J. Maxillofac. Oral Surg. (Apr–June 2019) 18(2):299–306
https://doi.org/10.1007/s12663-018-1140-1

ORIGINAL ARTICLE

The Interaction Between Craniofacial Computed Tomographic Dimensional Parameters and BMI in Obstructive Sleep Apnea

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Received: 5 January 2018 / Accepted: 25 July 2018 / Published online: 27 August 2018

Abstract

Introduction The impact of the dimensional parameters of the pharyngeal bony frame by its length, width and the position of the hyoid upon the severity of obstructive sleep apnea syndrome (OSAS) has not been investigated in depth. Interactions of those parameters with body mass index (BMI) and their overall reciprocal effect on OSAS severity have also not been established.

Materials and Methods This retrospective cross-sectional study was conducted on 108 male OSAS patients followed in OSAS outpatient clinics between November 2014 and October 2015. They all underwent a polysomnography test, and an apnea–hypopnea index (AHI) was calculated. They also underwent an upper airway computerized tomographic scan in which three craniofacial parameters were evaluated: inter-pterygoid distance (IPD), hard palate-to-hyoid (HP-H) distance, and gnathion plane-to-hyoid (GP-H) distance.

Results A longer pharynx and an inferiorly placed hyoid bone correlated with the AHI ($r = 0.33$, $p = 0.001$ and $r = 0.226$, $p = 0.03$, respectively). GP-H correlated with body mass index (BMI) ($r = 0.3243$, $p < 0.001$), while HP-H and IPD did not. We found an interaction between BMI and HP-H, but none between GP-H and BMI. IPD did not correlate with OSAS severity, but it correlates with the age of the OSAS patients ($r = 0.235$, $p = 0.015$).

Conclusion Pharynx length and hyoid position have significant effects upon OSAS severity, and they interact differently with BMI in terms of those effects. Hard palate width increases with age but has no correlation with OSAS severity.

Keywords Obstructive sleep apnea · Computed tomography · Imaging · Obesity · Upper airway dimensions · Pharyngeal dimensions

Introduction

Obstructive sleep apnea syndrome (OSAS) is a common condition associated with significant medical consequences [1–5]. The pathogenesis of OSAS is multifactorial and may be attributed to pharyngeal airway dimension, tissue composition of the pharynx and surrounding structures, as well as neuromuscular function. Obstructive events can be localized at any level of the soft part of the pharyngeal tube, from its inlet situated at the level of the hard palate down to its outlet at the level of the hyoid bone and thyroid cartilage [6].

Pharyngeal airway dimensions are determined by both the maxillofacial bony frame and the soft tissue composing the pharyngeal walls and surrounding anatomical structures. The width of the pharyngeal tube is limited by the

This work was presented at the AAO-HNSF annual meeting and OTO EXPO September 2016; This work was performed in fulfillment of Daniel Ben Ner's M.D. thesis requirements of the Sackler School of Medicine, Tel Aviv University, Israel.

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bony frame at the level of the velopharynx and the oropharynx. The pharyngeal length is determined by the distance between the hard palate and the tongue base at the level of the hyoid bone [6].

Obesity is a well-known risk factor for OSAS [7, 8]. Peppard et al. showed a direct relation between body mass index (BMI) and OSAS severity: a gain of 10% in body weight among mild OSAS patients increased their risk of progression of OSAS severity sixfold. Furthermore, an equivalent weight loss can reportedly result in a greater than 20% improvement in OSA severity [9]. Obesity has been shown to increase the soft tissue volume of the upper airways [10, 11], but the complex mechanisms and the nature of its interplay with pharyngeal dimensions have not yet been studied in depth. The objective of this study was to determine the impact of the bony frame of the soft pharyngeal tube upon OSAS severity. We aimed to characterize the bony frame by its length, width and the position of the hyoid, and to investigate the reciprocal effect of these parameters with BMI on OSAS severity.

Methods

This study was approved by the institutional review board (11-2015, 0611-15-TLV). All male patients followed in the OSAS outpatient clinics in the Otolaryngology Head & Neck Surgery and Maxillofacial Surgery Department of the Tel Aviv Sourasky Medical Center, Israel, between November 2014 and October 2015 were included in this retrospective study. All patients that were followed in this clinic and were found by a sleep study to have mild, moderate or severe OSAS were sent to a computed tomography (CT) imaging of the head and neck as part of the standard perioperative assessment in our clinic. They had undergone a sleep study no more than 3 years before the acquisition of the CT imaging. A patient whose BMI changed by more than 1 BMI unit between the sleep study and the CT imaging repeated the sleep study. Patients who did not meet these terms were not included in this cohort.

The head and neck CT was retrieved from participants' charts. All CT scans had been performed while the subjects were awake and in a supine position with their heads in a neutral position, and with closed occlusion. They were instructed to breathe normally, maintain a closed bite, and refrain from swallowing. Patients with CT scans with open occlusion or while swallowing were excluded from the study. Although the scans were performed in four different imaging facilities, the study protocols were similar in terms of slide thickness (1 mm), and all the scans included soft tissue and bone windows. Patients that did not meet the above criteria were not included in the study.

Data on age, BMI and apnea–hypopnea Index (AHI) were retrieved from the participants' medical charts. Sleep studies were performed by a number of sleep laboratory services that used a variety of sleep laboratory devices, including full polysomnography, home partial sleep studies and overnight peripheral arterial tonometry studies.

Upper airway parameters were manually measured by one investigator (DBN) who used electronic calipers. The investigator was unaware of the OSAS severity and BMI of the subjects. All measurements were taken using the same technique, considering the limitations of the software supplied with the CT scan compact disks and the technical quality of the test.

The Parameters

Three craniofacial parameters were evaluated (Fig. 1). The inter-pterygoid distance (IPD) was defined as the distance between the centers of the greater palatine foramina. It was measured in the axial section showing the greater palatine foramina and approximately at the lowest level of the hard palate. IPD represents the width of the bony frame of the soft pharyngeal tube inlet (Fig. 1). The hard palate-to-hyoid bone (HP-H) distance was measured in a midsagittal section that was found using multiplanar reconstruction (MPR). A horizontal line was drawn tangent to the base of the posterior tip of the hard palate and perpendicular to the horizon of the screen as an absolute reference. A vertical was drawn between this line and the upper tip of the hyoid bone (Fig. 1). The length of this vertical distance represented the length of the pharyngeal tube. The gnathion plane-to-hyoid bone (GP-H) distance was determined by drawing a second horizontal line tangent to the lowest tip of the gnathion plane and parallel to the first horizontal line on a midsagittal section (found using MPR). A perpendicular line was drawn from this second tangent line to the upper tip of the hyoid bone. Values were considered to be positive when the hyoid bone was lower than the second tangent line and negative when the hyoid bone was higher than the second tangent line. The GP-H parameter represents the hyomandibular interaction at the level of the soft pharyngeal tube outlet toward the glottis. Statistical analysis was performed using the computing environment "R" (Development Corps Team, version 3.3.0, 2016). All statistical tests were two-tailed, and a p value of < 0.05 was considered significant. Continuous variables were described as mean and standard deviation. A Pearson coefficient (r) was calculated to determine the correlation between two variables. In order to examine the interaction between BMI and the upper airway parameters, a multiple linear regression was applied to the OSAS patient dataset, including the main effects of an upper airway parameter

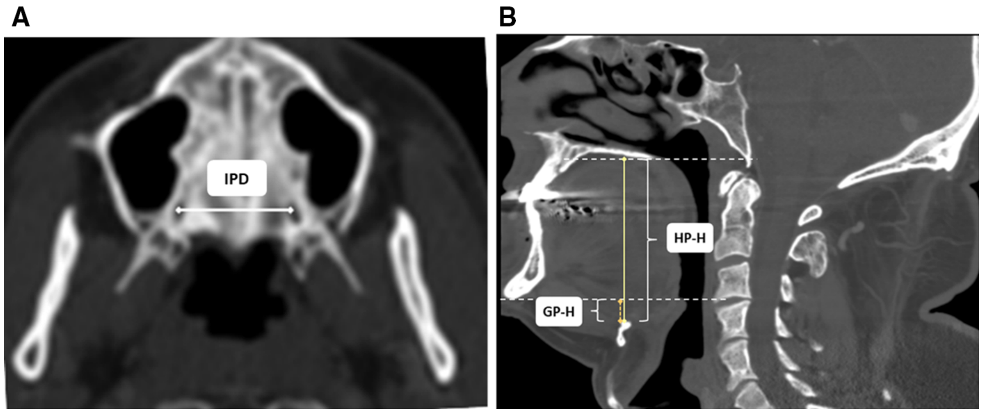

Fig. 1 **a** Measured dimensional CT parameters on a hard palate axial computerized tomographic (CT) scan. **b** Midsagittal CT scan. *IPD* inter-pterygoid distance, *HP-H* hard palate-to-hyoid distance, *GP-H* gnathion plane-to-hyoid distance

and BMI on disease severity. Effects significance was obtained by *t* tests.

Results

Our study included 108 males diagnosed as having OSAS. Their mean ± standard deviation age was 44.99 ± 13.29 years (range, 18–73 years), mean BMI 28.83 ± 3 0.32, and mean AHI 29.89 ± 19.99. Their demographics, sleep study results and upper airway parameters are summarized in Table 1. Their BMI and AHI results positively correlated with disease severity ($r = 0.282$, $p = 0.004$, $n = 100$, Fig. 2d). A positive correlation was found between HP-H and AHI ($r = 0.33$, $p = 0.001$, $n = 94$, Fig. 2g), indicating that a longer HP-H correlates with a more severe OSAS. GP-H also positively correlated with AHI ($r = 0.226$, $p = 0.03$, $n = 89$, Fig. 2f), indicating that the lower the hyoid was positioned relative to the gnathion plane, the more severe was the disease. No correlation was found between IPD and AHI or between age and AHI.

Table 1 Demographics, sleep study results and upper airway measurements of the OSAS study patients

Parameter	OSAS ($n = 108$)
Age	44.99 ± 13.29
Body mass index	28.83 ± 3.32
Inter-pterygoid distance	30.77 ± 2.47
Hard palate-to-hyoid distance	67.87 ± 6.78
Gnathion plane-to-hyoid bone distance	2.57 ± 10.65
Apnea–hypopnea index	29.89 ± 19.99

Values are presented as mean (± SD)

OSAS obstructive sleep apnea syndrome

We also detected a positive correlation between the demographic and upper airway CT parameters. Specifically, BMI positively correlated with age ($r = 0.323$, $p = 0.001$, $n = 102$, Fig. 2a), IPD also positively correlated with age ($r = 0.235$, $p = 0.015$, $n = 105$, Fig. 2b), GP-H positively correlated with both age and BMI ($r = 0.3243$, $p < 0.001$, $n = 93$, Fig. 2c; and $r = 0.341$, $p = 0.001$, $n = 87$, respectively, Fig. 2e), and GP-H strong correlated with HP-H ($r = 0.6$, $p < 0.0001$, $n = 93$, Fig. 2h). In contrast, HP-H did not correlate with either BMI or age, and IPD did not correlate with BMI.

After establishing correlations between HP-H, GP-H, BMI and AHI, we analyzed the interactions between those parameters. We plotted all of the OSAS patients by their BMI and an upper airway parameter (IPD, HP-H, and GP-H) in a scatterplot (Fig. 3). The median BMI of all of the OSA patients was 29.1, the median IPD was 30.68 mm, the median GP-H was 1.25 mm and the median HP-H was 68.9 mm. Each plot was divided into four areas according to the median BMI and the median of the relevant parameter. The mean AHI for each of the four areas is given in Fig. 3. The scatterplot of BMI and HP-H (Fig. 3c) demonstrated a reciprocal effect of BMI and HP-H on the AHI: area 4 had the largest mean AHI compared to the other areas, indicating that a larger HP-H and a larger BMI indicated a more severe OSAS.

In order to evaluate the quality of the reciprocal effect observed in Fig. 3c, we performed an analysis using multiple linear regressions including the AHI as dependent variable, and BMI and HP-H/GP-H/IPD as explanatory variables. The estimated effects for the regression model are shown in Table 3 in this model, both BMI and HP-H had significant positive effects on the AHI ($p = 0.02$ and $p = 0.004$, respectively, $B = 1.39$ and 0.88, respectively). This supports our previously noted descriptive observations: patients with a more severe OSAS were observed in the upper-right quarter of BMI and HP-H scatterplot

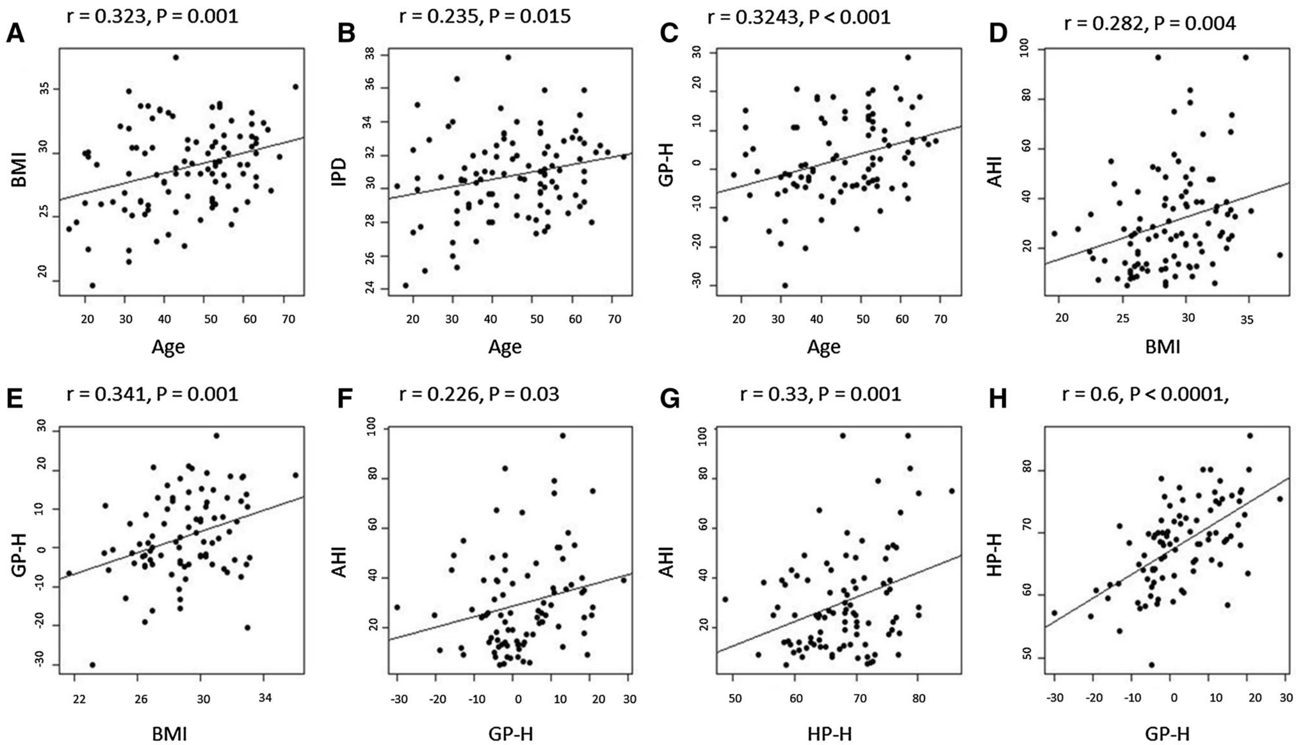

Fig. 2 Correlations between **a** BMI/Age, **b** IPD/Age, **c** GP-H/Age, **d** AHI/BMI, **e** GP-H/BMI, **f** AHI/GP-H, **g** AHI/HP-H and **h** HP-H/GP-H. *BMI* body mass index, *IPD* inter-pterygoid distance, *HP-H* hard palate-to-hyoid distance, *GP-H* gnathion plane-to-hyoid distance, *AHI* apnea–hypopnea index

(Fig. 3c). There were no significant additive effects for the combination of BMI with GP-H ($p = 0.13$ and $p = 0.19$, respectively). As shown before in Table 2 (correlation matrix) these variables are positively correlated with each other ($r = 0.341$, $p < 0.05$).Moreover, both GP-H and BMI correlated with disease severity ($r = 0.226$, $p < 0.05$ and $r = 0.282$, $p < 0.05$, respectively). This suggests that GP-H and BMI may be related in their individual effects on the AHI. Only the effect of BMI was significant in the model of BMI and IPD variables ($p = 0.001$ and $p = 0.99$, respectively). As shown both in the model (Table 3) and in the correlation matrix (Table 2), IPD was not associated with disease severity.

Discussion

In this study, we evaluated three new parameters representing the bony frame of the soft pharyngeal tube, IPD, HP-H and GP-H. The IPD represents the width of the velopharyngeal inlet, and it was not correlated with OSAS severity. IPD has not been reported in the literature in the setting of OSAS, and comparable anatomical markers of nasopharynx bony frame have rarely been measured as well. Kobayashi et al. [12] measured the pterygoid distance of normal Asian adults and found it to be about 32 mm. Manmohan Patel [13] measured the distance between the free edges of the medial pterygoid plates in dry skulls of Indian males, and reported a mean value of 30.44 ± 2.50 mm. Our measurements were shorter than the distances reported by Kobayashi et al. but similar to those reported by Patel. These differences between the two reported distances might be due to subtle, race-related variations in skull structure. Because of the limited data on the distance between the pterygoid plates in normal populations and in OSAS patients, we believe that further study in this field is required to examine its actual relevance to OSAS. Interestingly, the IPD was significantly correlated with age among our study participants. Age-dependent facial skeleton changes have been previously reported [14], but widening of the hard palate, to our knowledge, has not. The anthropometric implication of this finding has yet to be determined.

Our data indicate that a longer pharynx (HP-H) correlates with OSAS severity. We found no similar correlation between pharyngeal length and BMI. The association between pharyngeal length and OSAS was previously described by others [15–18]. Malhotra et al. showed via magnetic resonance imaging that male subjects have a longer pharynx (measured from hard palate to epiglottis base) compared with females, predisposing the male pharynx to collapse [17]. Genta et al. also concluded that

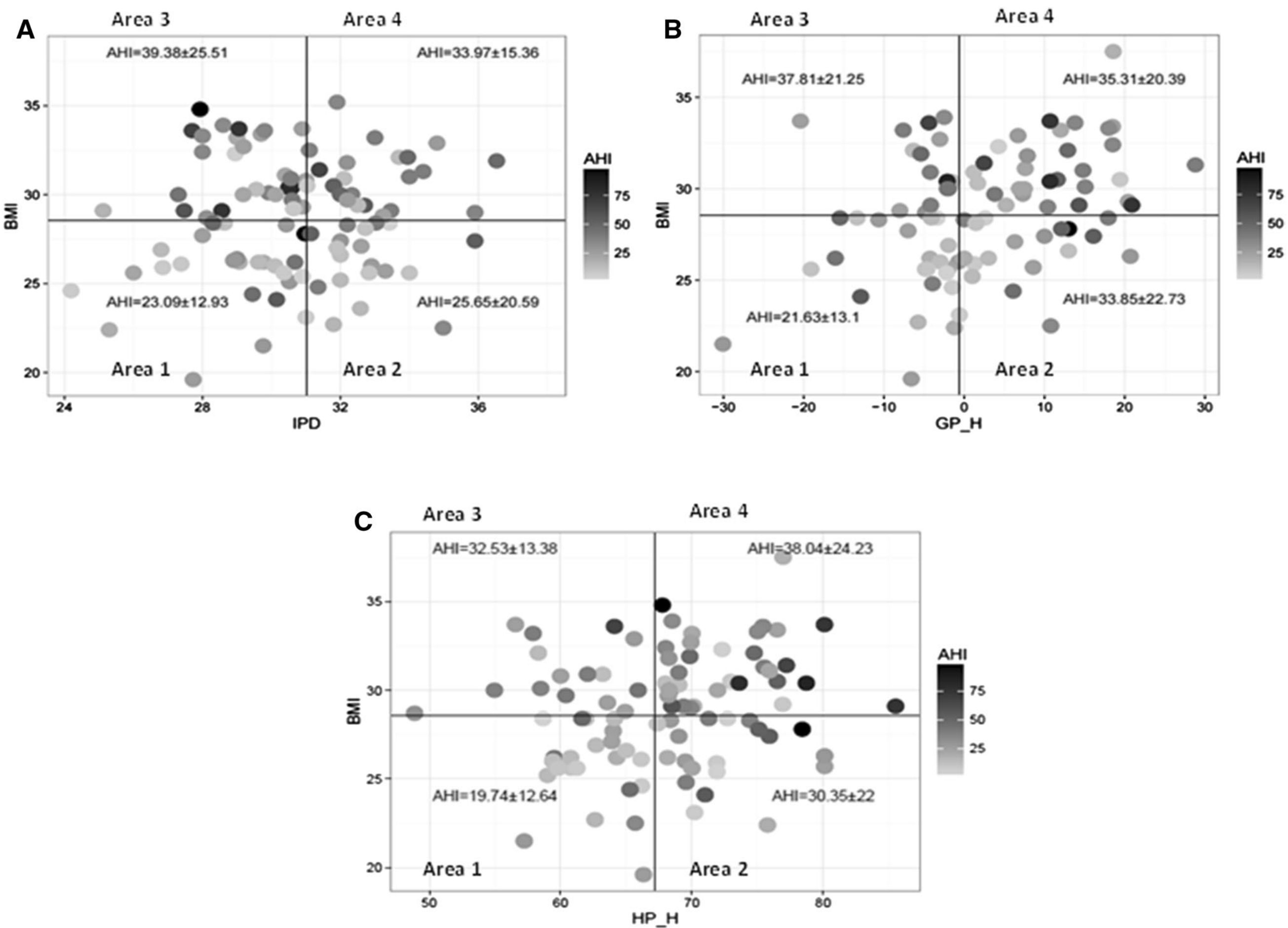

Fig. 3 Scatterplot of BMI and upper airway parameters. Each plot is divided into four areas according to the median of each variable. **a** BMI/IPD, **b** BMI/GP-H and **c** BMI/HP-H. *BMI* body mass index, *IPD* inter-pterygoid distance, *HP-H* hard palate-to-hyoid distance, *GP-H* gnathion plane-to-hyoid distance

Table 2 Correlation matrix: age, BMI, AHI and pharyngeal dimensional CT parameters

	BMI	AHI	IPD	GP-H	HP-H
AGE	0.323	NS	0.235	0.343	NS
BMI	–	0.282	NS	0.341	NS
AHI	–	–	NS	0.226	0.33
IPD	–	–	–	NS	NS
GP-H	–	–	–	–	0.6

Values are Pearson correlation coefficients (*r*)

CT computerized tomography, *NS* not significant, *BMI* body mass index, *IPD* inter-pterygoid distance, *HP-H* hard palate-to-hyoid distance, *GP-H* gnathion plane-to-hyoid distance

Significant is defined as $p < 0.05$

Table 3 Summary of multiple linear regression analysis for an additive model

	B	SE	*T*	*p* value
Additive model BMI + HP-H				
BMI	1.4	0.62	2.62	0.03*
HP-H	0.88	0.3	2.9	0.004*
Additive model BMI + GP-H				
BMI	1.03	0.66	1.55	0.13
GP-H	0.28	0.21	1.33	0.19
Additive model BMI + IPD				
BMI	1.95	0.61	3.2	0.001*
IPD	0.01	0.83	− 0.02	0.99

B estimated beta coefficient, *SE* estimation standard error, *t t* test statistic, *BMI* body mass index, *IPD* inter-pterygoid distance, *HP-H* hard palate-to-hyoid distance, *GP-H* gnathion plane-to-hyoid distance

*p value significant < 0.05

pharyngeal length is associated with increased collapsibility of the pharynx [18]. Additionally, Genta et al. [18] and Barkdull et al. [19] found that pharyngeal length is not correlated with BMI, similar to our findings.

We demonstrated that GP-H, a representative of hyoid position and the angulation of the geniohyoid muscle, positively correlated with OSAS severity, and that it positively correlated with BMI. Moreover, BMI alone also correlated with OSAS severity, as had been previously established in the literature [1–10]. Genta et al. [18] and Barkdull et al. [19] also showed that an inferiorly displaced hyoid correlates with both OSAS severity and BMI, but not with pharyngeal length.

By measuring pharyngeal length from the hard palate to the hyoid instead of from the epiglottis base, we showed that even though both the HP-H and GP-H measurements depend upon hyoid position and correlate strongly with each other, they differ in their interaction with BMI and in their effect on OSAS severity. Our regression models showed that HP-H is an independent factor in OSAS severity. GP-H correlated with BMI, and both BMI and GP-H affected OSAS severity, although neither showed an additive value.

The difference between the behavior of HP-H and GP-H in the different additive models and their different interactions with BMI may further imply the mechanism by which each of those three components affects OSAS severity. One mechanism of how pharyngeal length affects OSAS was explained by Pae et al. [20] Those authors hypothesized that a longer tube with the same diameter under the same tidal breathing produced larger negative pressure and thus contributed to collapsibility. Their hypothesis is in line with there being an independent role of HP-H in our regression model.

Our regression models on the interaction of GP-H and BMI showed no added value when using both parameters in a model for predicting OSAS severity. This suggests a shared mechanism between the two factors. Hyoid position, represented in our study by GP-H, is a well-known factor in OSAS pathogenesis [21, 22]. Lowe et al. [23] proposed that an inferiorly placed hyoid bone places the geniohyoid muscle at a mechanical disadvantage by its angulation, therefore exposing the patient to increased risk of collapse of the tongue base. The hypothesis of a shared mechanism may be further supported by the well-established effect of BMI on hyoid position: fat deposition in the neck and tongue was found by numerous studies to increase as BMI increases [15, 24–26], thus contributing to the displacement of the hyoid [27]. Moreover, Kim et al. [28] showed that fat distribution in the tongue is heterogeneous, and that it tends to accumulate in the tongue base. Thus, the correlation we found between GP-H and BMI might be explained by excess fat accumulation at the tongue base. Secondly, in the same study, Kim et al. noted that regardless of BMI, apneic patients have larger tongues compared to matched normal controls [28]. The latter finding may explain the lack of correlation between HP-H and BMI in the current study.

Age is another established risk factor for OSAS [29–33]. The prevalence of OSAS increases with age, with up to three times the prevalence among patients $\geq$ 65 years of age compared with middle-aged patients. However, the risk reaches a plateau around the age of 65 years [31]. According to our data, age did not correlate with the AHI scores, a finding that is consistent with some epidemiological studies [30, 31, 33] that showed that age was not in linear correlation with disease severity.

Our study has several limitations that bear mention. Our study group consisted solely of male patients. Women were not included due to the lack of information on menopause, which contributes to an increased risk of OSAS. Secondly, our patients underwent a CT scan of the upper airways as a routine preoperative evaluation. Selection bias might be suspected since most of our patients were first-line failures that were seeking surgical aid because they were unable to tolerate C-PAP treatment and were therefore referred to the OSAS otolaryngology surgical clinic. It is worth noting, however, that our group is very heterogeneous in their disease severity. Ranging from mild disease to severe with an average AHI score of 29.89 $\pm$ 19.9, which is at the edge of the moderate range. Thirdly, the acquisition of data on disease severity from medical charts was carried out in a retrospective manner. This resulted in there being no possibility of knowing the precise type of sleep study undergone by each participant. Nevertheless, all the sleep laboratory monitors used were FDA approved, and numerous validation studies demonstrated a high degree of correlation in the AHI between the various sleep laboratory monitoring systems. Moreover, the AHI scores are highly reproducible [34–38]. Fourthly, the CT scans of the upper airways were also performed in diverse facilities. All analyses, however, were performed on the original CT data and not on the interpretation of those data by the radiologists of those facilities. Finally, the study parameters were measured by means of the original software provided with each patient's dataset; therefore, slight changes due to software differences cannot be eliminated. Despite these limitations, the size of our OSAS study group is relatively large (n = 108) compared with other studies on the measurement of imaging parameters of OSAS patients whose cohorts ranged from 34 to 161 subjects [15, 20, 22, 24].

Conclusion

In conclusion, the results of our study showed that a longer pharynx and an inferiorly placed hyoid bone correlate with OSAS severity (AHI score). Our findings indicate an additive effect of BMI and pharynx length on OSAS severity but not of GP-H and BMI. IPD, a representative of the maximal width of the upper airway inlet, had initially been hypothesized to be correlated with OSAS' severity; however, it did not. Interestingly, IPD was found to increase with the age of our OSAS patients. The findings of this study provide additional insight into the factors contributing to upper airway obstruction during sleep, and unravel some of the complex interplay between upper airway parameters and BMI. The relevance of these interactions on surgical procedures and weight loss interventions for OSAS requires further research.

Acknowledgments This work was performed in fulfillment of Daniel Ben Ner's M.D. thesis requirements of the Sackler Faculty of Medicine, Tel Aviv University, Israel. We kindly ask to acknowledge Esther Eshkol for her editorial support.

Compliance with Ethical Standards

Conflict of interest There are no conflicts of interest to disclose.

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