CHEST

Original Research

SLEEP DISORDERS

Declining Kidney Function Increases the Prevalence of Sleep Apnea and Nocturnal Hypoxia

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Background: **Sleep apnea is an important comorbidity in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD). Although the increased prevalence of sleep apnea in patients with ESRD is well established, few studies have investigated the prevalence of sleep apnea in patients with nondialysis-dependent kidney disease, and no single study, to our knowledge, has examined the full spectrum of kidney function. We sought to determine the prevalence of sleep apnea and associated nocturnal hypoxia in patients with CKD and ESRD. We hypothesized that the prevalence of sleep apnea would increase progressively as kidney function declines.**
Methods: **Two hundred fifty-four patients were recruited from outpatient nephrology clinics and hemodialysis units. All patients completed an overnight cardiopulmonary monitoring test to determine the prevalence of sleep apnea (respiratory disturbance index ≥ 15) and nocturnal hypoxia (oxygen saturation < 90% for ≥ 12% of monitoring). Patients were stratified into three groups based on estimated glomerular filtration rate (eGFR) as follows: eGFR ≥ 60 mL/min/1.73 m² (n = 55), CKD (eGFR < 60 mL/min/1.73 m² not on dialysis, n = 124), and ESRD (on hemodialysis, n = 75).**
Results: **The prevalence of sleep apnea increased as eGFR declined (eGFR ≥ 60 mL/min/1.73 m², 27%; CKD, 41%; ESRD, 57%; *P* = .002). The prevalence of nocturnal hypoxia was higher in patients with CKD and ESRD (eGFR ≥ 60 mL/min/1.73 m², 16%; CKD, 47%; ESRD, 48%; *P* < .001).**
Conclusions: **Sleep apnea is common in patients with CKD and increases as kidney function declines. Almost 50% of patients with CKD and ESRD experience nocturnal hypoxia, which may contribute to loss of kidney function and increased cardiovascular risk.**

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Abbreviations: CKD = chronic kidney disease; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; CSR = Cheyne-Stokes respiration; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; OSA = obstructive sleep apnea; RDI = respiratory disturbance index; Sa_{O_2} = arterial oxygen saturation

Sleep apnea occurs in > 50% of patients with end-stage renal disease (ESRD),[1-6] which is considerably higher than in the general population.[7] In contrast to the extensive ESRD literature, few studies have investigated the prevalence of sleep apnea in patients with nondialysis-dependent chronic kidney disease (CKD). These studies have been limited by small sample size, selective recruitment, lack of appropriate comparison groups, and equivocal definitions of sleep apnea and CKD, and no single study, to our knowledge, has evaluated patients with the full spectrum of kidney function.[8-12]

The coexistence of sleep apnea in patients with CKD and ESRD is likely to have clinical relevance. In addition to impairment of sleep quality and daytime function,[13] sleep apnea increases the risk of hypertension,[14] atherosclerosis,[15] and vascular disease.[16-18] Vascular disorders are common to both patients with CKD and patients with ESRD, and their prevalence may be further increased by unrecognized sleep apnea.[19] Further, sleep apnea is characteristically associated with nocturnal hypoxia, which is the main biologic mechanism through which these vascular complications develop.[19-23] It is also possible that sleep apnea accelerates the deterioration of kidney function in patients with CKD either indirectly by increasing systemic BP, inflammatory cytokines, and sympathetic nervous system activity[24] (all of which

have been proposed to reduce kidney function[20,21,23]) or directly through the effect of hypoxia on the kidney.[25,26]

We sought to determine, through a cross-sectional study design, the prevalence of sleep apnea and nocturnal hypoxia in patients with CKD and to confirm the reported high prevalence of sleep apnea in patients with ESRD. We hypothesized that patients with CKD and ESRD have an increased prevalence of sleep apnea, which increases as kidney function declines.

Materials and Methods

Patient Selection and Recruitment

Adult patients (aged ≥ 18 years) attending outpatient nephrology clinics and hemodialysis units were invited to participate in the study. Exclusion criteria included supplemental oxygen use, tracheostomy, and inability to give informed consent. The study was approved by the University of Calgary Conjoint Health Research Ethics Board (E#20091). Informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

Patients were stratified according to their estimated glomerular filtration rate (eGFR) at the time of the study visit and classified into three groups based on the National Kidney Foundation staging system as follows: eGFR ≥ 60 mL/min/1.73 m^2, CKD (eGFR < 60 mL/min/1.73 m^2), and ESRD (on hemodialysis).[27] eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[28]

All patients completed a questionnaire that surveyed for demographic information; sleep and medical history, including hypertension, congestive heart failure, coronary artery disease (angina, myocardial infarction, and coronary artery bypass surgery), cerebrovascular disease (stroke or transient ischemic attack), diabetes, and COPD; and medication use. Medications included sedatives (benzodiazepines and hypnotics), antidepressants, and narcotics.

Sleep Apnea and Nocturnal Hypoxia

Patients performed an unattended, overnight cardiopulmonary monitoring study at home (Remmers Sleep Recorder Model 4.2; SagaTech Electronics Inc). Dialysis patients were asked to perform the overnight study on a dialysis-free day. The monitor consisted of an oximeter to record arterial oxygen saturation (Sa_{O_2}) and heart rate variability, a pressure transducer to record nasal airflow, a microphone to record snoring, and a body position sensor. The oximeter provided the data for an automated scoring algorithm, which calculated the respiratory disturbance index (RDI) based on the number of episodes of oxyhemoglobin desaturation ≥ 4% per hour of monitoring. Nocturnal oxygen saturation was sampled at 1 Hz. The Remmers Sleep Recorder was validated by comparison with attended polysomnography.[29,30] We defined sleep apnea as an RDI ≥ 15 because this reflects moderately severe sleep apnea that is likely to be clinically significant.[31,32] The Remmers Sleep Recorder has a sensitivity of 98% and specificity of 88% for a designation criteria of RDI ≥ 15.[30] A sleep medicine physician (P. J. H.) blinded to the patients' kidney function reviewed the raw data, confirmed that the estimated RDI was accurate, and determined whether apnea was central (Cheyne-Stokes respiration [CSR]) or obstructive (obstructive sleep apnea [OSA]) based on the morphology of the airflow recordings. Nasal pressure recordings with a characteristic crescendo/decrescendo pattern and no evidence of airflow limitation were classified as CSR, whereas recordings without a crescendo/decrescendo pattern and with airflow limitation were classified as OSA (Fig 1). Nocturnal hypoxia was defined as an Sa_{O_2} < 90% for ≥ 12% of monitoring, which has previously been used in the Sleep Heart Health Study.[33]

If the nocturnal cardiopulmonary monitoring test was nondiagnostic (patient did not sleep, unsatisfactory technical quality, or short monitoring time), the test was repeated. If the test remained nondiagnostic or was declined, it was classified as inconclusive, and the patient was excluded from further analysis. Patients with a previously completed sleep study, prior diagnosis of sleep apnea, or treatment with CPAP were included if their diagnostic sleep study was available for review and their eGFR was known at the time of the sleep study.

Statistical Analysis

Data are reported as mean ± SD for continuous variables and median (range) for categorical and nonnormally distributed variables. Parametric and nonparametric tests were used when appropriate. The unpaired *t* test or the Mann-Whitney *U* test was used for comparisons between two groups, whereas the one-way analysis of variance or the Kruskal-Wallis test was used for comparison among three groups. The Jonckheere-Terpstra test was used to examine trends among nonnormally distributed continuous variables. Categorical comparisons were analyzed using the χ^2 test and Fisher exact test. Univariate and multivariate logistic regression models were used to identify the factors associated with sleep apnea and nocturnal hypoxia. Traditional risk factors for sleep apnea (age, male sex, BMI, neck circumference, history of cardiovascular disease, cerebrovascular disease, diabetes, sedatives, and antidepressants) and kidney function status (eGFR ≥ 60, CKD, ESRD) were included. For nocturnal hypoxia, COPD and RDI were added to these variables. The Hosmer-Lemeshow goodness-of-fit test and omnibus tests of model coefficients were used to test the model fit for the logistic regression models. These tests demonstrated that the models were sensitive to differences in kidney function groups and that there was an adequate fit of the data to the model. All statistical analyses were two sided with a .05 significance level and were performed using SPSS version 17.0 (SPSS Inc) software.

Results

Patient Recruitment

A total of 403 patients (eGFR ≥ 60, n = 87; CKD, n = 185; ESRD, n = 132) were recruited (Fig 2);

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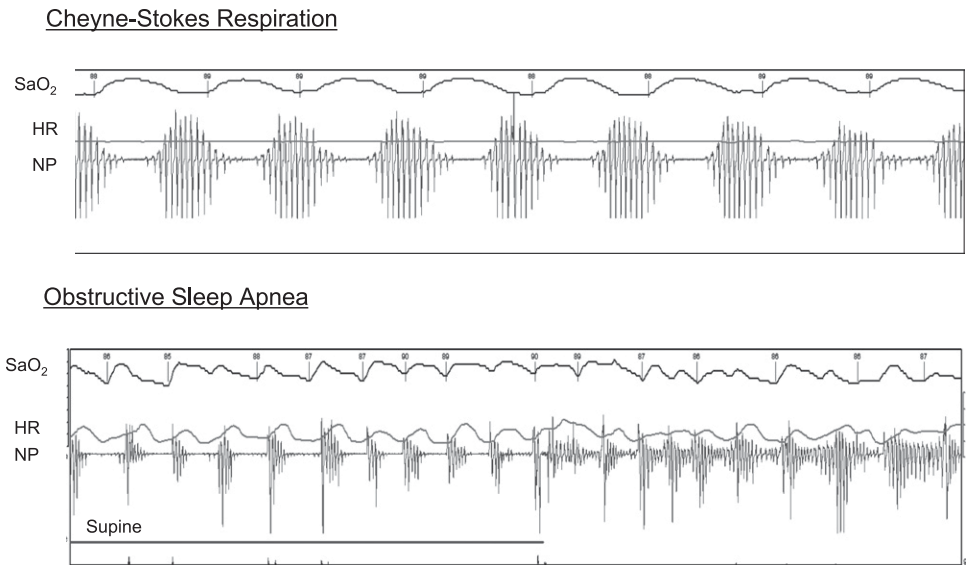

FIGURE 1. Nocturnal cardiopulmonary recording demonstrating Cheyne-Stokes respiration and obstructive sleep apnea. Each example is 10 min. HR = heart rate; NP = nasal pressure; SaO_2 = arterial oxygen saturation.

149 did not complete overnight cardiopulmonary monitoring for the following reasons: anxiety, travel distance, lack of time (n = 122); technical difficulties (n = 22); and receiving treatment with CPAP (n = 5). Comparison of the remaining 254 patients (eGFR ≥ 60, n = 55; CKD, n = 124; ESRD, n = 75) (Table 1) with the 149 who withdrew showed that those who completed the study were younger men with hypertension and larger neck circumferences.

Clinical Profile

Patients with CKD and ESRD were older than patients with eGFR ≥ 60 (Table 2). BMI also differed across groups. The prevalence of hypertension was > 50% in all patient groups and was significantly higher in those with CKD and ESRD. The prevalence of other comorbidities increased as eGFR declined. There was no difference in the prevalence of antidepressant medications, but sedatives and narcotics were used more frequently as kidney function declined. A history of snoring was reported equally across the three groups (eGFR ≥ 60, n = 35 [64%]; CKD, n = 93 [75%]; ESRD, n = 51 [68%]; $\chi^2 = 2.677$; $P = .262$). Unrefreshing sleep was also reported equally across the three groups (eGFR ≥ 60, n = 27 [49%]; CKD, n = 53 [43%]; ESRD, n = 47 [63%]; $\chi^2 = 2.677$; $P = .407$).

Sleep Apnea

The mean duration of nocturnal cardiopulmonary monitoring was 6.8 ± 1.5 h for patients with eGFR ≥ 60, 7.2 ± 1.5 h for patients with CKD, and 6.4 ± 2.0 h for patients with ESRD. Furthermore, the proportion of monitoring time that patients reported sleeping was 85.5% ± 12.5% for eGFR ≥ 60, 80.7% ± 14.9% for CKD, and 78.1% ± 17.8% for ESRD. Consequently, sleep efficiency and monitoring time were sufficiently long to capture important respiratory events (Fig 3, Table 3).

The proportion of patients with sleep apnea increased as kidney function decreased (eGFR ≥ 60, n = 15 [27%]; CKD, n = 51 [41%]; ESRD, n = 43 [57%]; $\chi^2 = 12.019$; $P = .002$). Sleep apnea was predominantly obstructive; however, the prevalence of CSR increased as eGFR decreased. The RDI was higher in groups with lower kidney function. Trend analysis

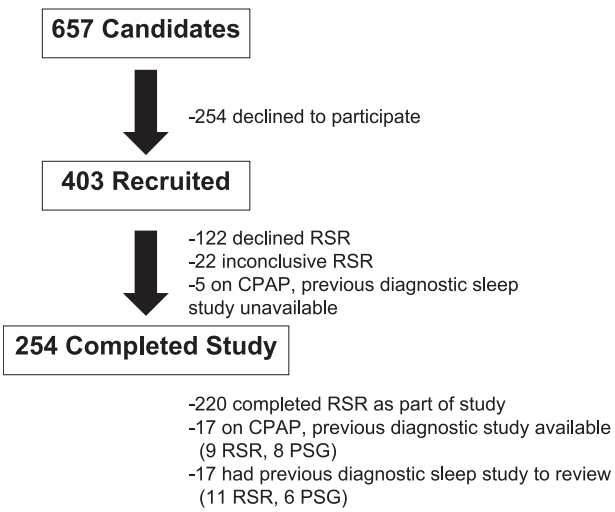

FIGURE 2. Patient recruitment. PSG = polysomnography; RSR = Remmers Sleep Recorder.

Table 1—*Clinical Profile of Patients Who Completed the Study Compared With Patients Who Withdrew From the Study*

	Completed	Withdrawn	*P* Value
No. patients	254	149	...
Age, y	59.5 ± 15.9	63.1 ± 15.3	.029
Male sex	164 (65)	77 (52)	.012
BMI, kg/m²	29.6 ± 7.5	28.4 ± 6.6	.145
Neck circumference, cm	40.9 ± 5.2	38.8 ± 4.6	< .001
Kidney function			
eGFR ≥ 60 mL/min/1.73 m²	55 (21)	32 (21)	1.000
CKD	124 (49)	61 (41)	.147
ESRD	75 (30)	56 (38)	.100
Comorbidities			
Hypertension	213 (84)	109 (73)	.014
Congestive heart failure	25 (10)	8 (5)	.134
Coronary artery disease	56 (22)	27 (18)	.304
Cerebrovascular disease	19 (7)	8 (5)	.537
Diabetes	95 (37)	60 (41)	.525
COPD	22 (9)	8 (5)	.245
Medications			
Sedatives	31 (12)	24 (16)	.294
Antidepressants	12 (5)	14 (9)	.091
Narcotics	16 (6)	11 (7)	.684

Data are presented as mean ± SD or No. (%), unless otherwise indicated. CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease.

indicated a significant increase in RDI as kidney function declined ($P < .001$).

Nocturnal Hypoxia

The proportion of patients who experienced nocturnal hypoxia increased as eGFR decreased (Fig 4). Nocturnal hypoxia was found in 9 patients (16%) with eGFR ≥ 60, 58 patients (47%) with CKD, and 36 patients (48%) with ESRD ($\chi^2 = 17.328$, $P < .001$) (Fig 4, Table 3). Trend analysis indicated a significant increase in the duration of $Sao_2 < 90\%$ as kidney function declined ($P = .004$).

Regression Analysis

Univariate logistic regression for sleep apnea revealed that ESRD, advanced age, male sex, increased BMI, increased neck circumference, congestive heart failure, coronary artery disease, and diabetes were associated with sleep apnea (Table 4). Multivariate analysis revealed that ESRD, advanced age, increased BMI, and increased neck circumference were associated with sleep apnea (Nagelkerke R^2, 0.400) (Table 4).

Univariate analyses for nocturnal hypoxia revealed that CKD, ESRD, advanced age, increased BMI, increased neck circumference, congestive heart failure, coronary artery disease, cerebrovascular disease, diabetes, COPD, and RDI were significant predictors of nocturnal hypoxia (Table 4). Multivariate analysis indicated that CKD, COPD, and RDI were significant predictors of increased risk for nocturnal hypoxia, with RDI being the strongest (Nagelkerke R^2, 0.480) (Table 4). ESRD, advanced age, and increased BMI were of borderline significance. Exclusion of the 14 patients who completed a polysomnography test instead of home cardiopulmonary monitoring did not alter the results.

Table 2—*Clinical Profile of All Patients Who Completed the Study*

	eGFR, mL/min/1.73 m²			
	≥ 60	CKD[a]	ESRD[b]	*P* Value
No. patients	55	124	75	
Age, y	43.7 ± 14.6	65.2 ± 12.1	61.9 ± 14.7	< .001
Male sex	32 (58)	80 (65)	52 (69)	.422
BMI, kg/m²	29.0 ± 6.9	31.3 ± 8.1	27.2 ± 6.4	.001
Neck circumference, cm	39.9 ± 4.9	41.1 ± 4.9	41.4 ± 5.8	.227
eGFR, mL/min/1.73 m²	84 (61-135)	30 (8-59)	...	< .001
Comorbidities				
Hypertension	32 (58)	113 (91)	68 (91)	< .001
Congestive heart failure	0 (0)	9 (7)	16 (21)	< .001
Coronary artery disease	4 (7)	25 (20)	27 (36)	< .001
Cerebrovascular disease	0 (0)	8 (6)	11 (15)	.006
Diabetes	7 (13)	48 (40)	39 (52)	< .001
COPD	4 (7)	7 (6)	11 (15)	.083
Medications				
Sedatives	4 (7)	10 (8)	17 (23)	.004
Antidepressants	2 (4)	5 (4)	5 (7)	.636
Narcotics	0 (0)	7 (6)	9 (12)	.019

Data are presented as mean ± SD, No. (%), or median (range), unless otherwise indicated. See Table 1 legend for expansion of abbreviations.
[a]CKD (eGFR < 60 mL/min/1.73 m²).
[b]ESRD (on hemodialysis).

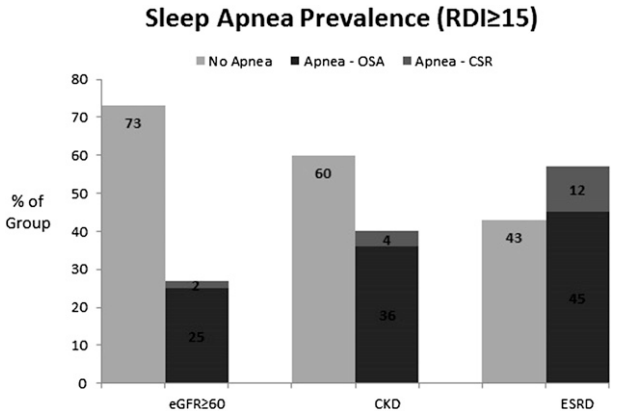

FIGURE 3. Prevalence of sleep apnea in all patients. CKD = chronic kidney disease; CSR = Cheyne-Stokes respiration; eGFR ≥ 60 = estimated glomerular filtration rate ≥ 60 mL/min/1.73 m²; ESRD = end-stage renal disease; OSA = obstructive sleep apnea; RDI = respiratory disturbance index.

Discussion

We found that the prevalence and severity of sleep apnea increased as kidney function declined. Furthermore, sleep apnea is common in patients with CKD in addition to those with ESRD. We also found a high prevalence of nocturnal hypoxia in patients with CKD and ESRD that appeared to be due to both sleep apnea and additional nonapneic factors.

Previous studies have evaluated the prevalence of sleep apnea in CKD. Markou et al[10] reported a 31.4% prevalence of sleep apnea in a cross-sectional study of 35 patients with CKD, but their study was limited by a small sample size and the absence of comparative groups with eGFR ≥ 60 and ESRD. Further, patients with cardiovascular disease were excluded, limiting the generalizability of their findings because cardiovascular comorbidities are common in this patient population.[19,23] Sim et al[12] reported an increased risk for sleep apnea in patients with mildly reduced eGFR. However, the prevalence of sleep apnea was low (2.5%), and the absence of BMI data precluded adjustment for the known association between obesity and sleep apnea.[7,34] Canales et al[8] reported an increased prevalence (27%) of sleep apnea in a cohort of elderly men but found no association with kidney function. Sakaguchi et al[11] reported an increased prevalence (32%) of sleep apnea in 100 patients with CKD in Japan, which may not be generalizable to non-Asian populations. Roumelioti et al[9] reported a high prevalence (22.5%) of severe sleep apnea in 89 patients with CKD but used historical control data where kidney function was undefined. Finally, in all of these studies, eGFR was determined using the Modification of Diet and Renal Disease Study equation, which is unreliable at eGFR ≥ 60, introducing potential misclassification bias.[35,36]

The present study addressed several of these limitations. First, we examined patients with the full spectrum of kidney function, ranging from those with eGFR ≥ 60 to ESRD. Second, all patients were recruited from nephrology clinics and hemodialysis units, including those with minimally impaired kidney function (eGFR > 60), which we believe is the most appropriate control group for this study. The high prevalence of sleep apnea in this group likely reflects the fact that the patients comprised a referred population with a high prevalence of hypertension and other renal symptoms. Third, patients were not excluded by age, sex, comorbidities, or medications, improving the generalizability of the findings to the CKD and ESRD populations. Comparison of the present ESRD population to a cohort of 237 patients with ESRD from the Southern Alberta Renal Program showed a similar clinical profile.[37] The present CKD population also had a similar clinical profile to the Chronic Renal Insufficiency Cohort study.[38] Consequently, we believe that the present study population is representative of the general CKD and ESRD populations. In addition, we determined eGFR using the CKD-EPI equation, which provides a more reliable classification of patients with an eGFR ≥ 60.[28,36]

Table 3—*Prevalence of Sleep Apnea and Nocturnal Hypoxia in All Patients*

	eGFR, mL/min/1.73 m²			
	≥ 60	CKD[a]	ESRD[b]	*P* Value
No. patients	55	124	75	
RDI, h	5.8 (0.2-115.3)	11.7 (0.5-127.0)	20.0 (0.4-112)	< .001
Sleep apnea, RDI ≥ 15	15 (27)	51 (41)	43 (57)	.002
SaO_2 < 90%, % of TTPO	0.8 (0-98.1)	9.7 (0-96.8)	10.6 (0-96.4)	< .001
Nocturnal hypoxia, SaO_2 < 90% for ≥ 12% of monitoring	9 (16)	58 (47)	36 (48)	< .001

Data are presented as median (range) or No.(%), unless otherwise indicated. RDI = respiratory disturbance index; SaO_2 = arterial oxygen saturation; TTPO = total time oximeter probe was on the patient. See Table 1 legend for expansion of other abbreviations.

[a]CKD (eGFR < 60 mL/min/1.73 m²).

[b]ESRD (on hemodialysis).

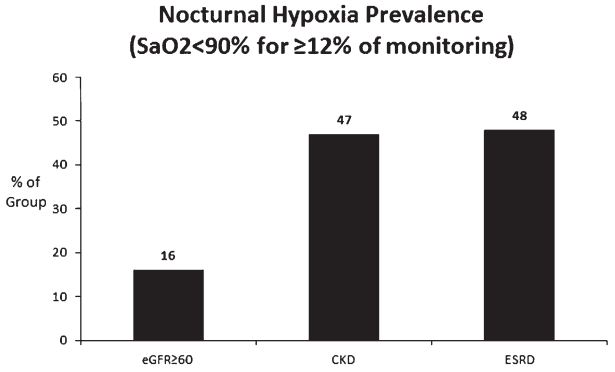

FIGURE 4. Prevalence of nocturnal hypoxia in all patients. See Figure 1 and 3 legends for expansion of abbreviations.

Among traditional risk factors, advanced age, increased BMI, increased neck circumference, cardiovascular disease, and diabetes were all associated with sleep apnea. Additionally, kidney disease status was associated with sleep apnea. Multivariate analysis did not show any association between sleep apnea and comorbid vascular disease. These data imply that reduced kidney function may contribute to the pathogenesis of sleep apnea independently of traditional risk factors for sleep apnea and coexisting vascular disease. Both fluid overload[39] and altered chemical control of breathing[40,41] have been proposed to cause sleep apnea in patients with ESRD. It is possible that similar mechanisms contribute to the pathogenesis of sleep apnea in patients with CKD prior to starting dialysis.

A striking finding was the high prevalence of nocturnal hypoxia in patients with CKD that was similar to that seen in patients with ESRD. Furthermore, only a portion of the nocturnal hypoxia in the CKD and ESRD groups was attributed to sleep apnea, suggesting that the pathogenesis was partly due to nonapneic factors. Two possible mechanisms are

Table 4—*Univariate and Multivariate Analyses for Sleep Apnea and Nocturnal Hypoxia*

	Univariate			Multivariate		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Sleep apnea[a]						
Kidney function						
eGFR ≥ 60 mL/min/1.73 m²	1	…	…	1	…	…
CKD	1.86	0.93-3.73	.078	0.85	0.32-2.26	.740
ESRD	3.58	1.69-7.58	.001	4.28	1.43-12.80	.009
Age, y	1.03	1.01-1.05	.001	1.03	1.01-1.06	.011
Male sex	2.96	1.69-5.17	< .001	1.83	0.73-4.62	.201
BMI, kg/m²	1.10	1.06-1.15	< .001	1.09	1.02-1.16	.008
Neck circumference, cm	1.25	1.17-1.33	< .001	1.18	1.05-1.32	.004
Congestive heart failure	3.16	1.31-7.64	.010	0.77	0.24-2.46	.663
Coronary artery disease	2.79	1.51-5.16	.001	1.21	0.54-2.74	.647
Cerebrovascular disease	1.92	0.75-4.96	.176	0.68	0.21-2.24	.523
Diabetes	1.88	1.13-3.15	.016	0.50	0.24-1.04	.063
Sedatives	0.70	0.32-1.53	.374	0.36	0.13-0.99	.047
Antidepressants	1.92	0.59-6.23	.276	3.31	0.67-16.41	.142
Narcotics	1.36	0.49-3.74	.555	0.98	0.27-3.58	.975
Nocturnal hypoxia[b]						
Kidney function						
eGFR ≥ 60 mL/min/1.73 m²	1	…	…	1	…	…
CKD	4.49	2.03-9.96	< .001	3.37	1.04-10.90	.043
ESRD	4.84	2.08-11.30	< .001	2.88	0.82-10.18	.100
Age, y	1.04	1.02-1.06	< .001	1.03	1.00-1.06	.062
Male sex	1.13	0.67-1.90	.661	0.37	0.14-1.01	.052
BMI, kg/m²	1.11	1.07-1.16	< .001	1.07	1.00-1.14	.061
Neck circumference, cm	1.15	1.09-1.22	< .001	1.06	0.94-1.18	.354
Congestive heart failure	2.88	1.22-6.80	.016	1.07	0.31-3.72	.917
Coronary artery disease	2.49	1.35-4.58	.003	1.24	0.53-2.90	.613
Cerebrovascular disease	3.47	1.27-9.45	.015	2.27	0.65-7.92	.198
Diabetes	2.12	1.26-3.57	.005	0.69	0.32-1.51	.356
COPD	4.41	1.66-11.71	.003	4.37	1.07-17.83	.040
Sedatives	1.66	0.78-3.52	.190	2.12	0.74-6.06	.162
Antidepressants	0.53	0.14-2.06	.361	0.14	0.02-0.86	.034
Narcotics	1.96	0.70-5.43	.198	0.92	0.25-3.42	.900
RDI, h[-1]	1.05	1.04-1.07	< .001	1.05	1.03-1.07	< .001

See Table 1 and 3 legends for expansion of abbreviations.

[a]Sleep apnea RDI ≥ 15.

[b]Nocturnal hypoxia SaO_2 < 90% for ≥ 12% of monitoring time.

comorbid pulmonary and cardiac disease and medications that can alter the mechanics and control of respiration.[40-43] Multivariate analysis revealed that COPD was associated with nocturnal hypoxia, but cardiovascular disease and use of sedatives and narcotics were not. Other potential causes, such as fluid overload, should be considered in future studies.

What are the clinical implications of the findings? Sleep apnea increases the risk of hypertension,[14] cardiovascular disease, and cerebrovascular disease,[16,18] all of which are important and highly prevalent complications of both CKD and ESRD.[19,22,23,37,38] These complications of sleep apnea are predominantly mediated through nocturnal hypoxia, which has been associated with elevated nocturnal BP,[20] left ventricular hypertrophy,[21] and adverse cardiovascular outcomes in patients with ESRD.[19,22] Although it is likely that sleep apnea may have a similar impact on clinical outcomes in patients with CKD, to our knowledge, this has not been studied to date. Furthermore, the potential interaction between nocturnal hypoxia and declining kidney function in patients with CKD is even more intriguing. Nocturnal hypoxia has been demonstrated to be independently associated with an increased risk for accelerated loss of kidney function.[44] The chronic hypoxia hypothesis suggests that chronic ischemic damage in the tubulointerstitium of the kidney is the final common pathway for the development of ESRD.[25,26] If such a process is already under way in patients with CKD, it is possible that ongoing nocturnal hypoxia will amplify the effect and accelerate the decline in kidney function. If so, identification and treatment of nocturnal hypoxia may provide a potential disease-modifying intervention that could delay or halt the progression of CKD to ESRD. Because a history of snoring and unrefreshing sleep were equally common among the three patient groups, objective cardiopulmonary evaluation may be required to identify these respiratory abnormalities.

The present study has a number of strengths. First, we recruited a relatively large sample from a renal population representative of the general CKD and ESRD populations. Second, we applied the same methodology to a broad spectrum of kidney disease, ranging from patients with eGFR $\geq$ 60 to ESRD. Third, we determined eGFR using the CKD-EPI equation, which is more reliable than what has been used in previous studies to estimate eGFR $\geq$ 60.

The study also has some limitations. First, the differences in neck size and prevalence of hypertension between the subjects who completed the study and those who withdrew raise the possibility of selection bias, which could result in an overestimation of the prevalence of sleep apnea. We tried to limit this by emphasizing that sleep-related symptoms were not required for recruitment and by using the same recruitment strategy and personnel for each group. Consequently, if such a selection bias did exist, we anticipate that it would have applied to all patients and that the difference in the prevalence of sleep apnea between groups would have been maintained. Further, as previously stated, the final study cohort was representative of the general CKD and ESRD populations. Second, we did not use a measurement of respiratory effort and, consequently, could only estimate the prevalence of central sleep apnea based on the morphology of the nasal pressure recording. Finally, we cannot comment on causality because of the cross-sectional nature of the study.

In conclusion, we have identified that patients with CKD are commonly exposed to nocturnal hypoxia related to both unrecognized sleep apnea and other factors. Nocturnal hypoxia has the potential to alter important clinical outcomes in this patient population, such as long-term cardiovascular risk and the rate of decline in kidney function. Further studies are required to determine whether treatment of sleep apnea and nocturnal hypoxia improves these clinical outcomes in patients with CKD.

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Dr Ahmed: contributed to the acquisition, analysis, and interpretation of the data and reviewed the manuscript for important intellectual content.
Dr Loewen: contributed to the conception and design of the study; acquisition, analysis, and interpretation of the data; and reviewed the manuscript for important intellectual content.
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Mr Beecroft: contributed to the acquisition, analysis, and interpretation of the data and final approval of the manuscript.
Dr Turin: contributed statistical expertise and reviewed the manuscript for important intellectual content.
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