Nasopharyngeal Morphometry in Adults with Cleft Lip/Palate and Obstructive Sleep Apnea: Analysis by Computed Tomography and Three-Dimensional Reconstruction

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Abstract

Objective: The aim of this article is to perform nasopharyngeal airway (NPA) morphometry of adults with cleft lip/palate (CL/P); verify correlation with obstructive sleep apnea (OSA) severity; and compare findings with CL/P without OSA (N-OSA) and OSA without cleft (N-CL/P).

Methods: Patients were divided into 3 groups: (G1) CL/P OSA; (G2) CL/P N-OSA; and (G3) N-CL/P OSA. Cone beam computed tomography images were used for three-dimensional reconstruction and morphometric analysis.

Results: Volume NPA was larger in G1 than in G3. Length, width, inferior depth, areas, and inferior perimeter of NPA in G1 did not differ from G2 or G3. The superior perimeter of G1 NPA differed significantly from G3. Severity of OSA did not differ between G1 and G3. Morphological variables and severity of OSA did not present a statistically significant correlation.

Conclusions: Cleft lip/palate obstructive sleep apnea patients presented larger nasopharyngeal areas than N-CL/P OSA. Findings suggest that OSA physiopathology in CLP patients has different pathways than in OSA patients without a cleft.

Keywords: Cleft palate, nasopharynx, sleep apnea obstructive, cone-beam computed tomography

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INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by intermittent obstruction of the upper airways during nocturnal sleep.[1] Certain anatomical characteristics of upper airways can impair airflow dynamics,[2-4] increasing the risk for OSA. This can be attributed to increased airflow resistance at rigid segments (nasal cavity and larynx) that lead to instability of the pharyngeal airway, which is a muscular and flexible structure with a high risk to collapse.[5]

Previous studies emphasize that patients with cleft lip/palate (CL/P) present atypical upper airway morphology in relation to controls without craniofacial anomalies, including reduced nasal cavity volume,[6,7] reduced pharyngeal dimensions,[8] and posterior airway space.[9,10] In addition, the pharyngeal dimensions of apneic patients with CL/P seemed to be smaller compared to non-apneic patients with CL/P.[11]

However, studies effectively associating atypical morphological upper airways in individuals with CL/P to OSA occurrence or severity are scarce. Recently, a study suggested that, contrary to the raised hypothesis, there does not seem to be an association between the nasal cavity dimensions of patients with CL/P and OSA occurrence.[12]

Moreover, the influence of the anatomical characteristics of specific airway segments, like the nasopharyngeal airway (NPA) for instance, on sleep-disordered breathing has not yet been fully elucidated. According to the literature, the NPA of individuals with CL/P can present an unfavorable relationship with the soft palate, which tends to have an impaired length, that can be a protective factor for OSA.[13] Also, the NPA of adults with CL/P would present an increased sagittal depth, especially following maxillary protraction therapy.[14] On the other hand, the NPA volume of those with

CL/P and OSA seems to be reduced compared to those with the craniofacial anomaly but without sleep-disordered breathing.[11] A previous report indicated that adults with CL/P and OSA have larger cross-sectional areas (CSAs) and perimeters of the superior limit of the nasopharynx than adults with OSA without craniofacial anomalies.[12] To what extent these characteristics would represent a risk or protective factor for OSA in those with CL/P requires further elucidation.

In this context, the morphometry of NPA in adults with craniofacial anomalies and OSA still needs a complete characterization. Therefore, this study aimed to perform the NSA morphometry of adults with CL/P, verify their correlation with OSA severity, and compare the findings to those with CL/P without OSA (CL/P N-OSA) and with OSA without craniofacial anomalies.

METHODS

Study Design and Settings

The study was conducted in a retrospective and cross-sectional manner, at a tertiary hospital, after approval by the Hospital de Reabilitação de Anomalias Craniofaciais da USP (Approval no.: 52430221.0.0000.5441, Date: October 29, 2021). Due to the use of secondary data sources in this study, with the use of cone beam computed tomography (CBCT) images, a request was made for the exemption from signing the Informed Consent Form to the hospital's Ethics Committee, which was approved on October 29, 2021.

Sample Characteristics

A convenient sample of cone-beam computed tomography (CBCT) was selected from the Radiology Unit. No CBCT exams were performed exclusively for research purposes. All CBCT sets were obtained using an i-CAT Next Generation scanner (ISI-iCAT Imaging System—cone beam, Next Generation i-CAT®), with the following settings: field of view of 16 × 13 cm, exposure time of 26.9 seconds, 120 Kv, 37.07 mA, and 0.25 voxel resolution.[15] Images were saved in Digital Imaging and Communications in Medicine (DICOM) format to be posteriorly processed.

Three groups of CBCT sets were constituted: (G1) CL/P OSA (n = 6, 3 males, mean age 38.70 ± 10.20 years); (G2) CL/P N-OSA (n = 11, 8 males, mean age 24.80 ± 3.00 years); and (G3) N-CL/P OSA (n = 13, 4 males, mean age 50.40 ± 9.70 years). The sample size represents all the available cases with complete data identified during a 6-month period in 2021 and meeting eligibility criteria.

Inclusion criteria for G1 (CL/P OSA) were CBCT of adults with CL/P (complete post-foramen cleft palate, incomplete post-foramen cleft palate, unilateral transforaminal CL/P, and bilateral transforaminal CL/P) and aged 18-65 years old, of both genders, who underwent primary and/or secondary lip and/or palate surgeries, and were diagnosed with OSA according to the American Academy of Sleep Medicine criteria.[16] G2 (CL/P N-OSA) inclusion criteria were the same as for G1, having a complete post-foramen cleft palate, incomplete post-foramen cleft palate, unilateral transforaminal CL/P, and bilateral transforaminal CL/P, with the exception of not having OSA. G3 (N-CL/P OSA) inclusion criteria differed from G1 exclusively for the absence of any craniofacial anomalies, and OSA criteria followed the recommendations of the Portable Monitoring Task Force of the American Academy of Sleep Medicine.[17]

All subjects of G1 and G2 underwent type I polysomnography and CBCT acquisition in a 1-month time-lapse. Polysomnographic recordings were performed using an EMBLA N7000 polygraph, type I setting, monitored by a polysomnography technician, with electroencephalogram, electrooculogram, submental electromyogram (EMG), right and left anterior tibial EMG, electrocardiogram, chest and abdominal effort plethysmographs, oronasal airflow sensors (thermistor and nasal cannula), oxygen saturation (SpO_2), and body position sensor. The parameter used to score the intensity of OSA was the Apnea/Hypopnea Index (AHI): snoring complaints and AHI <5 events/h = primary snoring; AHI ≥5 and <15 events/h = mild OSA; AHI ≥15 and <30 events/h = moderate OSA; and ≥30 events/h = severe OSA.[16]

Polysomnographic exams were performed on G3 (N-CL/P OSA) prospectively using the Oxistart sensor (Biologix Sistemas Ltd, Brazil), which evaluates oxyhemoglobin saturation, heart rate variation, patient positioning, and snoring. The main parameter analyzed is the Oxygen Desaturation Index (ODI), which measures the number of oxygen desaturations per hour of recording.[18,19] A ≥3% decrease in oximetry values prior to a respiratory event was considered a desaturation. Classification criteria were snoring complaints and ODI <5 events/h = primary snoring; ODI ≥5 and <15 events/h = mild OSA; ODI ≥15 and <30 events/h = moderate OSA; ≥ 30 events/h = severe OSA.[17-19] Four individuals underwent type I polysomnography (as previously described for G1 and G2).

Preliminarily, exclusion criteria included septoplasty, rhinoseptoplasty, turbinectomy, sinusectomy, pharyngoplasty, pharyngeal flap, history of previous nasal fracture, nasal polyps, or tumors. However, no cases were excluded for any of these reasons.

Three-Dimensional Nasopharynx Airway Reconstruction and Assessment

Digital Imaging and Communications in Medicine series were imported to ITK-SNAP software version 3.8.0[20] for three-dimensional (3D) reconstruction of the NPA, using the semiautomatic segmentation tool and a −400 to −1000 Hounsfield unit threshold. The region of interest was set using 3 anatomical points in the first sagittal plane, where the full crista galli was seen: the most anterior and superior point of the Sella, posterior nasal spine, and Basion. When the posterior nasal spine was not visible/present, the most inferior–posterior point of the concha nasalis inferior was considered instead. A triangle created out of these points encompassed the NPA and was the reference for segmentation.

Afterward, the NPA meshes were exported to the ANSYS SpaceClaim 2020 R2 software[21] for the creation of computer-aided design (CAD) models, allowing the acquisition of solid 3D models of each airway segment, as described in Loureiro et al[12] in detail. No structure simplification was done, preserving the real dimensions and morphological characteristics of each subject's NPA. From CAD models, the morphometric analyses were performed using software tools.

The assessed variables of the NPA were volume, length, inferior and superior width, inferior depth, inferior and superior CSAs, and inferior and superior perimeter. All these values were automatically provided by the ANSYS SpaceClaim 2020 R2 software using CAD.

Main Points

- *Differences in volume and cross-sectional area of the NPA.*
- *Anatomy of NPA and correlations with OSA severity.*
- *Obstructive sleep apnea severity and NPA morphology.*
- *Impact of CL/P on airway anatomy.*

All measures were performed twice by the same trained and calibrated examiner, with an interval period of 2 weeks between sessions. The mean values of both assessments were considered for statistical analysis. Intra-examiner reproducibility was calculated using the intraclass correlation coefficient (ICC), indicating good (≥0.75-<0.90) and excellent agreement (≥0.90) for all variables).

Cephalometric Analysis

The Sella-Nasion-Point A (SNA) angle, which indicates the position of the maxilla in the posteroanterior direction in relation to the anterior base of the skull, was measured in the 3 groups using ITK-SNAP software version 3.8.0.[20]

Data Analysis

Variables were submitted for normality analysis using the Kolmogorov–Smirnov test. Data with normal distribution were presented as mean ± SD and compared by ANOVA test with multiple comparisons.[22] Variables non-normally distributed were presented as median values and their 25% and 75% percentiles and compared by Kruskal–Wallis test with multiple comparisons.[23] Values of $P \leq .05$ were considered significant.

RESULTS

Descriptive and Comparative Analysis

Age (years) of G1 (38.67 ± 10.21) vs. G2 (24.82 ± 2.99) (mean difference = 13.85 years; $P = .004$), G1 vs. G3 (50.38 ± 9.67) (mean difference = −11.72 years; $P = .006$), and G2 vs. G3 (mean difference = −25.57 years; $P < .0001$) differed significantly from each other (Figure 1A). Considering body mass index (kg/m^2), G1 (25.63 ± 1.99) vs. G2 (22.85 ± 3.11) did not differ significantly ($P = .173$), while G3 presented overweight compared to G1 (mean difference = 6.90 kg/m^2; $P = .002$) and G2 (mean difference = 9.68 kg/m^2; $P < .0001$) (Figure 1B). Considering subjects' sex, G1 had 50% male, G2, 72.72%, and G3, 30.76%. Obstructive sleep apnea was detected in G1 (median = 8.90; 25% = 7.47; 75% = 23.90 AHI events/h) and G3 (median = 16.40; 25% = 7.50; 75% = 38.25 AHI events/h—4 individuals; and median = 15.50; 25% = 8.37; 75% = 23.20 ODI events/h—10 individuals), severity did not differ between groups ($P > .999$) (Figure 1C).

Considering the type of cleft, G1 had 2 cases of complete post-foramen cleft palate, 1 incomplete post-foramen cleft palate, 1 unilateral transforaminal CL/P, and 2 bilateral transforaminal CL/P. In G2, 7 individuals had unilateral transforaminal CL/P and 4 had bilateral transforaminal CL/P. Individuals of G1 presented an average SNA angle of 80.70° ± 2.09°; in G2, the average SNA was 75.1° ± 3.05°; and in G3, 82.10° ± 4.42°. G1 vs. G2 (mean difference = 4.30°; $P = .203$) and G1 vs. G3 (mean difference = −1.80°; $P = .737$) did not differ at the statistically significant level, considering SNA. However, G2 vs. G3 (mean difference = −6.10°; $P = .009$) differed, with the subjects in G2 presenting a comparatively more retruded maxilla than those in G3 (Figure 1D).

The volume of NPA was larger in G1 than in G3 (mean difference = 2445 mm^3; $P = .035$) but did not differ from G2 (mean difference = 1789 mm^3; $P = .165$) at the statistical level of significance, as well as G2 and G3 did not differ from each other (mean difference = 656.20 mm^3; $P = .674$) (Table 1; Figure 2A). Besides volume characteristics, the anatomical variability of the NPA observed in intra- and inter-groups was remarkable, as seen in Figure 3. Nasopharyngeal airway length did not differ among groups, G1 vs. G2 (mean difference = −0.04 mm; $P = .999$); G2 vs. G3 (mean difference = 3.26 mm; $P = .091$); and G1 vs. G3 (mean difference = 3.21 mm; $P = .191$) (Table 1).

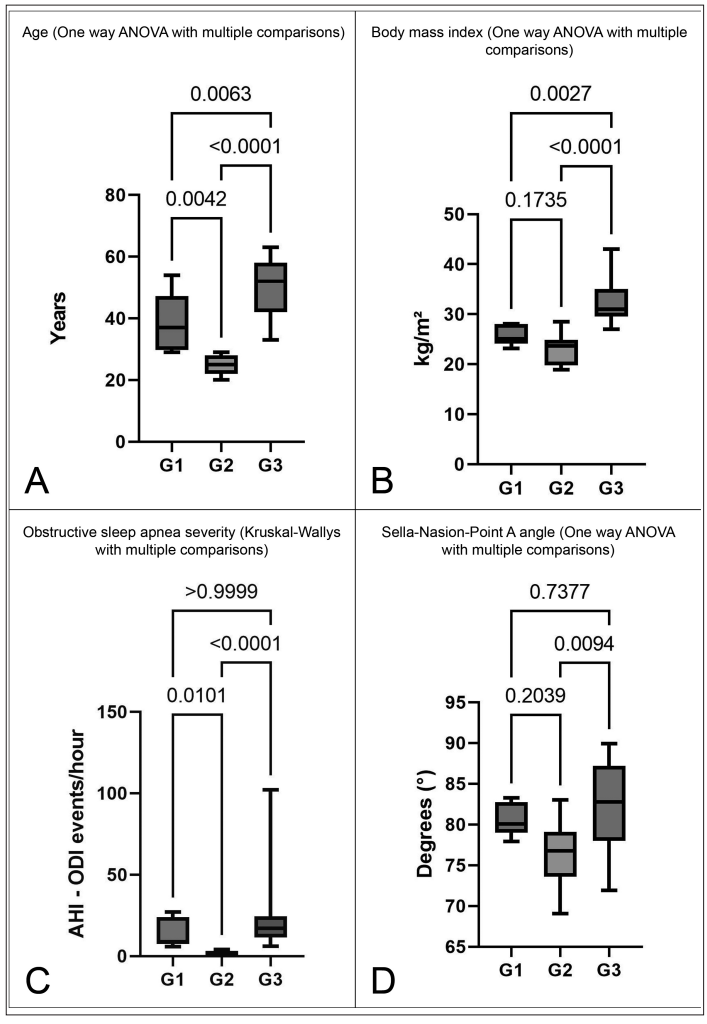

Figure 1. Comparative analysis of age (years), body mass index (kg/m^2), severity of OSA (AHI—ODI events/hour), and anterior–posterior maxilla positioning in relation to the base of the skull. AHI, Apnea/Hypopnea Index; ODI, Oxygen Desaturation Index; OSA, obstructive sleep apnea.

The CSA at the inferior limit of the NPA was larger in G1 than in G2 (mean difference = 121.40 mm^2; $P = .047$) and in G2 compared with G3 (mean difference = 105.30 mm^2; $P = .031$), but G1 and G3 did not differ from each other (mean difference = 16.16 mm^2; $P = .937$) (Table 1; Figure 2B).

Similar findings were observed for the perimeter of the inferior NPA limit, where G1 vs. G2 (mean difference = 12.08 mm; $P = .393$) and G1 vs. G3 (mean difference = −8.65 mm; $P = .596$) did not differ statistically, but G2 and G3 did (mean difference = −20.73 mm; $P = .023$) (Table 1; Figure 2C).

The inferior limit of the NPA width did not differ among groups, either between G1 and G2 (mean difference = 4.99 mm; $P = .138$); G1 and G3 (mean difference = 5.89 mm; $P = .059$); or G2 and G3 (mean difference = 0.901; $P = .898$) (Table 1).

Depth of NPA at its inferior limit did not differ between G1 vs. G2 (mean difference = 6.75 mm; $P = .391$); G1 vs. G3 (mean difference = 6.20 mm; $P = .459$); and G2 vs. G3 (mean difference = −0.55 mm; $P > .999$) (Table 1).

Table 1. Morphometric Variables Evaluated in the Studied Sample

Variables	G1 (CL/P OSA) n = 6	G2 (CL/P N-OSA) n = 11	G3 (N-CL/P OSA) n = 13
Volume (mm^3)	8624 ± 2744*	7077 ± 1487	6294 ± 1645*
Length (mm)	17.09 ± 5.11	17.13 ± 3.16	13.87 ± 3.25
Inferior limit cross-sectional area (mm^2)	486.50 ± 118.30*	365.00 ± 81.33*	470.30 ± 96.21*
Inferior limit perimeter (mm)	101.00 ± 14.51	88.90 ± 9.95*	109.60 ± 23.54*
Inferior limit width (mm)	32.45 ± 4.43	27.46 ± 3.70	26.55 ± 6.02
Inferior limit depth (mm)	27.78 ± 4.12	24.03 ± 3.32	24.91 ± 7.41
Superior limit cross-sectional area (mm^2)	479.70 ± 147.80	461.40 ± 68.53	386.00 ± 69.10
Superior limit perimeter (mm)	133.40 ± 18.00*	128.50 ± 11.50*	114.13 ± 12.50*

Comparisons were made through one-way ANOVA and Tukey's multiple comparisons. CL/P OSA, cleft lip/palate obstructive sleep apnea; CL/P N-OSA, cleft lip/palate without obstructive sleep apnea; N-CL/P OSA, obstructive sleep apnea without cleft lip/palate. *P < .05 were considered significantly different.

Considering the superior NPA limit toward the nasal cavity, CSAs did not differ between G1 vs. G2 (mean difference = 18.34 mm^3; P = .913); G1 vs. G3 (mean difference = 93.70 mm^3; P = .101); and G2 vs. G3 (mean difference = 75.36 mm^3; P > .115). On the other hand, the superior NPA perimeter was increased in G1 compared to G3 (mean difference = 19.07 mm; P = .019) and in G2 compared to G3 (mean difference = 14.25 mm; P = .038) but did not differ between G1 and G2 (mean difference = 4.82 mm; P = .758) (Table 1; Figure 2D).

The ICC showed excellent reproducibility of measurements: NPA volume (0.96) and length (0.90). For those parameters, whose dimensions were automatically provided by the ANSYS software—inferior limit CSA, inferior limit perimeter, inferior limit width, inferior limit depth, superior limit CSA, and superior limit perimeter—no ICC values were estimated.

Correlations

Neither G1 (CL/P OSA) nor G3 (N-CL/P OSA) exhibited correlations of OSA severity (AHI events per hour; ODI events per hour, respectively) with the assessed morphological variables of the NPA, or with age, body mass index, and SNA angle (Table 2).

DISCUSSION

Approximately 1 billion people are estimated to have OSA worldwide. The risk rises among those with obesity, advanced age,[24] and of the male sex.[25,26] Upper airway muscle responsiveness, arousal threshold, and loop gain are non-anatomical variables that have also been related to OSA severity in the general population.[27]

Among those with CL/P, however, there has been a particular interest in elucidating if anatomical factors, such as a reduced upper airway morphology[6,12] and unfavorable maxillo-mandibular relationship[8] are contributing features/phenotypes for the onset and severity of OSA. Notwithstanding, it remains unclear to what extent these characteristics correlate with OSA in adults with CL/P.[6-12]

Previously, Campos et al[11] reported in a similar sample that the total upper airway volume was significantly decreased in subjects with CL/P

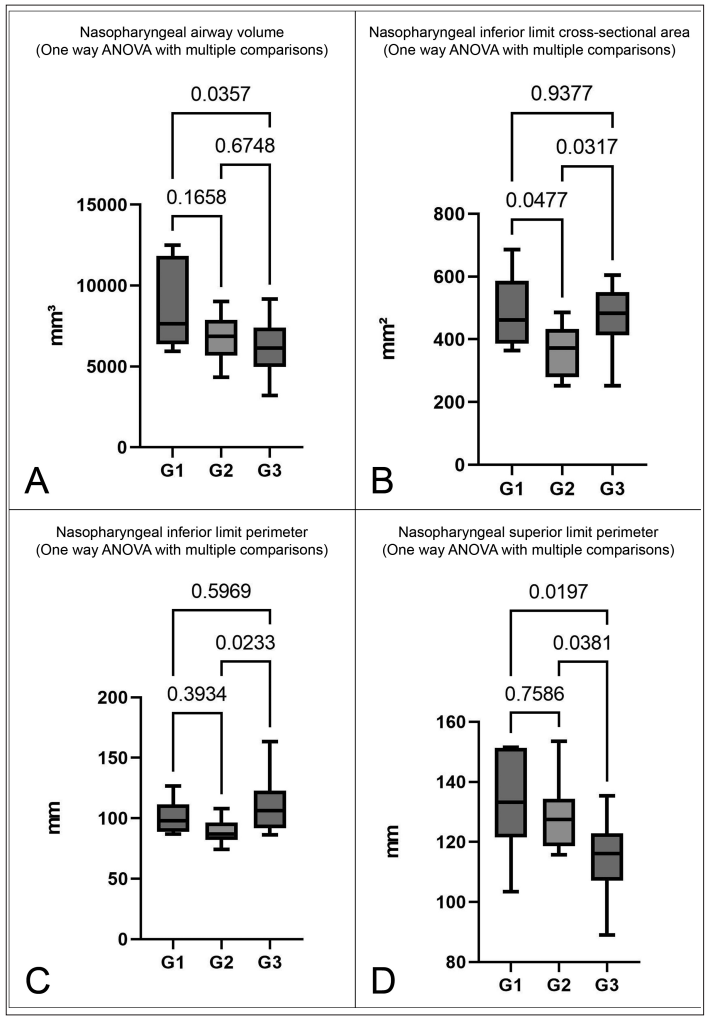

Figure 2. Comparative analysis of morphometric variables that differed at the statistical level of significance among groups.

and OSA, but not in those without sleep-disordered breathing. When segments of the airway were studied separately, the oropharyngeal segment seemed to be more critical for OSA etiopathogenesis in the population of adults with CL/P[11] than the nasal cavity.[12] It has been detected that this structure of adults with CL/P and mild OSA seems volumetrically smaller (but not at a statistical level of significance) than in those without craniofacial anomalies and more severe OSA.[12] However, in adults with CL/P and OSA, the nasal cavity tends to be volumetrically impaired, followed by a nasopharyngeal anatomy whose CSAs, perimeters,[12] airway volume and sagittal dimensions were more increased than in controls.[9,12] Therefore, it seems plausible that proper morphological aspects of the velar structure of individuals with CL/P act as a protective factor for OSA onset/severity, once impaired anatomy of the levator veli palatini and superior pharyngeal muscles[28] could reduce resistance to airflow.

On the other hand, a narrower nasopharynx might result in OSA, as expected in patients with CL/P after surgically reconstructing the palatal muscles.[28] Studies that evaluated nasopharyngeal characteristics among individuals with repaired CL/P, aiming to understand the relationship between airway morphology and the prevalence/severity of OSA, seem relevant and justifiable in this context.

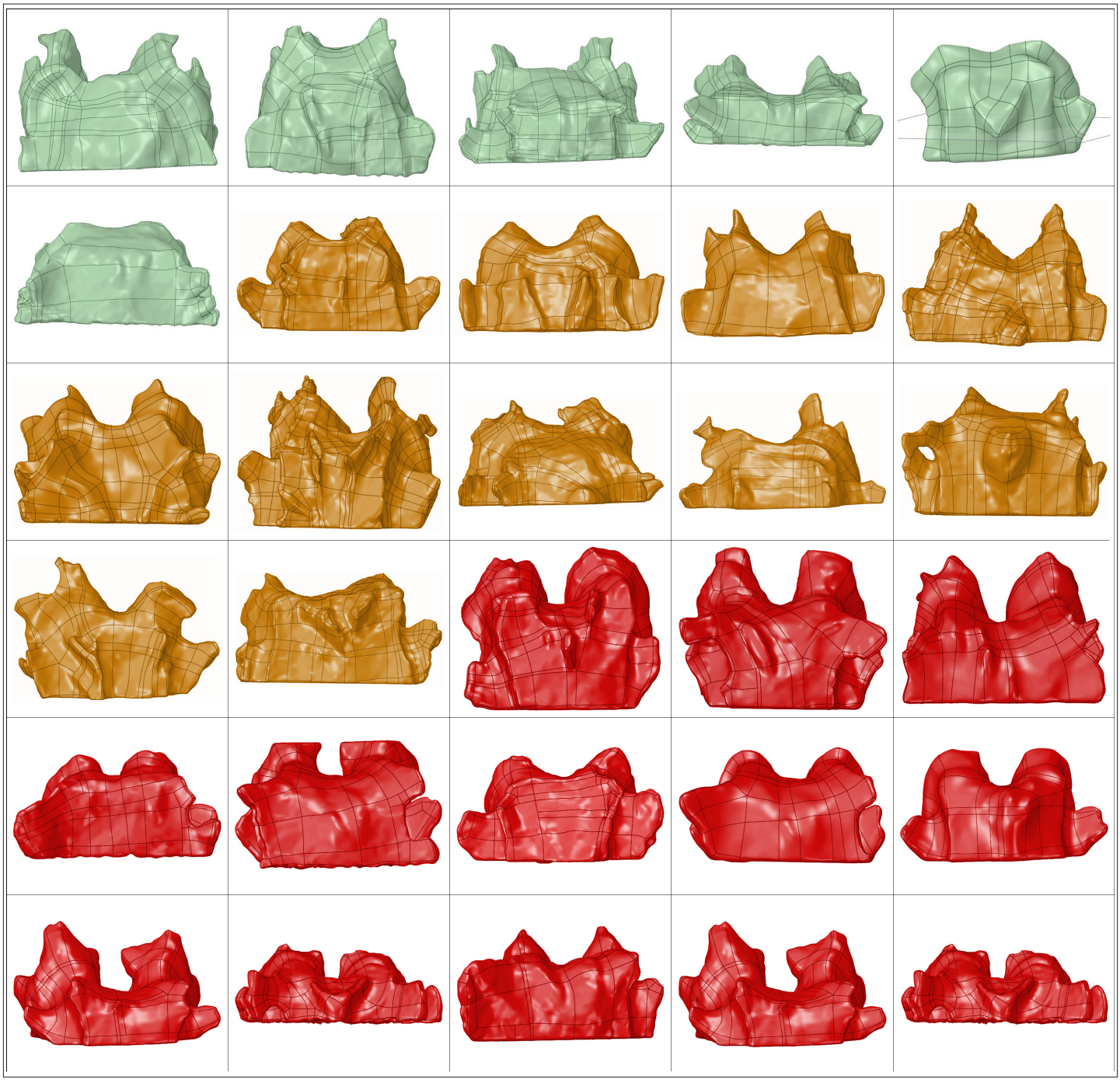

Figure 3. Posterior view of the nasopharyngeal airway 3D reconstructed. Light gray—G1 (CL/P OSA). Medium gray—G2 (CL/P N-OSA). Dark gray—G3 (N-CL/P OSA). 3D, three dimensional; CL/P OSA, cleft lip/palate obstructive sleep apnea; CL/P N-OSA, cleft lip/palate without obstructive sleep apnea; N-CL/P OSA, obstructive sleep apnea without cleft lip/palate.

The initial hypotheses of the present study were that (1) individuals with CL/P and OSA would have smaller NPA internal dimensions than those with CL/P N-OSA; (2) individuals with CL/P and OSA would have increased nasopharyngeal dimensions than those without craniofacial anomalies, but with OSA; and (3) nasopharynx dimension would be negatively correlated with OSA severity.

G1 vs. G2 did not differ in NPA volume ($P=.165$), length ($P=.999$), perimeter ($P=.393$), width ($P=.138$), and depth ($P=.391$). Also, the perimeter ($P=.758$) and CSA ($P=.913$) of the superior limit of the NPA were similar between G1 and G2. For instance, in the studied sample, hypothesis 1 would not be considered true as NPA morphometry did not differ between individuals with CL/P with OSA (G1) or without OSA (G2), except regarding the inferior limit of the NPA that was larger in G1 than in G2 ($P=.047$), unexpectedly.

A previous comparative analysis between adults with CL/P and OSA vs. CL/P N-OSA[11] had stated that the minimum CSA of the airway was found in the NPA in only 1 case per group (at a 7% and 17% frequency,

Table 2. Correlation Data of Obstructive Sleep Apnea Severity with Demographic, Anthropometric, Cephalometric, and Nasopharyngeal Airway Morphometry

	G1—AHI		G3—AHI/ODI	
Variables	Pearson-*r*	*P*	Pearson-r	*P*
Age	–0.187	.721	0.024	.937
Body mass index	0.398	.434	0.118	.696
Sella-Nasion-Point A	0.650	.234	0.340	.279
NPA				
Volume (mm^2)	0.272	.602	0.325	.277
Length (mm)	0.669	.145	–0.013	.964
Inferior limit cross-sectional area (mm^2)	0.077	.883	0.234	.440
Inferior limit perimeter (mm)	0.244	.641	0.044	.885
Inferior limit width (mm)	–0.157	.765	0.079	.796
Inferior limit depth (mm)	–0.485	.329	0.229	.451
Superior limit cross-sectional area (mm)	0.356	.640	–0.330	.270
Superior limit perimeter (mm)	0.763	.077	–0.124	.685

AHI, Apnea/Hypopnea Index; NSA, nasopharyngeal airway; ODI, Oxygen Desaturation Index.

respectively), while the more constricted area was the oropharynx, found in 66% of cases for both groups.[11] Indicating that, nasopharynx dimensions seem not to be a critical segment for airway patency reduction among those with craniofacial anomalies and OSA, which in a certain way corroborates our results.

Subjects of both groups had their palatoplasty done years ago (data not shown). Therefore, none of them were suffering from a transitory deleterious effect on airflow regulation expected during the immediate postoperative course, which has been associated with depression of SpO_2 due to OSA.[28] Consequently, OSA occurrence in G1 does not represent a consequence of recent rearrangement of NPA muscles through surgery.

On the other hand, the impact of palatoplasty impact on NPA dimensions in both groups is unknown because the size of the cleft and the preoperative nasopharynx morphometric parameters were not assessed. It has been proposed, though, that a higher risk of desaturation would be expected in patients who presented larger preoperative nasopharynx, leading to chronic OSA later.[29]

Perhaps, there is a certain threshold of NPA dimensions variation before and after palatoplasty that, when reached, leads to a clinically significant patency reduction and subsequent long-term OSA and nasal obstruction symptoms.[7] This would explain the fact that subjects from G1 presented increased CSA at the inferior limit of the NPA compared with G2 and still had OSA. Future studies should address the possible association between prepalatoplasty and postpalatoplasty NPA dimensions and the occurrence of OSA later in life for those with CL/P.

Lack of differences in G1 vs. G2 results analysis would be a consequence of the heterogeneous type of cleft intragroups and intergroups, which is a limitation of this study. However, this possible bias is debatable, since Fukushiro and Trindade[7] observed that the nasopharynx area does not differ among cleft types (unilateral CL/P, bilateral CL/P, or cleft palate) in adults from the same setting as ours.

Nasopharynx volume was larger in G1 than in G3 ($P = .035$), but no other variables differed between individuals with CL/P and OSA vs. N-CL/P and OSA. G2 (CL/P OSA) and G3 (N-CL/P with OSA) did not differ from each other regarding NPA: volume ($P = .674$), length ($P = .091$), inferior limit width ($P = .898$), and depth ($P > .999$). On the contrary, their CSA at the inferior limit of the NPA was larger in G2 than in G3 ($P = .031$), and the superior NPA perimeter was increased in G2 as well ($P = .038$). Hypothetically, the reduced dimensions in G3 may be associated with OSA severity.[12] However, it is not possible to state a cause-effect relationship between reduced NPA dimensions and increased severity of OSA in N-CL/P patients in the present study. A confirmatory analysis will require the evaluation of nasopharynx morphology among adults with primary snoring and/or mild OSA syndrome vs. moderate/severe OSA syndrome, which will not be performed in the present study.

Regarding the use of different types of PSG between groups G1 and G2 vs. G3, recent data showed a good correlation between AHI and ODI. In this way, type IV PSG in high OSA risk patients is an adequate tool for OSA diagnosis.[12,18,19]

Subjects in G2 presented a comparatively retruded maxilla than those in G3, with a mean difference of –6.10° ($P = .009$). A retruded maxilla is expected in adults with CL/P due to a growth restriction imposed by the sequela of reparative surgeries that result in fibrotic scar tissue, as proposed in the literature.[8] Although, this does not seem to have an influence on NPA patency.[8] On the other hand, the craniofacial anatomy in adult subjects with established OSA was previously evaluated in the meta-analysis by Neelapu et al.,[30] and despite their finding supporting the relationship between craniofacial disharmony and OSA, the SNA angle was not considered to be a risk factor for sleep-disordered breathing, supporting our findings.

Results indicate that despite differences among groups regarding NPA dimensions, no morphological characteristics correlated with OSA severity in G1 and G3. However, results should be confirmed by other studies with larger cohorts.

CONCLUSION

The present results suggest that the NPA dimensions of patients with CL/P do not seem to be part of the etiopathogenesis of OSA. In this way, OSA physiopathology in CLP patients might have different pathways than in OSA patients without craniofacial anomalies.

Data Availability Statement: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics Committee Approval: This study was approved by the Ethics Committee of Hospital de Reabilitação de Anomalias Craniofaciais da USP (Approval no.: 52430221.0.0000.5441, Date: October 29, 2021).

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Materials – institutional USP.; Data Collection and/or Processing – A.D.A., M.N.M.-R., N.B.L.; Analysis and/or Interpretation – A.D.A., M.N.M.-R., I.K.T.-S., S.H.K.T.; Literature Search – A.D.A., M.N.M.-R., N.B.L., I.K.T.-S., S.H.K.T.; Writing – A.D.A., S.H.K.T.; Critical Review – A.D.A., M.N.M.-R., N.B.L., I.K.T.-S., S.H.K.T.

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