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Acoustic Analysis of Snoring in the Diagnosis of Obstructive Sleep Apnea Syndrome: A Call for More Rigorous Studies

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Background: Snoring is a common symptom of obstructive sleep apnea syndrome (OSA) and has recently been considered for diagnosis of OSA.

Objectives: The goal of the current study was to systematically determine the accuracy of acoustic analysis of snoring in the diagnosis of OSA using a meta-analysis.

Methods: PubMed, Cochrane Library database, and EMBASE were searched up to July 15, 2014. A systematic review and meta-analysis of sensitivity, specificity, and other measures of accuracy of acoustic analysis of snoring in the diagnosis of OSA were conducted. The median of apnea-hypopnea index threshold was 10 events/h, range: 5–15 or 10–15 if aforementioned suggestion is adopted.

Results: A total of seven studies with 273 patients were included in the meta-analysis. The pooled estimates were as follows: sensitivity, 88% (95% confidence interval [CI]: 82–93%); specificity, 81% (95% CI: 72–88%); positive likelihood ratio (PLR), 4.44 (95% CI: 2.39–8.27); negative likelihood ratio (NLR), 0.15 (95% CI: 0.10–0.24); and diagnostic odds ratio (DOR), 32.18 (95% CI: 13.96–74.81). χ^2 values of sensitivity, specificity, PLR, NLR, and DOR were 2.37, 10.39, 12.57, 3.79, and 6.91 respectively (All $p > 0.05$). The area under the summary receiver operating characteristic curve was 0.93. Sensitivity analysis demonstrated that the pooled estimates were stable and reliable. The results of publication bias were not significant ($p = 0.30$).

Conclusions: Acoustic analysis of snoring is a relatively accurate but not a strong method for diagnosing OSA. There is an urgent need for rigorous studies involving large samples and single snore event tests with an efficacy criterion that reflects the particular features of snoring acoustics for OSA diagnosis.

Keywords: snoring, obstructive sleep apnea syndrome, acoustic analysis, review, meta-analysis

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Obstructive sleep apnea (OSA) syndrome is a serious sleep disorder characterized by the repeated closure of the upper airway during sleep, among adults 30–70 y of age, approximately 13% of men and 6% of women have moderate to severe OSA, 14% of men and 5% of women have an apnea-hypopnea index (AHI) ≥ 5 plus symptoms of daytime sleepiness.[1] It is also being recognized as an independent risk factor for several clinical consequences, including daytime sleepiness,[2] systemic hypertension,[3] increased risk of cardiovascular and cerebrovascular disease,[4–6] traffic accidents,[7–10] and impaired quality of life.[11]

Polysomnography (PSG) is currently the gold standard of OSA diagnosis.[12,13] Unfortunately, PSG requires a full-night hospital stay in a specifically equipped sleep suite, connected to more than 15 channels of measurements requiring physical contact with sensors.[14] PSG is inconvenient, expensive, and not suitable for mass screening. The limited number of PSG facilities around the world has long waiting lists, rendering it impossible to test all the patients in need of such assessment. Approximately 80–90% of patients with OSA are believed to be undiagnosed.[15] With advances in technology and the development of portable monitors, home testing for sleep related breathing disorders is now feasible and circumvents many of the limitations of an attended in-laboratory polysomnogram. Although the portable monitors may expedite the diagnosis of OSA for many, it is essential that health care professionals using these methods recognize several inherent limitations.[16] There is an enormous need for a simplified screening instrument capable of convenient and reliable diagnosis of OSA.

Snoring is one of the common and earliest symptoms of OSA. Snoring has long been viewed as a potential indicator for monitoring OSA. It has a unique advantage over other physiological signals, in that it can be acquired conveniently with only one to two low-cost noncontact or contact microphones. Importantly, the test does not affect the patient's sleep quality. Interest in the acoustic characteristics of snores began almost 2 decades ago. Recently several papers have proposed OSA detection systems[17] and AHI estimation based on whole-night audio recording of snoring [18,19] For devices utilizing acoustic signals, the data are insufficient to determine whether the use

Table 1—Characteristics of the eight studies finally selected.

Study	Publication Year	Country	Number of Patients	TP	FP	FN	TN	AHI Threshold	QUADAS Score
Nakano et al.[56]	2014	Japan	40	16	7	1	16	15	11
Ben-Israel et al.[18]	2012	Israel	30	13	3	2	12	10	13
Mesquita et al.[17]	2012	Spain	34	19	5	4	6	15	13
Karunajeewa et al.[37]	2011	Australia	41	25	1	3	12	10	11
de Silva et al.[40]	2011	Australia	51	35	1	4	11	15	12
Fiz et al.[19]	2010	Germany	37	12	2	3	20	15	13
Ng et al.[49]	2009	Singapore	40	27	1	3	9	10	12

of acoustic signals with other signals as a substitute for airflow is adequate to diagnose OSA.[20]

The aim of this review was to systematically determine the sensitivity and specificity of acoustic analysis of snoring in the diagnosis of OSA. In this paper, we (1) discuss the consistencies and differences across the existing research studies and (2) identify opportunities for methodological improvements.

METHODS

Search Strategy

This review was performed according to a protocol designed *a priori* and recommended for systematic reviews and meta-analyses.[21–23] We searched PubMed, Cochrane Library database, and EMBASE electronically up to July 15, 2014, utilizing combinations of the relevant medical subject heading terms, key words, and word variants for 'obstructive sleep apnea syndrome', 'snoring analysis', 'acoustic analysis', and 'diagnosis'. In addition, we reviewed the reference lists from all relevant articles to identify additional studies. All searches were conducted independently by 2 reviewers (H.J. & L.S.). The results were compared, and any questions or discrepancies were resolved through iteration and consensus.

Inclusion Criteria for Included Studies

A study was included if it met the following inclusion criteria: (1) the study was written in English; (2) full text literature was available; (3) AHI assessment was based mainly on acoustic analysis of snoring; (4) subjects underwent PSG monitoring; (5) the study reported the sensitivity and specificity of the acoustic analysis; (6) the study clearly stated the number of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) results in the diagnosis of OSA, or they could be calculated from the data; (7) the study was performed on adults (age 18 y or older); and (8) snore information was collected using microphones. We excluded a study from the analysis if it did not meet the above criteria or the experimental conditions were not clear.

Data Extraction and Quality Assessment

Data extraction was performed independently by two reviewers (H.J. & L.S.). The reviewers were blinded to publication details, and disagreements were resolved by consensus. Data retrieved from the reports included first author, country, publication year, participant characteristics, sensitivity and specificity data, diagnostic cutoff values, number of patients, and study design. **Table 1** demonstrates a summary of each study, including the number of TP, FP, FN, and TN. We did not contact the authors for further details. The methodological quality of each study was assessed by a quality assessment for studies of diagnostic accuracy (QUADAS) that is an evidence-based quality assessment tool for use in systematic reviews of diagnostic accuracy studies (maximum score, 13).[24] When a criterion was fulfilled, a score of 1 was given; 0 if a criterion was unclear; and −1 if a criterion was not achieved.

Ethical Considerations

This study was approved by the Ethics Committee of First Affiliated Hospital, Guangzhu Medical University (Guangzhou, Guangdong, China).

Statistical Analysis

We used standard methods recommended for meta-analyses of diagnostic test evaluations.[25] Analyses were performed using two professional statistical software programs (Meta-DiSc 1.4 for Windows, XI Cochrane Colloquium, Barcelona, Spain; and STATA version 12.0, STATA Corporation, TX, USA). Heterogeneity in meta-analysis refers to the degree of variability in results across studies. We used the Q statistic of χ^2 test and inconsistency index (I^2) to estimate the heterogeneity of individual studies contributing to the pooled estimate. For the χ^2 test, significance was set at $p < 0.05$; for I^2 statistics, significance was set at $p > 0.05$.[26] Because of a lack of standardization, different thresholds may have been used in the included studies to define a positive test result. To detect threshold effects, the relationship between sensitivity and 1-specificity was evaluated by using Spearman correlation coefficient. A strong positive correlation would suggest threshold effect.[27]

The following indices of diagnostic accuracy were calculated by using Meta-DiSc 1.4 for Windows and analyzed for each study: sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR). The pooled sensitivity, specificity, and other related indices across studies were calculated using both Mantel–Haenszel method (fixed effects model) and DerSimonian–Laird method (random effects model). In addition, diagnostic threshold variation among studies was assessed by using a summary receiver operating characteristic (SROC) curve. The SROC curve (and the area under the curve [AUC]) represents the overall performance

Figure 1—Flowchart of the study selection process.

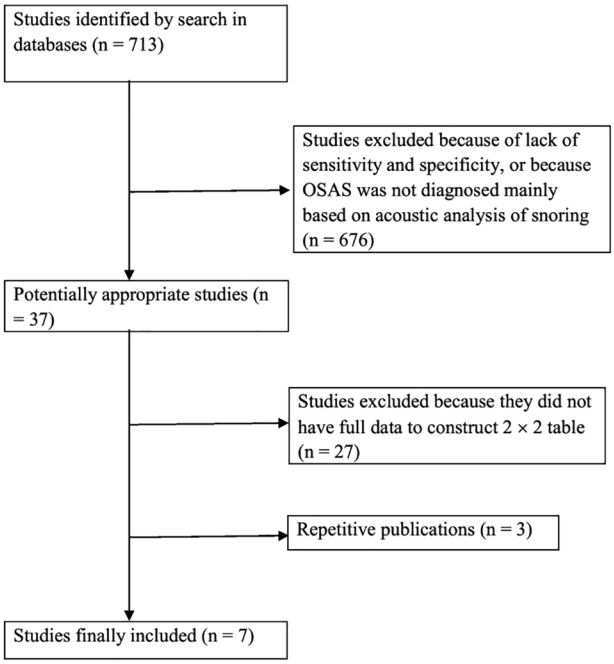
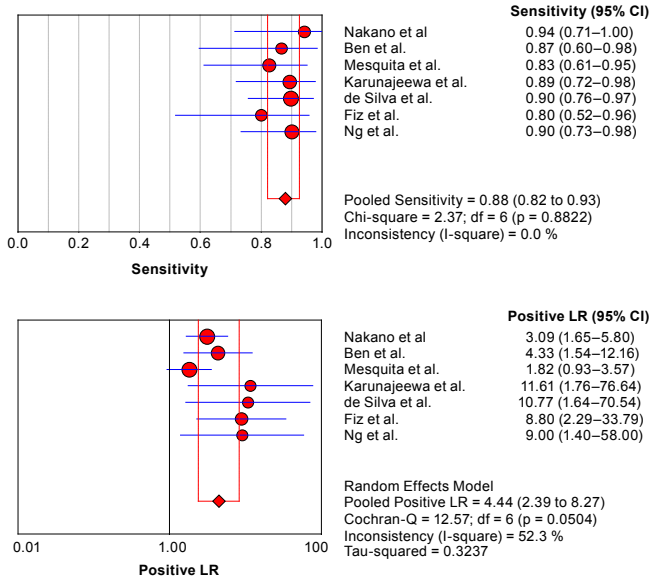


Figure 2—Forest plots of sensitivity and specificity estimates for acoustic analysis of snoring in the diagnosis of obstructive sleep apnea syndrome (OSAS) in the seven studies selected.



The point estimates of sensitivity and specificity from each study are shown as solid circles and the size of each study is indicated by the size of the solid circle. Error bars are 95% confidence intervals (CI). LR, likelihood ratio.

of the test and depicts the tradeoff between sensitivity and specificity. In order to evaluate the statistical outcome validity, we detected the pooled outcome by sensitivity analysis. We used a random-effects model to reanalyze the data as an alternative to the fixed effect model. Because publication bias is of concern for meta-analysis of diagnostic studies, we tested for the potential presence of this bias using Deeks funnel plots. Publication bias was assessed visually by using a scatter plot of the inverse of the square root of the effective sample size (1/root [effective sample size]) versus the DOR, which should have a symmetrical funnel shape when publication bias is absent.[28]

RESULTS

Study Selection Process

The primary search retrieved 713 studies. At review, 676 studies were excluded after reading the abstract and an additional 27 studies were excluded after reading the full text because they did not meet the inclusion criteria. In addition, three studies were excluded because of repetitive publication. We finally included seven studies. **Figure 1** shows a flowchart of the study selection process.

The characteristics of the seven studies finally selected are shown in **Table 1**. The publication years spanned from 2009 to 2014. The number of patients enrolled in single studies ranged from 30 to 51 patients. The total number of patients was 273. The selected AHI threshold value was 10 or 15 times per hour. All studies had a high QUADAS score (≥ 10).

Threshold Effect

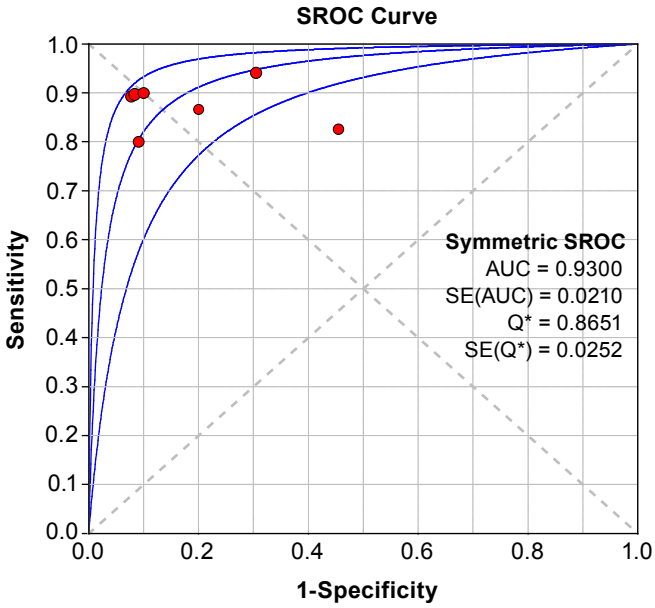
Computation of Spearman correlation coefficient between log of sensitivity and log of [1- specificity] of acoustic analysis of snoring was 0.00 (p = 1.00), indicating no statistically significant threshold effect.

Diagnostic Accuracy

Figure 2 shows the forest plot of sensitivity and specificity for acoustic analysis of snoring in the diagnosis of OSA for the seven studies. The sensitivity ranged from 0.80 to 0.94 (pooled: 0.88; 95% CI: 0.82–0.93), and the specificity ranged from 0.70 to 0.92 (pooled: 0.81; 95% CI: 0.72–0.88). We also found that pooled PLR was 4.44 (95% CI: 2.39–8.27), NLR was 0.15 (95% CI: 0.10–0.24), and DOR was 32.18 (95% CI: 13.96–74.18). χ^2 values of sensitivity, specificity, PLR, NLR, and DOR were 2.37 (p = 0.88), 10.39 (p = 0.10), 12.57 (p = 0.05), 3.79 (p = 0.71), and 6.91 (p = 0.33), respectively. I2 less than 50% in all parameters except pooled Positive LR (52.3%), indicating no significant heterogeneity between studies.

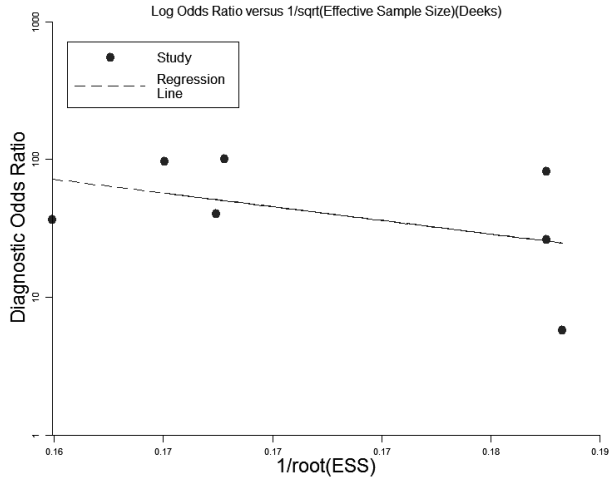
A SROC curve for acoustic analysis of snoring showing TP rates versus FP rates from individual studies is shown in **Figure 3**. As a global measure of test efficacy, we used the Q-value (the intersection point of the SROC curve with a diagonal line from the left upper corner to the right corner of the ROC space), which corresponds to the highest common value of sensitivity and specificity for the test. This point does not indicate the only or even the best combination of sensitivity and specificity for a particular clinical setting but represents an overall measure of the discriminatory power of a test. Our data showed that the SROC curve was positioned near the desirable upper left corner of the SROC curve. The maximum joint sensitivity and specificity (i.e., the Q-value)

Figure 3—Summary receiver operating characteristic (SROC) curves for acoustic analysis of snoring in the diagnosis of obstructive sleep apnea.



Each circle represents each of the seven studies included in the meta-analysis. The size of each study is indicated by the size of the solid circle. The regression SROC curve summarizes the overall diagnostic accuracy. AUC, area under the curve; SE, sleep efficiency.

Figure 4—Funnel graph for the assessment of potential publication bias in the 7 studies selected.



The funnel graph plots the diagnostic odds ratio against the 1/root (effective sample size). The dotted line is the regression line. The result of the test for publication bias was not statistically significant (p = 0.30). ESS, effective sample size.

was 0.87, and the AUC was 0.93, indicating a high level of overall accuracy.

Although the SROC curve and DOR are complicated as to their interpretation and use in clinical practice, the likelihood ratios (PLR and NLR) are more clinically meaningful for the measurement of diagnostic accuracy.[29] For these two ratios, the diagnostic value for OSA is considered high when PLR > 10 and NLR < 0.1, moderate when PLR = 5.0–10.0 and NLR = 0.1–0.2, and low when PLR < 5.0 and NLR = 0.2–0.5.[30]

Sensitivity Analysis and Publication Bias

As an alternative to the random effect model, we used a fixed-effect model. However, the new analysis produced results similar to those obtained by the fixed- effect model. After excluding suspicious studies, the results were still similar to the original results. Although the funnel plots for publication bias showed some asymmetry due to the limited number of studies (**Figure 4**), Deeks test showed no statistical significance (p = 0.30). These results indicated no potential for publication bias.

DISCUSSION

This is the first study to investigate the accuracy of acoustic analysis of snoring in the diagnosis of OSA using a critical literature review and meta-analysis. The current meta-analysis of seven high-quality studies indicates that acoustic analysis of snoring is a relatively highly accurate diagnostic tool for OAS, with the pooled sensitivity being 0.89, specificity 0.84, AUC 0.94, and DOR 48.06. The PLR value is 4.44 and the NLR was 0.15, the results of likelihood ratios suggest that acoustic analysis of snoring currently is inadequate as a robust method for diagnosing OSA.

The weakness of clinical studies that we reviewed prompted the following summary and suggestions.

First, some studies have been showing that snore-related sound (SRS) classification is a first step in the detection of snoring and OSA.[31–37] Duckitt et al.[38] recorded sound with an ambient microphone from six subjects that was segmented into snoring episodes, breathing, duvet noise, and silence periods using hidden Markov models and spectral-based features. Cavusoglu et al.[31] classified snore types with an accuracy ranging from 86.8% to 97.3% using a linear regression fed by sub-band spectral energy distributions processed by principal component analysis. Yadollahi and Moussavi[35] investigated the effect of body and neck position on the classification results. The overall accuracies were found to be 95.7% and 93.2% for tracheal and ambient recordings, respectively, regardless of the neck position. Karunajeewa et al.[37] used three noise reduction techniques and compared their performance with an overall classification accuracy of 90.74%; however, their accuracy was up to 96.78% with noise reduction techniques and a proper choice of features. However, only some studies took concerted effort to explore the effect of the signal-to-noise ratios on the methods proposed.[33,39,40] Noise reduction together with proper choice of parameters derived from SRS analysis could help develop an accurate and possibly automated diagnostic tool.

Second, it is important to note that snoring does not have a fixed and constant occurrence,[41] and not all snoring episodes are due to the same mechanisms during sleep.[42] Some studies have already reported significant differences between postapneic snores (snores that are produced immediately after an apnea) and all other snores.[43–45] Lee et al.[46] reported the existence of

monosyllabic low-frequency snore, duplex low- and mid-frequency snore, duplex low- and high-frequency snore, and triplex low-, mid-, and high-frequency snore in OSA. It is possible that some events were overscored and some were underscored with a reasonable overnight average, and thus, only a subset of snores may have utility for indicating OSA.

Third, the acoustic analysis of snoring has demonstrated good ability to discriminate between simple snorers and OSA patients.[47–51] Primary snoring was defined as snoring without further respiratory events such as apneas or hypopneas.[52] Sola-Soler et al.[53] mentioned there were normal snores in patients with OSA. Our recent study showed that 87.32%, 78.38%, and 39.55% of all snores were primary snores in patients with mild, moderate, and severe OSA, respectively.[54] The acoustic analysis of snoring could discriminate between "simple snorers" and patients with OSA, but it was difficult to estimate obstructive AHI accuracy without distinguishing the special characteristic of snore sound in OSA; this may be the most critical reason that acoustic analysis of snoring is inadequate as a robust method for diagnosing OSA.

Fourth, different studies have chosen different snoring parameters for acoustic analysis, such as pitch (sensitivity and specificity were 89.3% and 92.3%),[36] formant frequencies (sensitivity and specificity were 0.88% and 0.82%)[47] or peak frequencies (sensitivity and specificity were 97.7% and 85%),[48] sound intensity (sensitivity and specificity were 87.0% and 100%)[55] or power spectrum (sensitivity and specificity were 80.0% and 90.9%,[20] and 94.1% and 78.9%,[55] respectively), and mel-frequency cepstrum stability, pitch density, running variance, apnea phase ratio, and interevent silence (sensitivity and specificity were 87% and 80%).[17] The aforementioned findings indicate that many snoring parameters have relatively good diagnostic capacity. Further investigation is needed to understand which parameters or combinations of parameters are best.

Fifth, OSA was defined as mild, moderate, or severe depending on whether the AHI was between 5 and 15, 15 and 30, or greater than 30, respectively. The major challenge for the interpretation of the data presented is that the primary AHI cutoff across studies was highly variable. Mesquita et al.,[17] de Silva et al.,[40] Fiz et al.,[19] and Nakano et al.[56] report AHI cutoffs of 15 events/h. The other studies selected an AHI threshold value of 5 or 10 for distinguishing between simple snorers and patients with OSA. Already, using current technology, the data suggest that severe sleep apnea might be ruled out in a proportion of individuals, or sleep apnea ruled in for many individuals, based on snoring estimates of AHI. For example, according to Nakano et al.,[56] every individual with an estimated AHI of > 30 had moderate to severe OSA and should be expediently assessed for OSA and treated (regardless of symptoms, according to current recommendations). Likewise, every individual who had an estimated AHI < 15 did not have severe OSA and may not require prioritized assessment and intervention (unless symptoms of sleepiness/fatigue and cardiovascular comorbidities are present, or operates heavy machinery, etc). Sensitivity/specificity analysis using a single cutoff does not give credit for this potential utility, as the dependent variable is dichotomized.

Sixth, the samples were small in those seven publications, and the limited number of patients may have influenced the outcomes. Moreover, little attention has been placed on sex, age, or obesity, factors that may require adjustment of the thresholds used for each technology. At minimum, some mention that research of the utility of the approaches within sex, age and BMI subgroups will be important to study in the future. Furthermore, a very limited number of papers published in languages other than English were not included in this meta-analysis, which may be a potential source of bias. Based on those limitations, a definitive conclusion about the accuracy of diagnosis of acoustic analysis of snoring should not be drawn. Nevertheless, the studies included in our analysis are of high-quality research, and therefore may provide a considerable power, although further studies on a large scale are needed to confirm the diagnostic value of acoustic analysis of snoring for OSA.

In conclusion, acoustic analysis of snoring is a relatively accurate but not a strong method for diagnosing OSA. Appropriate methods for unequivocal classification of snoring and special characteristic of snore sound in OSA are to be elaborated. Although the acoustics of snoring, as a diagnostic tool, is from a burgeoning stage to growing maturity, there is an urgent need for a rigorous, large sample size, and a single snore event test with an efficacy criterion that reflects the particular features of snores to diagnose OSA, and that this information can ultimately be of benefit to public health.

ABBREVIATIONS

AHI, apnea-hypopnea index
ANFIS, adaptive network fuzzy inference system
AUC, area under the curve
DOR, diagnostic odds ratio
ESS, effective sample size
FN, false negative
FP, false positive
I^2, inconsistency index
NLR, negative likelihood ratio
OSA, obstructive sleep apnea syndrome
PLR, positive likelihood ratio
PSG, polysomnography
QUADAS, quality assessment for studies of diagnostic accuracy
SROC, summary receiver operating characteristic
SRS, snore-related sound
SVMs, support vector machines
TN, true negative
TP, true positive.

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