ODI	1.00	0.98–1.02	0.993	–	–	–
CRP	1.00	0.90–1.10	0.947	–	–	–
Leukocytes	1.17	0.935–1.46	0.171	–	–	–

OR, odds ratio; CI, confidence interval; univ., univariate model; multiv., multivariate model; BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; t90, percentage of sleep with peripheral oxygen saturation below 90%; CRP, C-reactive protein; PWR, platelet-to-white blood cell-ratio; NLR, neutrophil-to-lymphocytes ratio.

The variables included in the multivariate model were age, sum of comorbidities, t90, average saturation, PWR × 100 and CPAP adherence. Statistically significant predictors were age, t90, and non-adherence to CPAP.

Mortality

Mortality was significantly associated with older age, a greater number of comorbidities, a higher t90 value, lower average saturation, and non-adherence. The odds ratio for the number of comorbidities was small, and adherence was a major predictor. The other univariate regression variables were statistically significant but negligible in size. Multivariate analysis confirmed that age, t90, and non-adherence were significant predictors. However, only CPAP adherence was significant. Gender, BMI, ESS score, AHI and ODI did not predict death in our cohort (Table 5).

DISCUSSION

The results of our study confirm the importance of adherence to CPAP therapy in reducing CV risk, inflammatory activity, and overall mortality in patients with OSA. Analysis of data from 245 patients showed that non-adherence to CPAP therapy was associated with a higher incidence of CV complications and significantly higher mortality, which is consistent with previous findings^{7,17}.

Notably, the non-adherent group had significantly lower OSA parameters in both the subjective and objective domains. However, as shown in the Results and Discussion sections, despite seemingly having better OSA scores, the non-adherent group suffered more adverse outcomes, such as malignancies, CV events, and chronic inflammation. It should be noted that the non-adherent group was also older and had more comorbidities, which may have impacted their CPAP tolerance.

One of the fundamental mechanisms linking OSA and CV disease is chronic inflammation, a condition often presents in OSA patients that is characterized by increased levels of CRP, leukocytes, neutrophils, and other

markers of systemic inflammation⁵. The literature reports these inflammatory markers as significant predictors of CV complications and overall mortality^{2,18}.

In the present study, a positive correlation was found between AHI, ODI, and t90 values and the development of CV disease. Similarly, a meta-analysis by Tadic et al.² indicated that CPAP therapy significantly improved left and right ventricular longitudinal strain; global longitudinal strain of the left ventricle improved, with a medium effect size of 0.51.

Our results demonstrate that in addition to its direct effect on inflammatory markers and oxygen saturation, adhering to CPAP therapy may also protect the CV system. Recent studies have documented the reversal of left and right ventricular remodeling after three to six months of CPAP therapy, even in patients without heart failure^{2,5}.

Furthermore, chronic inflammation, demonstrated by an elevated NLR in baseline blood tests, was the only significant risk factor for developing malignancies during the follow-up period. Despite the seemingly plausible protective effect of CPAP therapy, multivariate analysis found NLR to be the only independent predictor of malignancy. However, OSA has been confirmed to be an independent risk factor for cancer incidence^{12,13}. Similar to our findings, Justeau et al.¹⁵ reported a slightly reduced incidence of new tumors in CPAP-treated patients; however, the result was not statistically significant. Jacobson et al.¹⁴ suggested that CPAP therapy may improve the effectiveness of radiation therapy in patients with breast cancer.

It should be noted that the effectiveness of CPAP therapy is significantly influenced by patient adherence, which remains low despite its proven benefits. Identifying patients at risk of non-adherence and providing targeted interventions, such as education and behavioral support, could reduce the incidence of CV complications and overall mortality in this population¹⁹.

In the present study, regression models identified age and total leukocyte count as independent predictors of CV complications. Non-adherence, age, and t90 were independent predictors of mortality, while NLR was the only independent predictor of incident malignancies. These results underscore the importance of a comprehensive assessment of OSA, including inflammatory markers and CV profiles.

Answers to research hypotheses:

H1: Patients non-adherent to CPAP therapy have a higher incidence of CV complications.

This hypothesis has been affirmed. The non-adherent group had a significantly higher incidence of CV complications ($P = 0.003$).

H2: Patients non-adherent to CPAP therapy have higher mortality.

This hypothesis is confirmed. The non-adherent group had a significantly higher mortality rate ($P = 0.003$). Multivariate analysis confirmed that non-adherence was an independent predictor of mortality (OR 4.42; $P = 0.012$).

H3: Patients non-adherent to CPAP therapy have a higher incidence of incident malignancies.

This hypothesis is rejected. Although the ORs for incident malignancies in univariate analysis were significant (OR for non-adherence 2.67; $P = 0.022$), multivariate analysis revealed that NLR was the only independent predictor of malignancy development (OR 2.69; $P = 0.008$).

H4: (a) AHI, (b) ODI, and (c) t90 values positively correlate with the incidence of CV complications.

All three hypotheses are affirmed. Correlation analyses demonstrated a positive relationship between t90 and the incidence of complications. Additionally, t90 proved to be an independent predictor of mortality. There was a statistically significant, albeit weak, correlation of AHI and ODI with CRP levels and leukocyte counts.

H5: Parameters of chronic inflammation positively correlate with the incidence of CV complications.

This hypothesis is affirmed. The multivariate model confirmed that age and total leukocyte count were independent predictors of CV complications (OR 1.09 and 1.47, respectively; $P < 0.001$). However, they were of negligible size, which may have reduced their significance.

Study limitations

Our study has several limitations. First, since this was a naturalistic and retrospective analysis, the demographic and clinical characteristics of the groups were not homogeneous and this may have influenced the results. Although the sample size was relatively large, the frequency of some of the observed outcomes (e.g. death and incident malignancies) was low. It was also not possible to measure sleep quality or the exact duration of nightly CPAP use in all patients. Additionally, we did not analyze possible changes in OSA severity during the follow-up period.

There were some discrepancies in the results of correlation and regression analyses, which may be attributed to the sample-size, especially the smaller number of patients

with observed outcomes. Our study also did not include an assessment of risk factors for non-adherence, which could act as a mediating factor. Furthermore, we did not evaluate some recently used biomarkers, such as galectin-3 or sST2, discussed in other studies^{5,20,21}. Finally, we did not perform repeated laboratory testing of inflammatory markers after CPAP therapy, a reasonable suggestion for further research.

CONCLUSION

Adherence to CPAP therapy in patients with OSA appears to play a significant role in reducing inflammatory burden, CV complications, and overall mortality. The present study also showed that several hematological and inflammatory parameters were able to predict serious complications, including malignancy and death. From a practical point of view, these findings underline the need for systematic monitoring of adherence to CPAP therapy, not only in terms of subjective symptoms, but also in terms of long-term prognosis. Supporting adherence through education, behavioral interventions, and personalized approaches should be an integral part of care for individuals with OSA. Prospective and interventional studies are needed in the future to confirm causal relationships and verify the effectiveness of strategies to increase adherence in clinical practice.

ABBREVIATIONS

CPAP, Continuous positive airway pressure; OSA, obstructive sleep apnea; CV, cardiovascular; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; t90 index, time spent below 90% oxygen saturation; ESS, Epworth Sleepiness Scale; BMI, body mass index; AHI, apnea-hypopnea index; ODI, oxygen desaturation index.

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