Diagnostic Value of Screening Instruments for Identifying Obstructive Sleep Apnea in Kidney Failure

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Background: Patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) have a high prevalence of obstructive sleep apnea (OSA) that can have significant clinical implications. An accurate clinical screening tool for OSA that identifies patients for further diagnostic testing would assist in the identification of this comorbidity. The Berlin Questionnaire (BQ), Adjusted Neck Circumference (ANC), and STOP-BANG questionnaire are 3 such instruments that have been validated in patients with normal kidney function.

Objective: The objective of this study was to determine the validity of these screening instruments in patients with CKD and ESRD, using overnight cardiopulmonary monitoring to diagnose OSA.

Methods: One hundred seventy-two patients were recruited from nephrology clinics and hemodialysis units (CKD: n = 109; ESRD: n = 63). All patients completed the BQ, ANC, STOP-BANG, and overnight cardiopulmonary monitoring to diagnose OSA (respiratory disturbance index [RDI] ≥ 15). Sensitivity, specificity, positive and negative predictive values, and accu-

acy were calculated for the BQ, ANC, and STOP-BANG.

Results: Obstructive sleep apnea was present in 41 CKD patients (38%) and 32 ESRD patients (51%). All screening instruments had satisfactory sensitivity (56% to 94%) but poor specificity (29% to 77%) and low accuracy (51% to 69%) in both CKD and ESRD patients with RDI ≥ 15 . Using an RDI ≥ 30 yielded similar results.

Conclusions: Current screening questionnaires do not accurately identify patients at high risk for OSA or rule out the presence of OSA in patients with CKD and ESRD. Consequently, objective monitoring during sleep is required to reliably identify sleep apnea in these patient populations.

Keywords: Obstructive sleep apnea, chronic kidney disease, end-stage renal disease, Berlin questionnaire, adjusted neck circumference, STOP-BANG questionnaire

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Obstructive sleep apnea (OSA) is common in patients with chronic kidney disease (CKD)¹⁻⁷ and end-stage renal disease (ESRD).^{1,8-12} The prevalence of OSA in these populations has been reported to range from 27% to 54% in CKD patients^{2,3,5-7} and 45% to 70% in ESRD patients,^{1,8-12} which is significantly higher than the general population.¹³ Further, the clinical presentation of OSA in the CKD and ESRD populations differs from that in the general sleep apnea population, reflected by a lower prevalence of sleep related symptoms.^{14,15} Consequently, OSA is more likely to be unrecognized in these populations.

The co-existence of OSA in patients with CKD and ESRD is clinically relevant and has potential to alter important outcomes. In addition to causing impairment of sleep quality and daytime function,^{16,17} OSA increases the risk of vascular disease^{18,19} and systemic hypertension,²⁰ both of which are common complications of CKD and ESRD.²¹ OSA may also accelerate the deterioration of kidney function in patients with CKD, either directly through the effect of hypoxia on the kidney²²⁻²⁴ or indirectly through increases in systemic blood pressure, inflammatory cytokines, and sympathetic nervous system activity.²⁵⁻²⁸ OSA can be effectively treated in many patients with continuous

BRIEF SUMMARY

Current Knowledge/Study Rationale: Patients with Chronic kidney disease (CKD) and end-stage renal disease (ESRD) have a high prevalence of obstructive sleep apnea (OSA) which can have a significant impact on clinical outcomes. We sought to determine the validity of existing OSA screening instruments in patients with CKD and ESRD.

Study Impact: Current OSA screening questionnaires do not accurately identify patients at risk for OSA and do not rule out the presence of OSA in patients with CKD and ESRD. Consequently, objective cardiopulmonary monitoring is needed to reliably identify OSA in these populations.

positive airway pressure (CPAP).²⁹ Consequently, it is important that OSA be recognized and formally diagnosed in these patient populations.

Several instruments have been developed to screen patients for OSA in order to direct objective diagnostic monitoring to those considered at high risk of having the disorder. Given the high prevalence of OSA in patients with CKD and ESRD, an instrument to screen for OSA in these populations would be useful. The Berlin Questionnaire (BQ),³⁰ adjusted neck circumference (ANC),^{31,32} and STOP-BANG³³ questionnaire are three such instruments that have been validated in patients with nor-

mal kidney function, but not in patients with CKD and ESRD. The objective of this study was to determine the diagnostic value of these screening instruments in patients with CKD and ESRD, using overnight cardiopulmonary monitoring to diagnose OSA.

METHODS

Study Subjects

Consecutive adult patients (≥ 18 years) with CKD (defined by an estimated GFR [eGFR] < 60 mL/min/1.73m²)³⁴ and ESRD (requiring thrice weekly conventional hemodialysis) attending outpatient nephrology clinics and dialysis units in Calgary, Alberta, Canada, were invited to participate in the study. eGFR at the time of the study visit was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.³⁵ Exclusion criteria were current treatment with supplemental oxygen, tracheostomy, Cheyne-Stokes respiration (CSR), and inability to give informed consent. Patients currently treated with CPAP therapy were included in the study if their original diagnostic sleep study and sleep questionnaire were available for review and their eGFR at the time of OSA diagnosis was known. The study was approved by the University of Calgary Conjoint Health Research Ethics Board. Informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

Screening Instruments

All patients completed a sleep history questionnaire, which included questions regarding a history of snoring, witnessed apnea during sleep, and nocturnal choking. Additionally, the questionnaire surveyed demographic information and medical history, including a history of hypertension, vascular disease (angina, myocardial infarction, coronary artery bypass surgery, congestive heart failure, stroke, or transient ischemic attack), and diabetes. Each patient's risk of having OSA was estimated from the BQ,³⁰ calculation of the ANC,^{31,32} and STOP-BANG questionnaire.³³

Based on the history of snoring (category 1), daytime sleepiness or fatigue (category 2), and hypertension/obesity (BMI > 30 kg/m²) (category 3), the BQ considers frequent and persistent symptoms in 2 of these 3 categories to indicate a high risk of OSA (**Appendix**).³⁰ The BQ has a sensitivity of 54% and specificity of 97% for a designation criterion of respiratory disturbance index (RDI) ≥ 15 and a sensitivity of 17% and specificity of 97% for a designation criterion of RDI ≥ 30 in a primary care population.³⁰

The ANC is calculated by measuring the patient's neck circumference (in centimetres) and adding additional centimetres if there is a history of hypertension (4 cm), habitual snoring (3 cm), and nocturnal choking (3 cm).^{31,32} An ANC < 43 indicates a low probability of sleep apnea, 43–48 intermediate probability (4 to 8 times as probable as low probability), and > 48 indicates a high probability (20 times as probable).^{31,32}

The STOP-BANG questionnaire consists of 4 simple yes/no questions regarding habitual snoring, tiredness/sleepiness, observed apneas, and high blood pressure.³³ An additional point is added for each of the following clinical characteristics: BMI > 35 kg/m², age > 50 years, neck circumference > 40 cm, and male gender. A score ≥ 3 out of a total possible score of 8

is considered high risk for OSA. The STOP-BANG questionnaire has a sensitivity of 92.9% and specificity of 43.0% for a designation criterion of RDI ≥ 15 , and a sensitivity of 100% and specificity of 37% for a designation criterion of RDI ≥ 30 .³³

Diagnosis of OSA

All patients, regardless of OSA symptoms, performed an unattended, overnight cardiopulmonary monitoring study at home (Remmers Sleep Recorder Model 4.2, Saga Tech Electronic, Calgary, AB, Canada) to determine OSA status. ESRD patients underwent the overnight study after a non-dialysis day. The monitor consists of an oximeter to record oxyhemoglobin saturation (SpO₂) and heart rate variability, a pressure transducer to record nasal airflow, a microphone to record snoring, and a body position sensor. The oximeter provides the data for an automated scoring algorithm, which calculates the RDI based on the number of episodes of oxyhemoglobin desaturation $\geq 4\%$ per hour of monitoring. Nocturnal oxygen saturation was sampled at 1 Hz. The Remmers Sleep Recorder has been validated by comparison to attended polysomnography.^{36,37} Sleep apnea was defined as RDI ≥ 15 and RDI ≥ 30 , which correspond with moderate-severe and severe sleep apnea, respectively, and are most likely to be clinically significant. The Remmers Sleep Recorder has a sensitivity of 98% and specificity of 88% for a designation criterion of RDI ≥ 15 , and a sensitivity of 95% and specificity of 93% for a designation criterion of RDI ≥ 30 .³⁷ The raw data were reviewed by a sleep medicine physician (PJH), blinded to patients' kidney function and symptoms, who confirmed that the estimated RDI was accurate and determined whether apnea was central (CSR) or obstructive (OSA), based on the morphology of the airflow recordings. Nasal pressure recordings with a characteristic crescendo/decrecendo pattern and no evidence of airflow limitation were classified as CSR, whereas recordings without a crescendo/decrecendo pattern and with airflow limitation were classified as OSA.

Analysis

Data are presented as mean $\pm$ standard deviation or number (percentage), unless otherwise indicated. Estimated OSA risk, as assessed by the BQ, ANC, and STOP-BANG questionnaire, was compared to the diagnosis of OSA (RDI ≥ 15 and ≥ 30 , respectively) as determined by objective cardiopulmonary monitoring for both CKD and ESRD patients. Subjects with CSR were excluded from our primary analyses, but were included as part of a sensitivity analysis. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), accuracy (total number of correct risk assessments divided by total number of risk assessments), and area under the receiver operating characteristic (ROC) curve (AUC) were calculated for high risk for the BQ, both moderate to high risk (≥ 43 cm) and high risk (> 48 cm) for the ANC, and high risk for the STOP-BANG questionnaire at moderate (RDI ≥ 15) and severe (RDI ≥ 30) diagnostic criteria for OSA. These were undertaken for CKD and ESRD patients separately. The unpaired t-test or the Mann-Whitney U-test was used for comparisons between continuous variables, while the χ^2 test with Fischer's Exact Test was used for dichotomous variables. Finally, we examined the impact of using higher thresholds to assess OSA risk in the ANC (> 53 cm) and the STOP-BANG questionnaire (≥ 4). All statistical analyses were two-sided and performed with SPSS

V.17.0 (SPSS, Chicago, IL, USA). P-values < 0.05 were considered statistically significant.

RESULTS

Patient Recruitment

Six hundred fifty-seven patients were informed of the study between May 2007 and November 2010 (**Figure 1**); 254 patients declined to participate. In addition, eGFR was too high (≥ 60) in 87 patients, and 14 patients did not complete the questionnaires. The remaining 302 patients (CKD, $n = 174$; ESRD, $n = 128$) were eligible for cardiopulmonary monitoring, which was declined by 116 patients (CKD: $n = 61$; ESRD: $n = 56$). One hundred thirteen CKD patients and 72 ESRD patients completed cardiopulmonary monitoring. Thirteen patients with CSR (CKD, $n = 4$; ESRD, $n = 9$) were excluded from further analyses, resulting in a final study population of 109 CKD patients and 63 ESRD patients. Eight CKD patients and 5 ESRD patients were currently treated with CPAP.

Chronic Kidney Disease

Patient Characteristics

CKD patient characteristics stratified by OSA status ($\text{RDI} \geq 15$) are presented in **Table 1**. The mean duration of nocturnal cardiopulmonary monitoring was 7.3 ± 1.5 h for CKD patients, while the proportion of monitoring time that patients reported sleeping was $81\% \pm 15\%$. Consequently, estimated sleep efficiency and monitoring time were sufficiently long to capture important respiratory events. Moderate to severe OSA ($\text{RDI} \geq 15$) was present in 38% of CKD patients. Using a more conservative definition of OSA ($\text{RDI} \geq 30$), the prevalence of OSA remained high at 23%. As expected, the severity of associated nocturnal hypoxemia was greater in CKD patients with OSA. CKD patients with OSA had an increased BMI and greater neck circumference, but did not differ from CKD patients without OSA in terms of age or gender distribution.

There were no differences in the individual categories or the final assessed risk of the BQ between CKD patients with and without OSA, although category 1 (snoring) and final risk were of borderline significance. Using the ANC, CKD patients with OSA had greater neck circumference than CKD patients without OSA, although nocturnal choking was of borderline significance. However, these components contributed to higher ANC scores, which resulted in a greater proportion of CKD patients with OSA being assessed as higher risk. Component analyses of the STOP-BANG questionnaire revealed that CKD patients with OSA were more likely to report a history of witnessed apneas, have a BMI > 35 kg/m², and neck circumferences > 40 cm. Male gender and age > 50 years were of borderline significance. Accordingly, this corresponded to higher STOP-BANG total scores and a greater proportion of CKD patients with OSA being assessed as high risk.

Performance of Screening Instruments

The sensitivity, specificity, PPV, and NPV for a positive BQ, ANC, and STOP-BANG to identify OSA in patients with CKD using RDI thresholds of 15 and 30 are shown in **Table 2**.

Figure 1—Patient recruitment

CSR, Cheyne-Stokes respiration; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; RSR, Remmers Sleep Recorder.

Using an $\text{RDI} \geq 15$, the BQ, $\text{ANC} \geq 43$, and STOP-BANG performed with good sensitivity but poor specificity; an $\text{ANC} > 48$ had a modest sensitivity and specificity. The BQ, ANC, and STOP-BANG had good NPVs, but poor PPVs. The accuracies of the BQ, $\text{ANC} \geq 43$, $\text{ANC} > 48$, and STOP-BANG were 52%, 58%, 69%, and 54%, respectively, for identifying OSA at an $\text{RDI} \geq 15$.

At an $\text{RDI} \geq 30$, the BQ, $\text{ANC} \geq 43$, and STOP-BANG had high sensitivity but poor specificity, while an $\text{ANC} > 48$ had both a modest sensitivity and specificity. The BQ, ANC, and STOP-BANG had good NPVs, but poor PPVs. The accuracies of the BQ, $\text{ANC} \geq 43$, $\text{ANC} > 48$, and STOP-BANG were 45%, 47%, 69%, and 45%, respectively, for identifying OSA using a $\text{RDI} \geq 30$.

Inclusion of the 4 subjects with CSR did not alter these results. Increasing the threshold for the ANC (> 53) resulted in improved specificity and PPV at the expense of reduced sensitivity and NPV. Accuracy was not improved at $\text{RDI} \geq 15$, but was improved to 76% at $\text{RDI} \geq 30$. Increasing the threshold for the STOP-BANG (≥ 4) improved specificity and PPV and mildly reduced sensitivity and NPV at both RDI thresholds. Accuracy was increased to 64% at $\text{RDI} \geq 15$ and 57% at $\text{RDI} \geq 30$.

End-Stage Renal Disease

Patient Characteristics

ESRD patient characteristics stratified by OSA status ($\text{RDI} \geq 15$) are presented in **Table 3**. The mean duration of nocturnal cardiopulmonary monitoring was 6.4 ± 2.0 h for ESRD patients, while the proportion of monitoring time that patients reported sleeping was $78\% \pm 18\%$ for ESRD. Consequently,

Table 1—Chronic kidney disease patient characteristics

Parameter	All Subjects N = 109	OSA N = 41	No Apnea N = 68	p-value
Nocturnal Monitoring				
RDI/h	10.5 (0.5, 127)	36.2 (15.0, 127)	6.5 (0.5, 14.6)	< 0.001
RDI ≥ 15	41 (38)	—	—	—
RDI ≥ 30	25 (23)	—	—	—
Mean SpO ₂ , %	91.6 ± 3.1	89.6 ± 3.2	92.8 ± 2.3	< 0.001
SpO ₂ < 90%, % monitoring time	7.5 (0.0, 94.0)	34.1 (1.2, 94.0)	1.9 (0.0, 82.9)	< 0.001
Demographics				
Age, years	65 ± 12	66 ± 10	64 ± 13	0.403
Male gender	67 (61)	30 (73)	37 (54)	0.068
BMI, kg/m ²	31.1 ± 8.3	34.1 ± 9.9	29.2 ± 6.6	0.007
Neck circumference, cm	40.7 ± 4.8	43.3 ± 4.5	39.2 ± 4.4	< 0.001
Berlin Questionnaire				
Category 1	70 (64)	31 (76)	39 (57)	0.065
Category 2	36 (33)	17 (41)	19 (28)	0.207
Category 3	103 (94)	39 (95)	64 (94)	1.000
High risk	79 (72)	34 (83)	45 (66)	0.077
Adjusted Neck Circumference				
Neck circumference, cm	40.7 ± 4.8	43.3 ± 4.5	39.2 ± 4.4	< 0.001
Hypertension	102 (94)	38 (93)	64 (94)	1.000
Habitual snoring	81 (74)	32 (78)	49 (72)	0.651
Nocturnal choking	34 (31)	17 (41)	17 (25)	0.089
Total score, cm	47.4 ± 5.4	50.3 ± 5.0	45.7 ± 5.0	< 0.001
Risk, ≥ 43 cm	81 (74)	38 (93)	43 (63)	0.001
Risk, > 48 cm	45 (41)	26 (63)	19 (28)	0.001
Risk, > 53 cm	21 (19)	14 (34)	7 (10)	0.005
STOP-BANG				
S: Do you snore loudly?	36 (33)	17 (41)	19 (28)	0.207
T: Do you often feel tired, fatigued, or sleepy during the daytime?	42 (39)	18 (44)	24 (35)	0.420
O: Has anyone ever observed you stop breathing during your sleep?	15 (14)	10 (24)	5 (7)	0.020
P: Do you have high blood pressure?	102 (94)	38 (93)	64 (94)	1.000
B: BMI > 35 kg/m ² ?	22 (20)	14 (34)	8 (12)	0.007
A: Age > 50 years?	95 (87)	39 (95)	56 (82)	0.076
N: Neck circumference > 40 cm?	59 (54)	34 (83)	25 (37)	< 0.001
G: Gender male?	67 (61)	30 (73)	37 (54)	0.068
Total Score, median (range)	4 (1, 8)	5 (2, 8)	3 (1, 7)	< 0.001
Risk, ≥ 3	85 (78)	38 (93)	47 (69)	0.004
Risk, ≥ 4	66 (61)	34 (83)	32 (47)	< 0.001

Data are mean ± SD or number (percentage) of patients within group unless otherwise indicated. OSA, obstructive sleep apnea; RDI, respiratory disturbance index; SpO₂, oxyhemoglobin saturation; BMI, body mass index.

monitoring time and estimated sleep efficiency were sufficiently long to capture important respiratory events. Moderate to severe OSA (RDI ≥ 15) was present in 51% of ESRD patients, and the prevalence of severe OSA (RDI ≥ 30) was also high at 40%. The severity of nocturnal hypoxemia was greater in ESRD patients with OSA. ESRD patients with OSA had an increased BMI and greater neck circumference, but did not differ from ESRD patients without OSA in terms of age or gender distribution.

There were no differences in the individual categories or the final assessed risk of the BQ between ESRD patients with and without OSA. Similarly, apart from neck circumference, there were no differences in the other components of the ANC between ESRD patients with and without OSA. However, the increased neck circumference resulted in higher ANC scores and corresponded to a greater proportion of ESRD patients

with OSA being assessed as higher risk. Component analyses of the STOP-BANG questionnaire revealed that ESRD patients with OSA were more likely to report loud snoring, a history of witnessed apneas, have a BMI > 35 kg/m², and neck circumferences > 40 cm. Accordingly, this resulted in higher STOP-BANG total scores and a greater proportion of ESRD patients with OSA being assessed as high risk.

Performance of Screening Instruments

The sensitivity, specificity, PPV, and NPV for a positive BQ, ANC, and STOP-BANG in identifying OSA in ESRD patients are shown in **Table 4**.

At an RDI ≥ 15, an ANC ≥ 43 and STOP-BANG had good sensitivity, but poor specificity. The BQ had modest sensitivity but poor specificity, while an ANC > 48 had both modest sensitivity and specificity. Each screening instrument had a moderate

Table 2—Diagnostic value of obstructive sleep apnea screening instruments in chronic kidney disease patients

		Adjusted Neck Circumference			STOP -BANG	
	Berlin	≥ 43	> 48	> 53	≥ 3	≥ 4
RDI ≥ 15						
Sensitivity, %	83	93	63	34	93	83
Specificity, %	34	37	72	90	31	53
PPV, %	43	47	58	67	45	52
NPV, %	77	89	77	69	88	84
Accuracy, %	52	58	69	69	54	64
AUC, % (95% CI)	58 (48-69)	65 (55-75)	68 (57-78)	62 (51-73)	62 (51-72)	68 (58-78)
RDI ≥ 30						
Sensitivity, %	88	96	72	40	100	88
Specificity, %	32	32	68	87	29	48
PPV, %	28	30	40	48	29	33
NPV, %	90	96	89	83	100	93
Accuracy, %	45	47	69	76	45	57
AUC, % (95% CI)	60 (48-72)	64 (53-75)	70 (58-82)	64 (50-77)	64 (54-75)	68 (57-79)

RDI, respiratory disturbance index; PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver operating characteristic curve; CI, confidence interval.

PPV and NPV. The accuracies of the BQ, ANC ≥ 43, ANC > 48, and STOP-BANG were 51%, 67%, 67%, and 62%, respectively, for determining OSA using RDI ≥ 15.

At an RDI ≥ 30, the BQ and an ANC ≥ 43 had moderate sensitivity and NPV, but poor specificity and PPV. An ANC > 48 had moderate sensitivity, specificity, PPV, and NPV. The STOP-BANG had excellent sensitivity and NPV, but poor specificity and PPV. The accuracies of the BQ, ANC ≥ 43, ANC > 48, and STOP-BANG were 55%, 56%, 71%, and 54%, respectively, for determining OSA using a RDI ≥ 30.

Inclusion of the 9 subjects with CSR did not alter these results. Increasing the threshold for the ANC (> 53) resulted in improved specificity and PPV at the expense of reduced sensitivity and NPV, but did not improve accuracy, at both RDI ≥ 15 and ≥ 30. However, increasing the threshold for the STOP-BANG (≥ 4) improved specificity and PPV, while maintaining good sensitivity and NPV at both RDI thresholds. Accuracy was increased to 75% at an RDI ≥ 15 and 67% at an RDI ≥ 30.

DISCUSSION

This is the first study to systematically examine the validity of OSA screening questionnaires in the CKD and ESRD populations using objective cardiopulmonary monitoring to diagnose OSA. We found that (a) OSA screening instruments had limited accuracy in the CKD and ESRD populations, with accuracies ranging between 45% to 69% in CKD patients and 51% to 71% in ESRD patients at RDI levels of 15 and 30, respectively; (b) the ANC was the most accurate screening tool in both the CKD and ESRD populations; (c) the ANC and STOP-BANG assigned more CKD and ESRD patients with OSA as high risk; and (d) the BQ was unable to distinguish between CKD and ESRD patients with and without OSA.

Several small studies have reported increased OSA risk in the dialysis³⁸⁻⁴⁰ and transplant⁴¹ populations using the Berlin questionnaire, but in contrast to this study, none included objective overnight monitoring to confirm the diagnosis of OSA.

We found that the BQ had a better sensitivity but poorer specificity and predictive value in both the CKD and ESRD populations compared to measures obtained in the initial validation in the primary care setting.³⁰ The ANC has not been validated outside of a sleep centre population.^{31,32} The STOP-BANG questionnaire performed similarly in our CKD and ESRD populations to what has previously been reported in the preoperative assessment of surgical patients³³ and in a more recent community study.⁴²

In order to screen patients for a disorder with an important health outcome, a good screening tool requires a high sensitivity with an acceptable specificity. Overall, we found the BQ, ANC, and STOP-BANG demonstrated high sensitivities, but the specificities were significantly below acceptable levels. High sensitivities are useful in order to avoid missing cases that may lead to adverse health outcomes and healthcare costs, but low specificities result in the inclusion of low-risk patients and higher false positive rates. This limits the utility of these screening tools in the patient population we studied. Given the good negative predictive values we found, there may be a role for these screening questionnaires to exclude OSA and avoid further testing. However, further evaluation will be required in those who have a positive screening questionnaire. Of interest, increasing the thresholds for the ANC and STOP-BANG questionnaire did improve accuracy in our CKD and ESRD patients. However, further studies are required to examine the use of alternative thresholds for OSA diagnosis in these populations, as well as to examine the implications and efficacy of these screening strategies. The poor performance of the BQ is consistent with what has been demonstrated in other disease-specific populations. Although the BQ performed well in the primary-care setting³⁰ and in patients with atrial fibrillation⁴³ and resistant hypertension,⁴⁴ it did not effectively screen for OSA in the stroke,⁴⁵ systemic hypertension,⁴⁶ and sleep clinic populations,⁴⁷ nor in patients who were evaluated following acute myocardial infarction.⁴⁸ To date, the ANC and the STOP-BANG have not been validated in disease-specific populations.

Table 3—End-stage renal disease patient characteristics

Parameter	All Subjects N = 63	OSA N = 32	No Apnea N = 31	p-value
Nocturnal Monitoring				
RDI/h	16.6 (0.4, 112)	41.0 (16.6, 112)	6.1 (0.4, 13.7)	< 0.001
RDI ≥ 15	32 (51)	—	—	—
RDI ≥ 30	25 (40)	—	—	—
Mean SpO ₂ , %	91.7 ± 3.7	90.3 ± 2.9	93.2 ± 3.2	< 0.001
SpO ₂ < 90%, % monitoring time	10.8 (0.0, 94.9)	30.9 (2.3, 94.9)	0.5 (0.0, 87.1)	< 0.001
Demographics				
Age, years	61 ± 14	62 ± 14	59 ± 16	0.501
Male Gender	42 (67)	24 (75)	18 (58)	0.188
BMI, kg/m ²	27.2 ± 6.5	30.0 ± 7.0	24.3 ± 4.5	< 0.001
Neck Circumference, cm	41.3 ± 5.9	44.0 ± 6.0	38.6 ± 4.5	< 0.001
Berlin Questionnaire				
Category 1	36 (57)	21 (66)	15 (48)	0.207
Category 2	20 (32)	8 (25)	12 (39)	0.287
Category 3	59 (94)	29 (91)	29 (94)	1.000
High Risk	41 (65)	22 (69)	19 (61)	0.603
Adjusted Neck Circumference				
Neck circumference, cm	41.3 ± 5.9	44.0 ± 6.0	38.6 ± 5.0	< 0.001
Hypertension	59 (94)	29 (91)	30 (97)	0.613
Habitual snoring	44 (70)	23 (72)	21 (68)	0.788
Nocturnal choking	14 (22)	10 (31)	4 (13)	0.129
Total score, cm	47.6 ± 6.5	50.4 ± 6.4	44.6 ± 5.4	< 0.001
Risk, ≥ 43 cm	45 (71)	28 (88)	17 (55)	0.005
Risk, > 48 cm	25 (40)	18 (56)	7 (23)	0.010
Risk, > 53 cm	13 (21)	11 (34)	2 (6)	0.011
STOP-BANG				
S: Do you snore loudly?	17 (27)	13 (41)	4 (13)	0.022
T: Do you often feel tired, fatigued, or sleepy during the daytime?	32 (51)	17 (53)	15 (48)	0.803
O: Has anyone ever observed you stop breathing during your sleep?	11 (17)	10 (31)	1 (3)	0.006
P: Do you have high blood pressure?	59 (94)	29 (91)	30 (97)	0.613
B: BMI > 35 kg/m ² ?	6 (10)	6 (19)	0 (0)	0.024
A: Age > 50 years?	46 (73)	24 (75)	22 (71)	0.782
N: Neck circumference > 40 cm?	36 (57)	26 (81)	10 (32)	< 0.001
G: Gender male?	42 (67)	24 (75)	18 (58)	0.188
Total Score, median (range)	4 (1, 7)	5 (2, 7)	3 (1, 5)	< 0.001
Risk, ≥ 3	52 (83)	30 (94)	22 (71)	0.022
Risk, ≥ 4	40 (63)	28 (88)	12 (39)	< 0.001

Data are mean ± SD or number (percentage) of patients within group unless otherwise indicated. OSA, obstructive sleep apnea; RDI, respiratory disturbance index; SpO₂, oxyhemoglobin saturation; BMI, body mass index; ANC, adjusted neck circumference.

The high prevalence of hypertension, which was found in over 90% of our patients and was equally common in those with and without OSA, is one reason the BQ, ANC, and STOP-BANG were unable to reliably distinguish patients with and without OSA in the CKD and ESRD populations. By definition, most CKD and ESRD patients have hypertension either as a cause or consequence of kidney disease.²¹ Additionally, the reliance of these screening questionnaires on sleep related symptoms, such as snoring, witnessed apneas, nocturnal choking, and daytime sleepiness, limit their accuracy in CKD and ESRD patients, as these populations are less likely to present with the stereotypical features of OSA.^{14,15} Furthermore, fatigue is a common symptom of CKD and ESRD, which can overlap with complaints of sleepiness and develop independently of sleep disordered breathing.^{49,50} Fluid status is another potential confounder that is thought to influence upper airway obstruction and neck cir-

cumference in kidney failure patients.⁵¹⁻⁵⁴ Although it is possible that fluid accumulation in the neck accounted for some of the increased neck circumference in patients with OSA, our study was not designed to evaluate this. However, we tried to minimize the potential for fluid status to confound our results by standardizing when ESRD patients were evaluated in relation to the time they received dialysis. Further, the dichotomous categorization of age (> 50 years) used in the STOP-BANG questionnaire is also a limitation as CKD and ESRD are more prevalent in the elderly.⁵⁵ Consequently, the presence of these factors could significantly reduce the accuracy of these screening tools.

Our study has a number of strengths. First, we recruited a relatively large sample size from a renal population representative of the general CKD and ESRD populations, which increases the relevance of our findings to these patient populations. In fact, our CKD population had a similar clinical profile to the Chronic

Table 4—Diagnostic value of obstructive sleep apnea screening instruments in end-stage renal disease patients

		Adjusted Neck Circumference			STOP -BANG	
	Berlin	≥ 43	> 48	> 53	≥ 3	≥ 4
RDI ≥ 15						
Sensitivity, %	69	88	56	34	94	88
Specificity, %	39	45	77	94	29	61
PPV, %	54	62	72	85	58	70
NPV, %	55	78	63	58	82	83
Accuracy, %	51	67	67	63	62	75
AUC, % (95% CI)	54 (39, 68)	66 (53, 80)	67 (53, 80)	64 (50, 78)	61 (48, 75)	74 (62, 87)
RDI ≥ 30						
Sensitivity, %	76	84	64	40	96	88
Specificity, %	42	37	76	92	26	53
PPV, %	46	47	64	77	46	55
NPV, %	73	78	76	70	91	87
Accuracy, %	55	56	71	71	54	67
AUC, % (95% CI)	59 (45, 73)	60 (46, 75)	70 (57, 84)	66 (52, 81)	61 (47, 75)	70 (57, 87)

RDI, respiratory disturbance index; PPV, positive predictive value; NPV, negative predictive value; AUC, area under receiver operating characteristic curve; CI, confidence interval.

Renal Insufficiency Cohort study,⁵⁶ and our ESRD population resembled a larger cohort of ESRD patients from the Southern Alberta Renal Program.⁵⁷ Second, we used the same methodology, including objective cardiopulmonary monitoring, in patients with a broad spectrum of kidney disease, which enabled us to compare the accuracy of these screening instruments in the CKD and ESRD populations. Third, no inclusion or exclusion criteria were set with respect to age, gender, comorbidities, or medications, which improved the generalizability of our findings to the CKD and ESRD populations. Notwithstanding these strengths, our study also has limitations. First, the potential for selection bias exists as patients attending the nephrology clinics may have been more likely to participate if they suspected they had sleep apnea. We tried to limit this by emphasizing that sleep related complaints were not required for recruitment. If such a bias did exist, it should have been reflected in a higher prevalence of sleep related symptoms and higher accuracy of the screening instruments, which was not the case. Second, we used portable monitoring in place of polysomnography. The RDI was calculated based on monitoring time rather than objective sleep duration and thus the frequency of OSA events could have been underestimated. Further, this methodology did not employ a measurement of respiratory effort and consequently we could only estimate the prevalence of central sleep apnea based on the morphology of the nasal pressure recording. We addressed these potential limitations by asking patients to estimate their sleep time, and having the portable monitoring results reviewed by a sleep medicine physician to determine whether the findings were consistent with either Cheyne-Stokes respiration or OSA.

In summary, our study demonstrates that current screening questionnaires do not accurately identify patients at high risk for OSA or rule out the existence of OSA in patients with CKD and ESRD. This is unfortunate given the high prevalence of OSA in these patient populations¹⁻¹² and its potential impact on important clinical outcomes.^{16-20,22-28} Further studies are required to develop and validate more accurate screening strate-

gies for OSA in patients with CKD and ESRD. In the meantime, objective cardiopulmonary monitoring during sleep is required to reliably identify sleep apnea in these patients.

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Appendix—Berlin Questionnaire and scoring algorithm

Category 1: snoring positive if ≥ 2 points scored for the following items:		Category 2: daytime fatigue and sleepiness positive if ≥ 2 points scored for the following items:	
Do you snore?		How often do you feel tired or fatigued after you sleep?	
Yes	1	Nearly every day	1
No/Don't Know	0	3-4 times a week	1
If you snore, your snoring is:		1-2 times a week	0
Slightly louder than breathing	0	1-2 times a month	0
As loud as talking	0	Never or nearly never	0
Louder than talking	1	During your waking time, do you feel tired, fatigued or not up to par?	
Very loud-can be heard in adjacent rooms	1	Nearly every day	1
How often do you snore?		3-4 times a week	1
Nearly every day	1	1-2 times a week	0
3-4 times a week	1	1-2 times a month	0
1-2 times a week	0	Never or nearly never	0
1-2 times a month	0	Have you ever nodded off or fallen asleep while driving a vehicle?	
Never or nearly never	0	Yes	1
Has your snoring ever bothered other people?		No	0
Yes	1	If yes, how often does this occur?	
No/Don't Know	0	Nearly every day	1
Has anyone ever noticed that you quit breathing during your sleep?		3-4 times a week	1
Nearly every day	1	1-2 times a week	0
3-4 times a week	1	1-2 times a month	0
1-2 times a week	0	Never or nearly never	0
1-2 times a month	0		
Never or nearly never	0		
		Category 3: is positive if ≥ 1 point scored for the following items:	
		Do you have high blood pressure?	
		Yes	1
		No/Don't Know	0
		OR BMI > 30 kg/m ²	
		> 30	1
		≤ 30	0

Participants are classified as high risk if two or more categories are positive and low risk if fewer than two categories are positive.