Unstable periodontal disease and its association with sleep-disordered breathing

Katherine C. Schacherl, DDS ■ Shengtong Han, PhD ■ John A. Schacherl, DDS ■ Andrew Dentino, DDS, PhD

Periodontal therapy results in successful disease management for some patients, but patients whose periodontal disease cannot be managed with standard-of-care protocols are treated repeatedly without success. For this set of patients, a systemic rather than an oral origin is possible. This clinical study investigated the connection between unresolved periodontal disease and sleep-disordered breathing (SDB) in 71 patients (44 women and 27 men), aged 19 to 75 years (mean, 45 years), who were enrolled in periodontal maintenance therapy for Stage I or II periodontitis. The results of an at-home sleep testing device served as the basis for evaluating 4 SDB screening tools: Papillary Bleeding Index (PBI), Epworth Sleepiness Scale (ESS) questionnaire, STOP-Bang questionnaire, and salivary cortisol testing. At-home sleep testing indicated that 33 participants had an apnea-hypopnea index ≥ 5, signifying probable obstructive sleep apnea. A finding of unstable periodontal disease (PBI ≥ 2) was able to identify 21 of these 33 participants, while the ESS and STOP-Bang questionnaires identified only 2 and 6 participants, respectively. The difference between the PBI and both the ESS and STOP-Bang questionnaires was statistically significant ($P < 0.05$; 2-sample proportion test). There was no relationship between participants' cortisol levels and the PBI findings. This clinical study found a link between unresolved periodontal disease and SDB. The results of this study suggested that the PBI is a reliable, objective means for general dentists to identify SDB in patients with unresolved periodontal disease. Once identified, these patients can be referred for treatment to address their SDB, which may positively impact management of their periodontal disease.

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Periodontal disease is a chronic inflammatory disease of the periodontium that affects an estimated 20% to 50% of the global population.[1,2] Its development begins with gingivitis, inflammation of the oral gingival tissues. Untreated gingivitis may develop into periodontal disease, a chronic, infectious inflammatory disease defined by hard and soft tissue loss. Its advanced form is characterized by periodontal ligament loss and destruction of the surrounding alveolar bone. Periodontal disease is the main cause of tooth loss and is considered a threat to both oral and systemic health.

Some patients with periodontal disease can manage their disease through conventional treatment. The goal of periodontal treatment is to help patients achieve control of their disease and stability of their periodontal health, preventing further bone and tissue loss. Nonsurgical treatments include manual scaling and root planing, ultrasonic scaling, guided biofilm therapy with airflow polishers, and localized and systemic delivery of antibiotics. Some patients may benefit from surgical treatment, which can include bony recontouring, pocket reduction surgery, and hard and soft tissue regeneration procedures. However, there is a subset of periodontal patients who are unable to manage their disease with the current standard of care. This group of patients never achieves stable periodontal health, despite repeated periodontal treatments performed at shorter recall intervals.

The long-term negative health effects of chronic oral inflammation continue to be extensively studied within medicine. Reports of the relationship between poor oral health and the risk of poor cardiovascular health (heart attack and stroke), neurologic health (Alzheimer disease), obstetric outcomes (low birth weight and premature birth), and diabetic health are widespread in the literature.[3-6] These relationships can be bidirectional.[3,5]

Another condition with multiple systemic ramifications is sleep-disordered breathing (SDB), characterized by repeated occurrences of hypopnea or apnea.[7] Prolonged overactivation of the sympathetic nervous system during SDB may induce unfavorable health consequences, including the creation of a chronic inflammatory state and hypothalamic-pituitary-adrenal axis hyperactivity, resulting in a constant presence of cortisol.[7,8] The cortisol from the prolonged sympathetic drive, in combination with the inflammation associated with periodontal disease, may be a reason that a subset of patients with periodontitis cannot heal.

In 2017, the American Dental Association adopted a policy encouraging dentists to screen patients for SDB as part of a comprehensive medical and dental history.[9] The policy suggests that dentists evaluate patients for risk factors such as obesity, retrognathia, or hypertension and learn to recognize symptoms of SDB, including daytime sleepiness, snoring,

choking, or witnessed apneas, so that they can refer patients for appropriate medical follow-up and diagnosis.[9]

Based on the hypothesis that some patients with unresolved Stage I or II periodontal disease may have undiagnosed and untreated SDB that creates a host environment conducive to unstable periodontal disease, the present study sought to evaluate changes in a participant's papillary bleeding index (PBI) before and after periodontal maintenance therapy as a potential screening tool for SDB in patients whose periodontal disease has not responded to standard-of-care protocols. The results of an at-home sleep testing device served as the basis for comparing the reliability of the PBI, Epworth Sleepiness Scale (ESS) questionnaire, STOP-Bang questionnaire, and salivary cortisol testing as screening tools for SDB.

Methods

This study was completed at the Marquette University School of Dentistry, Milwaukee, Wisconsin, and was approved by the Office of Research Compliance (reference HR-3522). Prior to signing an informed consent, participants were informed of their right to withdraw from the study at any time without consequence. Only the principal investigator (K.C.S.) had immediate access to all cortisol and sleep data to monitor for results that would require participant removal from the study.

A single examiner (J.A.S.) performed the PBI evaluations for all participants. The PBI examiner did not have access to any sleep, cortisol, or PBI data until after the second PBI examination at 8 weeks. All PBI examination data were entered by trained dental assistants.

Participants

The participants in this study were 71 patients (44 women [62%] and 27 men [38%]), aged 19 to 75 years (mean age, 45 years), attending a private practice for periodontal therapy. All of the patients had previously undergone treatment for Stage I or II periodontitis as defined at the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (Table 1).[10] The study criteria required participants to exhibit consistently good home care, have minimally visible clinical plaque or radiographic calculus, and have no current diagnosis of SDB.

Patients were excluded if they had severe chronic obstructive pulmonary disease, asthma, cardiac arrhythmias, atrial fibrillation, ventricular bigeminy, or medical adhesive allergy; if they used tobacco in any form; or if they were pregnant. Once a patient was enrolled in the study, there was an additional exclusion criterion to ensure patient safety, determined using the results of sleep screening with technology based on photoplethysmography (PPG). If the sleep screening completed as part of the study demonstrated severe SDB based on periodicity (defined as an elevated low-frequency coupling narrow band [greater than 40%]), the participant would be excluded from further participation in the study and referred directly to a sleep medicine specialist.[11] No participant met this exclusion criterion.

Examinations and maintenance therapy

Each study participant was seen at 2 in-clinic appointments. At the first appointment, the participant met with a trained dental assistant who screened the participant using the STOP-Bang and the Epworth Sleepiness Scale (ESS) questionnaires.[12-15] The participant's body mass index (BMI) was computed based on their self-reported height and weight. The participant then met with the PBI examiner, who performed the PBI examination and recorded the results.[16-18]

Following the PBI examination, the participant received a periodontal maintenance cleaning with a registered dental hygienist. The periodontal maintenance cleaning included the use of hand instruments, ultrasonic instruments, and airflow polishers to disrupt biofilm and completely remove all soft and hard deposits. Personalized home care instructions were given to each participant. At the conclusion of this appointment, the participant was given an at-home sleep testing device (SleepImage Pulse, model PO2, MyCardio) and instructed as to its use.[19,20] The participant was also given an at-home salivary cortisol testing kit (Sanesco International) and instructed as to its use.

The participant's second clinical appointment occurred 8 weeks later, when the PBI examiner performed the second PBI examination and recorded the results. The participant also received the results of the at-home sleep and cortisol tests at this appointment.

Papillary Bleeding Index

The study participants received 2 PBI examinations, 8 weeks apart. The PBI differentiates 4 intensities of bleeding after the gingival sulcus is swept with a blunt periodontal probe in defined papillary regions of the mouth. The sweeping is done in all 4 quadrants, in a specific order, to a maximum of 28 sites per participant. The oral/lingual regions are probed in the first (maxillary right) and third (mandibular left) quadrants, and the facial/buccal regions are probed in the second (maxillary left) and fourth (mandibular right) quadrants.[16-18] After the designated tissue in the quadrant is swept, 20 to 30 seconds are allowed to elapse, after which the intensity of the bleeding is assigned PBI grade 1 to 4 using the following parameters as defined by Saxer and Mühlemann's 1975 article and cited by Wolf et al in 2005: 1, a single point of bleeding is noted; 2, a fine line of blood or several bleeding points become visible at the gingival margins; 3, the interdental triangle becomes more or less filled with blood; or 4, there is profuse bleeding—immediately after probing, blood flows into the interdental area to cover portions of the tooth and/or gingiva (Figure).[17,18] The sum of all recorded scores provides the bleeding number. To calculate the PBI, the bleeding number is divided by the total number of papillae examined.

Epworth Sleepiness Scale

The daytime sleepiness experienced by participants was assessed with the ESS. The ESS is a subjective questionnaire comprising a series of questions that provides a score of 0 to 24 to describe daytime sleepiness.[12,13] A score of 0 to 5 indicates lower normal daytime sleepiness; 6 to 10 indicates higher normal daytime sleepiness; 11 to 12 indicates mild excessive daytime sleepiness; 13 to 15 indicates moderate excessive daytime sleepiness; and 16 to 24 indicates severe daytime sleepiness.[21]

Table 1. Stages of periodontitis.[a]

Periodontitis stage[b]		Stage I	Stage II	Stage III	Stage IV
Severity	Interdental CAL at site of greatest loss	1-2 mm	3-4 mm	≥ 5 mm	≥ 5 mm
	RBL	Coronal third (< 15%)	Coronal third (15% to 33%)	Extending to middle or apical third of the root	Extending to middle or apical third of the root
	Tooth loss	No tooth loss due to periodontitis		Tooth loss due to periodontitis of ≤ 4 teeth	Tooth loss due to periodontitis of ≥ 5 teeth
Complexity	Local	Maximum probing depth ≤ 4 mm Mostly horizontal bone loss	Maximum probing depth ≤ 5 mm Mostly horizontal bone loss	In addition to stage II complexity: Probing depth ≥ 6 mm Vertical bone loss ≥ 3 mm Furcation involvement (Class II or III) Moderate ridge defect	In addition to stage III complexity: Need for complex rehabilitation due to: Masticatory dysfunction Secondary occlusal trauma (tooth mobility degree ≥ 2) Severe ridge defect Bite collapse, drifting, flaring Less than 20 remaining teeth (10 opposing pairs)
Extent and distribution	Add to stage as a descriptor	For each stage, describe extent as localized (< 30% of teeth involved), generalized, or molar/incisor pattern			

Abbreviations: CAL, clinical attachment loss; RBL, radiographic bone loss.

[a]Reprinted with permission from Wiley. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: framework and proposal of a new classification and case definition. *J Clin Periodontol*. 2018;45(Suppl 20):S149-S161. Erratum: 2019;46(7):787. doi:10.1111/jcpe.12945 ©2018.[10]

[b]The initial stage should be determined using CAL; if not available then RBL should be used. Information on tooth loss that can be attributed primarily to periodontitis—if available—may modify stage definition. This is the case even in the absence of complexity factors. Complexity factors may shift the stage to a higher level; for example, furcation II or III would shift to either stage III or IV irrespective of CAL. The distinction between stage III and stage IV is primarily based on complexity factors. For example, a high level of tooth mobility and/or posterior bite collapse would indicate a stage IV diagnosis. For any given case, only some, not all, complexity factors may be present; however, in general it only takes one complexity factor to shift the diagnosis to a higher stage. It should be emphasized that these case definitions are guidelines that should be applied using sound clinical judgment to arrive at the most appropriate clinical diagnosis.

For posttreatment patients, CAL and RBL are still the primary stage determinants. If a stage-shifting complexity factor(s) is eliminated by treatment, the stage should not retrogress to a lower stage since the original stage complexity factor should always be considered in maintenance phase management.

STOP-Bang questionnaire

Each participant's probability of having obstructive sleep apnea (OSA) was evaluated with the STOP-Bang questionnaire, which classifies an individual's risk for OSA based on the following parameters: *s*noring; *t*iredness; *o*bserved breathing cessation, choking, or gasping; blood *p*ressure; *b*ody mass index; *a*ge; *n*eck size; and *g*ender. The STOP-Bang instrument is a subjective questionnaire comprising 8 yes/no questions.[14,15] A yes response to questions in the STOP section is more heavily weighted. An answer of yes to 0 to 2 questions indicates a low risk, 3 to 4 questions an intermediate risk, and 5 to 8 questions a high risk of OSA. The following scenarios are also indicative of high risk: yes to 2 or more of the 4 STOP questions and male sex; yes to 2 or more of the STOP questions and BMI > 35 kg/m^2; and yes to 2 or more of the STOP questions and a neck circumference of 43 cm (17 in) in men or 41 cm (16 in) in women.

Salivary cortisol test

The cortisol levels of the participants were assessed utilizing an at-home 4-point salivary cortisol test. Cortisol levels are known to peak in the morning, decrease throughout the day, and then rise again overnight following the body's circadian rhythm.[22] The purpose of testing cortisol at multiple reference points is to allow the clinician to determine if a patient has a normal or abnormal cortisol curve. Each testing laboratory has a specific reference range for the normal levels of cortisol expected at a particular time of day. The present study used the cortisol reference ranges established by the manufacturer of the testing kit for each of the 4 collection points: point 1, 5.1 to 11.6 nM; point 2, 2.3 to 5.3 nM; point 3, 1.0 to 2.4 nM; and point 4, 0.4 to 2.1 nM. Values above or below these ranges at a particular collection point would be considered high or low, respectively.

The test criteria required participants to collect saliva samples 4 times a day, with the first sample collected 1 hour after awakening. Subsequent samples were collected at 4- to 5-hour

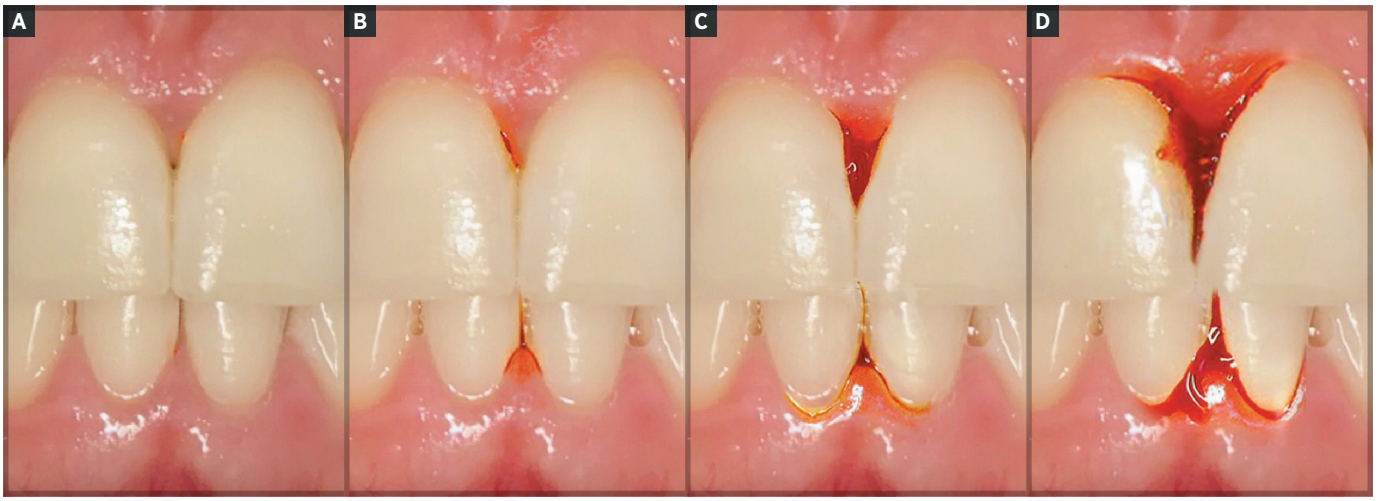


Figure. Simulated clinical examples of Papillary Bleeding Index scoring. A. Grade 1. B. Grade 2. C. Grade 3. D. Grade 4. (Graphic design courtesy of Kelly M. DeWald, Chicago, Illinois.)

intervals thereafter. No alcohol consumption was permitted within 12 hours of sample collection, and no application of topical hormones was permitted on the day of sample collection. Napping 90 minutes or longer during the day of sample collection was to be avoided. Study participants could not eat, chew gum, smoke, drink liquids other than water, or brush their teeth at least 1 hour prior to sample collection.

The study participants returned their salivary samples and recorded sampling times to the laboratory (Sanesco International) in prepaid mailers. The laboratory confirmed proper sample collection and the quality and quantity of all samples to the principal investigator.

At-home sleep test

The sleep quality of participants was assessed with the SleepImage at-home sleep testing system. This system evaluates sleep disorders by measuring sleep duration and stages to aid in the diagnosis of sleep apnea and manage sleep disorder treatment. The Food and Drug Administration has cleared its use in children aged 2 years and older as well as in adults, and it is intended for use by, or at the order of, a healthcare professional.[23,24] The system utilizes a small, finger-worn device with a PPG sensor to collect data. The sensor is paired to a smartphone application that transmits the collected data to cloud-based servers for automated analysis and generation of a sleep report. The sleep report assesses, among other things, a participant's apnea-hypopnea index (AHI), and the results are reported in the present study as software-generated AHI (sAHI).

The AHI is the primary metric used by medical providers and insurers to diagnose and stratify the severity of OSA. The AHI is determined by calculating the number of apnea and hypopnea events occurring per hour of sleep. An *apnea* is defined as cessation of airflow exceeding 10 seconds with a 3% drop in oxygen level, while a *hypopnea* is defined as at least a 30% reduction in airflow with a drop in oxygen level of at least 3%. The severity of OSA is defined based on the AHI results: AHI < 5 is an absence of OSA; AHI = 5 to 14 is mild OSA; AHI = 15 to 29 is moderate OSA; and AHI ≥ 30 is severe OSA.[25] The sleep reports of the study participants were available to the principal investigator immediately after completion of the test.

The SleepImage system is based on cardiopulmonary coupling calculations and spectrographic analysis to assess the coupled interactions between heart rate variability and respiratory activity. These are both strongly modulated by sleep, heart rate variability, and respiratory excursions (PPG-derived respiration or electrocardiogram-derived respiration) to generate metrics of sleep periods exhibiting stable, high-frequency coupling and unstable, low-frequency coupling. This method provides measures of sleep duration, sleep quality, and sleep pathology to guide clinical decisions and therapy management.[26-34]

Primary outcome variable

The primary outcome variable was the bleeding score as determined by the Saxer and Mühlemann PBI, calculated according to the methods described earlier.[16-18] The study parameters allowed the PBI examiner 20 to 30 seconds to determine whether bleeding occurred at each site. The presence of bleeding was determinative of periodontal instability.[16-18,35-42] Treatment outcomes were defined as successful (stable) if the 8-week PBI was < 2.0. Unstable periodontal disease was defined as an 8-week PBI ≥ 2.0. These 2 groups were then examined to determine the numbers of patients with an sAHI < 5 and sAHI ≥ 5.

Statistical analysis

Statistical analysis was conducted with statistical software (R, version 4.1.2). The statistical tests used were the 2-sample *t* test and 2-sample proportion test, and the level of significance was set at $P < 0.05$.

Results

At-home sleep test

The sleep quality of participants was assessed with the at-home system, with an emphasis on calculating the sAHI to identify OSA. The sleep test results found that 33 of 71 participants (46.48%) had an sAHI ≥ 5, signifying probable OSA. Of the

Table 2. Distribution of mean PBI ranges before and after periodontal maintenance therapy.[a]

	Participants with unstable disease, n	
Mean PBI range	Pretreatment	Posttreatment
0 to < 1.0	2	3
1.0 to < 2.0	15	23
2.0 to < 3.0	34	32
3.0 to < 4.0	20	13
4.0	0	0

[a]Posttreatment measurements performed 8 weeks after a single periodontal maintenance treatment.

Table 3. Comparison of participants' ESS and sAHI scores.

			sAHI	
ESS score	Daytime sleepiness	Participants, n	Mean (SD)	95% CI
0-5	Lower normal	46	4.85 (6.27)	2.99 to 6.71
6-10	Higher normal	17	11.94 (19.24)	2.05 to 21.83
11-12	Mild excessive	6	11.50 (7.29)	3.85 to 19.15
13-15	Moderate excessive	0	NA	NA
16-24	Severe	2	8.00 (4.24)	−30.12 to 46.12

Abbreviations: ESS, Epworth Sleepiness Scale; NA, not applicable; sAHI, software-generated apnea-hypopnea index.

participants with an sAHI ≥ 5, 20 were women and 13 were men. Nine (27.27%) participants, 5 women and 4 men, had an sAHI ≥ 15. All 33 participants were referred to their primary care providers for discussion of their findings and follow-up care. The sAHI metric provided the baseline for investigation of reliable SDB screening methods.

Papillary Bleeding Index

Periodontal instability was defined as a PBI ≥ 2.0 at the 8-week examination due to the continued presence of fine lines of blood or several bleeding points visible at the gingival margin. At the first PBI examination, prior to periodontal maintenance, 17 of 71 participants (23.94%) had a PBI < 2.0, and 54 participants (76.06%) had a PBI > 2.0 (Table 2). At the examination conducted 8 weeks after a single periodontal maintenance treatment, 26 participants (36.62%) had a PBI < 2.0, and 45 (63.38%) had a PBI of ≥ 2.0. Based on the continued presence of bleeding on instrumentation, a majority of the participants showed periodontal instability despite having received periodontal therapy and home care instructions 8 weeks earlier.

Epworth Sleepiness Scale

The ESS questionnaire was used to screen for daytime sleepiness. The ESS classified 63 participants (88.73%) with lower (n = 46; 64.79%) to higher (n = 17; 23.94%) normal daytime sleepiness, 6 participants (8.45%) with mild excessive daytime sleepiness, 0 participants (0.00%) with moderate excessive daytime sleepiness, and 2 participants (2.82%) with severe daytime sleepiness (Table 3).

The 2 participants found to have severe daytime sleepiness according to the ESS each had an sAHI ≥ 5 (Table 4). However, the remaining 31 of 33 participants with probable OSA were in the normal or mild excessive ranges of the ESS.

STOP-Bang questionnaire

The STOP-Bang questionnaire was used to assess the probability of OSA. The results of this assessment classified 57 participants (80.28%) as having low risk, 6 participants (11.27%) as having intermediate risk, and 8 participants (8.45%) as having high risk for OSA (Table 5).

Of the 33 patients who scored greater than sAHI ≥ 5 in the sleep study, screening with the STOP-Bang questionnaire showed 27 (81.82%) at low or intermediate risk of OSA and identified only 6 (18.18%) at high risk of OSA (Table 6). As previously stated, the STOP-Bang questionnaire identified 8 of 71 participants as high risk; however, the sleep testing found that 2 of these 8 had an AHI < 5, meaning that there was no probable OSA.

The mean BMI of all 71 patients in this study was 25.82 (Table 7). The mean BMI of participants with an sAHI < 5 was 24.52, classified on the higher end of normal according to the BMI scale of the National Institutes of Health (NIH). The mean BMI of participants with an sAHI ≥ 5 was 27.31. The mean BMI of the 8 participants with an sAHI ≥ 15 was 27.68. The difference in BMI between participants with an sAHI < 5 and

Table 4. ESS scores of participants with sAHI ≥ 5.

ESS	Daytime sleepiness	Participants, n	sAHI	
			Mean (SD)	95% CI
0-5	Lower normal	16	10.69 (7.64)	6.62 to 14.76
6-10	Higher normal	9	21.11 (23.21)	3.27 to 38.95
11-12	Mild excessive	6	11.50 (7.29)	3.85 to 19.15
13-15	Moderate excessive	0	NA	NA
16-24	Severe	2	8.00 (4.24)	−30.12 to 46.12

Abbreviations: ESS, Epworth Sleepiness Scale; sAHI, software-generated apnea-hypopnea index.

Table 5. Comparison of participants' STOP-Bang (OSA risk) and sAHI scores.

OSA risk	Yes responses, n	Participants, n	sAHI	
			Mean (SD)	95% CI
Low	0-2	57	6.33 (11.61)	3.25 to 9.41
Intermediate	3-4	6	11.33 (9.89)	0.95 to 21.72
High	5-8	3	11.00 (5.00)	−1.42 to 23.42
High	2 STOP + male	3	11.67 (13.20)	−21.13 to 44.47
High	2 STOP + high BMI[a]	2	7.00 (5.66)	−43.82 to 57.82
High	2 STOP + large neck[b]	0	NA	NA

Abbreviations: BMI, body mass index; NA, not applicable; OSA, obstructive sleep apnea; sAHI, software-generated apnea-hypopnea index.

[a]High BMI (men or women): > 35 kg/m^2.

[b]Large neck: men, 43 cm (17 in); women, 41 cm (16 in).

participants with an sAHI ≥ 5 was statistically significant (P = 0.02; 2-sample t test).

Salivary cortisol test

Of the 71 study participants, 61 (85.92%) had at least 1 cortisol test sample flagged as high or low compared to the reference range, while 10 participants (14.08%) had no high or low flags across any of the 4 time points.

Discussion

This study hypothesized that some patients with unresolved Stage I or II periodontal disease may have undiagnosed and untreated SDB, creating a host environment conducive to unstable periodontal disease. An at-home sleep test was used to establish whether the participants had probable SDB; the PBI was used to determine whether the participants had stable (PBI < 2.0) or unstable (PBI ≥ 2.0) periodontal disease; and the PBI, STOP-Bang, ESS, and cortisol testing were assessed for their potential to identify patients with SDB.

The SleepImage system was found to be a straightforward tool for at-home assessment of sleep quality. No participant required assistance completing their sleep test after in-clinic instructions regarding use of the device, and no participant reported difficulty with use. Test results were available to the principal investigator immediately following the conclusion of each participant's test. The sleep test findings were clearly reported and easily understood by the principal investigator. The study's sleep physician was able to read and interpret the sleep reports without any reported difficulties or further interaction with the principal investigator.

The sleep test results served as the basis for evaluating the SDB screening tools utilized in the study—the PBI examination, ESS questionnaire, STOP-Bang questionnaire, and salivary cortisol testing. The sleep test results found that 33 of 71 participants (46.48%) had probable OSA, defined as an sAHI ≥ 5. The PBI examination successfully identified 21 (63.64%) of these 33 participants: 15 of 20 women and 6 of 13 men.

At the 8-week PBI examination, 26 of 71 participants (36.62%) were in the stable periodontal health group with a PBI < 2.0, and 45 participants (63.38%) were in the unstable group with a PBI ≥ 2.0. According to the at-home sleep test, 21 (46.67%) of the participants in the unstable group had an sAHI ≥ 5. In the stable group, 12 participants (46.15%) had an sAHI ≥ 5.

The ESS questionnaire identified 2 of 20 female participants and 0 of 13 male participants, with the 2 female participants also being identified by PBI examination. Of the 33 study participants identified by the at-home sleep test as having probable OSA (sAHI ≥ 5), 2 were flagged by the ESS as exhibiting severe

Table 6. STOP-Bang (OSA risk) scores of participants with sAHI ≥ 5.

OSA risk	Yes responses, n	Participants, n	Mean (SD) sAHI
Low	0-2	21	13.46 (14.60)
Intermediate	3-4	6	11.33 (9.89)
High	5-8	3	11.00 (5.00)
High	2 STOP + male	2	17.50 (12.02)
High	2 STOP + high BMI[a]	1	11.00 (0.00)
High	2 STOP + large neck[b]	0	NA

Abbreviations: NA, not applicable; OSA, obstructive sleep apnea; sAHI, software-generated apnea-hypopnea index.

[a]High BMI (men or women): > 35 kg/m^2.

[b]Large neck: men, 43 cm (17 in); women, 41 cm (16 in).

Table 7. Comparison of participants' sAHI and BMI scores.

		BMI, kg/m^2	
sAHI	Participants, n	Mean (SD)	95% CI
Total	71	25.82 (5.21)	24.58 to 27.05
sAHI < 5	38	24.52 (4.70)	22.97 to 26.06
sAHI ≥ 5	33	27.31 (5.43)	25.39 to 29.24
sAHI ≥ 15	9	27.68 (3.66)	24.87 to 30.49

Abbreviations: BMI, body mass index; sAHI, software-generated apnea-hypopnea index.

daytime sleepiness; these individuals had a mean sAHI of 8. Despite the successful identification of these 2 patients who did have high risk for OSA, the ESS failed to identify 31 participants (93.94%) with an sAHI ≥ 5. There was a statistically significant difference between the PBI and the ESS questionnaire in the proportions of high-risk participants they identified ($P < 0.05$; 2-sample proportion test). The mean ESS for patients with an sAHI < 5 was 4, and for those with an sAHI ≥ 5 was 6. These means fall into the lower normal (range 0 to 5) and higher normal (range 6 to 10) scores for daytime sleepiness severity.

The results indicated that the PBI examination was a significantly more reliable method of SDB identification (63.64%) than STOP-Bang, which correctly identified only 6 of 33 participants (18.18%) as having probable OSA ($P < 0.001$; 2-sample proportion test). Thus, while STOP-Bang correctly identified a high risk of OSA in 6 participants (2 of 20 female and 4 of 13 male participants), STOP-Bang failed to identify the high risk in 27 participants (81.82%) who had an sAHI ≥ 5. Six participants were flagged as having intermediate risk for OSA. When the results of the STOP-Bang assessment fall into the intermediate risk category, the decision as to whether to refer a patient to a sleep medicine specialist is left to the judgment of the individual clinician, thus creating a gray area for clinicians and patients.

Of the 12 participants in the stable periodontal health group with an sAHI ≥ 5, STOP-Bang flagged only 2 (16.67%) as high risk and 3 (25.00%) as intermediate risk for OSA. None of these participants were identified by the ESS questionnaire.

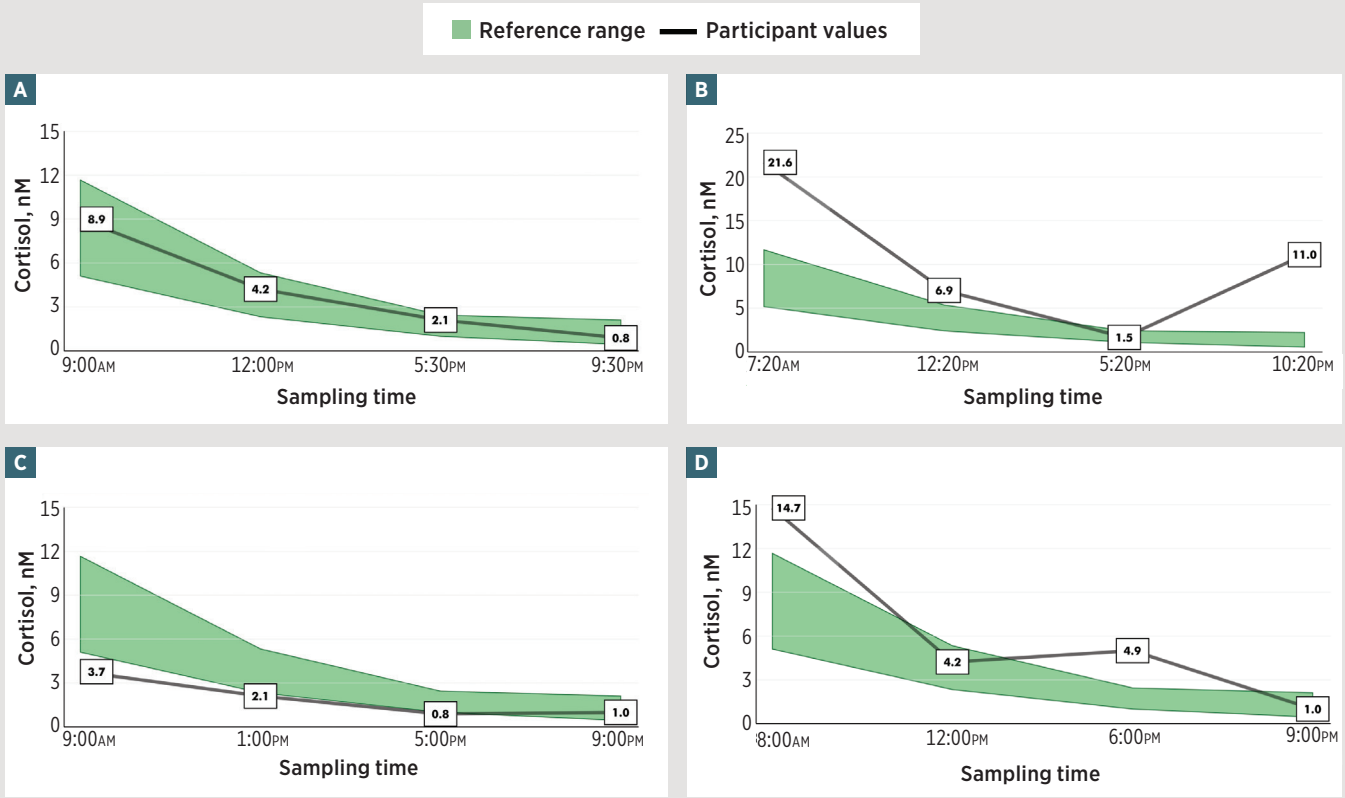
Nine of the 33 study participants (27.27%; 5 women and 4 men) had an sAHI ≥ 15. Of this group, 6 participants (66.67%) were classified as low risk for OSA by STOP-Bang even though the mean sAHI in this group was 30. One woman in the STOP-Bang low-risk group had an sAHI of 81. Another participant was classified as intermediate risk by STOP-Bang, despite having an sAHI of 31. Two participants (22.22%) were classified by STOP-Bang as high risk, with a mean sAHI of 21.

In the STOP-Bang questionnaire, patients with a BMI > 35 kg/m^2 are designated as having a high risk for OSA. In contrast, in the NIH classification, BMI > 30 kg/m^2 indicates obesity. The NIH classification of BMI defines underweight as < 18.5 kg/m^2, normal weight as 18.5 to 24.9 kg/m^2, overweight as 25.0 to 29.9 kg/m^2, and obesity as ≥ 30.0 kg/m^2.[43] Because the STOP-Bang questionnaire defines high risk as a BMI of > 35 kg/m^2 rather than using the NIH definition of BMI ≥ 30 kg/m^2 as the threshold for obesity, it may fail to identify some individuals with high BMI who are at risk for SDB.

In the group of sAHI ≥ 5, STOP-Bang identified 6 of 33 participants (18.18%) as having high risk for OSA, and the ESS identified 2 of 33 participants (6.06%) as having severe daytime sleepiness. STOP-Bang identified 2 participants not identified by PBI examination.

No participant identified as high risk by STOP-Bang was also identified by the ESS. Using STOP-Bang and ESS questionnaires alone as the basis for SDB and referral to sleep medicine would have identified only 10 study participants.

Chart. Cortisol curves. A. Example of a healthy participant. B to D. Examples of unhealthy participants.



STOP-Bang classified 8 participants as high risk for OSA, with 2 of these participants ultimately found to have no probable OSA due to an sAHI < 5, and ESS classified 2 participants as having severe daytime sleepiness. Furthermore, there was no overlap within these groups. The 2 participants identified by ESS were considered intermediate risk by STOP-Bang.

A 4-point salivary cortisol analysis was selected due to its ability to evaluate the curve of cortisol levels over the course of a day. A healthy cortisol curve peaks in the morning and decreases throughout the day, with the reference ranges for normal described previously. While some providers order a single blood draw to evaluate cortisol, this metric does not provide a full picture of the patient's cortisol health throughout the day like a 4-point salivary analysis. The Chart shows the cortisol curves of some participants in the study.

Long-term increased cortisol levels have negative medical sequelae and are well-documented within the literature.[44,45] SDB increases sympathetic output during sleep and affects cortisol levels.[46] Many research studies have investigated the links among cortisol levels, SDB, and health.[7,47-49] The present study looked at the wide variation of abnormal results from study participants and found no statistical relationship between patients' cortisol patterns and the PBI findings ($P > 0.05$; 2-sample t test). However, due to the high percentage (85.92%) of participants in the present study who had unhealthy cortisol curves, cortisol testing may prove useful for patients with unresolved periodontal disease.

Table 8. Number of participants with sAHI ≥ 5 (n = 33) identified by tested SDB tools.

SDB identification tool	Total, n	Male, n	Female, n
PBI	21	6	15
STOP-Bang[a]	6	4	2
ESS[b]	2	0	2

Abbreviations: ESS, Epworth Sleepiness Scale; PBI, Papillary Bleeding Index; sAHI, software-generated apnea-hypopnea index; SDB, sleep-disordered breathing.

[a]STOP-Bang identified 2 participants not identified by PBI or ESS, both male.

[b]Both female participants identified by ESS were also identified by PBI.

The 8-week PBI examination did not perfectly identify all participants with SDB but did identify more participants than the STOP-Bang and ESS questionnaires (Table 8). Whether a simpler dichotomous (yes/no) bleeding index would also identify such individuals is not clear. However, it is the opinion of the authors that the PBI examination represents increased discriminating power over the more commonly used bleeding indices due to the ability of the PBI to grade the levels of inflammation present rather than simply determining the presence or absence of bleeding.

The male-female participant imbalance may be a study limitation. The PBI in premenopausal women may be impacted by

timing of their menstrual cycle and/or the use of contraceptives, and perimenopausal or menopausal women may have different hormonal influences that impact their PBI. It is known that SDB affects about 34% of adult men, who have a 2-fold greater risk of OSA than premenopausal women. Both men and women are affected equally in the postmenopausal age range, and some patient groups, such as those with resistant hypertension, type 2 diabetes, and ischemic heart disease, have a higher prevalence.[50,51]

Conclusion

This study found an objective PBI examination to be a reliable SDB screening tool for patients with unresolved periodontal disease. The STOP-Bang and ESS questionnaires failed to identify participants who would benefit from referral and treatment for SDB. General dentists are uniquely familiar with periodontal inflammation, and the PBI examination is a rapid and easily implemented screening tool. Use of the PBI examination can contribute to more accurate screening and identification of patients at risk for SDB, especially women who may not have been identified through STOP-Bang or ESS screening.

A PBI protocol, followed by appropriate referrals, could be used for assessing whether a patient's inflammation is an oral presentation of a systemic problem. Identification of a systemic origin for unresolved periodontal disease could lessen the burden of periodontal disease in populations worldwide, reduce its associated systemic diseases, minimize the financial impact on healthcare systems, and improve patient outcomes.

Author affiliations

Marquette University School of Dentistry, Milwaukee, Wisconsin (K. C. Schacherl, Han, Dentino); Private practice, Verona, Wisconsin (J. A. Schacherl).

Correspondence

Katherine C. Schacherl, DDS
(katherine.schacherl@marquette.edu).

Conflicts of interest

None reported.

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