diabetology

MDPI

Article

Integrated Evaluation of CPAP Therapy in Type 2 Diabetic Patients with Sleep Apnea: Quality of Life and Effects on Metabolic Function and Inflammation in Outpatient Care

Petar Kalaydzhiev [1,2,*], Tsvetelina Velikova [3], Yanitsa Davidkova [4], Radostina Ilieva [1,2], Elena Kinova [1,2] and Emilia Naseva [5]

[1] Department of Emergency Medicine, Medical University of Sofia, 1606 Sofia, Bulgaria; radostilieva@yahoo.com (R.I.); kinova.e@abv.bg (E.K.)
[2] Cardiology Department, University Hospital "Tsaritsa Yoanna—ISUL", 1527 Sofia, Bulgaria
[3] Medical Faculty, Sofia University St. Kliment Ohridski, 1407 Sofia, Bulgaria; tsvelikova@medfac.mu-sofia.bg
[4] Department of Clinical Hematology, Specialized Hospital of Active Treatment of Hematological Diseases, 1000 Sofia, Bulgaria; yani.tihomirova@gmail.com
[5] Faculty of Public Health "Prof. Tzecomir Vodenitcharov, MD, DSc", Medical University of Sofia, 15 Acad. Ivan Evstratiev Geshov, 1606 Sofia, Bulgaria; e.naseva@foz.mu-sofia.bg
* Correspondence: pkalaidjiev@gmail.com

Abstract

Background. Type 2 diabetes mellitus (T2D) and moderate-to-severe obstructive sleep apnea (OSA) commonly coexist and exacerbate poor glycemic control, systemic inflammation, and diminished quality of life (QoL). Although continuous positive airway pressure (CPAP) therapy has demonstrated metabolic and anti-inflammatory benefits, its real-world impact in Bulgarian outpatient settings—where CPAP costs are borne entirely by patients—has not been characterized. **Objectives**. To evaluate the effects of six months of CPAP therapy on glycemic control (hemoglobin A_1c [HbA_1c]), systemic inflammation (high-sensitivity C-reactive protein [hsCRP]), body mass index (BMI), lipid profile (low-density lipoprotein [LDL]), QoL (Short Form 36 Physical Component Summary [SF-36 PCS] and Mental Component Summary [SF-36 MCS]), and survival among Bulgarian outpatients with T2D and moderate-to-severe OSA. **Methods**. In this prospective, multicenter cohort study conducted from January 2022 to July 2023, 142 adults with established T2D and OSA (apnea–hypopnea index [AHI] $\geq$ 15) were enrolled at three outpatient centers in Bulgaria. Fifty-five patients elected to purchase and use home-based CPAP (intervention group), while 87 declined CPAP—either because of cost or personal preference—and continued standard medical care without CPAP (control group). All participants underwent thorough outpatient evaluations at baseline (month 0) and at six months, including measurement of HbA_1c, hsCRP, BMI, fasting lipid profile (LDL), and patient-reported QoL, via the SF-36 Health Survey. Survival was tracked throughout follow-up. **Results**. After six months, the CPAP group experienced a significant reduction in HbA_1c from a median of 8.2% (IQR 7.5–9.5%) to 7.7% (6.7–8.7%), $p < 0.001$, whereas the control group's HbA_1c decreased modestly from a median of 8.6% (IQR 7.9–9.4%) to 8.3% (7.6–9.1%); $p < 0.001$), with a significant between-group difference at follow-up ($p = 0.005$). High-sensitivity CRP in the CPAP arm fell from a median of 2.34 mg/L (IQR 1.81–3.41) to 1.45 mg/L (IQR 1.25–2.20), $p < 0.001$, while remaining unchanged in controls ($p = 0.847$). BMI in the CPAP group declined significantly from 28.6 kg/m^2, IQR 26.6–30.6 to 28 kg/m^2, IQR 25.6–29.2 ($p < 0.001$), compared to no significant change in controls (median 28.9 kg/m^2), $p = 0.599$. LDL decreased in the CPAP group from a median of 3.60 mmol/L (IQR 3.03–3.89) to 3.22 mmol/L (IQR 2.68–3.48), $p < 0.001$, with no significant reduction in controls ($p = 0.843$). Within the CPAP arm, both SF-36 PCS and SF-36 MCS scores improved significantly from baseline ($p < 0.001$ for each),

check for updates

Academic Editor: Peter Clifton

Received: 1 July 2025
Revised: 30 July 2025
Accepted: 18 August 2025
Published: 1 September 2025

Citation: Kalaydzhiev, P.; Velikova, T.; Davidkova, Y.; Ilieva, R.; Kinova, E.; Naseva, E. Integrated Evaluation of CPAP Therapy in Type 2 Diabetic Patients with Sleep Apnea: Quality of Life and Effects on Metabolic Function and Inflammation in Outpatient Care. *Diabetology* **2025**, *6*, 87. https://doi.org/10.3390/diabetology6090087

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

although between-group differences at six months did not reach statistical significance (PCS: 48 ± 10 vs. 46 ± 9, $p = 0.098$; MCS: 46, IQR 40–54 vs. 46, IQR 39–53, $p = 0.291$). All-cause mortality during follow-up included 2 events in the CPAP group and 11 events in the control group (log-rank $p = 0.071$). **Conclusions**. In Bulgarian outpatients with T2D and moderate-to-severe OSA, six months of CPAP therapy significantly improved glycemic control, reduced systemic inflammation, lowered BMI and LDL, and enhanced QoL, with a non-significant trend toward reduced mortality. These findings underscore the importance of integrating CPAP into multidisciplinary management despite financial barriers.

Keywords: continuous positive airway pressure; type 2 diabetes mellitus; obstructive sleep apnea; quality of life

1. Introduction

In individuals with type 2 diabetes (T2D), the prevalence of moderate-to-severe obstructive sleep apnea (OSA) is estimated at 60–70%, according to observational studies and systematic reviews [1,2]. Several randomized controlled trials (RCTs) have shown that CPAP therapy can lead to improvements in glycemic parameters among patients with T2D and OSA. However, the effect varies depending on duration of use and level of adherence [3,4]. For example, a 12-week trial in which CPAP therapy did not significantly alter mean 24 h glucose levels demonstrated that wearing CPAP for at least four hours per night was associated with reduced glycemic variability, despite no change in average glucose values [3,5]. In another multicenter RCT, patients with T2D and OSA who received CPAP therapy versus a control group without CPAP exhibited a statistically significant reduction in HbA_1c (mean – 0.3%) after six months of treatment [5]. CPAP also improves QoL as measured by the SF-36 PCS and SF-36 MCS scores and reduces subjective daytime sleepiness as measured by the Epworth Sleepiness Scale (ESS), with well-adherent patients showing significantly higher SF-36 scores and correspondingly lower ESS values compared to those treated non-consistently [1,4]. Chronic low-grade inflammation characteristic of patients with T2D and OSA is reflected by elevated C-reactive protein (CRP) and interleukin 6 (IL-6) levels; meta-analyses indicate that regular CPAP use significantly decreases these markers, especially in patients with higher baseline CRP (>3 mg/L) and those with obesity (BMI > 30 kg/m^2) [1,2]. Furthermore, cross-sectional studies in ambulatory patients with T2D and sleep disturbances have established a relationship between poorer QoL (SF-36 PCS/MCS) and increased depressive symptoms, underscoring the importance of monitoring mental health in outpatient settings [6]. Meta-analyses confirm that the comorbidity of OSA and psychiatric disorders (such as depression and anxiety) reduces CPAP adherence and contributes to further deterioration of QoL in ambulatory populations [7].

Despite the existence of international RCTs and observational studies on the impact of CPAP on glycemic control and QoL, there remains a lack of data examining these effects in a Bulgarian outpatient population followed for at least six months. In our multicenter prospective cohort, patients with T2D and moderate-to-severe OSA are monitored over a half-year period at three Bulgarian outpatient centers to assess how CPAP therapy influences physical and mental components of QoL as measured by SF-36, as well as glycemic control assessed by HbA_1c. By generating real-world evidence within the Bulgarian healthcare context, this investigation aims to inform a multidisciplinary management strategy tailored to these patients.

2. Materials and Methods

This prospective, multicenter cohort study was conducted in an outpatient setting across three ambulatory medical centers in Bulgaria between January 2022 and July 2023. The study protocol was reviewed and approved by the Central Ethics Committee of the Medical University of Sofia (Protocol No. 3489/2021 25 October 2021), and written informed consent was obtained from all participants in accordance with the principles of the Declaration of Helsinki.

During the recruitment period, a total of 410 adult outpatients with established type 2 diabetes (T2D) were screened for symptoms suggestive of obstructive sleep apnea (OSA) during routine cardiology and endocrinology consultations. Of these, 186 individuals were diagnosed with moderate-to-severe OSA, defined as an apnea–hypopnea index (AHI) of $\geq$15 events per hour, confirmed using ApneaLink™ (ResMed®, San Diego, CA, USA), a validated home respiratory polygraphy system. The device captures nasal airflow, thoracic movements, heart rate, and peripheral oxygen saturation (SpO_2), and has demonstrated high diagnostic concordance with in-laboratory polysomnography [8,9].

Following clinical evaluation and application of predefined exclusion criteria, a total of 142 eligible patients were enrolled consecutively across the three centers. Participants were included based on confirmed diagnoses of both T2D and moderate-to-severe OSA (AHI $\geq$ 15), as well as their ability to understand the study protocol and provide written informed consent. No randomization procedure was applied.

Inclusion criteria required the presence of T2D and moderate-to-severe OSA, as well as the cognitive and physical ability to independently operate a CPAP device. Exclusion criteria included a diagnosis of type 1 diabetes, advanced heart failure (NYHA class III or IV), prior CPAP or other positive airway pressure therapy, prior upper airway surgery, active malignancy, autoimmune or corticosteroid-dependent disease, significant psychiatric or cognitive impairment, or logistical limitations that could prevent regular follow-up in the outpatient setting.

Participants were followed for six months. In Bulgaria, CPAP devices and related supplies are not reimbursed by the national health insurance system, requiring patients to bear the full cost out of pocket. This represents a substantial financial burden for many, and as a result, a significant proportion of eligible individuals ultimately opt not to initiate CPAP therapy. Taking into account both this economic constraint and individualized clinical assessment, 55 patients elected to purchase and use home-based CPAP (intervention group). In comparison, 87 patients declined CPAP—either due to cost or personal preference—and continued with standard medical care without CPAP (control group). All participants underwent clinical evaluations, laboratory testing (including HbA1c, hsCRP, fasting lipid profile [total cholesterol, LDL, HDL, triglycerides], fasting glucose, and serum creatinine for eGFR calculation), and patient-reported outcome assessments at baseline and again at six months.

At the 6-month follow-up, sleep-disordered breathing (SDB) parameters—including AHI, oxygen desaturation index (ODI), average and lowest SpO_2, and cumulative time with SpO_2 below 90%—were reassessed in both groups. For patients without CPAP therapy, a repeat recording was performed using ApneaLink™, with automated analysis and subsequent quality control review. For patients in the CPAP group, sleep-related data were obtained directly from their CPAP devices through telemonitoring platforms, which provided continuous data on respiratory events and oxygen saturation during therapy.

Patient-reported outcomes included the Bulgarian versions of the SF-36 Health Survey and ESS. Anthropometric measurements and vital signs were obtained using standardized procedures, and laboratory tests included markers of inflammation, renal function, glycemic control, and lipid profile, which were analyzed according to certified methods.

Primary outcomes were defined as the change from baseline to six months in QoL, assessed by SF-36 PCS and SF-36 MCS scores, and in subjective daytime sleepiness, measured by ESS. Secondary outcomes included changes in metabolic, inflammatory, hemodynamic, renal, and sleep-related parameters, as well as all-cause survival at six months [10,11].

The results were presented as numbers or proportions for categorical variables and as mean ± standard deviation (SD) or median and IQR for numerical variables, depending on their distribution. The distribution of continuous variables was tested for normality using the Kolmogorov–Smirnov test. Baseline comparability between groups was assessed using an independent samples *t*-test or the Mann–Whitney U test, where appropriate, as well as a Pearson chi-square test. Within-group differences between baseline and follow-up were analyzed using the paired-samples *t*-test or Wilcoxon signed-rank test.

Between-group comparisons of treatment effect were further evaluated using ANCOVA, with follow-up values as the dependent variable, group assignment as the fixed factor, and baseline scores as covariates. This approach allowed adjustment for initial between-group differences. Survival was analyzed using Kaplan–Meier estimates and the log-rank test. All statistical analyses were performed using IBM SPSS Statistics, version 29.0.2.0 (IBM Corp., Armonk, NY, USA), and $p < 0.05$ was considered statistically significant.

3. Results

3.1. Baseline Characteristics of the Study Groups

Both groups were similar in sex, comorbidities, and therapy ($p > 0.05$), Table 1.

Table 1. Baseline characteristics of the study groups.

Parameter		No CPAP Therapy		CPAP Therapy		*p*
		n	%	n	%	
Sex	f	29	33.3	18	32.7	0.940
	m	58	66.7	37	67.3	
Atrial Fibrillation	No	71	81.6	42	76.4	0.450
	Yes	16	18.4	13	23.6	
Dyslipidemia	No	40	46.0	32	58.2	0.156
	Yes	47	54.0	23	41.8	
Coronary artery disease	No	62	71.3	35	63.6	0.341
	Yes	25	28.7	20	36.4	
Beta blockers	No	23	26.4	21	38.2	0.140
	Yes	64	73.6	34	61.8	
ACE	No	55	63.2	33	60.0	0.700
	Yes	32	36.8	22	40.0	
ARB	No	50	57.5	31	56.4	0.897
	Yes	37	42.5	24	43.6	
HCTZ	No	47	54.0	26	47.3	0.433
	Yes	40	46.0	29	52.7	
Mineralocorticoid receptor antagonist	No	75	86.2	48	87.3	0.856
	Yes	12	13.8	7	12.7	
Loop diuretics	No	76	87.4	47	85.5	0.746
	Yes	11	12.6	8	14.5	
Statins	No	58	66.7	40	72.7	0.447
	Yes	29	33.3	15	27.3	

Table 1. *Cont.*

Parameter		No CPAP Therapy n	No CPAP Therapy %	CPAP Therapy n	CPAP Therapy %	*p*
Semaglutide or Liraglutide	No	65	74.7	43	78.2	0.690
	Yes	22	25.3	12	21.8	
SGLT2i	No	58	66.7	38	69.1	0.764
	Yes	29	33.3	17	30.9	
Metformin	No	15	17.2	14	25.5	0.237
	Yes	72	82.8	41	74.5	
Insulins	No	75	86.2	45	81.8	0.481
	Yes	12	13.8	10	18.2	
DPP4	No	68	78.2	48	87.3	0.171
	Yes	19	21.8	7	12.7	
Sulfonylureas	No	72	82.8	45	81.8	0.886
	Yes	15	17.2	10	18.2	
Chronic kidney disease	No	71	81.6	43	78.2	0.617
	Yes	16	18.4	12	21.8	

The groups were similar in age, as were most of the baseline measurements, except for two of them (Table 2). The lowest desaturation was significantly lower in the no CPAP group (median 85, IQR 83–87) compared to the CPAP group (median 87, IQR 85–88), $p = 0.023$. Similarly, Cheyne–Stokes respiration was significantly lower in the no-CPAP group (median 5.1, IQR 3.4–6.8) compared to the CPAP group (14.4, IQR 12.1–16.9), $p < 0.001$.

3.2. Follow-Up at the 6th Month

Adherence to CPAP therapy was objectively assessed via telemonitoring. The mean nightly usage among CPAP users was 5.2 ± 1.4 h, and 78% of patients met the adherence criterion of using the device for at least 4 h per night on ≥70% of nights. These data were automatically recorded and transmitted from the CPAP devices, allowing for continuous remote monitoring of treatment compliance.

A significant difference between the groups at the 6th month was observed in some parameters (Table 2). Epworth Sleepiness Scale (ESS), AHI, Oxygen Desaturation Index, Average SpO2, time spent with oxygen saturation below 90%, eGFR Cockroft (mL/min/1.73 m^2), HbA1c (%), hsCRP (mg/L), total cholesterol, LDL, triglycerides, and systolic blood pressure were significantly lower in the CPAP group ($p < 0.05$). The lowest desaturation, Cheyne–Stokes respirations, and HDL levels were significantly higher in the CPAP group.

However, no significant difference was found for the other parameters ($p > 0.05$).

3.3. Dynamics Between the Baseline and the 6th Month in the Study Groups

We assessed the change in each group between the baseline and the follow-up. Significant improvement was observed in both groups. However, the CPAP group showed an improvement in all parameters except for total cholesterol. No CPAP group did not experience improvement in BMI, Epworth Sleepiness Scale, SF-36 Mental Component, oxygen desaturation index, average SpO_2, lowest desaturation, Cheyne–Stokes respirations, hsCRP, LDL, HDL, and total cholesterol (Table 2).

Table 2. Comparison of the main parameters in the study groups at baseline and at the 6th month.

Parameter	Measure	No CPAP Therapy		CPAP Therapy		*p*	No CPAP Therapy		CPAP Therapy		*p* (6th Month)	*p* Baseline-6th Month No CPAP	*p* Baseline-6th Month CPAP
		Median/Mean	IQR/sd	Median/Mean	IQR/sd		Median/Mean	IQR/sd	Median/Mean	IQR/sd			
Age	Median; IQR	60	54–63	57	51–64	0.508							
Body mass index (BMI, kg/m^2)	Median; IQR	28.9	27.2–30.3	28.6	26.6–30.6	0.87	28.9	27.0–30.7	28	25.6–29.2	0.072	0.599	<0.001
Epworth Sleepiness Scale	Median; IQR	11	14-Jul	11	13-Aug	0.826	11	8–15	7	5–10	<0.001	0.702	<0.001
SF-36 Physical Component	Mean; sd	45	9	46	10	0.562	46	9	48	10	0.098	<0.001	<0.001
SF-36 Mental Component	Median; IQR	43	38–53	44	40–52	0.537	44	39–53	46	40–54	0.291	0.299	<0.001
AHI	Mean; sd	44.4	14.5	44.6	14.8	0.939	44.4	14.7	3.6	2.1	<0.001	<0.001	0.033
Oxygen Desaturation Index	Mean; sd	40.3	13.8	40.7	15.1	0.86	39.4	15.7	4.6	5.3	<0.001	0.594	<0.001
Average SpO_2	Median; IQR	91	89–92	90	90–92	0.992	91	89–92	97	97–97	<0.001	0.884	<0.001
Lowest desaturation	Median; IQR	85	83–87	87	85–88	0.023	85	83–87	94	92–95	<0.001	0.179	<0.001
Time spent with oxygen saturation below 90%	Mean; sd	11.4	6	12.2	6.9	0.439	11.1	6.3	5	3.2	<0.001	<0.001	<0.001
Cheyne–Stokes respirations	Median; IQR	5.1	3.4–6.8	14.4	12.1–16.9	<0.001	5.1	3.5–6.4	6.7	4.0–8.8	0.005	0.183	<0.001
eGFR Cockroft (mL/min/1.73 m^2)	Mean; sd	79.3	17.2	77.3	16.8	0.493	79.4	17.2	80.3	16.2	0.761	<0.001	<0.001
HbA1c (%)	Median; IQR	8.6	7.9–9.4	8.2	7.5–9.5	0.289	8.3	7.6–9.1	7.7	6.7–8.7	0.005	<0.001	<0.001
hsCRP (mg/L)	Median; IQR	2.68	2.08–3.39	2.34	1.81–3.41	0.309	2.76	2.09–3.27	1.45	1.25–2.20	<0.001	0.847	<0.001
Total cholesterol (mmol/L)	Median; IQR	5.52	4.92–6.10	5.33	4.87–6.02	0.487	5.37	4.88–5.84	4.95	4.58–5.41	0.004	0.673	0.852
LDL (mmol/L)	Median; IQR	3.61	3.02–4.10	3.6	3.03–3.89	0.857	3.68	3.04–4.08	3.22	2.68–3.48	<0.001	0.843	<0.001
HDL (mmol/L)	Median; IQR	1.36	1.16–1.54	1.46	1.22–1.62	0.205	1.37	1.17–1.54	1.59	1.38–1.73	<0.001	0.396	<0.001
Triglycerides (mmol/L)	Median; IQR	2.04	1.38–2.62	2.19	1.75–2.74	0.089	1.99	1.45–2.57	1.56	1.18–2.19	0.002	0.046	<0.001
Systolic blood pressure (mmHg)	Mean; sd	122	11	124	10	0.523	119	6	115	7	0.003	<0.001	<0.001
Diastolic blood pressure (mmHg)	Mean; sd	77	5	78	6	0.378	77	6	75	6	0.18	<0.001	<0.001

3.4. Survival Analysis

We observed two events in the CPAP group and 11 events in the no CPAP group during the follow-up. However, the short time did not allow for calculating quartiles. The log-rank test did not reveal a significant difference between the groups ($p = 0.071$) (Figure 1).

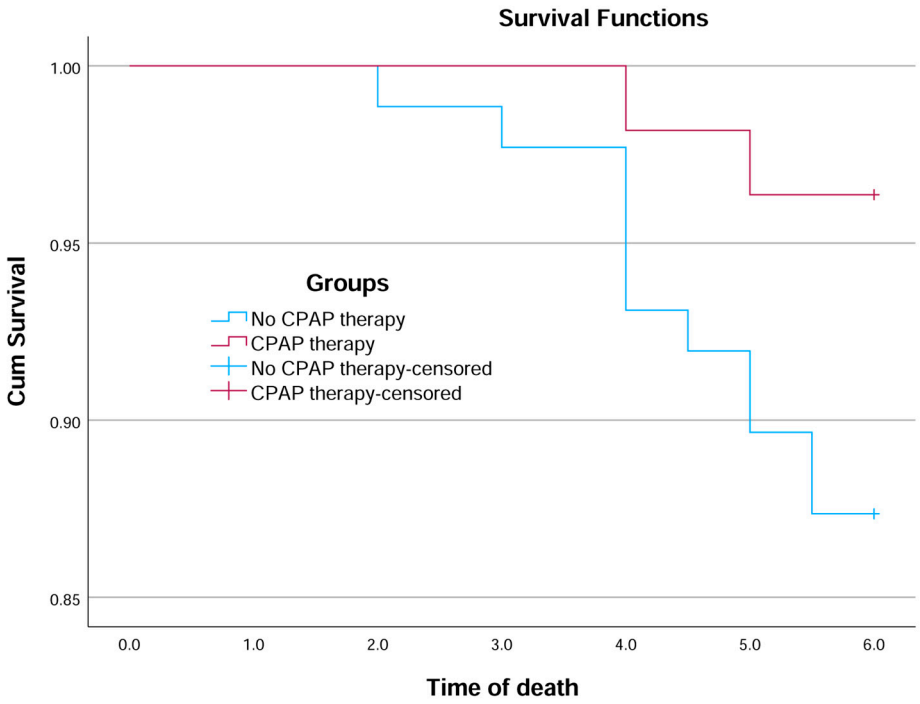


Figure 1. Kaplan–Meier survival curve comparing cumulative survival over time between patients receiving CPAP therapy and those without it. Although the CPAP group showed a trend toward improved survival, the difference between groups did not reach statistical significance ($p = 0.071$).

4. Discussion

This real-world, multicenter prospective study underscores the substantial multidimensional benefits of CPAP therapy in Bulgarian outpatients with T2D and moderate-to-severe obstructive sleep apnea (OSA). These findings provide strong support not only for the established metabolic effects of CPAP but also for its less frequently highlighted impacts on systemic inflammation, cardiovascular risk reduction, and QoL, which are particularly relevant in a healthcare setting where CPAP is not reimbursed and access is limited by financial constraints.

A notable finding in this study is the reduction in HbA_1c observed in the CPAP group. The mean decrease of approximately 0.8% is greater than what has been reported in previous randomized trials and meta-analyses, where reductions are typically around 0.3% [3,4,12]. This effect may be related to relatively good adherence (over four hours per night), as prior studies have shown a dose–response relationship between CPAP use and glycemic control [13]. Given the known association between elevated HbA_1c and vascular complications, such a change may be clinically relevant.

The observed reduction in hsCRP in our cohort is consistent with prior randomized studies and meta-analyses demonstrating CPAP's anti-inflammatory effects in patients with comorbid T2D and OSA [14]. These effects are particularly pronounced among individuals with elevated baseline CRP values and central obesity—two hallmarks of metabolic dysregulation and cardiometabolic risk. In such patients, even modest reductions in systemic inflammation are associated with improved vascular function and a lower incidence of major cardiovascular events [15]. A recent synthesis of pooled data underscores

that CPAP use may reduce hsCRP by up to 0.5–1.0 mg/L in high-risk subgroups, supporting its role as a non-pharmacologic modulator of vascular inflammation in diabetes care [16].

Notably, patients on CPAP experienced a mean BMI reduction of approximately 1.2 kg/m^2 over 6 months—a decrease that, despite not reaching conventional statistical significance (p = 0.098), aligns with emerging data on the interplay between adiposity, inflammation, and metabolic health. Evidence demonstrates that even modest weight loss in obese and overweight individuals with OSA (about 1 kg per unit weight lost) can lead to measurable declines in AHI and inflammatory markers [0.7 events/h AHI reduction per 1 kg lost] [17]. Further, observational data link CPAP usage to favorable body composition changes, such as reducing visceral adiposity and improving markers of cardiometabolic risk [18]. These weight-related improvements likely mediate the observed decreases in HbA_1c and hsCRP, reinforcing a mechanistic pathway where adipose tissue reduction attenuates insulin resistance and vascular inflammation—key contributors to diabetes progression and cardiovascular risk [19]. The trend toward lower BMI, even in a short 6-month follow-up, suggests that CPAP may support weight-related mechanisms in the control of glycemic and inflammatory markers. Extended follow-up could clarify the statistical and clinical significance of these effects.

Crucially, improvements in sleep-related indices, such as the AHI, ODI, and ESS, underscore the mechanical and physiological efficacy of CPAP. Better nocturnal ventilation not only improves sleep architecture but also restores sympathetic–parasympathetic balance, contributing to reductions in nocturnal blood pressure, daytime fatigue, and cardiovascular stress [20]. This translates to meaningful improvements in physical and mental components of QoL, as quantified by SF-36 scores [21]. However, the lack of significant between-group differences in SF-36 domains may reflect the relatively short follow-up period and the multifactorial nature of QoL, which is modulated by comorbid depression, socioeconomic factors, and patient expectations [22].

From a cardiometabolic standpoint, CPAP should be considered a complementary intervention to pharmacologic treatment, especially in light of the rising use of sodium–glucose co-transporter 2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in T2D management. SGLT2 inhibitors have been shown to significantly reduce heart failure hospitalizations and cardiovascular deaths [23], while GLP-1 RA lowers the incidence of major adverse cardiovascular events (MACEs) [24]. However, pharmacologic therapies may not be well-tolerated in all patients due to gastrointestinal side effects, volume depletion, or contraindications such as renal dysfunction. For such individuals, CPAP offers a valuable non-pharmacological strategy that addresses overlapping mechanisms, such as systemic inflammation, sympathetic activation, and endothelial dysfunction, especially in patients with combined T2D and OSA [25,26].

This study was conducted in Bulgaria, where CPAP therapy is fully patient-funded. This economic barrier introduces a potential selection bias, as individuals who can afford treatment are more likely to be health-literate, adherent, and engaged in their care. Nevertheless, the observed improvements across metabolic and quality-of-life domains highlight the need for healthcare policy reforms aimed at improving access. Previous studies have shown that reimbursement programs enhance CPAP adherence and improve long-term outcomes [27]. Given the high prevalence of T2D and OSA in aging populations, public investment in coverage strategies may yield significant benefits for both patient outcomes and healthcare sustainability.

In addition, the use of telemedicine holds potential for further optimizing CPAP adherence. Contemporary CPAP devices with cloud-based data transmission allow for remote monitoring, real-time feedback, and behavioral support, enabling a more personalized and scalable model of care. This is particularly relevant for patients with T2D, who often require

continuous, multifaceted management involving glucose control, weight regulation, blood pressure monitoring, and now, sleep quality optimization [28].

Although the present study did not show a statistically significant reduction in all-cause mortality in the CPAP-treated group, the trend toward lower mortality remains clinically meaningful. This aligns with evidence from large observational cohorts suggesting that consistent CPAP adherence reduces cardiovascular and overall mortality. In contrast, major randomized controlled trials such as SAVE, RICCADSA, and ISAACC failed to demonstrate a mortality benefit, likely due to poor adherence and limited nightly usage in these studies [29–31]. Recent meta-analyses, however, have confirmed that regular CPAP use—particularly $\geq$4 h per night—is associated with significant reductions in major adverse cardiovascular events and all-cause mortality [32]. Longer and adequately powered prospective studies are needed to verify the survival benefits of CPAP in this high-risk group.

Strengths and Limitations of the Study

Despite its clinically relevant findings, this study has several limitations that should be acknowledged. First, the non-randomized design introduces potential selection bias, as CPAP allocation was based on patient financial capacity rather than random assignment. This may have favored the inclusion of more health-conscious and adherent individuals in the intervention group, potentially exaggerating the observed benefits. Second, the relatively short follow-up period of six months limits the ability to evaluate long-term outcomes, particularly with respect to cardiovascular morbidity and mortality. Given that some benefits of CPAP, such as reductions in atherosclerotic burden or major adverse cardiovascular events, may only manifest over extended periods, longer-term prospective studies are necessary to confirm these initial findings.

Third, although sleep apnea was diagnosed using a validated home sleep apnea testing device, the gold standard for OSA diagnosis remains in-laboratory polysomnography. While HSAT has demonstrated acceptable accuracy in identifying moderate-to-severe OSA, it may underestimate certain sleep-related parameters such as sleep architecture, arousal index, or hypoventilation events. Thus, some degree of misclassification or underestimation of OSA severity cannot be excluded.

Fourth, quality of life and psychological outcomes, though measured via SF-36, may have been influenced by unmeasured psychosocial variables, including depression, anxiety, or socioeconomic stressors, which were not systematically captured. Lastly, the study was conducted in a single-country setting (Bulgaria), which presents unique healthcare financing challenges. Thus, the generalizability of the findings to other populations or healthcare systems with different reimbursement models and patient support structures may be limited.

Additionally, the unexpectedly high mortality rate in the non-CPAP group, despite their relatively young average age, may reflect unmeasured baseline risk factors or residual confounding. Since treatment allocation was not randomized, and CPAP users may have been more health-conscious, selection bias could have contributed to differences in outcomes, including mortality.

The strengths of our study include its prospective, multicenter design and real-world outpatient setting. We assessed both clinical outcomes and patient-reported measures, allowing us to capture the direct impact of CPAP therapy on quality of life. As a non-pharmacological intervention, CPAP contributes meaningfully to the prevention of cardiovascular and renal complications in patients with diabetes and sleep apnea. These findings support the role of CPAP in preventive medicine and reflect current guideline

recommendations. The study's design and outcomes help address its limitations and offer valuable directions for future research.

5. Conclusions

This study provides robust real-world evidence that CPAP therapy offers meaningful clinical and metabolic benefits for patients with type 2 diabetes and moderate-to-severe OSA, particularly in improving glycemic control, reducing systemic inflammation, and enhancing sleep-related outcomes. Despite financial and methodological limitations, the findings underscore the need for broader integration of CPAP into multidisciplinary diabetes care. Future long-term, randomized studies are essential to validate its impact on cardiovascular outcomes and mortality and to inform healthcare policy reforms aimed at improving access and adherence.

Author Contributions: Conceptualization, P.K.; methodology, P.K. and T.V.; software, E.N.; validation, P.K., Y.D., R.I. and E.K.; formal analysis, E.N.; investigation, P.K.; resources, P.K.; data curation, P.K., T.V. and E.N.; writing—original draft preparation, P.K., T.V. and E.N.; writing—review and editing, P.K. and T.V.; visualization, E.N.; supervision, P.K.; project administration, T.V.; funding acquisition, P.K. and T.V. All authors have read and agreed to the published version of the manuscript.

Funding: This study is financed by the European Union NextGenerationEU through the National Recovery and Resilience Plan of the Republic of Bulgaria, project BG-RRP-2.004-0004-C01 "Strategic research and innovation program for development of Medical University—Sofia".

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of the Medical University of Sofia, Protocol No. 3489/2021 25 October 2021.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data cannot be shared for ethical/privacy reasons. The data underlying this article cannot be shared publicly due to ethical reasons. The data contain sensitive information and are associated with questionnaires completed by patients. The data will be shared upon reasonable request to the corresponding author, after any sensitive information has been removed.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ACE	Angiotensin-Converting Enzyme
AHI	Apnea-Hypopnea Index
ARB	Angiotensin II Receptor Blocker
BMI	Body Mass Index
CPAP	Continuous Positive Airway Pressure
CRP	C-Reactive Protein
DPP4	Dipeptidyl Peptidase-4 Inhibitor
eGFR	Estimated Glomerular Filtration Rate
ESS	Epworth Sleepiness Scale
GLP-1 RA	Glucagon-Like Peptide-1 Receptor Agonist
HbA1c	Hemoglobin A1c
HDL	High-Density Lipoprotein
HR	Hazard Ratio
HSAT	Home Sleep Apnea Testing
hsCRP	High-Sensitivity C-Reactive Protein
IL-6	Interleukin 6

IQR	Interquartile Range
LDL	Low-Density Lipoprotein
MACE	Major Adverse Cardiovascular Events
MCS	Mental Component Summary (from SF-36)
NYHA	New York Heart Association
ODI	Oxygen Desaturation Index
OSA	Obstructive Sleep Apnea
PCS	Physical Component Summary (from SF-36)
QoL	Quality of Life
RCT	Randomized Controlled Trial
SDB	Sleep-Disordered Breathing
SF-36	36-Item Short Form Health Survey
SGLT2i	Sodium–Glucose Co-Transporter 2 Inhibitor
SpO2	Peripheral Capillary Oxygen Saturation
T2D	Type 2 Diabetes Mellitus

References

1. Zhao, X.; Zhang, W.; Xin, S.; Yu, X.; Zhang, X. Effect of CPAP on blood glucose fluctuation in patients with type 2 diabetes mellitus and obstructive sleep apnea. *Sleep Breath.* **2022**, *26*, 1875–1883. [CrossRef]
2. Shang, W.; Zhang, Y.; Wang, G.; Han, D. Benefits of continuous positive airway pressure on glycaemic control and insulin resistance in patients with type 2 diabetes and obstructive sleep apnoea: A meta-analysis. *Diabetes Obes. Metab.* **2021**, *23*, 540–548. [CrossRef] [PubMed]
3. Banghøj, A.M.; Krogager, C.; Kristensen, P.L.; Hansen, K.W.; Laugesen, E.; Fleischer, J.; Cichosz, S.L.; Poulsen, P.L.; Kirkegaard, M.G.; Thorsteinsson, B.; et al. Effect of 12-week continuous positive airway pressure therapy on glucose levels assessed by continuous glucose monitoring in people with type 2 diabetes and obstructive sleep apnoea; a randomized controlled trial. *Endocrinol. Diabetes Metab.* **2020**, *4*, e00148. [CrossRef]
4. Aurora, R.N.; Rooney, M.R.; Wang, D.; Selvin, E.; Punjabi, N.M. Effects of Positive Airway Pressure Therapy on Glycemic Variability in Patients With Type 2 Diabetes and OSA: A Randomized Controlled Trial. *Chest* **2023**, *164*, 1057–1067. [CrossRef]
5. Makhdom, E.A.; Maher, A.; Ottridge, R.; Nicholls, M.; Ali, A.; Cooper, B.G.; Ajjan, R.A.; Bellary, S.; Hanif, W.; Hanna, F.; et al. The impact of obstructive sleep apnea treatment on microvascular complications in patients with type 2 diabetes: A feasibility randomized controlled trial. *J. Clin. Sleep Med.* **2024**, *20*, 947–957. [CrossRef]
6. Hashimoto, Y.; Sakai, R.; Ikeda, K.; Fukui, M. Association between sleep disorder and quality of life in patients with type 2 diabetes: A cross-sectional study. *BMC Endocr. Disord.* **2020**, *20*, 98. [CrossRef] [PubMed]
7. Gupta, M.A.; Simpson, F.C. Obstructive sleep apnea and psychiatric disorders: A systematic review. *J. Clin. Sleep Med.* **2015**, *11*, 165–175. [CrossRef]
8. Chang, H.C.; Wu, H.T.; Huang, P.C.; Ma, H.P.; Lo, Y.L.; Huang, Y.H. Portable Sleep Apnea Syndrome Screening and Event Detection Using Long Short-Term Memory Recurrent Neural Network. *Sensors* **2020**, *20*, 6067. [CrossRef]
9. Araújo, I.; Marques, F.; André, S.; Araújo, M.; Marques, S.; Ferreira, R.; Moniz, P.; Proença, M.; Borrego, P.; Fonseca, C. Diagnosis of sleep apnea in patients with stable chronic heart failure using a portable sleep test diagnostic device. *Sleep Breath.* **2018**, *22*, 749–755. [CrossRef] [PubMed]
10. McHorney, C.A.; Ware, J.E., Jr.; Raczek, A.E. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med. Care* **1993**, *31*, 247–263. [CrossRef]
11. Johns, M.W. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep* **1991**, *14*, 540–545. [CrossRef]
12. Grimaldi, D.; Beccuti, G.; Touma, C.; Van Cauter, E.; Mokhlesi, B. Association of obstructive sleep apnea in rapid eye movement sleep with reduced glycemic control in type 2 diabetes: Therapeutic implications. *Diabetes Care* **2014**, *37*, 355–363. [CrossRef] [PubMed]
13. Martínez-Cerón, E.; Barquiel, B.; Bezos, A.M.; Casitas, R.; Galera, R.; Garcia-Benito, C.; Hernanz, A.; Alonso-Fernandez, A.; Garcia-Rio, F. Effect of Continuous Positive Airway Pressure on Glycemic Control in Patients with Obstructive Sleep Apnea and Type 2 Diabetes. A Randomized Clinical Trial. *Am. J. Respir. Crit. Care Med.* **2016**, *194*, 476–485. [CrossRef] [PubMed]
14. Heffernan, A.; Duplancic, D.; Kumric, M.; Ticinovic Kurir, T.; Bozic, J. Metabolic Crossroads: Unveiling the Complex Interactions between Obstructive Sleep Apnoea and Metabolic Syndrome. *Int. J. Mol. Sci.* **2024**, *25*, 3243. [CrossRef] [PubMed]
15. Kim, B.M.; Ryu, S.Y.; Han, M.A.; Choi, S.W. Loss of significant association between high-sensitivity C-reactive protein (hs-CRP) and metabolic syndrome after adjustment for waist circumference found in 2022 Korea National Health and Nutrition Examination Survey data. *J. Physiol. Anthropol.* **2025**, *44*, 16. [CrossRef]

16. Zhu, Q.; Luo, Q.; Wang, Z.; Chen, S.; Chen, G.; Huang, S. Effects of continuous positive airway pressure therapy on inflammatory markers in patients with obstructive sleep apnea: A meta-analysis of randomized controlled trials. *Sleep Breath.* **2025**, *29*, 182. [CrossRef] [PubMed]
17. Malhotra, A.; Heilmann, C.R.; Banerjee, K.K.; Dunn, J.P.; Bunck, M.C.; Bednarik, J. Weight reduction and the impact on apnea-hypopnea index: A systematic meta-analysis. *Sleep Med.* **2024**, *121*, 26–31. [CrossRef]
18. Miralles-Llumà, L.; Vilarrasa, N.; Monasterio, C.; López-Padrós, C.; Alves, C.; Planas, R.; Arribas, L.; Montserrat, M.; Pérez-Ramos, S.; Pallarès, N. Effects of a One-Year Intensified Weight Loss Program on Body Composition Parameters in Patients with Severe Obesity and Obstructive Sleep Apnea (OSA): A Randomized Controlled Trial. *Nutrients* **2024**, *16*, 4255. [CrossRef]
19. Pidd, K.; Breeze, P.; Ahern, A.; Griffin, S.J.; Brennan, A. Effects of weight loss and weight gain on HbA1c, systolic blood pressure and total cholesterol in three subgroups defined by blood glucose: A pooled analysis of two behavioural weight management trials in England. *BMJ Open* **2025**, *15*, e095046. [CrossRef]
20. Battisha, A.; Kahlon, A.; Kalra, D.K. Sleep-Disordered Breathing and Hypertension-A Systematic Review. *J. Clin. Med.* **2025**, *14*, 3115. [CrossRef]
21. Onyegbule, C.J.; Muoghalu, C.G.; Ofoegbu, C.C.; Ezeorah, F. The Impact of Poor Sleep Quality on Cardiovascular Risk Factors and Quality of Life. *Cureus* **2025**, *17*, e77397. [CrossRef]
22. Abbasi-Ghahramanloo, A.; Soltani-Kermanshahi, M.; Mansori, K.; Khazaei-Pool, M.; Sohrabi, M.; Baradaran, H.R.; Talebloo, Z.; Gholami, A. Comparison of SF-36 and WHOQoL-BREF in Measuring Quality of Life in Patients with Type 2 Diabetes. *Int. J. Gen. Med.* **2020**, *13*, 497–506. [CrossRef]
23. Wiviott, S.D.; Berg, D.D. SGLT2 Inhibitors Reduce Heart Failure Hospitalization and Cardiovascular Death: Clarity and Consistency. *J. Am. Coll. Cardiol.* **2023**, *81*, 2388–2390. [CrossRef]
24. Stefanou, M.I.; Theodorou, A.; Malhotra, K.; Aguiar de Sousa, D.; Katan, M.; Palaiodimou, L.; Katsanos, A.H.; Koutroulou, I.; Lambadiari, V.; Lemmens, R.; et al. Risk of major adverse cardiovascular events and stroke associated with treatment with GLP-1 or the dual GIP/GLP-1 receptor agonist tirzepatide for type 2 diabetes: A systematic review and meta-analysis. *Eur. Stroke J.* **2024**, *9*, 530–539. [CrossRef]
25. Yu, Z.; Cheng, J.X.; Zhang, D.; Yi, F.; Ji, Q. Association between Obstructive Sleep Apnea and Type 2 Diabetes Mellitus: A Dose-Response Meta-Analysis. *Evid. Based Complement. Altern. Med.* **2021**, *2021*, 1337118. [CrossRef] [PubMed]
26. Xu, P.H.; Hui, C.K.M.; Lui, M.M.S.; Lam, D.C.L.; Fong, D.Y.T.; Ip, M.S.M. Incident Type 2 Diabetes in OSA and Effect of CPAP Treatment: A Retrospective Clinic Cohort Study. *Chest* **2019**, *156*, 743–753. [CrossRef] [PubMed]
27. Billings, M.E.; Kapur, V.K. Medicare long-term CPAP coverage policy: A cost-utility analysis. *J. Clin. Sleep Med.* **2013**, *9*, 1023–1029. [CrossRef]
28. Murase, K.; Tanizawa, K.; Minami, T.; Matsumoto, T.; Tachikawa, R.; Takahashi, N.; Tsuda, T.; Toyama, Y.; Ohi, M.; Akahoshi, T.; et al. A Randomized Controlled Trial of Telemedicine for Long-Term Sleep Apnea Continuous Positive Airway Pressure Management. *Ann. Am. Thorac. Soc.* **2020**, *17*, 329–337. [CrossRef]
29. McEvoy, R.D.; Antic, N.A.; Heeley, E.; Luo, Y.; Ou, Q.; Zhang, X.; Mediano, O.; Chen, R.; Drager, L.F.; Liu, Z.; et al. CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea. *N. Engl. J. Med.* **2016**, *375*, 919–931. [CrossRef] [PubMed]
30. Peker, Y.; Glantz, H.; Eulenburg, C.; Wegscheider, K.; Herlitz, J.; Thunström, E. Effect of Positive Airway Pressure on Cardiovascular Outcomes in Coronary Artery Disease Patients with Nonsleepy Obstructive Sleep Apnea. The RICCADSA Randomized Controlled Trial. *Am. J. Respir. Crit. Care Med.* **2016**, *194*, 613–620. [CrossRef]
31. Sánchez-de-la-Torre, M.; Sánchez-de-la-Torre, A.; Bertran, S.; Abad, J.; Duran-Cantolla, J.; Cabriada, V.; Mediano, O.; Masdeu, M.J.; Alonso, M.L.; Masa, J.F.; et al. Effect of obstructive sleep apnoea and its treatment with continuous positive airway pressure on the prevalence of cardiovascular events in patients with acute coronary syndrome (ISAACC study): A randomised controlled trial. *Lancet Respir. Med.* **2020**, *8*, 359–367. [CrossRef] [PubMed]
32. Patil, S.P.; Ayappa, I.A.; Caples, S.M.; Kimoff, R.J.; Patel, S.R.; Harrod, C.G. Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline. *J. Clin. Sleep Med.* **2019**, *15*, 335–343. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.