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Different Craniofacial Characteristics Predict Upper Airway Collapsibility in Japanese-Brazilian and White Men

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BACKGROUND: OSA pathogenesis is complex and may vary according to ethnicity. The anatomic component predisposing to OSA is the result of the interaction between bony structure and upper airway soft tissues and can be assessed using passive critical closing pressure (Pcrit). We hypothesized that Japanese-Brazilians and whites present different predictors of upper airway collapsibility, suggesting different causal pathways to developing OSA in these two groups.

METHODS: Male Japanese-Brazilians (n = 39) and whites (n = 39) matched for age and OSA severity were evaluated by full polysomnography, Pcrit, and upper airway and abdomen CT scans for determination of upper airway anatomy and abdominal fat, respectively.

RESULTS: Pcrit was similar between the Japanese-Brazilians and the whites (-1.0 ± 3.3 cm H_2O vs -0.4 ± 3.1 cm H_2O, $P = .325$). The Japanese-Brazilians presented smaller upper airway bony dimensions (cranial base, maxillary, and mandibular lengths), whereas the whites presented larger upper airway soft tissue (tongue length and volume) and a greater imbalance between tongue and mandible (tongue/mandibular volume ratio). The cranial base angle was associated with Pcrit only among the Japanese-Brazilians ($r = -0.535$, $P < .01$). The tongue/mandibular volume ratio was associated with Pcrit only among the whites ($r = 0.460$, $P < .01$). Obesity-related variables (visceral fat, BMI, and neck and waist circumferences) showed a similar correlation with Pcrit in the Japanese-Brazilians and the whites.

CONCLUSIONS: Japanese-Brazilians and whites present different predictors of upper airway collapsibility. Although craniofacial bony restriction influenced Pcrit only in the Japanese-Brazilians, an anatomic imbalance between tongue and mandible volume influenced Pcrit among the whites. These findings may have therapeutic implications regarding how to improve the anatomic predisposition to OSA across ethnicities.

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KEY WORDS: computed tomography; Pcrit; ethnicity; OSA

ABBREVIATIONS: AHI = apnea-hypopnea index; MPH = distance from the hyoid to the mandibular plane; Pcrit = passive critical closing pressure; PSG = polysomnography; TV/MV = tongue/mandibular volume; Vimax = peak inspiratory flow

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OSA is a common disorder among adults that is defined and graded by severity by the apnea-hypopnea index (AHI).[1] The mechanisms that lead to OSA are complex and not completely understood. The balance between the craniofacial bony structure and the upper airway soft tissues is thought to determine an anatomic predisposition to OSA.[2] Obesity may modify the upper airway through the enlargement of the upper airway soft tissues, especially the tongue.[3,4] Several other factors, including neuromuscular modulation, control of breathing, and arousal threshold, may contribute to OSA severity as expressed by AHI.[5,6] All these factors may interact differently according to sex, age, and ethnicity. Because of the differences in craniofacial characteristics and body composition among ethnicities, interethnic studies provide an attractive model for studying the anatomic component of OSA pathogenesis. Asians are thought to be predisposed to OSA because of craniofacial bony restriction. Asians with OSA have been shown to have a shorter cranial base length than do whites.[7-9] In contrast, whites have been shown to have larger upper airway soft tissue, such as enlarged tongue dimensions, when compared with Asians.[7,8] Despite all these differences, OSA prevalence is strikingly similar in Asian and Western countries.[1,10-12]

Several issues may have limited our understanding of the ethnic differences in OSA. Some interethnic studies included only people with OSA and may have not been able to characterize the full spectrum of the differences among ethnicities. In addition, most studies were controlled by BMI or AHI.[7-9,13] BMI may not be a good metric to compare ethnicities because of ethnic differences in body composition.[14-16] AHI cannot distinguish between anatomic predisposition and the other factors that lead to OSA. The passive critical closing pressure (Pcrit) can assess anatomic predisposition to OSA.[5,17] With a view toward understanding the causal pathways to OSA development, we hypothesized that Japanese-Brazilians and whites would present different predictors of upper airway collapsibility. To test this hypothesis, Japanese-Brazilian and white men well matched for age and OSA severity (full polysomnography [PSG]) underwent Pcrit measurements and had their upper airway anatomy studied by CT scan and body fat composition determined by abdominal CT scan.

Materials and Methods

Study Design

The study consisted of a clinical interview and physical examination, baseline PSG, upper airway and abdominal CT scans, and Pcrit determination. All procedures were performed within 14 days; however, in most subjects, CT scans were performed during the afternoon before baseline PSG, and Pcrit determination was performed the following morning. The study was approved by the Hospital das Clínicas ethics committee (protocol number 0230/09; SDC 3235/08/151). All subjects gave written informed consent before the study started.

Subjects

Male Japanese-Brazilians and whites (18 to 70 years old) referred to the Hospital das Clínicas sleep clinic were recruited. To study the full spectrum of airway collapsibility, healthy subjects from the outpatient primary care clinic were also included. We excluded women; subjects with craniofacial abnormalities; those with comorbidities as defined by COPD, heart failure, chronic kidney disease, or neuromuscular diseases; and those currently using sedative medications. The Japanese-Brazilians and the whites were matched for age (± 7 years) and OSA severity by AHI (± 7 events/h). All subjects underwent a detailed clinical evaluation and a physical examination including height, weight, and waist and neck circumference. Ethnicity was self-reported. All the Japanese-Brazilians confirmed that the previous three generations in their family were either Japanese or Japanese-Brazilian without any miscegenation with other races.

Polysomnography

Subjects were evaluated by full PSG during natural sleep to identify the presence and severity of OSA. Monitoring included EEG, electrooculography, chin and leg electromyography, electrocardiography, oximetry, measurements of airflow (pressure cannula and oronasal thermistor), and measurements of ribcage and abdominal movements during breathing (Alice 5; Philips Respironics). Sleep stages were scored manually according to American Academy of Sleep Medicine recommendations.[18] Apnea was defined as complete cessation of airflow (thermistor) for ≥ 10 s. Hypopnea was defined as a > 30% reduction in airflow (nasal pressure) for at least 10 s associated with a 3% oxygen desaturation or cortical arousal.[18]

Upper Airway Collapsibility Determination

Passive Critical Closing Pressure: During Pcrit determinations, all polysomnographic channels used in the diagnostic PSG were recorded, except for nasal pressure and thermistor. Pcrit measurements were performed with subjects in the supine position. Each subject was fitted with a nasal mask attached to a heated pneumotachograph (3700A; Hans Rudolf, Inc) and a differential pressure transducer (MP45-14-871; Validyne Engineering) for measurement of airflow. Mask pressure was measured by another pressure transducer (MP45-30-871; Validyne Engineering). Respiratory signals (airflow and mask pressure) were conditioned (CD 280; Validyne Engineering) and recorded on a personal computer using an analog-to-digital converter (PCI-6014; National Instruments) and custom-designed data-acquisition software (LabVIEW; National Instruments). A modified CPAP device (Philips Respironics) that could deliver both positive and negative airway pressure was attached to the mask. Sleep was induced with midazolam as described previously.[17] Briefly, 0.5 mg of midazolam diluted in a saline solution was slowly infused IV (3 min). If the subject awoke and was not able to fall asleep again within 10 min, an additional dose of midazolam was administered until stable sleep was achieved. After sleep onset, CPAP was increased to abolish airflow limitation. This level was used as the holding

pressure for each individual. Once stable stage 2 (N2) or 3 (N3) sleep was observed at the holding pressure, CPAP was reduced abruptly by 1 to 2 cm H_2O during expiration and was held at this level for five breaths. The pressure was then returned to the holding pressure for 1 min before being dropped a further 1 to 2 cm H_2O for another five breaths. This process of progressively dropping CPAP continued until obstructive apnea occurred. If arousal occurred during any pressure drop, CPAP was returned to the holding pressure until stable sleep resumed. The entire procedure of progressively dropping CPAP until obstruction was repeated three to five times in each subject. Data were analyzed using custom-designed software (Matlab; MathWorks) to determine the peak inspiratory flow (Vimax) for breaths 3 to 5 during the pressure drop. Each of these breaths was assessed for the presence or absence of inspiratory flow limitation.[17] Breaths associated with arousal were excluded from the analysis. Vimax and nasal pressure from flow-limited breaths were plotted. Pcrit was determined as the zero-flow intercept from the linear regression of Vimax vs nasal pressure as described previously.[17]

Upper Airway CT Scan

All subjects underwent a CT scan of the upper airway (Discovery CT 750 HD; GE Healthcare). Image acquisition was performed during quiet tidal breathing with subjects supine and with a neutral head position. Each subject's head was positioned according to the Frankfurt plane, a plane from the inferior margin of the orbit to the superior portion of the external auditory meatus, perpendicular to the scanner table.[19] The scans were acquired at a 2.5-mm collimation/interval and were reconstructed at a 0.625/0.625-mm thickness/interval, with 120 kV, 100 mA, and a rotation time of 0.8 s. Axial and sagittal image reconstructions were performed to allow linear and volumetric measurements using an Advantage Workstation, version 4.5 (GE Healthcare).[20]

We identified the following landmarks on sagittal CT scan (Fig 1): point A, point B, anterior nasal spine, posterior nasal spine, nasion, center of the sella turcica, cranial base, hyoid bone, incisors occlusion, epiglottis base, most prominent point of the anterior surface of the mandibular symphysis in respect to the mandibular plane (pogonion), and medial condylar point of the mandible. Based on these landmarks, the following measurements were made: angle measurement from the sella to the nasion to point A, angle measurement from the sella to the nasion to point B, cranial base angle, distance from the nasion to the sella, distance between medial condylar point of the mandible and point A, distance between medial condylar point of the mandible and the most prominent point of the anterior surface of the mandibular symphysis in respect to the mandibular plane, distance between the angle of mandible and the center in the condylar surface, perpendicular distance from the mandibular plane to the hyoid, distance between two horizontal lines passing at the level of the posterior nasal spine and the epiglottis, and distance from the anterosuperior point of the hyoid to the incisors occlusion. The sagittal measurements were performed using the landmarks shown in Figure 1.[2,7,19-23] Tongue area was measured by tracing the contours on the sagittal plane, whereas lateral wall thickness and parapharyngeal fat were quantified on the axial plane. Mandible volume was determined by a technique based on the threshold characteristic of bone (160-3,000 Hounsfield units). To determine tongue volume, the tongue limits were identified and traced manually on each axial image obtained. Airway volume was determined by a segmentation technique based on the threshold characteristic of air (−1,024 to −800 Hounsfield units).[24,25] Volumetric reconstructions were performed to determine mandible, tongue, and airway volume. All measurements were performed by a single investigator.

Abdominal CT Scan

Abdominal CT scanning was performed immediately after upper airway CT scanning to measure visceral fat volume. Cross-sectional images were acquired with the subject in maximal inspiration, with a section thickness of 5 mm and a scanning time of 2 s, with 120 kV and 200 mA. Subcutaneous and visceral fat areas were measured on one cross-sectional scan obtained at the level of the umbilicus. The visceral fat area measured by this technique was shown to be highly correlated with total visceral fat volume.[26] The range of attenuation for fat tissue (in Hounsfield units) was determined for each subject and included the mean ± 2 SD as described previously. The region of interest (visceral fat) was defined by tracing its contour. The volume of the outside (subcutaneous fat) was excluded, with only the visceral fat volume remaining.[26]

Statistical Analysis

Data were analyzed using a statistical package (SPSS for Windows, version 17.0; IBM Corporation). Normal distribution of continuous variables was tested using the Kolmogorov-Smirnov test. Continuous variables were compared between the Japanese-Brazilians and the whites using an unpaired Student t test or a Mann-Whitney U test as appropriate. Correlation analysis (Pearson or Spearman as indicated) was used to test the associations between Pcrit and variables of interest. The Benjamini-Hochberg false discovery rate control procedure was used to adjust for multiple comparisons.[27] Multiple linear regression analysis was performed to identify the independent predictors of Pcrit in each ethnicity. Additional linear regression models were built that included the entire group to test the association between obesity or craniofacial features and Pcrit, and the interaction of these variables with ethnicity. The sample size calculation was based on a multiple linear regression analysis for each ethnicity. Assuming a power of 80%, α of 0.05, r^2 of 0.5, and seven variables, we obtained a sample of 37 subjects in each group.

Results

One hundred two subjects were screened for the study. We excluded 24 subjects (13 Japanese-Brazilians and 11 whites) who did not consent to participate (n = 18) or because of previous uvulopalatopharyngoplasty (n = 3), severe asthma (n = 1), use of sedatives (n = 1), or severe retrognathia (n = 1). The final sample was composed of 78 subjects (39 Japanese-Brazilian and 39 white men). Thirteen subjects in each ethnicity did not have OSA (AHI < 15 events/h). Among all the included subjects, 19 were recruited from the outpatient primary care clinic (nine Japanese-Brazilians and 10 whites). As expected by the study design, the two groups were similar with respect to age and OSA severity. The Japanese-Brazilians were shorter and had a lower weight and smaller waist circumference than did the whites. Pcrit was similar between the Japanese-Brazilians and the whites (Table 1).

Upper airway tomographic variables and abdominal fat measurements are shown in Figure 1 and Table 2. The

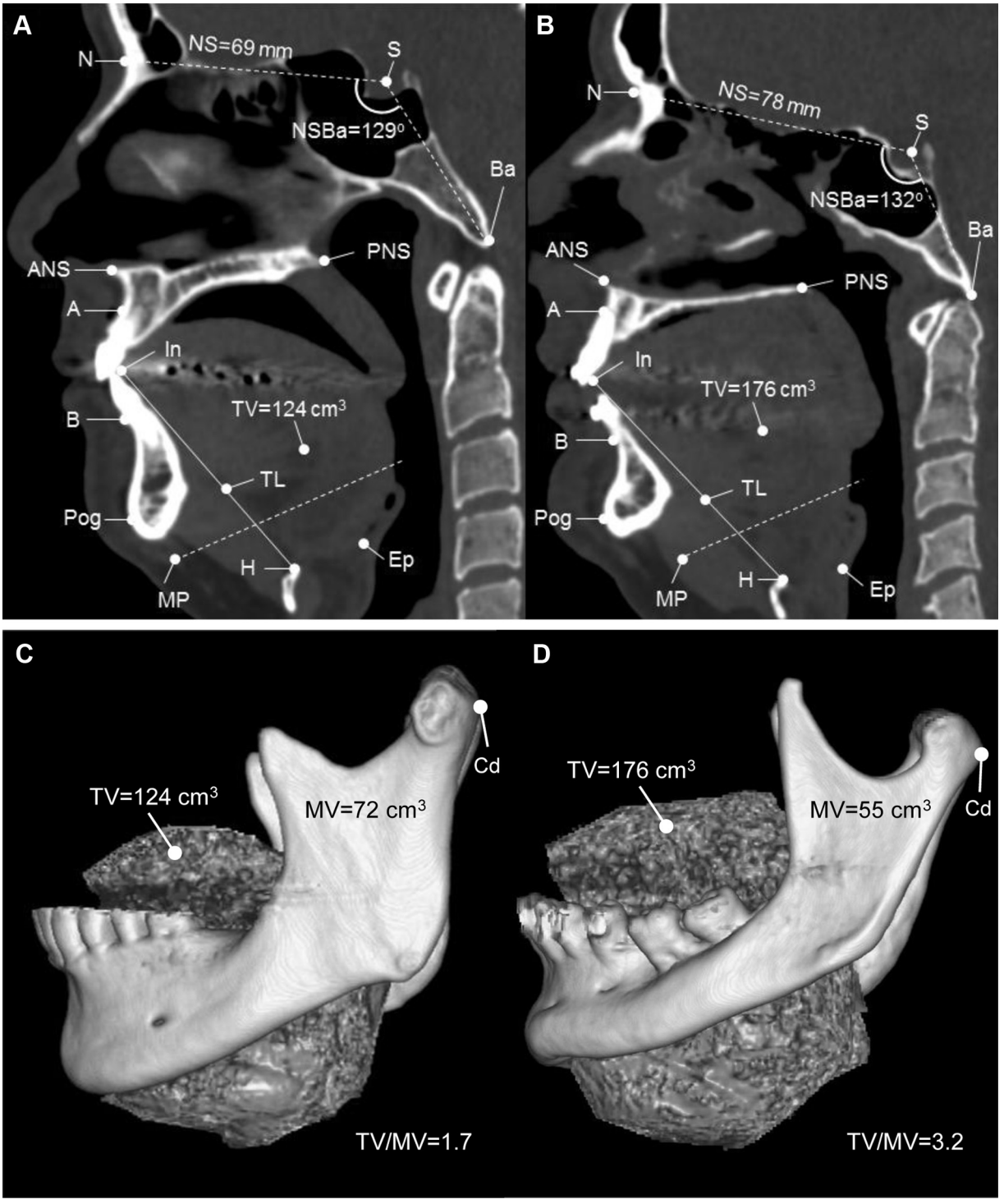

Figure 1 – *A-D, Representative sagittal and volumetric CT scan reconstructions of a Japanese-Brazilian (A and C) and a white (B and D) subject matched for age and OSA severity. Cephalometric landmarks used are shown in A and B. Volumetric reconstructions of the tongue and mandible are shown in C and D. The Japanese-Brazilian subject was 49 years old with a BMI of 28 kg/m^2 and an apnea-hypopnea index (AHI) of 60 events/h. The white subject was 46 years old with a BMI of 30 kg/m^2 and an AHI of 60 events/h. The Japanese-Brazilian subject presented smaller cranial base dimensions (NS and NSBa) (A), suggesting increased bony restriction, but smaller tongue volume and tongue/mandibular volume ratio (C), suggesting a better balance between bony and soft tissue, as compared with the white subject (B and D). Pharyngeal critical closing pressure (Pcrit) was similar (−0.4 and −0.2 cm H_2O, Japanese-Brazilian and white, respectively). A = point A; ANS = anterior nasal spine; B = point B; Ba = cranial base; Cd = medial condylar point of the mandible; Ep = epiglottis base; H = hyoid bone; In = incisors occlusion; MP = mandibular plane; MV = mandibular volume; N = nasion; NS = cranial base length; NSBa = cranial base angle; PNS = posterior nasal spine; Pog = pogonion; S = sella; TL = tongue length; TV = tongue volume; TV/MV = tongue/mandibular volume ratio.*

TABLE 1] Baseline Characteristics

Characteristic	Total (N = 78)	Japanese-Brazilians (n = 39)	Whites (n = 39)	*P* Value
Age, y	47.5 ± 12.8	47.2 ± 13.3	47.8 ± 12.5	.840
Height, m	1.70 ± 0.01	1.67 ± 0.01	1.74 ± 0.01	< .001
Weight, kg	85.1 ± 14.8	80.6 ± 2.1	89.6 ± 2.4	.006
BMI, kg/m^2	29.2 ± 4.1	28.8 ± 3.9	29.6 ± 4.2	.380
Neck circumference, cm	41.4 ± 3.1	41.5 ± 3.4	41.3 ± 2.8	.768
Waist circumference, cm	101.4 ± 11.2	98.8 ± 11.2	104.0 ± 10.8	.041
AHI, events/h	36.7 ± 27.8	36.7 ± 27.5	36.6 ± 28.3	.986
Minimum oxygen saturation, %	83.0 (73.7-88.0)	83.0 (70.0-88.0)	82.0 (74.0-88.0)	.631
Midazolam dose, mg/kg	0.043 ± 0.022	0.043 ± 0.020	0.043 ± 0.025	.996
Pcrit, cm H_2O	−0.7 ± 3.2	−1.0 ± 3.3	−0.4 ± 3.1	.325
Holding pressure, cm H_2O	9.0 (7.5-11.0)	9.0 (7.5-11.0)	8.5 (7.0-11.0)	.677

Data are presented as mean ± SD or median (interquartile range). AHI = apnea-hypopnea index; Pcrit = passive critical closing pressure.

Japanese-Brazilians had smaller maxillary, mandibular, and cranial base lengths than did the whites. Mandibular volume was greater among the Japanese-Brazilians than the whites. The whites had greater tongue length and volume than did the Japanese-Brazilians. Other soft tissue structures, such as lateral wall thickness and parapharyngeal fat, were similar between the two groups. The whites also had a greater imbalance of soft tissue/bony structure, expressed by greater tongue/mandibular volume (TV/MV) ratio (Fig 1), as compared with the Japanese-Brazilians. Upper airway length, MPH, and visceral fat volume were similar

TABLE 2] Upper Airway and Abdominal Tomographic Measurements in Japanese-Brazilians and Whites

Tomographic variables	Total (N = 78)	Japanese-Brazilians (n = 39)	Whites (n = 39)	*P* Value
Bony structures				
Maxillary length, mm	86.5 ± 4.3	85.2 ± 3.6	88.0 ± 4.5	.004
Mandibular length, mm	114.2 ± 5.4	112.0 ± 4.6	116.4 ± 5.4	< .001
Mandibular height, mm	65.4 ± 4.7	66.4 ± 4.3	64.5 ± 4.9	.073
Mandibular volume, cm^3	62.9 ± 10.2	66.0 ± 9.9	59.8 ± 9.6	.007
Cranial base length, mm	69.0 ± 3.8	66.9 ± 2.5	71.1 ± 3.7	< .001
Cranial base angle, °	128.1 ± 4.9	127.6 ± 5.4	128.6 ± 4.3	.350
SNA, °	82.0 ± 3.9	82.4 ± 4.2	81.6 ± 3.7	.399
SNB, °	79.0 ± 4.0	79.5 ± 3.7	78.5 ± 4.4	.295
MPH, mm	16.1 ± 8.0	15.0 ± 7.9	17.2 ± 8.0	.226
Soft tissues				
Lateral wall thickness, mm	14.9 ± 4.3	15.7 ± 3.9	14.0 ± 4.6	.081
Parapharyngeal fat, mm	6.0 ± 2.5	6.4 ± 2.7	5.7 ± 2.3	.262
Upper airway length, mm	70.8 ± 8.6	70.5 ± 8.7	71.0 ± 8.6	.785
Upper airway volume, cm^3	9.9 ± 4.0	9.6 ± 3.6	10.3 ± 4.4	.427
Tongue length, mm	67.9 ± 7.7	66.1 ± 7.7	69.6 ± 7.3	.042
Tongue volume, cm^3	140.8 ± 18.7	136.1 ± 16.8	145.5 ± 19.6	.025
Tongue/mandibular volume ratio	2.3 ± 0.4	2.1 ± 0.3	2.5 ± 0.4	< .001
Visceral fat				
Visceral fat volume, cm^3	120.3 ± 48.4	113.8 ± 52.8	125.9 ± 44.0	.290
% visceral fat /% total abdominal fat	38.7 ± 10.4	38.2 ± 10.1	39.1 ± 10.7	.722

Data are presented as mean ± SD. MPH = distance from the hyoid to the mandibular plane; SNA = angle measurement from the sella to the nasion to point A; SNB = angle measurement from the sella to the nasion to point B.

between the Japanese-Brazilians and the whites (Table 2).

Several anthropometric and tomographic variables were correlated with Pcrit (Fig 2 and Table 3). The cranial base angle was associated with Pcrit only among the Japanese-Brazilians, making evident the importance of craniofacial bony dimensions in this ethnicity. On the other hand, a greater TV/MV ratio was associated with Pcrit among the whites, suggesting that the imbalance of soft tissue/bony structure is a determinant of upper airway collapsibility within this ethnic group.

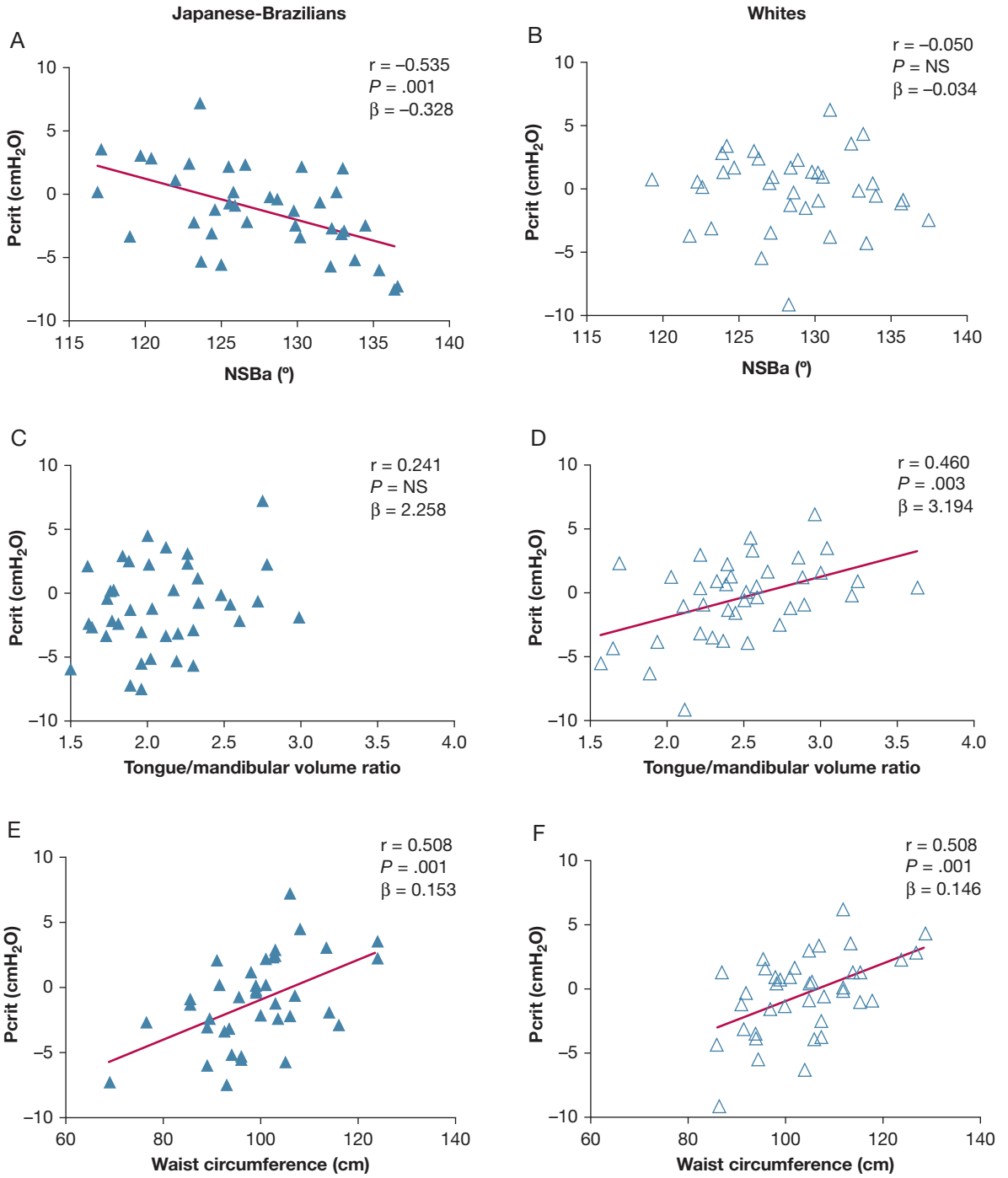

Figure 2 – *A-F, Correlations between Pcrit and tomographic and demographic variables according to ethnicity. Relationship between Pcrit and NSBa (A and B), tongue/mandibular volume ratio (C and D) and waist circumference (E and F) in the Japanese-Brazilians and the whites, respectively.* β = *unstandardized* β *coefficient. See Figure 1 legend for expansion of other abbreviations.*

TABLE 3] Univariate Correlation (Pearson) between Pcrit, Obesity Variables, and Tomographic Upper Airway Measurements in Japanese-Brazilians and Whites

Variable	Japanese-Brazilians (n = 39)			Whites (n = 39)		
	Pearson Correlation *r*	*P* Value (Unadjusted)	*P* Value (After Adjustment)	Pearson Correlation *r*	*P* Value (Unadjusted)	*P* Value (After Adjustment)
Obesity variables						
BMI	0.396	.013	.026	0.443	.005	.025
Neck circumference	0.465	.003	.019	0.551	< .001	.004
Waist circumference	0.508	.001	.007	0.508	.001	.011
Visceral fat volume	0.502	.002	.016	0.448	.004	.023
Tomographic variables						
Maxillary length	0.145	.378	ns	−0.140	.403	ns
Mandibular length	0.073	.658	ns	−0.242	.137	ns
Mandibular volume	0.132	.423	ns	−0.100	.546	ns
Cranial base length	0.038	.825	ns	−0.034	.840	ns
Cranial base angle	−0.535	.001	.009	−0.050	.771	ns
SNA	0.065	.704	ns	−0.084	.624	ns
SNB	−0.220	.190	ns	−0.149	.385	ns
MPH	0.557	< .001	.001	0.609	< .001	.006
UA length	0.566	< .001	.003	0.491	.001	.013
UA volume	0.229	.530	ns	0.264	.764	ns
Tongue length	0.508	.001	.010	0.483	.002	.018
Tongue volume	0.464	.003	.020	0.516	.001	.015
TV/MV ratio	0.241	.139	ns	0.460	.003	.022

The Benjamini-Hochberg false-discovery rate control procedure was used to adjust for multiple comparisons. ns = nonsignificant *P* value; TV/MV = tongue/mandibular volume; UA = upper airway. See Table 1 and 2 legends for expansion of other abbreviations.

Obesity-related variables such as BMI, neck and waist circumferences, and visceral fat revealed a similar correlation with Pcrit in the Japanese-Brazilians and the whites.

A multiple linear regression model using Pcrit as the dependent variable showed different variables associated with Pcrit in each ethnicity. An obesity variable and a craniofacial feature were included in each model. Waist circumference was chosen for both ethnicities because this variable presented the highest association with Pcrit in the univariate analysis among other obesity variables (BMI, neck circumference). The cranial base angle was used for the Japanese-Brazilians because it was the only craniofacial variable associated with Pcrit in the univariate analysis in this ethnicity. The TV/MV ratio was used for the whites because it was the only craniofacial feature variable associated with Pcrit among the whites. Although among the Japanese-Brazilians cranial base angle and waist circumference were independent predictors of Pcrit ($r^2 = 0.375$, $P < .001$), waist circumference and TV/MV ratio were independently associated with Pcrit among the whites ($r^2 = 0.344$, $P = .001$) (Table 4).

TABLE 4] Multiple Linear Regression Model of the Variables Associated With Pcrit in Japanese-Brazilians and Whites

Variable	Japanese-Brazilians (n = 39)				Whites (n = 39)			
	β Coef	Sβ Coef	r^2	*P* Value	β Coef	Sβ Coef	r^2	*P* Value
Cranial base angle,°	−0.230	−0.374	…	.020	…	…	…	…
Waist circumference, cm	0.102	0.338			0.113	0.391		.011
TM/MV ratio	…	…	…	…	2.190	0.316	…	.036
Model	…	…	0.375	< .001	…	…	0.344	.001

β Coef = unstandardized coefficient B; Sβ Coef = standardized β coefficient. See Table 1 and 3 legends for expansion of other abbreviations.

Another model tested the association among a measure of obesity (waist circumference), ethnicity, and the interaction of waist circumference with Pcrit. Waist circumference was an independent predictor of Pcrit ($P < .001$), but ethnicity and the interaction were not significant predictors. To test the association among craniofacial features, ethnicity, and the interaction between craniofacial features and ethnicity, two different models were built, one using the cranial base angle and another using the TV/MV ratio. In the first model, the cranial base angle ($P = .005$) and the interaction between cranial base angle and ethnicity ($P = .045$) were independent predictors of Pcrit, whereas ethnicity was marginally significant ($P = .054$). The other model using the TV/MV ratio showed that it was significantly associated ($P = .016$) with Pcrit, but that ethnicity and the interaction between TV/MV ratio and ethnicity were not.

Discussion

In the current study, we compared a well-characterized and similar sample of male Japanese-Brazilians and whites. Despite similar age, BMI, visceral fat, OSA severity, and upper airway collapsibility (Pcrit), the Japanese-Brazilians had smaller upper airway bony dimensions (cranial base and maxillary and mandibular length) as compared with the whites. In contrast, the whites had larger upper airway soft tissue (tongue length and volume). The major findings of our study were as follows. First, obesity, as assessed by different markers including BMI, neck and waist circumference, and visceral fat, contributed similarly to the determination of upper airway collapsibility among the Japanese-Brazilians and the whites. Second, Pcrit was associated with the cranial base angle among the Japanese-Brazilians, independent of obesity, highlighting the contribution of craniofacial bony restriction to upper airway collapsibility among the Japanese. In contrast, the cranial base angle was not associated with upper airway collapsibility among the whites (Fig 2, Table 3). Third, although tongue volume contributed similarly to Pcrit among both the Japanese-Brazilians and the whites, the TV/MV ratio was associated with Pcrit only among the whites. These findings may reflect different factors contributing to the imbalance between soft tissue and bony structures among ethnicities.

Interethnic studies provide a good opportunity to explore the role of craniofacial characteristics and obesity in the genesis of OSA. Our study is unique because upper airway collapsibility, upper airway anatomy, and obesity were assessed and compared among Japanese-Brazilians and whites. Pcrit was similar among the Japanese-Brazilians and the whites. However, several bony and soft tissue dimension differences were observed. Moreover, despite similar obesity measurements, different craniofacial characteristics predicted Pcrit within each ethnicity. We speculate that upper airway collapsibility is a result of complex interactions between upper airway anatomic characteristics.

We showed that Japanese-Brazilians have a shorter cranial base and maxilla and mandible length, which is in agreement with previous studies comparing Asian and white subjects with OSA.[7,8] In addition, cranial base angle and waist circumference were independently associated with Pcrit among the Japanese-Brazilians (Table 4). Sforza et al[28] studied the association between Pcrit and cephalometric variables among whites male subjects with OSA and did not find an association between Pcrit and cranial base angle.

Several evolutionary changes in the human upper airway have been described, such as a steeper and shorter cranial base. These anatomic adaptations are thought to have facilitated speech acquisition but may also have increased upper airway collapsibility and predisposed man to the development of OSA.[29] Previous interethnic studies have shown that Asians with OSA present a steeper cranial base angle when compared with whites.[7-9] A steeper cranial base angle approximates the spine and posterior pharyngeal wall to the posterior portion of the tongue (which defines the pharynx anteriorly). This may result in pharyngeal narrowing and an increase in its collapsibility, as also suggested by the findings of the current study. Therefore, our findings emphasize the importance of craniofacial bony restriction on upper airway collapsibility among Japanese-Brazilians.

Obesity, as measured by BMI, neck and waist circumference, and visceral fat, was highly correlated with Pcrit in both ethnicities, which is consistent with the findings of previous studies.[30-32] In addition, in the current study, obesity predicted Pcrit independent of ethnicity. We and others have shown that obesity may affect the upper airway through tongue enlargement, caudal hyoid displacement (MPH), and upper airway lengthening.[20,33] In the current study, tongue volume, MPH, and upper airway length were associated with Pcrit. However, tongue volume was greater among the whites. An anatomic balance model has been proposed

to explain the contribution of upper airway anatomy to OSA. Tsuiki et al[22] showed that an imbalance between tongue and maxillomandibular size as measured by lateral cephalometry was present among subjects with OSA as compared with control subjects. In another study, Iida-Kondo et al[34] used upper airway MRI and showed that subjects with OSA had a larger tongue/oral cavity volume ratio than did control subjects. Mostafiz et al[35] showed that the imbalance between the tongue and the oral cavity predicted a positive response to mandibular advancement splint. We showed that the whites had larger tongues and more upper airway anatomic imbalance (higher TV/MV ratio) than did the Japanese-Brazilians. In addition, the TV/MV ratio was a predictor of Pcrit independent of waist circumference among the whites (Table 4). These findings suggest that the imbalance between soft tissue and craniofacial dimensions plays an important role in upper airway collapsibility among whites.

Our study has several limitations. First, because of the cross-sectional design of our study, we cannot establish a causal relationship between the studied variables. Second, ethnicity is influenced by local culture and interactions with the environment, which modify the original characteristics of the ethnic group.[36] A Brazilian study compared the association of nutritional factors with body fat deposition in Japanese immigrants. The authors observed that first-generation Japanese-Brazilians presented a lower BMI, a shorter waist circumference, and less abdominal obesity than did their second-generation descendants.[37] An unexpected finding of our study was the similar BMI and abdominal fat between the Japanese-Brazilians and the whites. Previous reports that compared Asian and white subjects with OSA have shown a lower BMI among Asians.[8-10,13] A possible explanation for our finding is the incorporation of habits and a Western diet followed by Japanese-Brazilians. Third, Pcrit was determined after sleep induction with small doses of midazolam. Nevertheless, this technique has been validated and shown to be comparable to the standard technique.[17] Finally, our findings cannot be extrapolated to women. However, by including only male subjects, we reduced the variability of the studied variables. Further work will clearly be required to broaden our findings to other demographic and ethnic/racial groups.

Conclusions

In summary, this study has shown that the Japanese-Brazilians and the whites presented different predictors to upper airway collapsibility. We found that craniofacial bony restriction influenced Pcrit only in the Japanese-Brazilians. On the other hand, the anatomic imbalance between the tongue and mandible volume was higher among the whites than the Japanese-Brazilians and was associated with Pcrit. Although the Japanese-Brazilians and the whites had similar upper airway collapsibility, different predictors of Pcrit among ethnicities were observed, and this finding may help us to understand the complex interactions between upper airway bony and soft tissue. Future studies that include a larger sample, other ethnicities, and both sexes are necessary to expand our understanding of how craniofacial characteristics and obesity predispose to OSA.

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