REVIEW ARTICLES

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Anatomically Based Outcome Predictors of Treatment for Obstructive Sleep Apnea with Intraoral Splint Devices: A Systematic Review of Cephalometric Studies

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Aims: The aim of this review is to summarize data from the literature on the predictive value of anatomy-based parameters, as identified by cephalometry, for the efficacy of mandibular advancement devices (MAD) for the treatment of obstructive sleep apnea (OSA).

Methods: Articles were initially selected based on their titles or abstracts. Full articles were then retrieved and further scrutinized according to predetermined criteria. Reference lists of selected articles were searched for any missed publications. The selected articles were methodologically evaluated.

Results: Of an initial 311 references, 13 were selected that assessed correlations between polysomnographic and cephalometric variables. The majority of studies demonstrated a correlation between treatment effectiveness and features as determined by cephalometric analysis, such as the mandibular plane angle, hyoid bone distance to mandible, antero-posterior diameter of the maxilla, tongue area, cranial base, and soft palate.

Conclusions: The mandibular plane angle and the distance between hyoid bone and mandibular plane was found to have a predictive value for MAD effectiveness in OSA patients. However, the relative weak and somewhat inconsistent cephalometric data suggest that decisions based solely on these factors cannot be recommended, especially because an integrated analysis of other risk factors (e.g., age, sex, BMI) should also be taken into account.

Keywords: cephalometry, mandibular advancement device, OSA, predictors, splint

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Population-based studies suggest that approximately 13% of middle-aged men and 6% of middle-aged women suffer from symptomatic obstructive sleep apnea (OSA). OSA is associated with clinical, psychological, and social impairment, and is currently viewed as a major risk factor for several medical disorders.[1–3] The pathogenesis of OSA is complex, involving a combination of neurological, anatomic, and demographic factors that may influence the onset of upper airways obstruction, such as, for example, a high body mass index (BMI) and an adult age—the two main demographic risk factors for sleep disordered breathing.[3,4] At present, full-night polysomnography (PSG) is the standard of reference for the diagnosis and severity rating of OSA.[5] Treatment options range from conservative measures, such as weight loss and continuous positive airway pressure (CPAP), to more invasive soft-tissue surgery. Despite the fact that CPAP is the standard for treatment, it must be pointed out that it has strong limitations due to poor patient tolerance.

Recently, the use of oral appliances (OA) has evolved into a viable alternative to CPAP. Importantly, findings from studies adopting custom-made mandibular advancement devices (MAD) are encouraging and may suggest that anatomical predisposition plays an important role as a risk factor for OSA.[6–11] Based on that, the need for identifying potential anatomy-based outcome predictors for MAD treatment has emerged.

At present, practical parameters for OSA treatment with MAD have been mainly focused on the relative indications with respect to CPAP, supporting, for instance, their use in patients with mild-to-moderate OSA who prefer them to CPAP, who do not respond to CPAP, or are not appropriate candidates for CPAP.[9] In any case, in the clinical setting, it is also important to identify which patients may expect benefits from treatment with MAD. For this purpose, several previous studies suggest that the assessment of various cephalometric features may help predicting the response to OA treatment.[12–15] Notwithstanding, the literature findings on this topic have never been systematically summarized, and the actual clinical value of cephalometric assessments for MAD treatment planning is yet to be determined.

Based on these premises, this manuscript is a qualitative systematic review of data found in the literature on the predictive value of cephalometry-based parameters for the effectiveness of MAD treatment in OSA patients.

Table 1A—Grading the evidence statements for case control studies.

	Selection									
Case control studies	Is the case definition adequate?			Representativeness of the cases		Selection of controls			Definition of controls	
	yes, with independent validation	yes, e.g., record linkage or based on self-reports	no description	consecutive or obviously representative series of case	potential for selection biases or not stated	community controls	hospital controls	no description	no history of disease (endpoint)	no description of source
Mayer et al. 1995	♦			♦		♦			♦	

	Comparability		Exposure									
	Comparability of cases and controls on the basis of the design or analysis		Ascertainment of exposure					Same method of ascertainment for cases and controls		Non response rate		
	study controls for cephalometric predictors for MAD efficacy in OSA	study controls for any additional factor	secure record	structured interview where blind to case/ control status	interview not blinded to case/control status	written self-report or medical report only	no description	yes	no	same rate for both group	non respondents described	rate different and no designation
Mayer et al. 1995	♦		♦					♦		♦		

METHODS

Search Strategy

The search strategy was designed to include articles on the basis of their relevance for answering the clinical research question, "Is it possible to predict the effectiveness of MAD therapy in patients with OSA, as assessed by PSG, using cephalometric parameters?"

The inclusion criteria were based on the type of the study: articles published after 1990, focusing on the PSG-assessed effects of MAD treatment in adult OSA patients without any other concurrent pathological syndromes who have undergone baseline cephalometric evaluation.

In order to identify relevant studies, as the first step, a search was carried out in the Medline and the Cochrane Library databases using a combination of MeSH and keyword terms related to OSA (i.e., obstructive sleep apnea), anatomy-based outcome predictors (i.e., anatomic obstruction; cephalometry; cephalometric parameters or analysis), oral appliances (i.e., oral device or appliance; mandibular advancement device, MAD; treatment or efficacy/effectiveness). No language limitations were set.

This first search step allowed the identification of a list of potential citations for inclusion in this review. Titles and abstracts on this list were screened by two independent reviewers (MM, RM-R), who then determined whether or not to retrieve the full text on the basis of the citations' potential relevance to the review's clinical research question.

As a further expansion of the search, searches were performed "by hand" within the Scopus database, the authors' personal libraries, and the reference lists of the full-text studies were performed to identify potential additional relevant citations. All the retrieved full texts were included in the review by consensus of all authors.

Data extraction from the included publications was performed by the same two authors who performed the initial search. Data regarding the demographic features of the sample, the time span between baseline and follow-up observation points, as well as the relevant cephalometric parameters that were assessed and placed into descriptive tables. All data are represented as they appeared in the original publication.

Quality Assessment

Critical appraisal of studies included in the review was performed according to the Newcastle-Ottawa Scale ([NOS] **Table 1A**, **1B**). For case-controls studies, NOS assigns a score for selection (case definition, representativeness of cases, selection and definition of controls), comparability (comparability of cases and controls on the basis of the design and analysis), and exposure (ascertainment of exposure, same method of ascertainment for cases and controls, non-response rate). Based on NOS guidelines, we considered as matched studies only those investigations in which cases and controls were actually matched in the design, and did not consider generic statement regarding the absence of between-group differences.

For cohort studies, NOS assigns a score for selection (representativeness of the exposed cohort, selection of non-exposed cohort, ascertainment of exposure, demonstration that outcome of interest was not present at the start of the study), comparability (comparability of cohort on the basis of the design and analysis), and outcome (assessment of outcome, length of follow-up, adequacy of follow-up of cohorts). The highest quality studies are assigned a score of 9.

RESULTS

Literature Search

Three hundred eleven citations were retrieved from the first phase of the search. A total of 270 references were excluded after screening of the titles and abstracts, because they were clearly not relevant for this review, were published before the year 1990, were not relevant to the clinical research question, or were duplicate studies. Full texts of the remaining 31 references were retrieved, along with 10 additional full-text articles that were identified as potentially relevant for the second-step search expansion. Based on the inclusion criteria, 13 articles were selected for this review (**Figure 1**).

Overview of Study Design, Diagnosis of OSA, and Outcome Measures

Of the 13 studies included in the review, all except one[16] had a retrospective design with a single observation point to assess

Table 1B—Grading the evidence statements for cohort studies.

	Selection												
Cohort studies	Representativeness of the exposed cohort				Selection of the non-exposed cohort			Ascertainment of exposure				Demonstration that outcome of interest was not present at start of study	
	truly representative in the community	somewhat representative in the community	selected group of users, e.g., nurses, volunteers	no descript of the derivation of the cohort	drawn from the same community as the exposed cohort	drawn from a different source	no descript	secure record	structured interview	self-report	no descript	yes	no
Eveloff et al. 1994		♦			♦			♦				♦	
Shen et al. 2012		♦			♦			♦				♦	
Liu et al. 2000		♦			♦			♦				♦	
Rose et al. 2002		♦			♦			♦				♦	
Skinner et al. 2002		♦			♦			♦				♦	
Mostafiz et al. 2011		♦			♦			♦				♦	
Ng et al. 2012		♦			♦			♦				♦	
Liu et al. 2001		♦			♦			♦				♦	
Otsuka et al. 2006		♦			♦			♦				♦	
Poon et al. 2008		♦			♦			♦				♦	
Iwamoto et al. 2012		♦			♦			♦				♦	
Marklund et al. 1998		♦			♦			♦				♦	

	Comparability		Outcome									
Cohort studies	Comparability of cohorts on the basis of the design or analysis		Assessment of outcome				Was follow up long enough for outcomes to occur		Adequacy of follow up of cohorts			
	study controls for cephalometric predictors for MAD efficacy in OSA	study controls for any additional factors	independent blind assessment	record linkage	Self-report	no descript	yes	no	complete follow up - all subjects accounted for	subjects lost to follow up unlikely to introduce bias - small number lost	big number lost and non-description of those lost	no statement
Eveloff et al. 1994	♦	♦		♦			♦					♦
Shen et al. 2012	♦			♦			♦					♦
Liu et al. 2000	♦	♦		♦			♦					♦
Rose et al. 2002	♦			♦			♦					♦
Skinner et al. 2002	♦	♦		♦			♦					♦
Mostafiz et al. 2011	♦			♦			♦					♦
Ng et al. 2012	♦			♦			♦					♦
Liu et al. 2001	♦			♦			♦					♦
Otsuka et al. 2006	♦			♦			♦					♦
Poon et al. 2008	♦			♦			♦					♦
Iwamoto et al. 2012	♦			♦			♦					♦
Marklund et al. 1998	♦			♦			♦					♦

treatment effectiveness. The study duration was specified in only 3 papers, adopting a 6-months, 6- to 12-week, and 6- to 8-week follow-up, respectively.[17–19] Three of the studies[16,20,21] specified that participants underwent an accommodation period of 6–8 weeks to adapt to the device. The sample sizes varied considerably from 9 to 89 subjects, with an average of 39 participants per study.

In accordance with the criteria for inclusion in the review, the diagnosis of OSA was based on baseline PSG recordings, even if the diagnostic cutoffs were set at different thresholds: for example, 2 studies[22,23] recruited patients with an apnea-hypopnea index (AHI) > 15/h, while 5 other studies recruited patients with an AHI > 10/h.[13,16,19–21] In another study,[17] OSA was diagnosed based on a respiratory disturbance index (RDI) > 10/h plus an apnea index (AI) > 5/h. Patients taking part in another study[26] had a supine AHI/h ≥ 10 and a lateral AHI/h < 10. Finally, another study[14] included patients with AI > 30/h. As a further aspect of heterogeneity, in some studies, participants were grouped based on OSA severity, while in other studies they were not. The 3 studies classifying the severity of OSA based on AHI adopted different thresholds to identify mild, moderate, and severe OSA patients.[16,19,24]

As for cephalometric analysis, it was performed at baseline, based on latero-lateral teleradiography, in all 13 studies, with the addition of dental impressions in one article.[20] Importantly, the parameters that were measured with cephalometry as well as the software that was used to identify the reference points for cephalometry varied widely among studies.

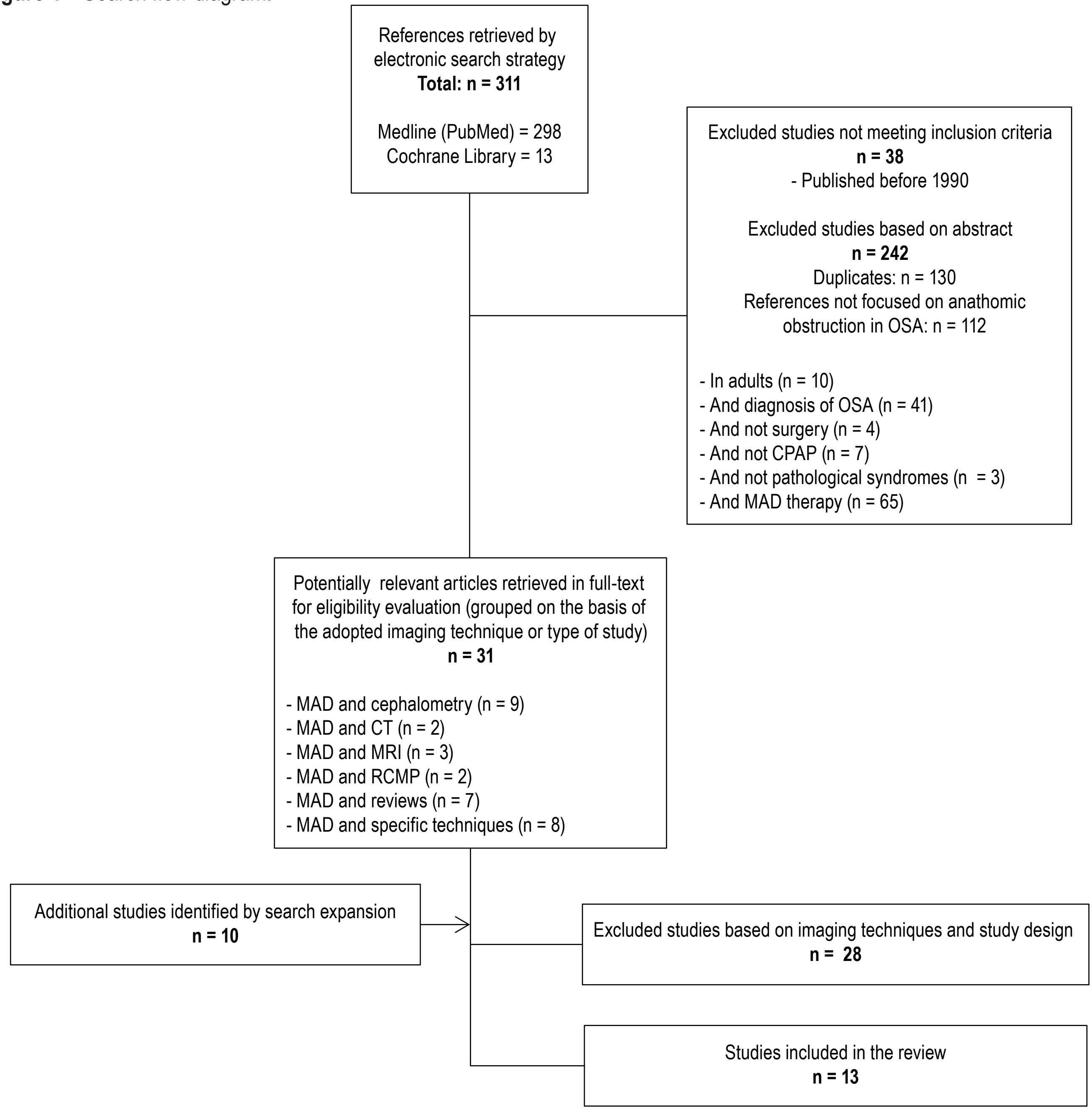
The primary outcome variable was AHI or AI in 12 studies, while one study adopted the RDI. All the studies described results in terms of the average AHI/AI/RDI values, except for one study[26] reporting the median values. Based on treatment outcome, patients were classified as complete responders, partial responders, or non-responders in 2 studies,[20,22] while in 5 studies[13,16,21,23,25] the participants were simply divided in responders and non-responders.

In accordance with the clinical research question underlying this review, the correlation between treatment outcome based on PSG data and the anatomical variables based on cephalometry was assessed in all studies.

Overview of MAD Design

The majority of articles reviewed provided some information on the design of the appliance, even if the manufacturing details were reported heterogeneously in only one paper[22] described the material that was used in the fabrication of the appliances. Five papers[17,22–24,26] provided details regarding the degree of mandibular protrusion, also indicating the

Figure 1—Search flow diagram.



percentage of maximum mandibular protrusion, ranging between 67% and 75%). The amount of vertical opening was not reported in any study.

Correlation Analysis

In accordance with the main criterion for inclusion in this review, all the studies reported the effectiveness of MAD treatment with respect to the cephalometric variables; few were specifically designed to assess the correlation between treatment-related changes in PSG data and cephalometric features (**Table 2A**, **2B**, **2C**). Results of such correlation analyses are summarized below. Findings are grouped based on the cephalometric variables under investigation (**Table 3**).

Mandibular Plane Angle

One study demonstrates an association between a greater post-MAD AHI reduction and a low mandibular plane angle ($p < 0.05$).[26] This finding is supported by another study,[17] which reports that the larger the mandibular plane angle the lower the AHI decrease ($r = 0.61$, $p < 0.05$).

Hyoid Bone Distance to Mandible

One study[13] reports that the hyoid-to-mandibular plane distance is smaller in the MAD-responders ($p = 0.01$). This finding is also supported by 3 studies, with p values ranging from $p = 0.001$ to $p = 0.012$.[14,18,19] In addition, another investigation finds that a higher AHI reduction is related to a higher

Table 2A—Correlation between polysomnographic and cephalometric variables according to AHI change (%).

Author	Demographic Data	PSG Data	Pre-MAD AHI (n/h)	Pre-MAD minSpO$_2$ (%)	Post-MAD AHI (n/h)	Post-MAD minSpO$_2$ (%)	Cephalometric Parameters	AHI change (%)	p
Mayer et al. 1995	Patients (n): 30 (24 M, 6 F)	All patients	64.6 ± 19.4	72.9 ± 17.1	31.3 ± 31.9	81.7 ± 10.9	Angle from sella-nasion-sub.spinale	16.98	0.0001
	Age: 38–74 y						Angle from sella-nasion-sub.mentale	−17.43	0.0008
	Height (cm): 172 ± 8.86						Length of soft palate	3.31	0.0146
	Weight (kg): 93.7 ± 19.9						Position of the base of the tongue	−2.87	0.0202
							Width of poster. airway space	−4.34	0.0528
							Width of middle oropharynx	−4.19	0.0870
Liu et al. 2000	Patients (n): 22	All patients	15.9 ± 16.82	73.44 ± 7.78	3.31 ± 4.61	81.32 ± 8.74	Anterior cranial base	0.6	< 0.05
	Age: 40–68 y	RDI	40.3 ± 21.71		11.72 ± 11.76		Mandibular plane angle	−0.61	< 0.05
	Mild/moderate OSA (n): 8						Upper to lower facial height ratio	0.73	< 0.01
	Severe OSA (n): 14								
Liu et al. 2001	Patients (n): 47 (42 M, 5 F)	All patients	40.3 ± 16.63	75.62 ± 14.09	17.07 ± 12.27	80 ± 15.97	Overjet	−0.32	< 0.05
	Age: 25–80 y	Complete R	44.21 ± 11.57	81.61 ± 10.43			Maxillary molar point-Frankfort plane	−0.32	< 0.05
	BMI (kg/m^2): 29.61 ± 6.49	Partial R	42.46 ± 19.33	71.91 ± 14.3			Hyoid-retrognathion	−0.29	< 0.05
		NR	28.69 ± 8.8	77.24 ± 16.95			Superior posterior airway space	−0.34	< 0.05
							Superior anterior airway space	−0.30	< 0.05
							Oropharyngeal CSA	−0.30	< 0.05
							Vertic. airw. length to oroph. CSA ratio	−0.29	< 0.05
Poon et al. 2008	Patients (n): 14 (8 M, 6 F)	All patients	38.4 ± 17.2	75.5 ± 11.1	10.9 ± 14.7	86 ± 8.4	Hyoid-mandibular plane	0.703	0.023
	Age: 20–60 y								
	Mild OSA (n): 2								
	Moderate OSA (n): 9								
	Severe OSA (n): 3								
Mostafiz et al. 2011	Patients (n): 53 (42 M, 11 F)	All patients	33 ± 14.4	83.4 ± 8.1	10.8 ± 12.5	86.7 ± 6.6	Upper facial height	0.311	0.024
	Age: 49.5 ± 11.8 y	Complete R	28.4 ± 14.4	84.2 ± 7.8	2.5 ± 1.4	89.9 ± 3.4	Tongue CSA	−0.478	0.008
	Height (cm): 173.8 ± 9.3	Partial R	34.8 ± 15.1	83.2 ± 8.4	10.8 ± 4.8	86.2 ± 5.9			
	Weight (kg): 86.9 ± 16.3	NR	40.6 ± 12.7	81.9 ± 9.1	29.4 ± 15.1	80.1 ± 8.2			
	BMI (kg/m^2): 28.7 ± 4.2								

Table 2B—Correlation between polysomnographic and cephalometric variables according to responders and non responders.

Author	Demographic Data	PSG Data	Pre-MAD AHI (n/h)	Post-MAD AHI (n/h)	Cephalometric Parameters	R	NR	p
Otsuka et al. 2006	Patients(n): 9 (9 M)	Responders	31.6 ± 12.44	8.3 ± 6.27	Mandibular position-cervical spine	108.1 ± 12	120 ± 9.02	< 0.05
	Age: R: 52.6 ± 8.09 NR: 51.1 ± 9.12	NR	29 ± 11.47	37.8 ± 16.97	Middle air way space	9.8 ± 4.35	15.2 ± 4.5	< 0.05
	BMI: R: 29.9 ± 4.08 NR: 29.4 ± 3.9				Inferior air way space	7.6 ± 3.63	12.5 ± 4.54	< 0.05
					Oropharyngeal CSA	541.5 ± 240.2	779.5 ± 204.22	< 0.05
					Airway to tongue ratio	0.111 ± 0.05	0.173 ± 0.05	< 0.05

reduction in the hyoid-to-mandibular plane distance when wearing the MAD ($r = 0.703$, $p = 0.023$).[24]

Facial Height

A higher AHI reduction is shown to correlate with a shorter upper or anterior facial height[16,20,26] and a larger lower facial height.[25] The smaller the upper-to-lower facial height ratio, the lower the MAD-related AHI decrease ($r = 0.71$, $p < 0.01$).[17]

Antero-Posterior Diameter of the Maxilla

One study suggests that MAD effectiveness is higher in OSA patients with a large antero-posterior diameter of the maxilla.[25]

Cranial Base Features

According to one study,[17] a significant linear correlation also exists between the decrease in AHI and some features of the anterior cranial base: in particular, the shorter the anterior cranial base, the lower decrease in AHI ($r = 0.60$, $p < 0.05$). Another study[16] reports that the mandibular position relative to the cranial base is lower in responders than non-responders ($p < 0.013$), as also described in an investigation reporting a correlation with the angle between the anterior cranial base and the mandibular plane.[18] Another study shows that an increased cranial base angulation is predictive of MAD treatment effectiveness ($p = 0.05$).[21]

Tongue Area

Tongue area was related with AHI decrease in one study ($r = −0.478$, $p = 0.008$).[20] In particular, a larger tongue cross-sectional area (CSA) seems to be associated with greater AHI reduction. In that study, the ratio between the tongue CSA and the volume of the oral cavity differs significantly between responders and non-responders ($p = 0.012$), with the former showing a higher ratio, i.e., a larger tongue area with respect to the oral cavity volume. According to the same study, maxillary length is significantly shorter in responders. On the contrary, another study[22] reports that a longer maxilla is associated to an improved MAD treatment response.

Soft Palate Features

Two studies[13,21] find that the soft palate length is significantly shorter in MAD responders ($p = 0.01$ and $p = 0.005$,

Table 2C—Correlation between polysomnographic and cephalometric variables according to odds ratio and R-squared.

			Pre-MAD		Post-MAD					
Author	**Demographic Data**	**PSG Data**	**AHI (n/h)**	**minSaO$_2$ (%)**	**AHI(n/h)**	**minSaO$_2$ (%)**	**Cephalometric Parameters**	**OR**	**R^2**	**p**
Eveloff et al. 1994	Patients (n): 19 (16 M, 3 F)	All patients	34.7 ± 5.3	96 ± 0.2	12.9 ± 2.4	88 ± 1	Posterior facial height		0.393	0.02
	Age: 45 ± 1.8	Responders	25		5.6		Mandibular-hyoid distance		0.688	0.002
	BMI (kg/m^2): 31.1 ± 1.2	NR	45		21		Posterior airway space		0.732	0.002
Marklund et al. 1998	Patients (n): 32 (M)	All patients	23 (2.2–66)		7.6 (0–32)		Mandibular plane angle	0.74		0.02
	Age: 37–72 y	In supine pos.	39 (0–84)		11 (0–60)		Lower anterior face height	0.75		0.04
	Height (cm):179 (166–190)	In lateral pos.	15 (0–70)		2.6 (0–31)					
	BMI (kg/m^2): 28 (23–37)									
Rose et al. 2002	Patients (n): 57 (51 M, 6 F)	All patients	22 ± 12.2	80.7 ± 6.8	10.4 ± 9.7	83.2 ± 7.5	Angle anter. cran. base/mand plane	1.295		
	Age: 56.5 ± 7.3 y						Hyoid-mandibular plane	1.14		
	BMI (kg/m^2): 26.4 ± 2									
Skinner et al. 2002	Patients (n): 14 (13 M, 1 F)	All patients	34 ± 22	76 ± 6	10 ± 5	82 ± 4	Hyoid-mandibular plane		0.37	0.012
	Age: 25–63 y									
	BMI (kg/m^2): 18.5–35.6									
Ng et al. 2012	Patients (n): 72 (55 M, 17 F)	All patients	27.4 ± 16.6	85 ± 4.2	13.3 ± 13.7	88 ± 2.4	Soft palate length	0.84		0.005
	Age: 49 ± 11	Responders	26.8 ± 14.4	85.2 ± 2.6	5.8 ± 5	88.4 ± 1.6	Cranial base angulation	1.13		0.05
	BMI (kg/m^2): 30.2 ± 5.6	NR	28.1 ± 19.3	84.7 ± 5.7	22.7 ± 15.3	87.4 ± 3.1				
Iwamoto et al. 2012	Patients (n): 89 (77 M, 12 F)	Responders	21 (5.3–67.5)		4.9 (0.2–10.9)		Anter-poster diameter maxilla	0.35		0.035
	Age: 20–78 y	NR	20 (7.2–43.7)		16.6 (7.4–41.6)		Lower facial height	0.28		0.01
	BMI (kg/m^2): 17.3–32.2									
Shen et al. 2012	Patients (n):52 (48 M, 4 F)	All patients	36.1 ± 17	80.8 ± 8.1			Minimal retroglossal airway	0.72		0.018
	Age: 43.4 ± 10.3	Responder	34.1 ± 15.1	82.8 ± 2.9			Posit.of mandible rel. to cran. base	0.685		0.013
	BMI (kg/m^2): 24.8 ± 2.6	NR	38.6 ± 19.1	78.3 ± 8.1			Anterior face height	0.835		0.006
	Mild/moderate OSA (n):25									
	Severe OSA (n): 27									

Table 3—Correlation between treatment effectiveness and the main groups of cephalometric features.

	Low Mandibular Plane Angle	Small Hyoid Distance to Mandible	Large and Short Facial Height	Large Antero-Posterior Diameter of Maxilla	Cranial Base Features	Tongue Area	Short Soft Palate
Marklund et al. 1998	X						
Liu et al. 2000	X		X		X		
Eveloff et al. 1994		X					X
Mayer et al. 1995		X					X
Rose et al. 2002		X			X		
Skinner et al. 2002		X					
Poon et al. 2008		X					
Iwamoto et al. 2012			X	X			
Shen et al. 2012					X		
Ng et al. 2012					X		X
Mostafiz et al. 2011						X	
Liu et al. 2001						X	

respectively). Another study[14] reports that the AI improved most in patients with a short soft palate ($p = 0.01$), a more rostral position of tongue basis ($p = 0.02$), a reduced width of the posterior airway space ($p = 0.05$), and middle oropharynx ($p = 0.08$).

Other Findings

One study[23] finds that the only significant skeletal differences between MAD responders and non-responders is the mandibular position relative to cervical spine. Two airway-space variables (i.e., middle and inferior airway space) are significantly larger in non-responders, as well as the oropharyngeal CSA and the airway-to-tongue ratio. These findings are supported by another study[22] reporting that responders have a significantly narrower inferior airway space ($p < 0.05$). Likewise, it is found that the minimal retroglossal airway is narrower in responders ($p < 0.018$).[16]

Assessment of Studies' Quality

Of the 13 papers included in the review, all except one[14] were cohort studies. The NOS scores were 8 for the majority of included papers, while 3 studies[13,17,19] achieved a score of 9. Thus, when considering the quality of those selected, the assessment showed the excellent level of the reviewed articles as well as their qualitative homogeneity. However, their methodological heterogeneity prevented a meta-analysis of data.

DISCUSSION

A variety of neurological, demographic, and anatomical factors interact to determine the onset of sleep disordered breathing and OSA. While the former include ventilation control instability and upper airway dilator muscle abnormalities, overweight and obesity are the main epidemiological risk factors.[3] On the other hand, it was also suggested that an unfavorable relationship between the soft tissues and the bony enclosure size represents a possible anatomically based predisposition towards OSA.[27–29] Based on that, the need to evaluate the skeletal features in the treatment planning phases seems to emerge. Furthermore, it is important to point out that anatomical variables depend on ethnic differences.[22]

The mechanism of action of MAD in treating OSA is complex. It is likely to involve positive anatomical changes related to an increased upper airways volume. Indeed, the forward displacement of the mandible moves the tongue base anteriorly and increases the retroglossal airway space. Moreover, an anterior movement of the tongue decreases the gravitational effect on the soft palate and a forward displacement of the mandible decreases the collapsibility of the velopharynx. On the other hand, data from the literature suggested that not all OSA patients markedly improved with mandibular advancement strategies. Based on that, some possible hypotheses to predict MAD effectiveness on the basis of individual skeletal features is proposed. For instance, Mehta et al.[30] presented an equation to predict MAD effects on AHI. These authors suggest that MAD effects positively correlate with neck circumference and baseline AHI and negatively correlate with the retropalatal airway width and the angulation of the mandibular plane with respect to the anterior cranial base. In addition, Hoekema et al.[31] found that the outcome of oral appliance therapy is favorable in less obese patients with milder sleep apnea and mandibular retrognathism. A better treatment response with an adjustable MAD was also seen in younger patients with a lower BMI, further suggesting that the interaction between soft and hard tissues is a key factor to understand the predictability of OSA treatment.[22]

Despite the aforementioned efforts, definitive evidence on the anatomical predictors of MAD effectiveness is still lacking, and a summary of the role of skeletal factors is important in this review.

The reviewed studies were selected on the basis of their PSG-based evaluation of MAD effectiveness with respect to skeletal features, as assessed with cephalometry. The choice to limit the included studies to those that adopted a cephalometric assessment was based on the need for increasing the internal validity of the review's findings. In addition, it must be kept in mind that this is the most commonly used first-step imaging technique for gross screening to evaluate the possible influence of skeletal features in the occurrence of OSA, thus reducing the possibility of a generalization of this review's findings. In spite of this strategy, unfortunately, the study designs were so heterogeneous that meta-analysis of data could not be performed. Thus, the extraction of methodologically sound, clinically useful, conclusions was difficult to perform. As a point of strength, the reviewed studies had the common feature of relying on PSG-diagnosed assessment of OSA events in the supine position, which was selected as the reference sleep position, because of the much lower prevalence of apnea events in other sleep positions.[26]

Within these limitations, some correlations between the outcomes of MAD therapy and cephalometric variables were reported, both in terms of positive and negative treatment effectiveness.

Some morphologic features were associated with poor response to MAD treatment. For example, the insertion of a MAD in patients with a steep mandibular angle is not supported. Indeed, it is likely to rotate the mandible, so that the genioglossus and hyoid muscles move closer to the posterior pharyngeal wall, thus limiting the benefit of mandibular advancement.

On the contrary, as far as potentially positive anatomical predictors are concerned, some authors[13,14] report a significantly smaller mandible-hyoid bone distance in MAD responders than in non-responders. Two mechanisms are suggested to explain such a correlation. First, it should be noted that MAD, while forcing the mandible forward, also pulls the muscles attached to the hyoid bone forward, thus reducing the distance between the hyoid bone and the mandibular plane, improving pharyngeal airway patency. Second, the mandibular advancement achieved with the MAD alters compliance of the muscles and improves the tonicity of pharyngeal dilator muscles.

Notwithstanding this interesting information, it must be recognized that the available literature is too limited to permit a recommendation of any particular strategy in the clinical setting. Additionally, it must be borne in mind that cephalometry provides only 2-dimensional information, while 3D imaging techniques or dynamic nasopharyngoscopy during sleep could detect additional skeletal/morphological features that predict MAD effectiveness because of the ability to analyze the transverse airways diameter. However, such methods are primarily reserved for research or to a highly specialized setting and are not suitable for use on a routine basis due to cost and limited availability. Thus, considering the clinical applicability of MAD to large patient populations, the ease of assessment, ability for evaluation while awake, and availability, cephalometry can be useful to investigate OSA patients on a large scale. It is important that more information is obtained on the correlation on the modifications of the bony tissues when the patient is in a supine position and when sleeping. The relatively weak and somewhat inconsistent cephalometric data now available suggest that decisions based solely on these factors cannot be recommended, particularly because an integrated analysis of other risk factors (e.g., age, sex, BMI) should be taken into account. According to some authors,[32] determination of the facial phenotype via photographic documentation may help in unraveling some aspects of craniofacial skeletal abnormalities associated with OSA. Therefore, facial photographic phenotyping may be a useful tool to assess intermediate phenotypes for OSA. As a further aspect for investigation, more information should be drawn from the amount of the advancement that is required to achieve the best balance between benefit and discomfort, which was shown to be a critical aspect in the OSA literature.[33] Moreover, as a further limitation of this review, it should be noted that the external validity is not optimal due to the poor consistency between the reviewed studies as far as the methodological features are concerned.

Thus, simply stated, further studies are required before the fragmental literature on the cephalometric predictors of MAD treatment in OSA patients can be translated into evidence-based clinical recommendations.

CONCLUSIONS

This systematic review identified 13 studies in an attempt to relate specific cephalometric variables to the effectiveness of MAD treatment for OSA patients. Some interesting findings were retrieved, suggesting that the outcome may depend on the assessment of soft-tissue volumes relative to their bony confinements. In particular, the mandibular plane angle and the distance between hyoid bone and mandibular plane emerged as possible predictors of MAD effectiveness: low mandibular angle and reduced hyoid bone-to-mandible distance were positively correlated with treatment outcome. These findings suggest that MAD may help restoring airway patency in patients with specific anatomic imbalances. Notwithstanding, the overall conclusions that can be drawn from this review are still limited by the somewhat inconsistent findings and the heterogeneity of study designs. Thus, it is suggested that further trials are performed before recommending any suggestions in the clinical setting.

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