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Effect of continuous positive airway pressure on albuminuria in patients with obstructive sleep apnea: a meta-analysis

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Abstract

Purpose A relationship between albuminuria and obstructive sleep apnea (OSA) has been documented in previous studies. Nevertheless, the impact of continuous positive airway pressure (CPAP) treatment on albuminuria in subjects with OSA is debated. This meta-analysis was carried out to investigate whether or not CPAP treatment affected urinary albumin-to-creatinine ratio (UACR) in subjects with OSA.

Methods A comprehensive literature search was conducted on Web of Science, Embase, and PubMed from January 1990 to December 2020. Information on patients' characteristics, features of the studies, and UACR of pre- and post-CPAP treatment was collected. For estimation of the pooled effects, standardized mean difference (SMD) was applied.

Results This meta-analysis included 6 articles and 211 subjects. The pooled analysis suggested that CPAP therapy exerted a favorable effect on the decrease of UACR in subjects with OSA (SMD = 0.415, 95% CI = 0.026 to 0.804, z = 2.09, p = 0.037). Subgroup analyses revealed that the CPAP treatment effect was not influenced by sample size, BMI, age, or AHI.

Conclusion The present meta-analysis indicated that UACR was significantly reduced by CPAP therapy in subjects with OSA. Further well-designed randomized controlled trials with large sample size are required to confirm the benefits.

Keywords Continuous positive airway pressure · Obstructive sleep apnea · Albuminuria · Urinary albumin-to-creatinine ratio · Meta-analysis

Introduction

Obstructive sleep apnea (OSA) is a common disease that affects approximately 2 to 4% general population [1]. It is characterized by repetitive upper airway collapse during sleep. This results in both oxyhemoglobin desaturation and sleep fragmentation [2]. It is increasingly recognized that the OSA is an important risk factor for abnormal glycolipid metabolism [3], fatty liver [4], cardiovascular diseases [5], hypertension [6], and kidney injury [7].

The correlation between OSA and kidney injury has been evaluated in numerous studies [7]. The overlap of OSA and chronic kidney disease (CKD) is common [8]. Patients with OSA are at increased risk of developing kidney injury [9, 10]. A cross-sectional study including 7700 subjects suspected of OSA reported that worse lowest nocturnal oxygen saturation was an independent predictor of estimated glomerular filtration rate (eGFR) < 60 [10]. A prospective study following up elderly patients found that apnea hypopnea index (AHI) remained significantly associated with eGFR decline after multi-adjustment [9]. Furthermore, OSA is also a risk factor of developing hypertension and diabetes, which are closely associated with CKD. Microalbuminuria represents an early marker of renal damage, which can be used as a screening and diagnostic tool for early kidney dysfunction [11]. OSA was reported to be independently associated

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with increased microalbuminuria, as indexed by the urinary albumin-to-creatinine ratio (UACR) [12].

Continuous positive airway pressure (CPAP), as the standard therapy for moderate/severe OSA, is effective in preventing collapse of the airway during sleep and normalizing oxyhemoglobin desaturation and sleep disruption. It is hypothesized that CPAP treatment is able to attenuate the adverse physiological changes associated with OSA. Lowering albuminuria is correlated with reduced risk of development of renal disease and better health outcomes [13]. However, the evidence whether the CPAP treatment can lower UACR in OSA patients remains controversial. The purpose of this study was to quantitatively evaluate the efficacy of CPAP treatment on UACR in OSA subjects.

Methods

The meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement for the conduct of meta-analyses of intervention studies [14].

Search strategy

A comprehensive literature search was performed using the following electronic databases from January 1990 to December 2020: Web of Science, Embase, and PubMed. The following search terms were combined: ("sleep apnoea" OR "sleep apnea" OR "sleep disordered breathing" OR "sleep-disordered breathing") AND ("continuous positive airway pressure" OR "CPAP") AND ("urine albumin" OR "urinary albumin" OR "albuminuria" OR "albumin-to-creatinine ratio" OR "albumin creatinine ratio"). Searches combined free-text and MeSH terms. We further hand searched the reference lists of relevant articles. There was no language restriction.

Study selection

The inclusion criteria were as follows: (1) all participants were adults aged 18 years and above; (2) all participants were diagnosed with OSA based on AHI $\geq$ 5 events/h; (2) all patients received CPAP treatment and the mean daily CPAP usage was $\geq$ 4 h/night; (3) all included study contained UACR measurements pre- and post-CPAP therapy; and (4) the studies consisted of sufficient data to conduct a meta-analysis. If studies contained the same group of participants, the study containing the largest sample size was chosen.

The exclusion criteria were as follows: conference articles, review articles, editorials, letters, abstracts, animal studies, case reports. Two authors reviewed the titles, abstracts, and complete articles to determine if they met inclusion criteria.

Data extraction

Data were collected by two independent reviewers from the eligible studies. For each study, the following information was collected: participant characteristics, sleep parameters, year of publication, the first author, the locations where the work was carried out, duration of CPAP treatment, patient inclusion criteria, number of patients, mean daily CPAP treatment time, study design, and the value of UACR pre- and post-CPAP therapy.

Quality assessment

The Newcastle–Ottawa Scale (NOS) was adopted to examine the quality as the included studies were all non-randomized. The NOS was applied to rate observational studies based on 3 parameters (selection, comparability, and outcome) with a maximum total score of 9 stars. Among the 9 stars, 4 stars were assigned for patient selection, 2 stars were assigned for comparability, and 3 stars were assigned for outcome. A higher number of stars represent a higher study quality.

Statistical analysis

Stata statistical software (Version 13.0, Stata Corporation) was utilized in this study. Standardized mean difference (SMD) and 95% CI was applied for estimation of the pooled effects. A fixed effects model was applied when there is no significant heterogeneity. If significant heterogeneity was present ($p < 0.10$ or $I^2 > 50\%$), we used the random effects model. Subgroup analyses were also performed to assess whether there was any factor influencing the treatment effect. Sensitivity analysis was performed to find the potential sources of heterogeneity. Publication bias was assessed visually using the funnel plot and statistically using Egger's regression and Begg's correlation.

Results

Search results

Figure 1 shows the flow chart of search for eligible studies. Seventy-eight papers were identified from the initial manual and electronic searching. After review of their titles and abstracts, 42 papers were excluded. Five of the remaining 11 papers were subsequently excluded for the following

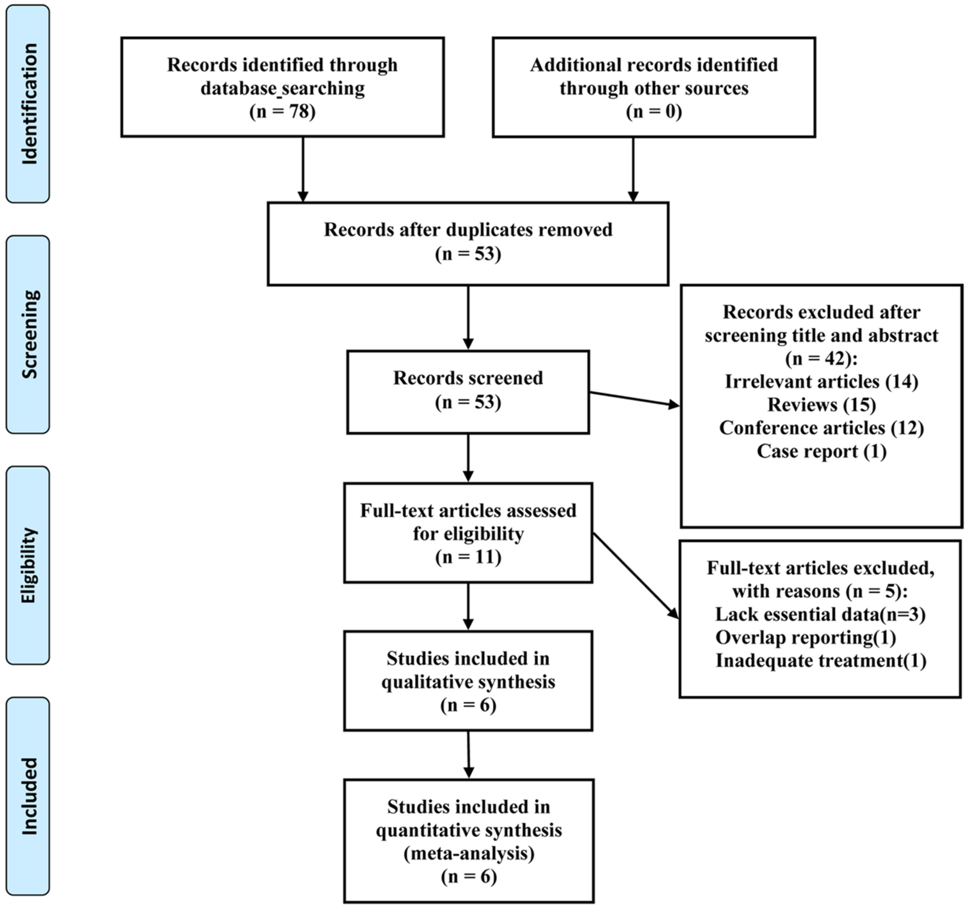

Fig. 1 Flow diagram of study selection

reasons: 3 studies lacked adequate data to perform a meta-analysis; overlapping patient group was reported in one study; and the daily treatment time in one study was less than 4 h/night. Finally, 6 studies were eligible for the meta-analysis [15–20].

Characteristics of the studies

All studies were observational. The majority of the patients were men. The range of mean age was from 46.4 ± 8.7 to 63 ± 9 years old. The AHI ranged from 35.2 ± 23.7 to 64.8 ± 26.6. The body mass index (BMI) ranged from 25.7 ± 5.0 to 33.66 ± 6.34 kg/m^2. The duration of CPAP therapy was from 1 month to 7.8 months. One study separated patients into severe OSA alone group and severe OSA plus high periostin group. Tables 1 and 2 show the characteristics of the studies and the patients' characteristics, respectively.

Pool analysis

The heterogeneity test revealed that there was a high heterogeneity among these studies (Chi-squared = 22.19, $p = 0.001$; $I^2 = 73.0\%$). So pooled analysis was conducted using the random effects model. The results reported that CPAP therapy exerted a favorable effect on the decrease of UACR in OSA subjects (SMD = 0.415, 95% CI = 0.026 to 0.804, $z = 2.09$, $p = 0.037$) (Fig. 2).

Sensitivity and subgroup analyses

The sensitivity analysis indicated that the study performed by Chen et al. [17] significantly affected the pooled SMD (Fig. 3). The heterogeneity was lowered to 0.0% after excluding the data reported by Chen et al. [17]. Subgroup analyses revealed that the differences in AHI, BMI, age, or sample size could not influence the effect of CPAP treatment (Table 3).

Publication bias

The funnel plot (Fig. 4) seemed to be slightly skewed, but neither the Begg's adjusted rank correlation test ($p = 0.230$) nor the Egger's regression asymmetry test ($p = 0.553$) showed publication bias.

Table 1 Characteristics of include studies

Study	Year	Nation/region	Sample size/ male	Inclusion criteria	ventilation duration/night (h)	Therapy duration (M)	Comorbidity	Study design	NOS
Daskalopoulou a	2011	Greece	46/NR	AHI > 15	6.04 ± 1.03	3	No diabetes; No hypertension	Observational study	8
Yasar a	2014	Turkey	18/14	AHI ≥ 15	6.12 ± 1.06	1	No any chronic disease	Observational study	7
Chen	2016	Taiwan	32/29	AHI ≥ 15	≥ 4	7.8	No CKD; No diabetes	Observational study	7
Matsumoto	2016	Japan	36/32	AHI ≥ 20	> 4	3	No CKD	Observational study	8
Parmaksiz	2020	Turkey	36/26	AHI ≥	≥ 4	3	No CKD	Observational study	7
Sunadome A	2020	Japan	35/NR	AHI ≥ 30	5.1 ± 1.3	3	NR	Observational study	9
Sunadome B	2020	Japan	8/NR	AHI ≥ 30	6.4 ± 1.2	3	NR	Observational study	9

Abbreviations: *NR* not reported, *AHI* apnea hypopnea index, *CKD* chronic kidney disease, *NOS* Newcastle–Ottawa Scale

Discussion

To our best knowledge, this was the first meta-analysis examining the effect of CPAP therapy on UACR, an early marker of renal damage, in OSA patients. The results of this meta-analysis including 6 studies demonstrated that CPAP treatment was associated with a statistically significant reduction in UACR in the OSA subjects. Subgroup analyses did not find discrepant effect of CPAP treatment on UACR in the subjects with OSA.

Albuminuria is considered a marker of renal damage in the early stage of CKD and also a well-established marker of increased risk of coronary heart disease and death [21, 22]. Previous studies have demonstrated that OSA was independently associated with albuminuria. Tsioufis et al. [23] compared 62 untreated hypertensive OSA patients with 70 hypertensive non-OSA patients and found that albuminuria was greater by 57% in OSA subjects than that in non-OSA subjects. Further multivariable linear regression analysis demonstrated that the independent predictors of ACR were AHI and 24-h pulse pressure. Another cross-sectional study including 273 type 2 diabetes mellitus, patients found that the higher respiratory event index category was significantly associated with albuminuria after adjusting for other risk factors for albuminuria [24]. This association was also noted in pediatric population. A study focusing children patients suggested that moderate-to-severe OSA children had significantly higher risk of increased low-grade albuminuria than non-OSA group [25].

The mechanisms whereby OSA predisposed to albuminuria were probably multifactorial. OSA was known to be associated with developing hypertension and diabetes, both of

Table 2 Patients' characteristics of the trials included in the meta-analysis

Author	Age	BMI	AHI	$LowSO_2$	Pre-CPAP UACR	Post-CPAP UACR
Daskalopoulou	46.16 ± 10.84	33.66 ± 6.34	60.58 ± 20.79	69.82 ± 12.10	19.71 ± 35.52 mg/g	11.78 ± 20.86 mg/g
Yasar	46.4 ± 8.7	31.9 ± 5.5	46.7 ± 25.3	NR	32.81 ± 26.63 mg/g	20.05 ± 31.21 mg/g
Chen	46.6 ± 9.1	29.7 ± 4.5	64.8 ± 26.6	NR	32.0 ± 9.5 mg/g	19.2 ± 6.5 mg/g
Matsumoto	60.5 ± 10.5	25.7 ± 5.0	35.2 ± 23.7	76.3 ± 12.1	1.93 ± 0.90 Logarithm ACR (mg/g)	1.68 ± 0.85 Logarithm ACR (mg/g)
Parmaksız	55.0 ± 9.6	29.9 ± 5.3	43.4 ± 23.1	68 ± 17	10.98 ± 19.79 mg/mol	12.67 ± 23.75 mg/mol
Sunadome A	58 ± 12 (*n* = 41)	28.7 ± 4.8	52.3 ± 18	75.5 ± 7.8	25.6 ± 96.6 mg/g	12.7 ± 34.2 mg/g
Sunadome B	63 ± 9(*n* = 12)	28.2 ± 3.5	51.3 ± 15.9	72.9 ± 8.5	132.1 ± 306.5 mg/g	60.6 ± 121 mg/g

Abbreviations: *BMI* body mass index, *AHI* apnea hypopnea index, $LowSO_2$ lowest O_2 saturation, *CPAP* continuous positive airway pressure, *UACR* urinary albumin-to-creatinine ratio

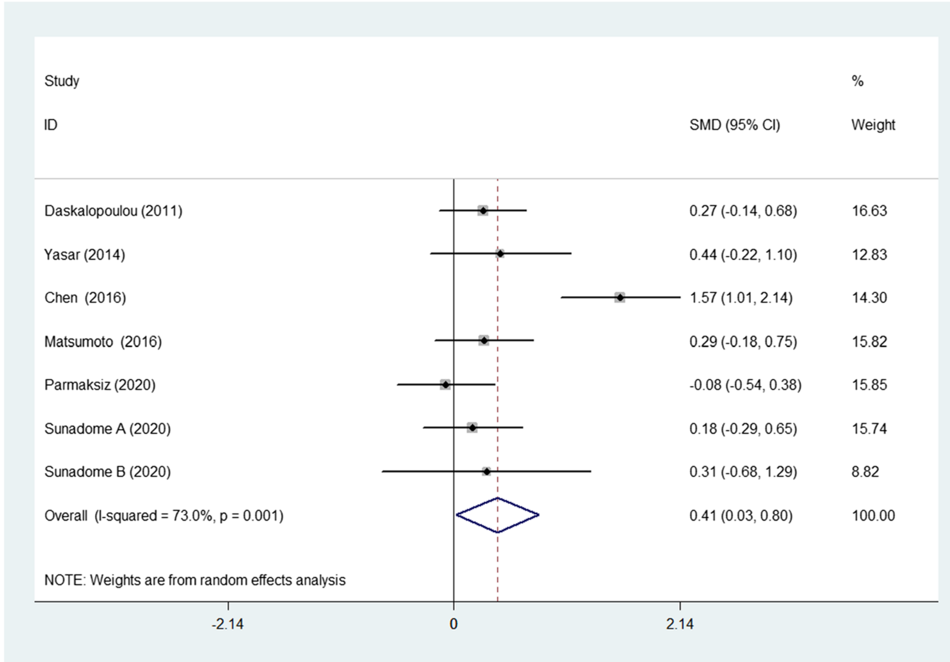

Fig. 2 Forest plot for the change in UACR before and after CPAP treatment. Abbreviations: *SMD* standardized mean difference, *UACR* urinary albumin-to-creatinine ratio, *CPAP* continuous positive airway pressure

which were main risk factors for albuminuria. Other factors such as oxidative stress, sympathetic nervous overactivity, and activation of the renin-angiotensin system all contributed to the OSA-related albuminuria independent of diabetes and high blood pressure [26].

Our results indicated that CPAP therapy exerted a favorable effect on the decrease of UACR in the OSA patients. The findings of the present study have important clinical implications. Evidences have demonstrated that patients with intermediate albuminuria had increased risk for CKD, heart failure, hypertension, and death from cardiovascular diseases. Furthermore, the risk was positively correlated with levels of albuminuria [27]. CPAP was another option for OSA patients with diabetes or hypertension to treat albuminuria. Early intervention by CPAP might be helpful in preventing occurrence of CKD and cardiovascular event and then improving outcomes. In the present study, there is considerable heterogeneity among individual studies. The

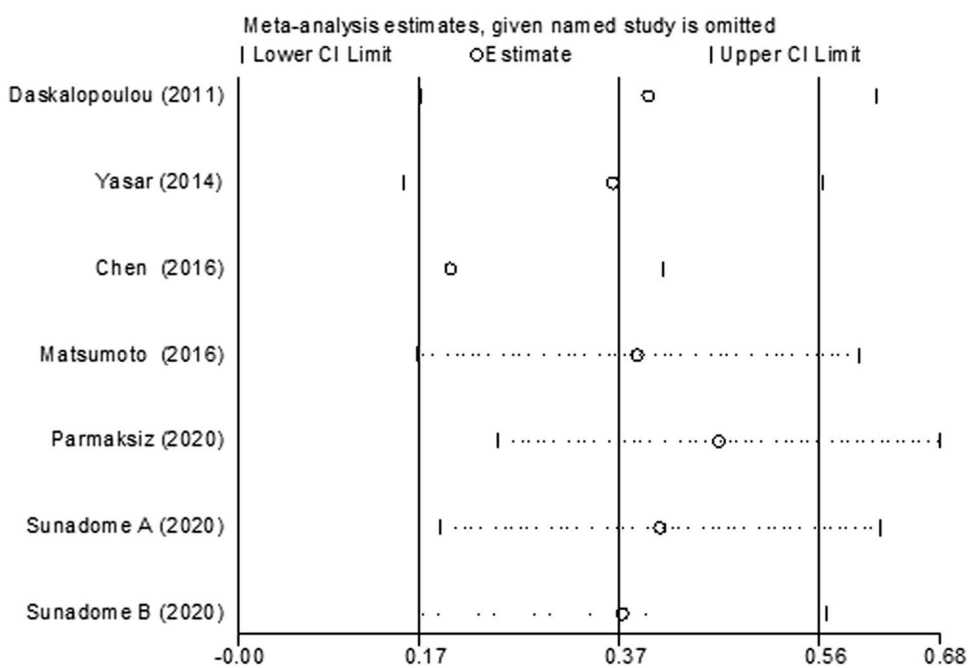

Fig. 3 Sensitivity analysis of the included studies

Table 3 The results of subgroup analyses

Subgroup	Number of studies/ patients	Heterogeneity			SMD			
		X^2	*p*	I^2(%)	SMD	95%CI	Z	*p*
Age								
< 50	3/96	13.95	0.001	85.7	0.755	-0.066 to 1.576	1.80	0.072
≥ 50	4/115	1.36	0.714	0.0	0.140	-0.119 to 0.399	1.06	0.289
BMI								
< 30	5/147	21.90	0.000	81.7	0.449	-0.123 to 1.020	1.54	0.124
≥ 30	2/64	0.18	0.673	0.0	0.319	-0.030 to 0.668	1.79	0.073
AHI								
< 50	3/90	1.98	0.372	0.0	0.415	0.026 to 0.804	1.13	0.258
≥ 50	4/121	17.05	0.001	82.4	0.588	-0.076 to 1.252	1.74	0.082
Sample size								
< 20	2/26	0.05	0.826	0.0	0.399	-0.151 to 0.948	1.42	0.155
≥ 20	5/185	22.12	0.000	81.9	0.427	-0.067 to 0.922	1.69	0.090

Abbreviations: *SMD* standardized mean difference, *BMI* body mass index, *AHI* apnea hypopnea index

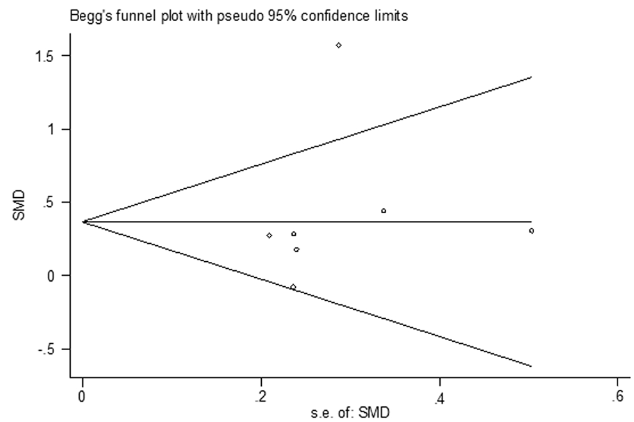

Fig. 4 Funnel plots for assessing publication bias of studies included. Abbreviations: *SMD* standardized mean difference, *SE* standard error

heterogeneity was lowered to 0.0% after excluding the data reported by Chen et al. [17]. This indicated that the greatest source of heterogeneity came from the study by Chen et al. [17]. The heterogeneity generally comes from clinic or methodology. The sex ratio, therapy duration, and albuminuria measurement of the study by Chen et al. [17] were different from other studies. It was speculated that the discrepancy of sex ratio, therapy duration, and albuminuria measurement might account for the heterogeneity across studies.

Four randomized controlled trials (RCTs) were excluded because of lacking adequate data to perform a meta-analysis and inadequate treatment. A randomized controlled trial (RCT) showed potential benefits of CPAP treatment in decreasing UACR in the OSA patients [28]. A recent RCT reported that there was no significant difference in decreasing UACR between the CPAP and control groups [29]. The factors such as baseline OSA severity and therapy duration might partially explain the inconsistent results. Subgroup analyses revealed that the differences in BMI, age, AHI, and sample size did not influence effect of CPAP treatment. The non-significance might be due to small sample size, which did not have adequate statistical power to explore the real association. The results of subgroup analyses needed to be interpreted cautiously.

This study had some limitations. Firstly, the total sample size in this meta-analysis was small, and larger sample size could yield more precise effect size estimation. Secondly, all of the included studies were observational trials but not RCTs. Thirdly, there was considerable heterogeneity among individual studies. Finally, the measurement of UACR was various in different studies; SMD was chosen as effect estimates.

In conclusion, the present meta-analysis demonstrated that CPAP treatment was associated with a statistically significant reduction in UACR in the subjects with OSA. The results suggested that CPAP therapy exerted favorable effect on attenuating albuminuria in the subjects with OSA.

However, body of evidence is weak, and well-designed randomized controlled trials with large sample size are further required to confirm the benefits.

Declarations

Ethics approval and consent to participate All analyses were based on previous published studies; thus, no ethical approval and patient consent are required.

Conflict of interest The authors declare no competing interests.

References

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 328:1230–1235
2. Simon S, Collop N (2012) Latest advances in sleep medicine: obstructive sleep apnea. Chest 142:1645–1651
3. Reutrakul S, Mokhlesi B (2017) Obstructive sleep apnea and diabetes: a state of the art review. Chest 152:1070–1086
4. Lin QC, Chen LD, Chen GP, Zhao JM, Chen X, Huang JF, Wu LH (2015) Association between nocturnal hypoxia and liver injury in the setting of nonalcoholic fatty liver disease. Sleep Breath = Schlaf & Atmung 19:273–280
5. Chami HA, Resnick HE, Quan SF, Gottlieb DJ (2011) Association of incident cardiovascular disease with progression of sleep-disordered breathing. Circulation 123:1280–1286
6. Peppard PE, Young T, Palta M, Skatrud J (2000) Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 342:1378–1384
7. Lin CH, Perger E, Lyons OD (2018) Obstructive sleep apnea and chronic kidney disease. Curr Opin Pulm Med 24:549–554
8. Chou YT, Lee PH, Yang CT, Lin CL, Veasey S, Chuang LP, Lin SW, Lin YS, Chen NH (2011) Obstructive sleep apnea: a stand-alone risk factor for chronic kidney disease. Nephrol Dial Transplant 26:2244–2250
9. Jaussent I, Cristol JP, Stengel B, Ancelin ML, Dupuy AM, Besset A, Helmer C, Ritchie K, Berr C, Dauvilliers Y (2016) Impact of sleep disturbances on kidney function decline in the elderly. Eur Respir J 47:860–868
10. Marrone O, Battaglia S, Steiropoulos P, Basoglu OK, Kvamme JA, Ryan S, Pepin JL, Verbraecken J, Grote L, Hedner J, Bonsignore MR (2016) Chronic kidney disease in European patients with obstructive sleep apnea: the ESADA cohort study. J Sleep Res 25:739–745
11. Ruggenenti P, Remuzzi G (2006) Time to abandon microalbuminuria? Kidney Int 70:1214–1222
12 Bulcun E, Ekici M, Ekici A, Cimen DA, Kisa U (2015) Microalbuminuria in obstructive sleep apnea syndrome. Sleep Breath = Schlaf & Atmung 19:1191–1197
13. Andrassy KM (2013) Comments on “KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease.” Kidney Int 84:622–623
14. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 339:b2535
15 Daskalopoulou EG, Liavvas C, Nakas CT, Vlachogiannis EG, Bouros D, Dombros NV (2011) Obstructive sleep apnoea syndrome promotes reversal albuminuria during sleep. Sleep Breathing = Schlaf & Atmung 15:589–597
16 Yasar ZA, Ucar ZZ, Demir AU, Kirakli C, Kalenci D, Tibet G (2014) Does CPAP therapy alter urinary albumin level in adult patients with moderate to severe obstructive sleep apnea syndrome? Sleep Breath = Schlaf & Atmung 18:525–532
17. Chen NH, Chou YT, Lee PH, Lin SW, Chuang LP, Lin YS, Yang CT (2016) Reversibility of albuminuria and continuous positive airway pressure compliance in patients of obstructive sleep apnea syndrome. Medicine 95:e4045
18. Matsumoto T, Murase K, Tachikawa R, Minami T, Hamada S, Tanizawa K, Inouchi M, Handa T, Oga T, Yanagita M, Mishima M, Chin K (2016) Microalbuminuria in patients with obstructive sleep apnea-chronic obstructive pulmonary disease overlap syndrome. Ann Am Thorac Soc 13:917–925
19. Parmaksiz E, Torun Parmaksiz E (2020) Reversibility of microalbuminuria with continuous positive airway pressure treatment in obstructive sleep apnea syndrome. Int Urol Nephrol 52:1719–1724
20. Sunadome H, Matsumoto H, Tachikawa R, Matsumoto T, Tanizawa K, Oga T, Ono J, Ohta S, Izuhara K, Hirai T, Chin K (2020) Role of serum periostin in severe obstructive sleep apnea with albuminuria: an observational study. Respir Res 21:143
21. Levey AS, de Jong PE, Coresh J, El Nahas M, Astor BC, Matsushita K, Gansevoort RT, Kasiske BL, Eckardt KU (2011) The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney Int 80:17–28
22. Klausen K, Borch-Johnsen K, Feldt-Rasmussen B, Jensen G, Clausen P, Scharling H, Appleyard M, Jensen JS (2004) Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes. Circulation 110:32–35
23. Tsioufis C, Thomopoulos C, Dimitriadis K, Amfilochiou A, Tsiachris D, Selima M, Petras D, Kallikazaros I, Stefanadis C (2008) Association of obstructive sleep apnea with urinary albumin excretion in essential hypertension: a cross-sectional study. Am J Kidney Dis 52:285–293
24. Nishimura A, Kasai T, Kikuno S, Nagasawa K, Okubo M, Narui K, Mori Y (2018) Effect of sleep-disordered breathing on albuminuria in 273 patients with type 2 diabetes. J Clin Sleep Med 14:401–407
25. Varlami V, Malakasioti G, Alexopoulos EI, Theologi V, Theophanous E, Liakos N, Daskalopoulou E, Gourgoulianis K, Kaditis AG (2013) Low-grade albuminuria in children with obstructive sleep apnea. J Sleep Res 22:289–294
26. Hanly PJ, Ahmed SB (2014) Sleep apnea and the kidney: is sleep apnea a risk factor for chronic kidney disease? Chest 146:1114–1122
27. Romundstad S, Holmen J, Kvenild K, Hallan H, Ellekjaer H (2003) Microalbuminuria and all-cause mortality in 2,089 apparently healthy individuals: a 4.4-year follow-up study. The Nord-Trondelag Health Study (HUNT), Norway. Am J Kidney Dis 42:466–473
28. Comondore VR, Cheema R, Fox J, Butt A, John Mancini GB, Fleetham JA, Ryan CF, Chan S, Ayas NT (2009) The impact of CPAP on cardiovascular biomarkers in minimally symptomatic patients with obstructive sleep apnea: a pilot feasibility randomized crossover trial. Lung 187:17–22
29. Rimke AN, Ahmed SB, Turin TC, Pendharkar SR, Raneri JK, Lynch EJ, Hanly PJ (2021) Effect of CPAP therapy on kidney function in patients with chronic kidney disease: a pilot randomized controlled trial. Chest 159(5):2008–2019