Point-of-Care Ultrasound for Obstructive Sleep Apnea Screening: Are We There Yet? A Systematic Review and Meta-analysis

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BACKGROUND: Perioperative diagnosis of obstructive sleep apnea (OSA) has important resource implications as screening questionnaires are overly sensitive, and sleep studies are expensive and time-consuming. Ultrasound (US) is a portable, noninvasive tool potentially useful for airway evaluation and OSA screening in the perioperative period. The objective of this systematic review was to evaluate the correlation of surface US with OSA diagnosis and to determine whether a point-of-care ultrasound (PoCUS) for OSA screening may help with improved screening in perioperative period.

METHODS: A search of all electronic databases including Medline, Embase, and Cochrane Database of Systematic Reviews was conducted from database inception to September 2017. Inclusion criteria were observational cohort studies and randomized controlled trials of known or suspected OSA patients undergoing surface US assessment. Article screening, data extraction, and summarization were conducted by 2 independent reviewers with ability to resolve conflict with supervising authors. Diagnostic properties and association between US parameters (index test) and OSA diagnosis using sleep study (reference standard) were evaluated. The US parameters were divided into airway and nonairway parameters. A random-effects meta-analysis was planned, wherever applicable.

RESULTS: Of the initial 3865 screened articles, 21 studies (7 airway and 14 nonairway) evaluating 3339 patients were included. Majority of studies were conducted in the general population (49%), respirology (23%), and sleep clinics (12%). No study evaluated the use of US for OSA in perioperative setting. Majority of included studies had low risk of bias for reference standard and flow and timing. Airway US parameters having moderate–good correlation with moderate–severe OSA were distance between lingual arteries (DLAs > 30 mm; sensitivity, 0.67; specificity, 0.59; 1 study/66 patients); mean resting tongue thickness (>60 mm; sensitivity, 0.85; specificity, 0.59; 1 study/66 patients); tongue base thickness during Muller maneuver (MM; sensitivity, 0.59; specificity, 0.78; 1 study/66 patients); and a combination of neck circumference and retropalatal (RP) diameter shortening during MM (sensitivity, 1.0; specificity, 0.65; 1 study/104 patients). Nonairway US parameters having a low–moderate correlation with moderate–severe OSA were carotid intimal thickness (pooled correlation coefficient, 0.444; 95% confidence interval [CI], 0.320–0.553; P value = .000, 8 studies/727 patients) and plaque presence (sensitivity, 0.24–0.75; specificity, 0.13–1.0; 4 studies/1183 patients).

CONCLUSIONS: We found that a number of airway and nonairway parameters were identified with moderate to good correlation with OSA diagnosis in the general population. In future studies, it remains to be seen whether PoCUS screening for a combination of these parameters can address the pitfalls of OSA screening questionnaires.   (Anesth Analg 2019;129:1673–91)

KEY POINTS

- **Question:** To what extent has previously published literature evaluated the use of surface ultrasound (US) measurement to diagnose and screen for obstructive sleep apnea (OSA), and whether a point-of-care ultrasound (PoCUS) tool can be used to address pitfalls of available screening questionnaires?
- **Findings:** In this systematic review, we identified a set of airway and nonairway US parameters that have fair to good correlation with OSA diagnosis in the general population but not in the perioperative setting.
- **Meaning:** Use of PoCUS is an exciting area of research in the perioperative setting, and future studies should aim to systematically validate this set of airway and nonairway parameters and to determine whether surface US can screen for OSA and address pitfalls of OSA screening questionnaires.

GLOSSARY

AHI = apnea–hypopnea index; **AUC** = area under curve; **BA** = brachial artery; **BMI** = body mass index; **CI** = confidence interval; **cIMT** = carotid intimal media thickness; **CPAP** = continuous positive airway pressure; **CT** = computed tomography; **CV** = coefficient of variation; **DLAs** = distance between lingual arteries; **HSS** = habitual simple snoring; **LPW** = lateral pharyngeal wall; **MM** = Muller maneuver; **MRI** = magnetic resonance imaging; **OR** = odds ratio; **NA** = not applicable; **NPV** = negative predictive value; **NR** = not reported; **OR** = odds ratio; **OSA** = obstructive sleep apnea; **OSAS** = obstructive sleep apnea syndrome; **PoCUS** = point-of-care ultrasound; **PPV** = positive predictive value; **PRISMA** = Preferred Reporting Items for Systematic Reviews and Meta-analysis; **PSG** = polysomnography; **QUADAS** = Quality Assessment of Diagnostic Accuracy Studies; **RDI** = respiratory disturbance index; **ROC** = receiver operating curve; **RP** = retropalatal; **RR** = relative risk; **Sao₂** = oxygen saturation; **SE** = standard error; **SFT** = subcutaneous fat thickness; **SROC** = summary receiver operating curve; **STARD** = Standards for Reporting of Diagnostic Accuracy Studies; **UA** = upper airway; **US** = ultrasound

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder, characterized by repeated upper airway (UA) obstruction, hypoxemia, and associated with increased morbidity and mortality.[1,2] OSA is considered an independent risk factor for postoperative cardiorespiratory complications[3,4] and increased perioperative utilization of health care resources.[5]

OSA is characterized by repeated episodes of complete (apnea) or partial (hypopnea) closure of the UA in the presence of breathing effort during sleep. These episodes are accompanied by oxygen desaturation (Sao₂) and hypoventilation of varying severity and terminated by cortical arousal to increase UA dilator activity and increase UA caliber.[6–8] OSA severity is classified based on apnea–hypopnea index (AHI) as mild (AHI = 5–15/h), moderate (AHI > 15–30/h), or severe (AHI > 30/h).[9]

Various OSA phenotypes can be explained physiologically by a decreased UA dilator muscle tone during sleep, low arousal threshold, or high loop gain.[10] However, the predominant feature is a narrow and collapsible UA anatomy determined by an interplay between redundant soft tissue, impaired genioglossus muscle tone and the bony confines of UA,[11] amounting to two-thirds of the variation in the AHI.[10,12] In patients with OSA, not only is the UA typically narrower and more collapsible while awake,[8,13–17] it collapses readily during sleep as the UA dilator muscle activity diminishes at sleep onset.[16,17] Identification of moderate–severe OSA is crucial to prevent potential life-threatening cardiopulmonary complications perioperatively. However, a large proportion of patients with OSA remain undiagnosed at the time of surgery.[18] Current screening tools are mainly questionnaire based and are largely sensitive but not specific[19,20] resulting in many false positives, unnecessary increased resource utilization, cost burden, and legal implications.[5,21] Gold standard laboratory polysomnography (PSG) study is expensive and not widely available. Point-of-care ultrasound (PoCUS) is a readily available, portable, noninvasive tool that has been used for airway evaluation and may be useful for OSA screening. PoCUS applications involve a focused ultrasound (US) examination that aims at answering well-defined clinical questions to guide patient management and improve clinical outcomes.[22–24] Focused airway assessment to diagnose OSA adds to an expanding list of well-established PoCUS applications for pulmonary,[25,26] diaphragmatic,[27,28] gastric assessment,[29] fluid status, and hemodynamic instability.[30,31] The objective of this systematic review was to evaluate the utility of surface US measurements for detection and assessment of OSA based on currently available literature and to determine whether a PoCUS tool may be utilized as a screening tool for OSA.

METHODS

Search Strategy and Study Selection

The current review was designed and prepared according to recommended standards[32] and reported as per the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.[33–35] A PRISMA checklist is provided in Supplemental Digital Content 1, Appendix 1, http://links.lww.com/AA/C913. A review protocol was prepared and followed before commencing the review. Search strategy was designed according to the PRISMA guidelines and implemented with the help of an expert medical librarian. The search was conducted on August 6, 2016 and updated on September 25, 2017. The literature databases searched from database inception to September 25, 2017, including MEDLINE, ePub ahead of print, MEDLINE in-process, and other nonindexed citations, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science (Thomson Reuters), Scopus (Elsevier), ClinicalTrials. Gov, WHO ICTRP, ProQuest Digital Dissertations, and UHN OneSearch for books/book chapters.

A literature search was done for OSA and US/ultrasonography/sonography: limited to human, adults, English where possible. The search used the Medical Subject Heading keywords "obstructive sleep apnea" and "ultrasonography" or "ultrasound" or "sonography." Also, the following text keywords were used for the literature search: "obstructive sleep apnea syndrome," "sleep disordered breathing," "obesity hypoventilation syndrome," "apnea or apnoea," "hypopnea or hypopnoea," "radiology," "magnetic resonance," "x-ray," "radiography," "Doppler," "radiological procedures," "radiologist," " radiology department," "radiology information

systems," " computed tomography," "tomography," "spectroscopy," "cephalometry," "echography," "imaging," and "diagnostic imaging."

Inclusion criteria were as follows: (1) observational studies or randomized controlled trials; (2) adult patients (>18 years old) with information available on OSA; (3) surface US imaging used for correlation with OSA diagnosis; and (4) all studies published in English. Exclusion criteria were as follows: (1) case reports; (2) review articles; (3) studies with no information on OSA status; (4) studies without ultrasonography; and (5) studies with ultrasonography but unrelated to OSA.

Studies were selected independently by 2 reviewers (A.G. and A. Tuteja) who screened the titles and abstracts to determine whether the studies met the eligibility criteria using the Covidence platform.[36] Disagreements were resolved by consensus or by other authors (M.S. and V.C.). A citation search by manual review of references from primary or review articles was also performed. Corresponding authors were contacted via email to provide missing data.

The US upper airway parameter was classified according to the anatomical location, suprahyoid versus infrahyoid region, as described before,[24] recognizing that the type of anatomical structures and US probes for examination can be quite different. Studies looking at other surface US parameters were classified separately.

Data Extraction

The following information was collected from each study: author, year of publication, type of study, sample size of OSA and non-OSA group, age, sex, body mass index (BMI), OSA status of patients, OSA diagnosis modality, AHI, PSG data, sleep questionnaire data, US variables and parameters, type of sonography, scanner, and transducer, sonographer intra- and interrater variability, and US methodology for each of the parameters examined.

Study Quality Assessment

We assessed risk of bias and generalizability using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool for diagnostic tests. The QUADAS-2 tool comprises 4 domains: patient selection (appropriateness of patients for the study question, including study design), index test (the surface US measure), reference standard (sleep study diagnostic test), and flow and timing (eg, the index and reference tests were performed within a reasonable time frame of up to 1 year). All 4 domains were assessed for risk of bias, and the first 3 domains (patient selection, index test, and reference standard) were assessed for applicability by indicating a "low," "high," or "unclear" rating. In the QUADAS-2, "applicability" refers to whether certain aspects of an individual study matched the review question. The QUADAS-2 does not generate a comprehensive quality score, but rather an overall judgment of low, high, or unclear risk. To have an overall judgment of a low risk of bias or a low concern regarding applicability, a study needed to be low on all relevant domains. If a study received a high or unclear rating in ≥1 domains, then it was judged as being at risk of bias or having concerns regarding applicability. Reference standards were rated as low risk of bias if all parameters of PSG recording were utilized, as unclear risk if 1 or 2 parameters were missing, and as high risk if >2 parameters were missing.

Data Analysis

Diagnostic properties of the various US parameters for OSA diagnosis and severity were extracted or calculated. The correlation coefficient between a specific airway or nonairway US parameter and OSA severity (AHI or oxygenation parameter) was extracted or calculated from the reported P value and sample size. Sensitivity and specificity of specific US parameter for a specific OSA severity cutoff (mild, moderate, or severe) were reported or calculated (if not reported) by construction of 2 × 2 tables directly from studies. Forest plots were constructed for (1) correlation coefficients between US parameters and OSA severity and (2) sensitivity and specificity of US parameters for diagnosing OSA. Pooled estimates based on DerSimonian and Laird random-effects models were calculated where appropriate. Heterogeneity was evaluated qualitatively and, where there were sufficient studies reporting on the same US parameter/OSA pairing, quantitatively with the I^2 statistic. Publication bias was investigated using funnel plots and the Duval and Tweedie trim-and-fill approach, a method that first identifies potentially unpublished estimates based on funnel plot asymmetry and then includes these unpublished estimates in a revised the pooled value. Summary receiver operating curves (ROCs) were also generated where ≥3 studies reported sensitivity and specificity for the same US parameter/OSA combination. Analyses were conducted in Review Manager (RevMan, London, UK, v5.3),[37] Comprehensive Meta-analysis (Biostat, Inc, Englewood, NJ),[38] and R[39] software tools (R Foundation for Statistical Computing, Vienna, Austria), as appropriate.

RESULTS

Study Selection

Our initial electronic search identified 3865 articles, and after deduplication, and applying eligibility criteria, 69 articles were included for full-text screening and a total of 21 studies were included in the qualitative synthesis (Figure 1). Studies were excluded mainly for the following reasons (Figure 1): surface US not used (21), no abstract of interest (7), duplicate (7), clinical trial registration or case series (5), editorial (3), pediatric population (3), no OSA diagnosis (3), and same study population (1). The complete search strategy is provided as Supplemental Digital Content 2, Search Strategy, http://links.lww.com/AA/C926.

Of these 21 studies, 7 airway studies (n = 430) and 14 nonairway studies (n = 2909) evaluating 3339 patients were included (Table 1). The studies were conducted in Bulgaria, China, France, Israel, Italy, Hong Kong, Taiwan, Turkey, and the United States. Studied patients were recruited from sleep clinics (12%), respiratory clinics (23%), cardiology (6%), internal medicine (5%), otolaryngology clinics (5%), and from the general population (49%). None of the studies included patients in the perioperative setting or patients with any other forms of sleep-disordered breathing, such as central sleep apnea, or sleep-related hypoventilation syndromes.

Quality of Included Studies

According to the QUADAS-2 tool, only 3 studies[40,43,44] had low risk of bias and low concern regarding applicability. Risk of bias and applicability concerns were marked high for patient selection in 4 studies, where Altin et al[47] included only men suspected to have OSA, 2 studies included patients
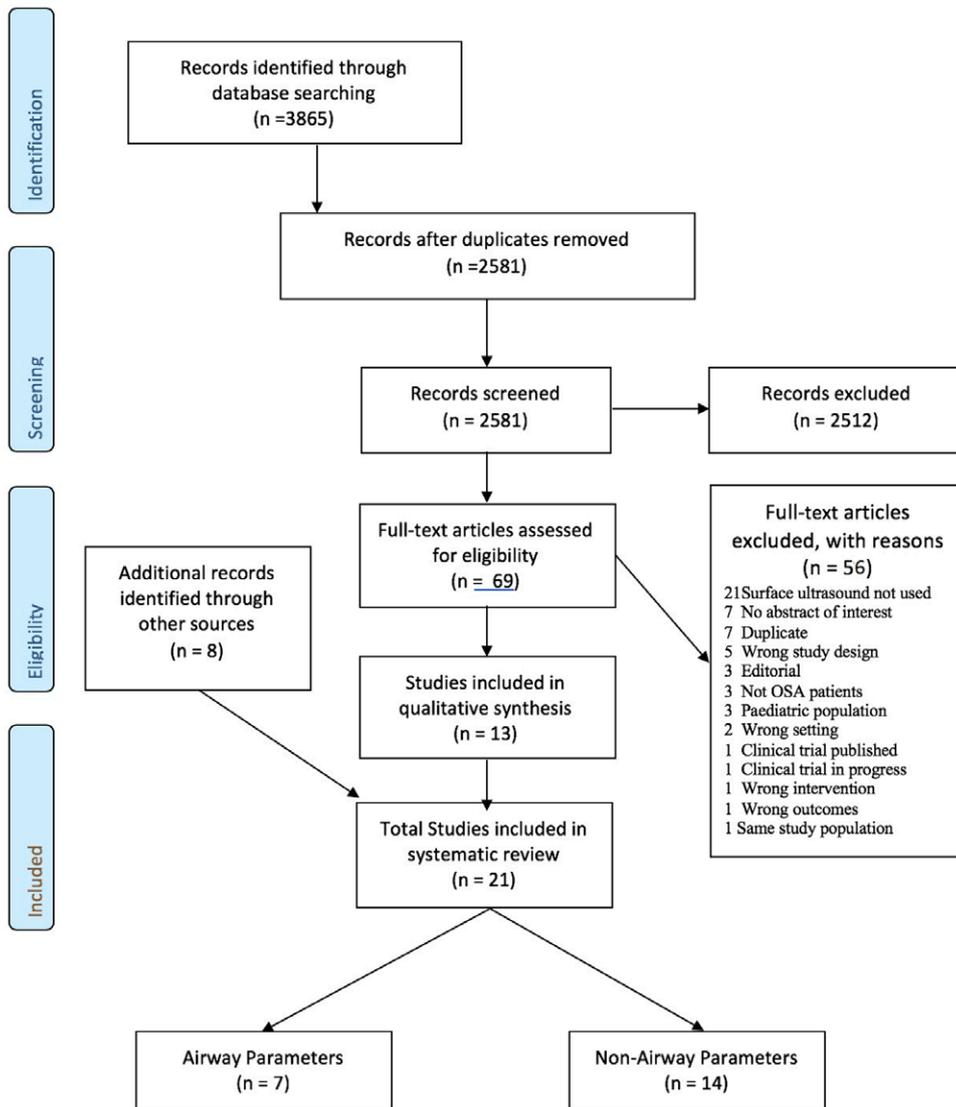
Figure 1. PRISMA flowchart. OSA indicates obstructive sleep apnea; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis.

with known diagnosis of OSA,[45,52] and in the study by Meng et al[55] where patients undergoing percutaneous coronary intervention, 1 week after acute coronary syndrome were included. Risk of bias and applicability concerns were marked high for index test for 1 study[45] due to unclear US scanning technique (Supplemental Digital Content 3–4, Figure 1a, http://links.lww.com/AA/C896, Figure 1b, http://links.lww.com/AA/C897). Most of the studies adequately described the tests, number of patients, recruitment methods, and dropouts. Risk of bias for flow and timing was unclear in 6 studies,[41,42,49,50,52,53,56] mainly due to inadequate information on the timing between the sleep study results and the US scan, and high in 1 study[45] where simultaneous US and sleep study were performed in 1 setting with little information about feasibility. Applicability concerns were low in majority of the studies for patient selection and index test but unclear for reference standard in 2 studies due to limited information about the number of sleep study parameters used to classify OSA[46,52] (Supplemental Digital Content 3–4, Figure 1a, http://links.lww.com/AA/C896, Figure 1b, http://links.lww.com/AA/C897). No included study used screening tools to identify OSA.

The interrater and intrarater variability for the use of US was reported in 2 airway studies[43,44] and 1 nonairway study[47] with moderate to good performance (Table 2; Supplemental Digital Content 5, Table 1, http://links.lww.com/AA/C898). None of the studies reported having used the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines[58] in the article.

Airway Parameters
Suprahyoid Region.
Tongue Parameters. Tongue dimensions in relation to respiration and Muller maneuver (MM; a maneuver where the patient is requested to perform a forced inspiratory effort against an obstructed airway by closing the nose and mouth to induce UA collapse in the awake state) were described and listed in Table 2. Lahav et al[41] examined the distance between lingual arteries (DLAs), tongue base width (coronal plane), and tongue base height (sagittal plane). For moderate to severe OSA (AHI > 15 events/h), a DLA cutoff of >30 mm had a sensitivity and specificity of 80% and 67%, respectively. Chen et al[40] showed that compared to controls (AHI < 5), tongue base thickness in response to negative

Table 1. Table of Demographics

Study	No. of Subjects	Age (y, Mean ± SD)	Sex (M:F)	BMI (kg/m², Mean ± SD)	Neck Circumference (cm, Mean ± SD)	AHI (Events/h, Mean ± SD)	Epworth Sleepiness Scale (Score, Mean ± SD)	Comorbidities (Control)	Comorbidities (OSA)
Airway parameters									
Chen et al[40]	Total: 40 Control (AHI < 5): 20 OSA (AHI > 5): 20	Control: 43 ± 13 OSA: 43 ± 11	Control: 13/7 OSA: 14/6	Control: 24.9 ± 2.5 OSA: 28.9 ± 3.2	Control: 39.3 ± 3.6 OSA: 41.4 ± 3.8	Control: 3.0 ± 1.9 OSA: 35.8 ± 27.1	Control: 6.3 (range, 0–14) OSA: 8.0 (2–16)	Hypertension: 4 (20%) DM: 2 (10%) Hyperlipidemia: 1 (5%) Cardiac disease: 2 (10%)	Hypertension: 8 (40%) DM: 2 (10%) Hyperlipidemia: 7 (35%) CV disease: 2 (10%)
Lahav et al[41]	Total: 40 No OSA: (AHI < 5): 11 Mild OSA (AHI = 6–15): 10 Moderate OSA (AHI 16–30): 4 Severe OSA (AHI > 30): 16	All patients: 49 (range, 20–71)	All males	All subjects: 28 (range, 23–41)	NR	NR	ESS: NR Daytime somnolence (n) None: 7 Mild: 4 Moderate: 16 Severe: 14	NR	NR
Liao et al[42]	Total: 66 AHI < 30: 27 AHI ≥ 30: 39	Total cohort: 42.8 ± 11.7 Control: mean, 39.86; SD, NR OSA: mean, 44.77; SD, NR	Control: 21/6 OSA: 36/3	Total: 27.5 ± 4.7 Control: mean, 24.57 OSA: mean, 29.65	Total: 40.8 ± 4.7 Control: mean, 38.08; SD, NR OSA: mean, 42.7; SD, NR	Total: 43.2 ± 26.7 Control: NR OSA: NR	Total: 8.9 ± 4.3 Control: mean, 7.59; SD, NR OSA: mean, 9.74; SD, NR	Hypertension (4/27) DM (1/27) Smoking (6) Alcohol (2)	Total: Hypertension (15/39) DM (7/39) Smoking (12) Alcohol (8)
Liu et al[43]	Total: 76 No OSA (AHI < 10): 18 OSA (AHI ≥ 10): 58	Control: 53.6 ± 11.2 OSA: 50.3 ± 10.7	Control: 11:7 OSA: 51:7	Control: 25.6 ± 3.1 OSA: 28.4 ± 4.4	Control: 37.6 ± 3.17 OSA: 40.1 ± 3.5	Control: 5.7 ± 2.8 OSA: 37.0 ± 19.9	NR	NR	NR
Shu et al[44]	Total: 105 No OSA: 25 Mild–moderate OSA (AHI = 5–30): 30 Severe OSA (AHI > 30): 50	No OSA: 38.2 ± 12.1 Mild–moderate OSA: 41.4 ± 12.6 Severe OSA: 49.2 ± 14.4	No OSA: 20/5 Mild–moderate OSA: 22/3 Severe OSA: 45/5	Control: 22.7 ± 2.8 Mild–moderate OSA: 25.7 ± 5.5 Severe OSA: 28.2 ± 4.0	Control: 35.9 ± 2.9 Mild–moderate OSA: 16.5 ± 7.5 Severe OSA: 41.1 ± 3.7	Control: 2.4 ± 1.5 Mild–moderate OSA: 16.5 ± 7.5 Severe OSA: 59.4 ± 16.3	NR	NR	NR
Siegel et al[45]	5 patients with OSA (AHI > 35)	Range: 35–57	All Males	NR	NR	NR	NR	NR	NR
Ugur et al[46]	Total: 97 Control: 24 OSA: 73	Control: 47.4 ± 14.6 OSA: 51.6 ± 12.8	Control: 14/10 OSA: 53/20	Control: 29.0 ± 5.5 OSA: 32.4 ± 5.8	Control: 42 (range, 32–46) OSA: 42 (36–45)	Control: 2.6 (range, 0.2–4.8) OSA: 18.7 (0.7–99.3)	NR	NR	NR

(Continued)

Table 1. Continued

Study	No. of Subjects	Age (y, Mean ± SD)	Sex (M:F)	BMI (kg/m², Mean ± SD)	Neck Circumference (cm, Mean ± SD)	AHI (Events/h, Mean ± SD)	Epworth Sleepiness Scale (Score, Mean ± SD)	Comorbidities (Control)	Comorbidities (OSA)
Nonairway parameters									
Altin et al[47]	Total: 70 Controls: 20 Mild OSA (AHI < 20): 20 Severe OSA (AHI > 20): 30	Control: 44.7 ± 6.2 (32–57) Mild: 47.5 ± 9.1 (33–63) Severe: 46.0 ± 8.1 (28–60)	Control: Males only OSA: Males only	Control: 27.4 ± 3.0 Mild: 47.5 ± 9.1 Severe: 30.0 ± 4.1	NR	Control: 2.0 ± 1.6 Mild: 12.9 ± 3.8 Severe: 42.3 ± 24.0	NR	NR	NR
Andonova et al[48]	Total: 54 Non-OSA: 27 OSA: 27	Control: 56.1 ± 1.4 OSA: 55.7 ± 1.4	Control: 26/1 OSA: 26/1	Control: 56.1 ± 1.4 OSA: 55.7 ± 1.4	NR	OSA: 60.8 ± 36.9	NR	Cardiac disease: 23%; Smoking: 60% DM: 37% Hypercholesterolemia: 52%	Cardiac disease: 19%; Smoking: 37% DM: 20% Hypercholesterolemia: 69%
Apaydin et al[49]	Total: 87 HSS(non-OSA): 20 Mild–moderate OSA (AHI = 5–30): 27 Severe OSA (AHI>=30): 40	Control: 47.4 ± 9.6 Mild–moderate OSAS: 52.9 ± 10.5 Severe OSAS: 51.1 ± 10.1	HSS: 13/7 OSA: 53/14 Mild–moderate OSA: 20/7 Severe OSA: 33/7	Control: 27.4 ± 5 Mild–moderate OSAS: 30 ± 4.7 Severe OSAS: 51.1 ± 10.1	Control: 30 ± 4.1 Mild–moderate OSAS: 39.7 ± 3.1 Severe OSAS: 41.1 ± 3.8	Control: 2.4 ± 1.5 Mild–moderate OSAS: 16.2 ± 7.3 Severe OSAS: 68.7 ± 22.7	NR	NR	NR
Baguet et al[50]	Total: 83	Control: NA OSA: 48 ± 11	Control: NA OSA: 74/9	Control: NA OSA: 27.4 ± 4.2	NR	NR	NR	NR	DM: 3 (4%) On statins: 9 (11%) Current smokers: (49%)
Chami et al[51]	Total: 682	Controls: AHI < 1.5: 56 (8) AHI = 1.5–4.9: 61 (10) OSA mild (AHI = 5–15): 60 (9) Moderate (AHI = 15–30): 63 (8) Severe (AHI ≥ 30): 62 (9)	Control: NA OSA: 327/355	Control: AHI < 1.5: 26.1 (4.5) AHI = 1.5–4.9: 28.2 (4.2) OSA mild (AHI = 5–15): 30.1 (5.4) Moderate (AHI = 15–30): 31.4 (5.7) Severe (AHI ≥ 30): 32.7 (5.6)	NR	NR	NR	DM Smoking Cardiovascular disease Hypertension	DM Smoking Cardiovascular disease Hypertension
Ciccone et al[52]	Total: 156	Control: NA OSA: 60 ± 12	Control: NA OSA: 125/31	Control: NA OSA: 34 ± 7	NR	IMT < 0.9: 20 (14–28) IMT ≥ 0.9: 41 (32–58)	NR	NR	Hypertension: 102 (65%) Dyslipidemia: 52 (33%) Diabetes: 38 (24%)

(Continued)

Table 1. Continued

Study	No. of Subjects	Age (y, Mean ± SD)	Sex (M:F)	BMI (kg/m², Mean ± SD)	Neck Circumference (cm, Mean ± SD)	AHI (Events/h, Mean ± SD)	Epworth Sleepiness Scale (Score, Mean ± SD)	Comorbidities (Control)	Comorbidities (OSA)
Ciccone et al[53]	Total: 120; Non-OSA: 40; Mild OSA (AHI = 5–15): 26; Moderate–severe OSA (AHI ≥ 15): 54	Control: 52.27 ± 10.52; Mild OSA: 53.65 ± 11.47; Moderate–severe OSA: 52.33 ± 10.19	Control: 34/6; OSA: 68/12	Control: 28.24 ± 2.7; Mild OSA: 28.13 ± 3.04; Moderate–severe OSA: 28.8 ± 3.03	Control: 40.03 ± 3.07; Mild OSA: 40.12 ± 2.91; Moderate–severe OSA: 40.61 ± 3.41	Control: 2.11 ± 1.14; Mild OSA: 10.55 ± 3.14; Moderate–severe OSA: 45.13 ± 16.08	Control: 6.72 ± 4.03; Mild OSA: 10.03 ± 4.16; Moderate–severe OSA: 11.25 ± 4.81	NR	NR
Drager et al[89]	Total: 81 (MS); OSA: 51	MS-OSA: 45 ± 7; MS + OSA: 47 ± 7	MS-OSA: 57% M; MS + OSA: 76% M	MS-OSA: 31.6 ± 2.7; MS + OSA: 31.9 ± 3.3	NR	MS-OSA: 4.4 ± 3.3; MS + OSA: 51 ± 27	MS-OSA: 9 [7–10]; MS + OSA: 10 [7.3–12]	NR	NR
Liu et al[54]	Total: 242; Non-OSA: 21; OSA (AHI > 5): 221	Controls: 49.5 ± 11.3; OSA: 50.3 ± 9.2	Control: 12/9; OSA: 169/52	Control: 24.8 ± 3.2; OSA: 28.1 ± 4.4	Control: 36.1 ± 3.06; OSA: 39.3 ± 3.58	Control: 3.23 ± 1.32; OSA: 32.5 ± 23.2	NR	NR	NR
Meng et al[55]	Total: 123; OSA (AHI > 5): 75; Non-OSA: 48	OSA: 66.5 ± 1.3; Non-OSA: 66.8 ± 1.3	OSA: M: 53 (70.7), F: 22; Non-OSA: M: 32 (66.7), F: 16	OSA: 24.1 ± 0.3; Non-OSA: 23.0 ± 0.5	NR	NR	NR	Hypertension, n (%): 38 (79.2); Hypercholesterolemia, n (%): 32 (66.7); Diabetes mellitus, n (%): 11 (22.9)	Hypertension, n (%): 56 (75.7); Hypercholesterolemia, n (%): 51 (68.9); Diabetes mellitus, n (%): 19 (25.9)
Minoguchi et al[56]	Total: 52; Obese control: 16; Mild OSA: 13; Moderate–severe OSA: 23	Obese control: 46.5 ± 3.8; Mild OSA: 48.6 ± 3.9; Moderate–severe OSA: 23	All males	Obese control: 16; Mild OSA: 13; Moderate–severe OSA: 23	Obese control: 41.0 ± 0.9; Mild OSA: 40.8 ± 0.8; Moderate–severe OS: 42.1 ± 0.7	Obese control: 3.3 ± 0.6; Mild OSA: 11. ± 0.9; Moderate–severe OSA: 48.4 ± 4.0	Obese control: 7.8 ± 1.1; Mild OSA: 10.4 ± 1.4; Moderate–severe OSA: 12.9 ± 0.1	NR	NR
Schulz et al[90]	Total: 70; Control: 35; OSA: 35	OSA: 55.7 ± 1.4 (52.0–58.4); Control: 56.1 ± 1.4 (53.2–59.2)	OSA 34/1 (M:F); Control: 34/1 (M/F)	OSA: 31.9 ± 0.6 (29.4–33.5); Control: 31.3 ± 0.5 (28.9–33.1)	NR	OSA: 57 ± 3 (45–66); Control: 4 ± 1 (2–6)	NR	Hypertension: 60%; CAD: 23%; PVD: 3%; DM: 37%; Hypercholesterolemia: 57%; Smoking: 60%	Hypertension: 69%; CAD: 19%; PVD: 3%; DM: 20%; Hypercholesterolemia: 59%; Smoking: 37%
Wattanakit et al[57]	Total: 985	Mean age: 62; Carotid plaque: Yes, 64 (5.3); No, 61 (5.3)	Carotid plaque: Yes, M: 52%; No, M: 41%	Carotid plaque: Yes, 27.9 (4.5); No, 28.4 (5.0)	NR	NR	NR	No carotid plaque: diabetes (%): 7.0; Hypertension (%): 25.4; Current smokers (%): 8.3	Carotid plaque: diabetes (%): 14.7; Hypertension (%): 34.7; Current smokers (%): 13.4
Yun et al[91]	Total: 104; OSA: 82; Non-OSA: 22	OSA: 41.5 ± 9.8	OSA: M, 75 (91.5%); Non-OSA: M, 19 (86.4%)	OSA: 26.0 ± 3.6; Non-OSA: 26.2 ± 2.8	NR	OSA: 39.1 (20.2–58); Non-OSA: 2.5 (0.9–3.2)	NR	Hyperlipidemia: 2 (9.1%); Smoking: 14 (63.6%); Alcohol: 10 (45.5%)	Hyperlipidemia: 18 (22%); Smoking: 45 (54.9%); Alcohol: 37 (45.1%)

Abbreviations: AHI, apnea–hypopnea index; BMI, body mass index; CAD, coronary artery disease; CV, cardiovascular; DM, diabetes mellitus; ESS, Epworth Sleepiness Scale; F, female; HSS, habitual simple snoring; IMT, intimal media thickness; M, male; MS, metabolic syndrome; NA, not applicable; NR, not recorded; OSA, obstructive sleep apnea; OSAS, obstructive sleep apnea syndrome; PVD, peripheral arterial disease; SD, standard deviation.

Table 2. Summary of Findings: Airway Ultrasound Parameters

Study Name	Study Design	Sample Size and Setting	Index Test: Ultrasound Variable	Reference Test for OSA Diagnosis	OSA Scoring Criteria (If Different From Criteria in Legend Below)	Blinding	Intra-/Interrater Variability	Correlation With AHI or RDI	Diagnostic Accuracy Metrics (Sensitivity, Specificity, PPV, NPV)	Correlation With OSA Diagnosis (OR)
Suprahyoid region										
Chen et al[40]	Cohort prospective	N = 40 (Taiwan): recently diagnosed OSA (AHI ≥ 5); Controls: AHI < 5	Dynamic TBT: TBT = maximum distance between the submental skin and the dorsal surface of the tongue base	Laboratory PSG, Embla N7000; Medcare, Reykjavik, Iceland	Same as below; oxygen desaturation threshold: 3% criteria	US scan: Yes; PSG results: Yes	NR	NR	NR	OSA: AHI > 5 events/h 1. TBT during MM (OR = 2.11; 95% CI, 1.15–3.87; P < .05) 2. Difference between TBT with the MM and that without the MM (OR = 2.47; 95% CI, 1.09–5.58; P < .05)
Lahav et al[40]	Cohort prospective	N = 41 (Israel) Sleep clinic: Only males	1. DLA 2. Tongue base width and height (maximal)	PSG: Embla: the Somnologica 3.2 (Embla, Denver, CO)	NR	US scanner: NR; PSG results: NR	NR	Correlation with AHI 1. Positive for DLA as continuous variable (coefficient, 0.557; P <.001) 2. No significant relationship with BMI, Tongue base width and height	For moderate to severe OSA (AHI > 15): sensitivity, 80%; specificity, 67% for DLA > 30 mm cutoff SROC value: NR	OS: AHI > 15 1. For a DLA > 30 mm: RR = 3.13 (95% CI, 1.26–7.74)[a]
Liao et al[42]	Prospective	N = 66– suspected OSA, snoring; Clinic	1. Resting Tongue base thickness 2. Muller Tongue base thickness 3. DLA 4. Retropalatal diameter, resting and during MM	Overnight PSG	NR	US scan: NR; PSG results: NR	NR	NR	For resting TBT ≥ 60 mm with severe OSA: 84.9%; sensitivity, 59.3%; specificity, 75.0%; PPV, 72.7%; NPV, 74.2% accuracy SROC value: Mean resting tongue base Thickness ≥ 60 mm: 0.74 (95% CI, 0.61–0.87) TBT during MM > 63 mm: 0.68 (0.55–0.80) DLA: 0.69 (0.55–0.83) All P < .05	Correlation with severe OSA (AHI ≥ 30) Univariate analysis: significant predictors: mean resting TBT > 60 mm, [OR = 8.0; 95% CI, 22.5–25.2], mean TBT in MM > 63.5 mm, [OR = 5.0; 95% CI, 11.7–15.2)], and mean DLA > 30 mm, [OR = 2.91; 95% CI, 11.05–8.0] Multivariate analysis: only resting TBT > 60 mm was found to be a significant predictor with OR = 5.18; 95% CI, 11.07–25.0; P = .041

(Continued)

Table 2. Continued

Study Name	Study Design	Sample Size and Setting	Index Test: Ultrasound Variable	Reference Test for OSA Diagnosis	OSA Scoring Criteria (If Different From Criteria in Legend Below)	Blinding	Intra-/Interrater Variability	Correlation With AHI or RDI	Diagnostic Accuracy Metrics (Sensitivity, Specificity, PPV, NPV)	Correlation With OSA Diagnosis (OR)
Liu et al[43]	Cohort prospective	N = 76 (Hong Kong) Respirology clinic	LPW thickness was correlated with AHI and MRI	Laboratory PSG, Healthdyne Alice 4, Atlanta, GA	Same as below; oxygen desaturation threshold: 3% criteria	US scan: NR PSG results: Yes	Intraoperator variability: ICC, 0.90; 95% CI, 0.71–0.97; SEM: 0.24 cm Interoperator variability: ICC, 0.97; 95% CI, 0.92–0.99; SEM: 0.13 cm	Correlation with AHI: Univariate analysis: positive correlation with neck circumference, BMI, and LPW thickness ($r = 0.37$; $P = .001$) Multivariate linear regression: LPW thickness: positive and independent association ($r^2 = 0.12$, $P = .002$) with AHI	NR (correlation with MRI): good correlation between LPW thickness by ultrasound and LPW-transverse thickness measured by MRI ($r = 0.78$; $P = .001$) Bland–Altman plots: Overestimation of LPW when using the transverse thickness on MRI (the limits of agreement: −0.62 cm; −2.54 cm), but better correlation when using oblique planes on the MRI images (limits of agreements: 1.28 cm; −1.30 cm)	NR
Shu et al[44]	Cohort Prospective	N = 105 (Taiwan) Sleep laboratory Total: 105 No OSA: 25 Mild-moderate OSA (AHI = 5–30): 30 Severe OSA (AHI > 30): 50	UAL, RP, and RG diameter under expiration at tidal breathing, FI, and MM	Lab PSG, Embla N7000, Medcare Flaga, Reykjavik, Iceland	Same as below, except; oxygen desaturation threshold: 4% criteria	US scan: Yes PSG results: Yes	The intra- and interobserver CV ranged from 2.3 (tongue thickness) to 9.1 (forced inspiration of RP diameter) and 3.0 (tongue thickness) to 10.4 (expiration of RG diameter), respectively The intraobserver CV for RP diameter was 7.5 on expiration, 6.4 on forced inspiration, and 8.3 on MM	Factors correlated with AHI (univariate analysis): age, BMI, neck circumference, UAL, tongue thickness, RP diameter at expiration, and 3 breathing maneuvers. The RG diameter on forced inspiration and MM and male sex were not correlated with AHI. Pearson coefficients: neck circumference ($r = 0.659$; $P = .001$), RP diameter on MM ($r = −0.624$; $P = .001$), %RP shortening on MM ($r = 0.584$; $P = .001$), and BMI ($r = 0.531$; $P = .001$)	Neck circumference and %RP shortening during MM, with severe OSA (AHI > 30) Validation group Sensitivity, 100% Specificity, 65% SROC value, 0.889; 95% CI, 0.774–1.004; $P = .001$ Model development group: AUC was 0.893 (95% CI, 0.816–0.970; $P = .001$	Severe OSA (AHI > 30) Multivariate analysis: %RP shortening during MM (OR = 1.087; 95% CI, 1.022–1.156; $P = .008$) and neck circumference (OR = 1.379; 95% CI, 1.138–1.617; $P = .001$)

(Continued)

Table 2. Continued

Study Name	Study Design	Sample Size and Setting	Index Test: Ultrasound Variable	Reference Test for OSA Diagnosis	OSA Scoring Criteria (If Different From Criteria in Legend Below)	Blinding	Intra-/Interrater Variability	Correlation With AHI or RDI	Diagnostic Accuracy Metrics (Sensitivity, Specificity, PPV, NPV)	Correlation With OSA Diagnosis (OR)
Siegel et al[45]	Prospective	N = 5 (the United States) OSA patients on CPAP Asleep patients on outpatient basis	Submental Ultrasound: Tongue Base Movement (not specified)	PSG: No details	NR	US scan: NR PSG results: NR	NR	In some subjects, obstruction may be detected earlier than PSG on US visualization of floor muscles	NA	NR
Infrahyoid region										
Ugur et al[46]	Cross-sectional	N = 97 (Turkey): OSA patients; Tertiary care university hospital	Subcutaneous fat tissue thickness, anterior neck and umbilicus	PSG, Grass Technologies, Twin PSG Software, West Warwick, Rhode Island	Same as below; except; oxygen desaturation threshold: 4% criteria No arousal.	US scan: NR PSG results: NR	NR	No significant correlation between ultrasound parameters and OSA	NR	NR

Scoring criteria: Obstructive apnea was defined as complete cessation of airflow or a ≥90% reduction in the peak thermal sensor signal for ≥10 seconds; a hypopnea episode was defined as ≥50% reduction in the nasal pressure signal for ≥10 seconds in association with oxygen desaturation >3% and/or arousal.

Diagnostic accuracy values calculated from the original article cited in the Study Name column.

Abbreviations: AHI, apnea–hypopnea index; AUC, area under curve; BMI, body mass index; CI, confidence interval; CPAP, continuous positive airway pressure; CV, coefficient of variation; DLAs, distance between lingual arteries; FI, forced inspiration; ICC, intraclass correlation coefficient; LPW, lateral pharyngeal wall; MM, Muller maneuver; MRI, magnetic resonance imaging; NA, not applicable; NPV, negative predictive value; NR, not recordable; OR, odds ratio; OSA, obstructive sleep apnea; PPV, positive predictive value; PSG, polysomnography; RDI, respiratory disturbance index; RG, retroglossal; RP, retropalatal; RR, relative risk; SEM, standard error of measurement; SROC, summary receiver operating curve; TBT, Tongue Base Thickness; UAL, upper airway length; US, ultrasound.

[a]The revised calculated RR and 95% CI are reported based on calculation of data reported in the 2x2 table of this study.[41]

airway pressure during MM (odds ratio [OR] = 2.11; 95% confidence interval [CI], 1.15–3.87; P < .05) and difference between tongue base thickness with or without MM (OR = 2.47; 95% CI, 1.09–5.58; P < .05) were associated with OSA diagnosis (AHI ≥ 5). Liao et al[42] found that out of tongue base width using DLA (30 mm), mean resting tongue base thickness (60 mm), and mean tongue base thickness during MM (63 mm), only resting tongue base thickness (cutoff >60 mm thickness) was found to be the sole predictor for severe OSA (OR = 5.18; 95% CI, 1.07–25.0; P = .04) on multivariable regression. Siegel et al[45] found that UA obstruction using US was detected 5–10 seconds before the onset of apnea (full cessation of airflow) during simultaneous overnight PSG; however little description was provided about how the events were identified.

Pharyngeal Parameters. Liu et al[43] found that US measurement of lateral pharyngeal wall (LPW) thickness had good correlations with magnetic resonance imaging (MRI) measurement (r = 0.78; P = .001) and the fair to moderate correlation with severity of OSA (r = 0.37; P = .001). Moreover, LPW thickness was found to have a positive and independent correlation (r = 0.12; P = .002) with AHI after adjustment for age, sex, neck circumference, and BMI in this study. Shu et al[44] performed dynamic assessment of pharyngeal parameters such as retropalatal (RP) and retroglossal diameters, during tidal breathing, forced inspiration, and MM. Multivariable analysis indicated that AHI was positively associated with percentage shortening of RP diameter during MM (OR = 1.09; 95% CI, 1.02–1.16; P = .008) and neck circumference (OR = 1.38; 95% CI, 1.14–1.62; P = .001).

Infrahyoid Region.
Subcutaneous Fat Tissue. Ugur et al[46] measured subcutaneous fat tissue thickness (mm) at the level of the submandibular gland, thyroid isthmus, suprasternal notch, hyoid, and umbilicus by US and concluded that these measurements had no correlation with AHI.

Nonairway Parameters
We examined studies providing information on correlation with US-identified nonairway structures and OSA diagnosis based on AHI cutoffs or AHI as a measure of OSA severity as a continuous measure.

Carotid Intimal Media Thickness. A number of studies evaluated correlation of the carotid intimal media thickness (cIMT) with OSA diagnosis (Table 3; Supplemental Digital Content 5, Table 1, http://links.lww.com/AA/C898). Studies where no data could be extrapolated for either correlation or diagnostic property metrics were excluded. Ciccone et al[52] studied the correlation between OSA duration and severity with cIMT US measurements.[53] Altin et al[47] found ultrasonographic evidence of increased atherosclerotic changes in both left and right common carotid arteries in OSA (P < .05). Andonova et al[48] found that the presence of atherosclerotic plaques in common carotid artery was predictive of moderate OSA (sensitivity = 59%, specificity = 70%), and mean cIMT was positively correlated with AHI (r = +0.43; P < .05). Apaydin et al[49] found that a higher cIMT was present in patients with OSA compared

to habitual snorers. However, cIMT did not correlate with OSA severity. Wattanakit et al[57] found a positive relationship between carotid plaque formation and cIMT with OSA severity on a univariate analysis; however, multivariate adjustment for demographic and metabolic factors attenuated with effect. Baguet et al[50] showed that nocturnal mean Sao_2 (<92%) was associated with cIMT and plaque formation, and minimal nocturnal desaturation (Sao_2 < 80%) was associated with plaque formation.

Other Parameters. Liu et al[60] found that mesenteric fat thickness had a positive association with the presence of moderate OSA (AHI > 15 events/h; OR = 7.18; 1.05–49.3; P value = not reported) for every 1-cm increase in mesenteric fat thickness and severe OSA (AHI > 30 events/h; OR = 7.45; 1.12–49.6; P value = not reported), after accounting for age, sex, BMI, neck circumference, preperitoneal, and subcutaneous fat thickness. In a follow-up study involving a larger sample size, they found that mesenteric fat thickness and AHI predicted metabolic syndrome only in men (OR = 1.02; 95% CI, 1.0–1.04; P = .027) for the increase of 1 event per hour, not in all patients (OR = 1.01; 95% CI, 1.0–1.03; P = .11) or in women (OR = 0.98; 95% CI, 0.95–1.01; P = .19).[54] Chami et al[51] evaluated US-identified brachial artery (BA) diameter by US and peripheral blood flow dynamics by flow-mediated dilation. A positive association was observed with increasing BA diameter and AHI, where the mean BA diameter (mm) was 4.5 (standard error [SE] = 0.11), 4.55 (0.07), 4.33 (0.04), 4.32 (0.04) for severe, moderate, mild, and no OSA, respectively (P < .05). However, no relation between OSA and flow-mediated dilation was identified.

Correlation With AHI
Various airway and nonairway tools were examined for the strength of correlation with AHI as a continuous measure (Supplemental Digital Content 6, Figure 2, http://links.lww.com/AA/C899). A random-effects meta-analysis (8 studies, 727 patients) was performed to evaluate the pooled estimates for the correlation between cIMT and AHI, where the pooled correlation coefficient was 0.44 (95% CI, 0.320–0.553; Q value = 26.1; P value < .001; I^2 = 73%; Figure 2). For the other OSA-related parameters, the data were insufficient to perform a meta-analysis, and summary measures were reported and assessed qualitatively (Supplemental Digital Content 6, Figure 2, http://links.lww.com/AA/C899). Airway measures such as DLAs, RP diameter and %RP diameter shortening during MM, lateral pharyngeal thickness, and UA length were found to have a moderate correlation with AHI (r values range between 0.37 and 0.624; Supplemental Digital Content 6, Figure 2, http://links.lww.com/AA/C899). The correlation between AHI and nonairway parameters such as mesenteric fat thickness and preperitoneal fat thickness was lower (r values range between 0.09 and 0.71; Supplemental Digital Content 6, Figure 2, http://links.lww.com/AA/C899).

Heterogeneity and Publication Bias
There was significant heterogeneity in the US measures used for evaluating UA that limited the generation of pooled estimates. In the random-effects meta-analysis of the

Table 3. Ultrasound Scanning Technique Table

Study Name	Sonography	Scanner	Transducer	Sonographers	Methodology
Suprahyoid region					
Chen et al[40]	Gray-scale 2D mode	Nemio SSA-550A (Toshiba Medical Systems, Otawara, Japan)	6-3 MHz curvilinear transducer	Certified sonographer with experience in ultrasound scanning of the head and neck region. The examiner was blinded to PSG results	All ultrasound examinations performed on frozen ultrasound images at the end of expiration during eupneic breathing. The varying shape of the tongue base during the MM was again observed dynamically by grey-scale real-time ultrasound. TBT and SFT were recorded and measured on frozen ultrasound images on performance of the MM with the tongue base positioned farthest away from the transducer (ie, with the pharyngeal airway presumably decreased to its smallest caliber). The maximum TBT and SFT on the MM were measured 3 times on 3 separate images.
Lahav et al[41]	NR	Acuson Super Sequoia 512 (Siemens Medical Solutions, Malvern, PA)	Convex transducer in the frequencies 4 and 6 MHz	All examinations were conducted by trained US technicians under the supervision of the first author.	With the patient in a seated position, the transducer was introduced to the skin of the neck in the submental region in coronal plane, immediately cephalad to the body of the hyoid bone, and in sagittal plane, in the area between the hyoid bone and the symphysis of the mandible.
Liao et al[42]	NR	Toshiba Aplio 500 Platinum platform (Otawara, Japan)	1-to 6-MHz convex transducer	Submental US performed by a head and neck surgeon experienced in neck US, triplicate measurements.	Triplicate measurements of DLA, retro palatal diameter in transverse dimension, and tongue base thickness in sagittal plane. Methods described in Lahav et al,[41] Chen et al,[40] and Shu et al[44] studies were used.
Liu et al[43]	Gray-scale real-time ultrasound	ATL HDL5000 (Bothell, CA)	C5-2 or C7-5 MHz curvilinear transducer	Same operator (LKH), who was experienced in ultrasound scanning and was blinded to the polysomnographic data	With the patient in supine position and slight neck extension, with 35° soft pad under neck, oblique coronal plane of parapharyngeal space scanned with transducer longitudinal on lateral side of neck, just underneath lateral border of occipital bone. Distance between internal carotid artery and echogenic surface of pharynx represented the LPW thickness in an oblique coronal plane. All measurements were recorded when lateral wall of pharynx moved farthest away from transducer. Maximum thickness of LPW on both sides measured 3 times on 3 separate images and mean value taken
Shu et al[44]	Gray-scale 2-dimensional mode	Aplio XV (Toshiba Medical Systems, Tokyo, Japan)	5.0-MHz convex transducer	An independent operator (Shu CC) who was blinded to the PSG results	Supine patient with orbitomeatal line vertical to horizon. Scanned from hyoid bone to EAM at level of oral pharynx. The probe is tilted up and down to locate RP and RG Pharynx. The probe was tilted to scan coronal plane and measure tongue thickness. Scanned sagittal plane along midline and measure UAL from anterior edge of hyoid to edge of hard palate
Siegel et al[45]	NR	Real-time mechanical sector ultrasonic machine (ATL HDI 5000; Advanced Technology Laboratories, Bothell, WA)	Ultrasonic transducer (P5-3 phased array or L12-5 linear array)	NR	Polysomnography and ultrasound recorded simultaneously. The ultrasonic transducer (P5-3 phased array or L12-5 linear array) was fastened around the head and positioned submentally, resting just above the sternum in a sling fastened around the neck with Velcro bands for position stabilization during sleep
Infrahyoid region					
Ugur et al[46]	NR	SONOLINE Antares system (Siemens, Erlangen, Germany)	13.5-MHz linear probe	NR	Subcutaneous fat tissue thicknesses (mm) of anterior neck and umbilicus assessed. Five parameters were measured: thickness of subcutaneous fat tissue adjacent to submandibular gland, thyroid isthmus, hyoid, suprasternal notch, and umbilicus.

(Continued)

Table 3. Continued

Nonairway structures

Study Name	Sonography	Scanner	Transducer	Sonographers	Methodology
Altin et al[47]	Gray scale	5000 HDI scanner (Philips ATL, Bothell, WA)	5- to 12-MHz linear array transducer	2 sonographers on 2 separate, minimum 1-week interval between visits. US data were average of the 2 measurements	IMT defined as distance between leading edge of the luminal echo to leading edge of the media/adventitia echo. CCA-IMT measured over a distance of about 1 cm proximal to the bulb. ICA-IMT measured over a distance of about 1 cm distal to the bulb. IMT of carotid bulb measured between these 2 sites
Andonova et al[48]	Color-coded duplex Real-time B-mode imaging	Sonix SP (Burnaby, BC, Canada)	7.5-MHz transducer	NR	Carotid IMT (mm) measured with a standard method, using a program for automatic value averaging. The rate of the stenosis determined with the morphologic method in longitudinal and transversal slice of the examining vessel.
Apaydin et al[59]	NR	Logic S8; GE Medical Systems, Milwaukee, WI	8-MHz linear probe	Analyzed by the same experienced physician, blinded to the snoring and/or sleep disturbance	Far-wall CCA-IMT measured in the distal of each CCA in the proximal 1 cm of carotid bulb in areas free of plaque. CCA-IMT manual measurement repeated 6 times and results were averaged. Plaque was defined as focal wall being 50% thicker than the surrounding wall.
Baguet et al[50]	B-mode ultrasonography	HP Sonos 2500; Hewlett-Packard, Santa Clara, CA	Sectorial probe of 7.5 MHz with axial and lateral resolution of 0.15 mm	NR	Both CCA studied consecutively in the long axis with a probe incidence allowing good-quality images. Image defined by presence of 2 hyperechogenic lines separated by a hypoechogenic zone from the posterior artery wall. IMT defined as distance separating the most internal parts of these lines, and the luminal diameter was the distance between the blood/intima interfaces on the anterior and posterior walls. For all patients, a zoom was used to define a zone of interest of 20 mm in length (stretching from 10 to 30 mm above the carotid bifurcation)
Chami et al[51]	NR	Toshiba SSH-140A ultrasound system	7.5-mHz linear array transducer	Blinded sonographers analyzed the images offline using a special software	A randomly assigned sonographer blinded to the FMD measurements and SDB status visually confirmed the timing of peak flow, inspected the raw spectral analysis, and selected the appropriate beats representing peak flow. Baseline and hyperemic flow velocities were multiplied by the baseline cross-sectional area to obtain the respective flow volumes.
Ciccone et al[52]	Two-dimensional echo-color Doppler of the carotid arteries	High-definition vascular echo graph Philips Sonos 5500, Bothell, WA	10-3 MHz linear electronic probe	Same physician	Supine position, with the neck extended and turned contra laterally by about 45°. The IMT was defined as the distance between the lumen-intima and media-adventitia borders of the vessel, ultrasonographically identified by a double hypoechoic line not projecting into the vessel lumen. Echo measurements were made in 3 zones: proximal zone: about 2 cm above the flow divider; distal zone: about half centimeter above the flow divider; and middle zone.
Ciccone et al[53]	Two-dimensional echo-color Doppler of the carotid arteries	Philips Sonos 5500 (Bothell, WA)	10-3 MHz linear electronic probe	Same physician.	cIMT defined as distance between the lumen-intima and media-adventitia borders of the vessel, ultrasonographically identified by a double hypoechoic line not projecting into the vessel lumen. Intima-media thickness of distal wall of right CCA on lengthwise axis, echo measurements made in 3 zones: (1) proximal zone: about 2 cm before the flow divider; (2) distal zone: about half centimeter before the flow divider; and (3) middle zone.
Drager et al[89]		Complior (Colson, Garges les Gonesses, France)	TY-306-Fukuda pressure-sensitive transducer (Fukuda, Tokyo, Japan)	Experienced observer, blinded to the polysomnographic data	IMT was measured on the right common carotid arteries 1 cm below the bifurcation at the site of the distal wall. IMT was measured at the thickest point, not including plaques, on the near and far walls with a specially designed computer program. Plaque was defined as a localized thickening >1.2 mm that did not uniformly involve the whole artery, and if present the measurement was taken ≥1 cm away from plaque

(Continued)

Table 3. Continued

Study Name	Sonography	Scanner	Transducer	Sonographers	Methodology
Liu et al[54]	NR	Philips ATL HDI 5000 (Bothell, CA) or Philips iU22 (Eindhoven, the Netherlands)	NR	Same ultrasonographer who was blinded to the clinical and PSG results.	For abdominal fat thickness, mesenteric leaves identified in central abdomen, tubular structures with linear hyperechoic peritoneal layers. Different mesenteric leaves were separated by thin hyperechoic peritoneal layers. Mean value of 3 thickest measurements taken. Preperitoneal and subcutaneous fat thicknesses measured in midline between xiphoid process and umbilicus.
Meng et al[55]	B-mode ultrasonography of both common carotid arteries	iU22 Ultrasound System; Philips Healthcare, Best, the Netherlands	A sectorial probe of 7.5 MHz with an axial and lateral resolution of 0.15 mm	2 sonographers who were blinded to the other study data. Analysis of the carotid parameters used the internal software of the iU22 Ultrasound System and was performed by the same operator.	Carotid IMT was determined over a 20 mm length above the carotid bulb on both arteries and the mean of 2 values was used
Minoguchi et al[56]	High-resolution B-mode ultrasonography	PEL-705S; Toshiba, Tokyo, Japan	A 7.5-MHz linear array transducer	All subjects were examined by the same investigator who was blinded to clinical characteristics.	The mean IMT was calculated as the average of 8 measurements (excluding sites of plaque) in the right and left sides during end diastole. Plaques were defined as the presence of focal, severe wall thickening (IMT > 1.2 mm), wall irregularity, and calcification. Plaque formation was graded as absent (0), mild (1: <30% of the vessel diameter), moderate (2: 30%–50% of the vessel diameter), or severe (3: > 50% of the vessel diameter
Schulz et al[90]	High-resolution B-mode ultrasonography	Sonoline Elegra, an 8-MHz transducer (Fa.; Siemens, Erlangen, Germany)	An 8-MHz transducer	All measurements were performed with the investigator blinded to the status of the individual patient	Longitudinal images obtained at the far wall of the distal 1.0 cm of both CCAs A plaque was defined as a localized thickening >1.2 mm
Wattanakit et al[57]	High-resolution B-mode ultrasound	Biosound 2000 II SA; Biosound Inc, Indianapolis, IN	Not mentioned	Examinations and readings were performed by trained and certified sonographers and readers	Measurements of carotid IMT were derived in the far wall of 3 segments of the right and left extracranial carotid arteries: the common carotid artery (1 cm proximal to the dilation of the carotid bulb), the bifurcation (the 1-cm segment proximal to the flow divider), and the internal carotid artery (the 1-cm segment in the internal branch distal to the flow divider).
Yun et al[91]	High-definition B-mode ultrasonography	10L5, Terason 2000; Terason Ultrasound, Burlington, MA	10.0-MHz linear array transducer	IMT was measured in the morning after polysomnography by one of the investigators who was blind to other subject information	Average IMT from both sides was recorded. The presence of plaques was documented in the exposed areas of the bilateral common, external, and internal carotid arteries, and bulbs. A plaque was defined as a localized thickening >1.2 mm that did not uniformly involve the entire artery. The degree of plaque formation was defined as follows: 0 = no plaque, 1 = 1 small (<30% of the diameter), 2 = 1 medium (between 30% and 50% of the diameter) or multiple small, and 3 = 1 large (>50% of the diameter) or multiple with ≥1 medium

Abbreviations: 2D, 2 dimensional; CCA, common carotid artery; DLAs, distance between lingual arteries; EAM, external auditory meatus; FMD, flow-mediated dilation; ICA, internal carotid artery; IMT, intimal media thickness; LPW, lateral pharyngeal wall; MM, Muller maneuver; PSG, polysomnography; RG, retroglossal; RP, retropalatal; SDB, sleep-disordered breathing; SFT, subcutaneous fat thickness; TBT, tongue base thickness; UAL, upper airway length; US, ultrasound.

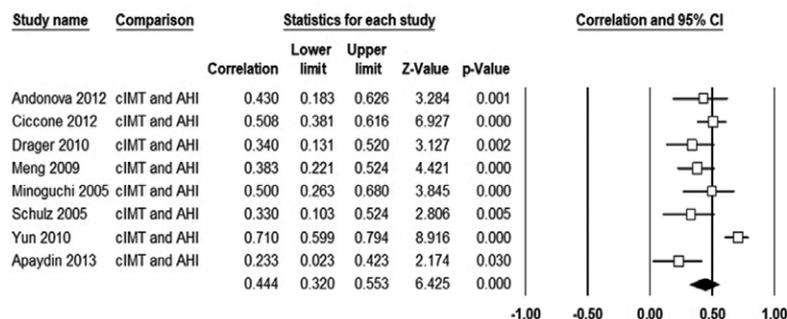**Correlation between Carotid Intimal Media Thickness and AHI**

Figure 2. Meta-analysis of correlation between cIMT and AHI. AHI indicates apnea–hypopnea index; CI, confidence interval; cIMT, carotid intimal media thickness.

correlation between AHI and cIMT (see above), there was a moderate amount of heterogeneity (I^2 = 73%). In a visual inspection of the funnel plot used to check for publication bias in this meta-analysis, studies were distributed symmetrically around the pooled estimate, suggesting no publication bias (Supplemental Digital Content 7, Figure 4, http://links.lww.com/AA/C900). The trim-and-fill method also suggested that there were no unpublished studies.

Diagnostic Properties of Various US Tools

Wherever applicable, diagnostic properties of US tools were examined. Relevant cutoffs examined were AHI > 5, AHI ≥ 15, and AHI ≥ 30 events/h (Figure 3). Overall 8 studies, of which 3 airway[41,42,44] and 5 nonairway parameter studies,[47,48,52,57,59] were included due to availability of data. The significant airway parameters were tongue base width (DLA > 30 mm), resting tongue base thickness ≥60 mm, resting tongue base thickness during MM, and combination of neck circumference with %RP diameter shortening during MM. These parameters had a high sensitivity (80%–100%), but moderate specificity for moderate to severe OSA diagnosis. On the other hand, the specificity of cIMT thickness (≥0.9 mm) and plaque presence was high (80%–100%) and was found to have a low to moderate sensitivity (20%–50%) for moderate OSA. The data were inadequate to pool results and evaluate for summary estimates, and no meta-analysis was performed.[61,62] However, graphical estimation of indirect comparison of the US parameters was conducted by generating ROCs wherever applicable for US parameters against OSA severity levels (Supplemental Digital Content 8, Figure 3, http://links.lww.com/AA/C901).[62] Overall, findings indicated that the strength of association was highest for the combination of neck circumference and %RP shortening during MM (sensitivity = 1.0, 95% CI, 0.93–1.0; specificity = 0.65, 95% CI, 0.51–0.77). Although data from Ciccone et al[52] indicated a good diagnostic profile for moderate to severe OSA for carotid plaque presence (sensitivity = 1.0, 95% CI, 0.93–1.0; specificity = 0.65, 95% CI, 0.51–0.77), the results should be read with caution as this study only included patients with OSA with no control group, with >70% on continuous positive airway pressure (CPAP) with varying compliance, thereby impacting the negative predictive value in this study.

DISCUSSION

To our knowledge, this is the first systematic review evaluating utility of surface US measurements for OSA diagnosis and correlation with its severity. Although a number of US determined airway and nonairway parameters were found to be associated with OSA diagnosis, there was significant heterogeneity and scarcity of well-designed studies to validate US as a useful OSA screening tool.

Many surgical patients with OSA remain undiagnosed at the time of surgery.[18] The gold standard for OSA diagnosis is an overnight laboratory-based PSG; however, due to increased cost and resource burden, this could potentially impact timely diagnosis and treatment.[63,64] Although portable sleep devices are gaining popularity and are less costlier than PSG, they are not suitable as a bedside, point-of-care tool in the preoperative setting. Patient questionnaires and scoring systems developed for OSA screening[65–69] are largely sensitive but less specific[19,20] with increased false positives leading to increased resource utilization and cost burden. US is a noninvasive, portable, and affordable clinical tool that is fast becoming a core skill set of physicians and health care providers.
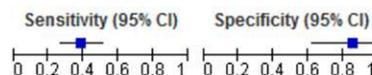
Anatomical factors of the UA account for two-thirds of the variation in OSA severity.[10,11] Past computed tomography (CT) and MRI studies of the UA have identified various anatomical risk factors for OSA including enlargement of the tongue,[70,71] soft palate,[72] adenotonsillar tissue,[73] parapharyngeal fat pads,[73] and LPWs[70] in conjunction with retrognathia. Airway obstruction at the RP and retroglossal regions of the pharynx,[74] an inferiorly displaced hyoid,[75,76] increased UA length,[77] increased pharyngeal length, and increased tongue dimensions[76] have been linked to OSA. Although CT and MRI are excellent airway evaluation tools, they are costly and inaccessible, thus not practical for OSA diagnosis. US scanning protocol of the UA has been described in the suprahyoid and infrahyoid regions.[78] Subsequent studies showed good correlation of US with CT-derived measured airway parameters,[78,79] with good inter- and intraobserver reliability.[80] Another study in OSA patients also successfully correlated the LPW thickness detected by US with MRI.[43] US has the potential to study UA collapse, and predict the site of UA obstruction.[81]

In this review, we identified a combination of neck circumference and %RP diameter shortening during MM, tongue base thickness during MM, resting tongue base thickness, tongue base width (DLA > 30 mm), and LPW
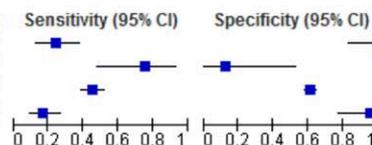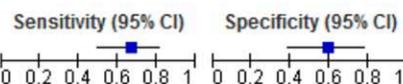
Figure 3. Diagnostic properties of the relevant US measures based on various AHI cutoffs. AHI indicates apnea–hypopnea index; CI, confidence interval; FN, false negative; FP, false positive; MM, Muller maneuver; NC, neck circumference; OSA, obstructive sleep apnea; RP diameter, retropalatal diameter; TN, true negative; TP, true positive.

thickening to be useful US parameters for future exploration. Mueller's Maneuver, performed by requesting the patient to perform a forced inspiratory effort against an obstructed airway by closing the nose and mouth, has been shown to be correlated with endoscopic findings of UA collapse.[82] Shu et al[44] proposed a prediction model combined with neck circumference and a percentage reduction in RP diameter during MM. Chen et al[40] evaluated tongue base thickness during MM and difference between tongue base thickness with or without MM were independent predictors of OSA (AHI > 5 events/h). Using static and dynamic measures of airway, US has the potential in establishing the site of obstruction[42–44,83] and potentially evaluate treatment effectiveness following CPAP or airway surgeries.

In addition, we found that US airway parameters had a high sensitivity for diagnosis of moderate to severe OSA, whereas surrogate metabolic sequelae of OSA such as carotid plaque formation and carotid intimal thickness were more specific (Table 2; Supplemental Digital Content 5, Table 1, http://links.lww.com/AA/C898). A combination of US airway parameters can likely increase diagnostic performance of this examination, but this needs to be evaluated in future studies. Several patient questionnaires and scoring systems have already incorporated nonairway parameters such as hypertension diagnosis.[19,20,84,85] It remains to be seen how the incorporation of nonairway measures would increase both sensitivity and specificity of a PoCUS-OSA tool.

Our review has certain limitations, and the use of PoCUS in the perioperative period needs to be investigated further before becoming mainstream. Even if 21 studies were included in this systematic review, most of the results were based on only the small subset of studies. Although we successfully identified a number of abnormal airway and nonairway US parameters correlating with OSA severity, all of these were from the general population with increased heterogeneity thereby decreasing the generalizability and application in the perioperative setting. Patients with significant craniofacial abnormalities or previous neck surgeries were excluded from most studies, and utility of US in this patient population would need to be investigated. Nevertheless, our findings will stimulate further prospective research to evaluate the usefulness compared to current questionnaire-based OSA screening tools, as in the ongoing trial at our institution (NCT03361553).[86] In addition, although AHI has for the longest time been an index to gauge severity of the condition, other parameters such as severity of Sao_2 could be important parameters linked with postoperative complications.[87,88] Furthermore, there is emerging knowledge to classify OSA patients based on the physiological response during breathing events, such as low arousal threshold or high loop gain that has important treatment implications in the perioperative setting.[10–12] However, the equipment used for these measures is bulky and currently limited to the research setting. The PoCUS-OSA screening tool on the other hand, arguably, has the potential to circumvent this limitation due to the increased availability and portability in the perioperative setting.

CONCLUSIONS

We identified a number of airway and nonairway US parameters having moderate to strong correlation with OSA that may be incorporated in a PoCUS-OSA screening tool. Among the airway parameters, a combination of neck circumference and %RP diameter shortening during MM, tongue base thickness during MM, resting tongue base thickness, tongue base width (DLA > 30 mm), and LPW thickening best predicted moderate to severe OSA diagnosis. Nonairway parameters including carotid plaque formation and carotid intimal thickening may be included in combination with symptoms and airway parameters to increase diagnostic performance (both sensitivity and specificity) of surface US. Although PoCUS is a potential tool for screening OSA, all past study data had significant heterogeneity and were obtained from studies conducted outside of the perioperative setting. This is a new exciting area of investigation, and future studies should build on this work to determine whether a perioperative PoCUS can further improve diagnostic accuracy of OSA questionnaire-based tools. ■

DISCLOSURES

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