Pharyngeal Airway Assessment in Children with Non-Syndromic Cleft Palate and Cleft Lip and Palate: A CBCT Study

Thesis

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Abstract

Purpose: The purpose was to assess the volumetric and linear dimensions of the pharyngeal airway in nonsyndromic cleft palate and cleft lip and palate patients compared to noncleft controls using cone beam computed tomography (CBCT).

Methods: Retrospective assessment of 567 CBCT scans was completed. Following strict exclusion criteria, 154 patients were selected: 78 cleft and 76 noncleft. The patients were divided by age (7-11 and 12-17 years). Upper airway measurements were taken with Invivo6 (Anatomage, California, USA). The airway was evaluated for volume, minimum cross-sectional area (MCSA), and linear measurements. Intergroup statistics were completed using Welch's t-tests, Cohen's d, and multiple linear regression.

Results: Velopharyngeal volume was significantly lower in cleft patients than controls in both age groups (7-11 $P=0.03$, 12-17 $P=0.002$). Distance from the posterior nasal spine (PNS) to the posterior pharyngeal wall (PPW) was significantly larger for cleft patients than controls in both age groups (7-11 $P<0.001$, 12-17 $P<0.001$). PPW length was larger in controls than cleft patients for both age groups (7-11 $P<0.001$, 12-17 $P<0.001$). MCSA was significantly smaller in cleft patients than control patients for the 12-17 age group ($P=0.001$). After adjustment, the cleft sample overall had smaller velopharynx volumes ($P=0.003$), oropharyngeal MCSA ($P=0.01$), transverse dimension of MCSA ($P=0.02$), and PPW length ($P<0.001$) with larger PNS to PPW distance ($P<0.001$).

Conclusions: Nonsyndromic children with palatal clefts have narrowed airways with reduced volumes, increasing risk for airway obstruction. Palatal deficiency and reduced pharyngeal height may lead to impairment of velopharyngeal closure.

Dedication

I dedicate this thesis to my incredible wife, Erin, and my loving parents, Andy and Debbie. Without your support, nothing I have accomplished would have been possible. Thank you.

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I would like to primarily acknowledge my committee members. Over the past two years, Dr. Dan Claman, Dr. Erin Gross, Dr. Ana Mercado, and Dr. Sonya Kalim have been instrumental in the completion of this project. From the initial brainstorming to the final edits, you have all played an unforgettable role. Thank you for the wisdom, guidance, reassurance, inspiration, training and teaching along the way.

I would also like to thank Dr. Anita Gohel, who brainstormed the initial concept for the project. Although you have moved on from Ohio State, you inspired this work.

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Chapter 1. Introduction

The field of dentistry has seen a growing interest in diagnostic screening and assessment of the airway. Measurements taken of the airway provide a better understanding of anatomic proportions and their relation to physiology. Historically, airway evaluation in dentistry has consisted of utilizing radiological means for assessing orthodontic and surgical treatment outcomes. Additionally, as our knowledge of conditions such as velopharyngeal insufficiency (VPI), sleep disordered breathing (SDB), and obstructive sleep apnea (OSA) has progressed, airway evaluation has provided the opportunity to evaluate skeletal, oral, and pharyngeal dimensions of affected patients. As technology has continued to advance, more medical and dental providers have implemented advanced, point-of-care radiologic techniques into their practice.

Though traditional techniques for airway measurement used lateral cephalometric radiographs, there is debate regarding interpretation of those measures. Superimposition of anatomic structures and restriction to linear measures of a three-dimensional space, as seen in lateral cephalometric films, complicate airway analysis. Previous research has demonstrated weak correlations between cross-sectional area and airway volume when related to linear measurements obtained from 2D images.[1] The lateral cephalometric film has a litany of limitations, including low reproducibility from difficulty in landmark identification, distortion errors, and magnification problems.[2,3] However, the

implementation of low-dose Cone Beam Computed Tomography (CBCT) has provided three-dimensional imaging with high accuracy and low distortion for airway analysis.[4] These images can be used for segmentation and visualization of the airway in three dimensions, allowing the viewer to quantify volumetric and surface area dimensions.[5] CBCT has been shown to provide repeatable volumetric measurements.[6,7] In a recent systematic review, van Vlijmen et al.[8] determined that CBCT offers better diagnostic potential than conventional 2D imaging modalities. This translates to improved treatment planning, results, and treatment outcomes. Though patients are exposed to an increased radiation dose with CBCT relative to cephalometric films, they are not exposed to the same extent of "medical" multislice CT. The lower relative dose, combined with high spatial resolution, fast acquisition speed, and definable contrast between empty space and soft tissue, enables CBCT to be a safe and valuable means to evaluate the upper airway.[9,10]

An important feature of the airway space is that it is dynamic, reflected by dimensional changes with varying head positioning, swallowing, tongue positioning, and breathing phase. Additionally, the airway possesses a complex relationship with its surrounding structures, including muscle, bone, soft tissue, and cartilage. In addition to the physiologic functions of these structures, they also can modify the morphology of the surrounding structures, typically through muscle balance and altered pressure.[11] The upper airway has been shown to be associated with dentofacial development, as removal of upper airway obstructions has been suggested to be a causative factor in changes to craniofacial morphology.[12]

Orofacial clefts are a heterogenous group of common congenital defects with complex etiologies.[13] Much of the existing literature suggests that orofacial clefts are a product of genetics and gene-environment interactions. Some of the suggested etiologies for clefting include malnutrition, maternal illness, and drugs.[14] Most often, clefting is divided into two categories: cleft lip with or without cleft palate (CL+/-CP) and cleft palate only (CP). These different forms of orofacial clefts possess varying developmental considerations.[15] Additionally, clefts can be subcategorized into non-syndromic and syndromic variants. Individuals with non-syndromic clefts do not possess the accompanying physical or developmental abnormalities as seen with the syndromic variant. It is estimated that about 70% of CL+/-P and 50% of CP are non-syndromic.[16,17,18] Clefting leads to a series of impairments in early childhood, including poor suckling, failure to thrive, and deafness. As children continue to grow, malocclusion, facial deformities, speech difficulties, and severe psychological problems can develop.[19,20] Early recognition of cleft conditions and their consequences are critical for management, as treatments are complex and multidisciplinary teams are necessary for optimal outcomes.

Craniofacial anomalies such as cleft palate can predispose and individual for OSA, a sleep-related breathing disorder in which normal ventilation is altered by upper airway obstruction resulting in sleep fragmentation.[21,22] Though criteria for sleep apnea varies, it remains common in the pediatric population with a prevalence of 1.2% to 5.8%.[21,23,24] Craniofacial anomalies, including cleft palate, have been shown to reduce airway patency and anatomically narrow the airway through decreased maxillary and

mandibular length, decreased maxillary height, midface hypoplasia, basal maxillary retrognathia, and mandibular retrognathia.[22,25,26] Obstructive symptoms, such as snoring, have been reported more frequently in children with CLP during sleep which can be an indication of obstruction[27]. Reduced, incompetent nasal airways in cleft patients lead to mouth-breathing, with as much as 70% of CLP patients exhibiting mouth-breathing tendency when compared to 30% in the non-cleft population.[28,29] Mouth-breathing is commonly found in younger and older children with SDB and it has been shown to be a significant predictor for OSA.[30,31] Leaving OSA undiagnosed and untreated can be severely detrimental to a developing child, with related complications including behavioral problems such as attention-deficit/hyperactivity disorder (ADHD) symptoms, depression, and aggression; lowered school performance; abnormal social behaviors; and hypersomnolence.[21,32] Severe cardiovascular complications from OSA include pulmonary hypertension, in which increases in pulmonary vascular resistance can progress to right heart failure and death. Though rare, children affected often require surgery to reduce airway obstructions impairing cardiac health, typically adenotonsillectomy and/or tracheostomy.[33,34,35]

Congenital conditions such as cleft palate as well as post-operative results from surgical procedures, including tonsillectomy, can predispose an individual for a condition called velopharyngeal insufficiency (VPI), in which the normal function of the velopharyngeal closure is disturbed due to abnormal anatomic structures. In the velopharynx region, the muscles of the pharynx and soft palate open and close the airway between the oropharynx and nasopharynx by constricting the posterior and lateral

pharyngeal walls and elevating the soft palate.[36] This closure forms the foundation for normal swallowing and production of speech sounds. Though there are many possible etiologies for VPI, cleft palate and unrepaired submucous cleft palate are noted to be the most common.[37] Even after cleft palate repair, one-third of patients will be diagnosed with VPI and require additional surgery to improve speech.[38,39,40] It is important to distinguish velopharyngeal insufficiency from velopharyngeal incompetence, which is due to abnormal velopharyngeal movements oftentimes stemming from a neuromuscular or traumatic etiology. Cleft palate can predispose an individual for secondary velopharyngeal incompetence when abnormalities in velum tension or pharyngeal muscle contraction are present.[41,42] VPI can lead to a variety of adverse effects, some more debilitating than others. The characteristic effect of VPI is nasal air emission leading to hypernasal resonance or rhinophonia. Additionally, articulation difficulties are common in children with VPI. The confluent nasal passage can also result in nasal reflux and dysphagia.[43,44] VPI leads to increased risk for psychological and developmental difficulties. These include impaired relationships, reduced psychosocial functioning, and lower quality of life.[45,46]

Though VPI itself may not be associated with OSA, treatment of the disorder has been associated with sleep disorders. Correction of VPI requires surgical flap, sphincter pharyngoplasty, or palatoplasty. Following surgical procedures, airway constriction results from decreasing the cross-sectional area of the velopharynx. This narrowing is associated with increased risk of snoring and sleep disordered breathing.[47,48] Data varies on the exact prevalence of OSA following surgical velopharynx repair, with it being

reported as high as 94% on polysomnography 6-months following pharyngeal flap surgery for unilateral cleft palate patients[49] versus a later study finding only 24% of unilateral cleft palate patients reported symptoms indicative of OSA.[50] Additional surgical treatment may be required for revision if OSA occurs as a result of the VPI repair procedures.

Considering the possible conditions and complications that can result from clefts, morphometric evaluation of the pharyngeal airway for children with CP and CLP can provide valuable information for medical and dental providers. Though there are many studies assessing effects of orthodontic or surgical treatment on the airway, few studies have focused on normative volumetric measures of the pediatric airway with CBCT. Beyond that, there is limited analysis when it comes to the airway in pediatric cleft palate patients, with many articles exhibiting small sample sizes or broad age ranges. To date, no studies have addressed the specific velopharyngeal dimensional differences found in CBCTs of children with and without cleft palate diagnoses. Furthermore, much of the airway literature cited in modern cleft studies was completed on adults. There is a clear lack of well-controlled, randomized, three-dimensional studies on the pediatric pharyngeal airway and velopharynx. This retrospective study conducted at Nationwide Children's Hospital and The Ohio State University in Columbus, Ohio aimed to assess the volumetric and linear dimensions of the pharyngeal airway in nonsyndromic cleft palate and cleft lip and palate patients compared with noncleft, nonsyndromic controls using CBCT.

Chapter 2. Methods

A. Patient Selection

The institutional review board of Nationwide Children's Hospital (NCH) approved the present study (No. 00001243) with a data usage agreement for The Ohio State University. Patients of the NCH Orthodontic Treatment Program aged 7-17 that had a CBCT taken as a part of their routine initial diagnostic records were selected via data query. Two population subsets were defined: children with cleft palate diagnoses and children without any cleft diagnosis. Inclusion criteria for the cleft group consisted of patients with diagnoses of cleft palate (ICD-10-CM Diagnosis Code Q35) and cleft lip and palate (ICD-10-CM Diagnosis Code Q37) with a CBCT taken between 2010 and 2020 (CPT Code 70486 and CDT Code D0367). This diagnosis criteria included multiple cleft variations, including hard palate, soft palate, submucous, unilateral and bilateral clefts. Inclusion criteria for the non-cleft group included CBCT taken between 2010 and 2020 using the same ICD and CDT codes. Exclusion criteria for both groups consisted of any malformations of the nervous system, eye, ear, face, and neck (Q00-Q18); congenital musculoskeletal deformities of head, face, spine and chest (Q67); congenital malformations of skull and face bones (Q75); osteosarcomas, congenital malformations of musculoskeletal system (Q77-79); other congenital malformations (Q87); chromosomal abnormalities (Q90-99); sleep disorders (G47); and respiratory disorders

(J98). For the non-cleft group, all patients with cleft diagnoses were additionally excluded (ICD-10 codes Q35-39). Each patient's chart was evaluated to verify presence or absence of appropriate inclusion and exclusion criteria following group allocation. Limited CBCT assessment was completed to verify initial criteria. Patients were excluded from the study if there were abnormal interferences in the airway that resulted in a non-uniform volumetric rendering or for presence of dramatic positioning or movement errors. This was evaluated and decisions to include or exclude were subjective and tied to ease of measurement. Patients were not excluded for signs of pharyngeal flap surgery. Additional exclusion criteria included CBCTs that did not show the entirety of the pharyngeal airway, including the complete nasopharynx, oropharynx, or hypopharynx.

Following initial data query, patients were subdivided further into two age cohorts: 7-11 years old and 12-17 years old. This was done to separate out pre-adolescent and adolescent subgroups, since each has specific developmental considerations. This also allowed for more multi-group comparison and narrowed analysis. The initial data query revealed lists of all CBCTS for cleft patients and control patients, which were then placed into subgroups as described earlier based on age at CBCT. From these lists, patients were randomly selected within excel based on medical record numbers (MRN) and were placed into the appropriate sample grouping. Once allocated, the age at initial CBCT for each subject was verified. If their age at first CBCT was older or younger than the appropriate age group, the patient was removed from the group and another patient was selected. Additionally, the entire selected population was analyzed to verify that only one CBCT was selected per patient and that no patients were measured twice. Of the total

of 567 of CBCTs reviewed, 154 met criteria. The means and standard deviations from previous studies were used to assist in power analysis.[51,52] A sample size of 38 patients in the cleft group and 38 patients in the noncleft group was required for a power of 0.80 ($P < 0.05$). As two age groups were utilized, this power calculation was attributed to each of the four subgroups, leading to 38 patients in both 7-11 and 12-17 age groups for both cleft and noncleft populations. The required sample sizes for power of 0.8 were met for this study.

After patients were allocated into subgroups, CBCT initial assessment was completed using Dolphin 3D (Dolphin Imaging & Management Solutions, CA, USA). Airway renderings for each patient were reviewed to verify that the entire pharyngeal airway was complete without distortion with no exaggerated positioning errors or artifacts from movement during image capture. If patients did not meet criteria, the subject was removed and a new patient was randomly selected from the initial data query using the same methods cited above. If the patient did meet criteria, the CBCT volume was exported anonymously as a no loss, 1:1 uncompressed DICOM (.dcm) file to a secured hard drive. From there, 154 CBCTs were transferred to a secured OneDrive server (Microsoft, WA, USA), with verification from NCH information services (IS). The CBCTs were then re-accessed at The Ohio State University in a radiological assessment room and analyzed using Invivo6 (Anatomage Inc, CA, USA). The flowsheet for group allocation and sample selection is demonstrated in Figure 1.

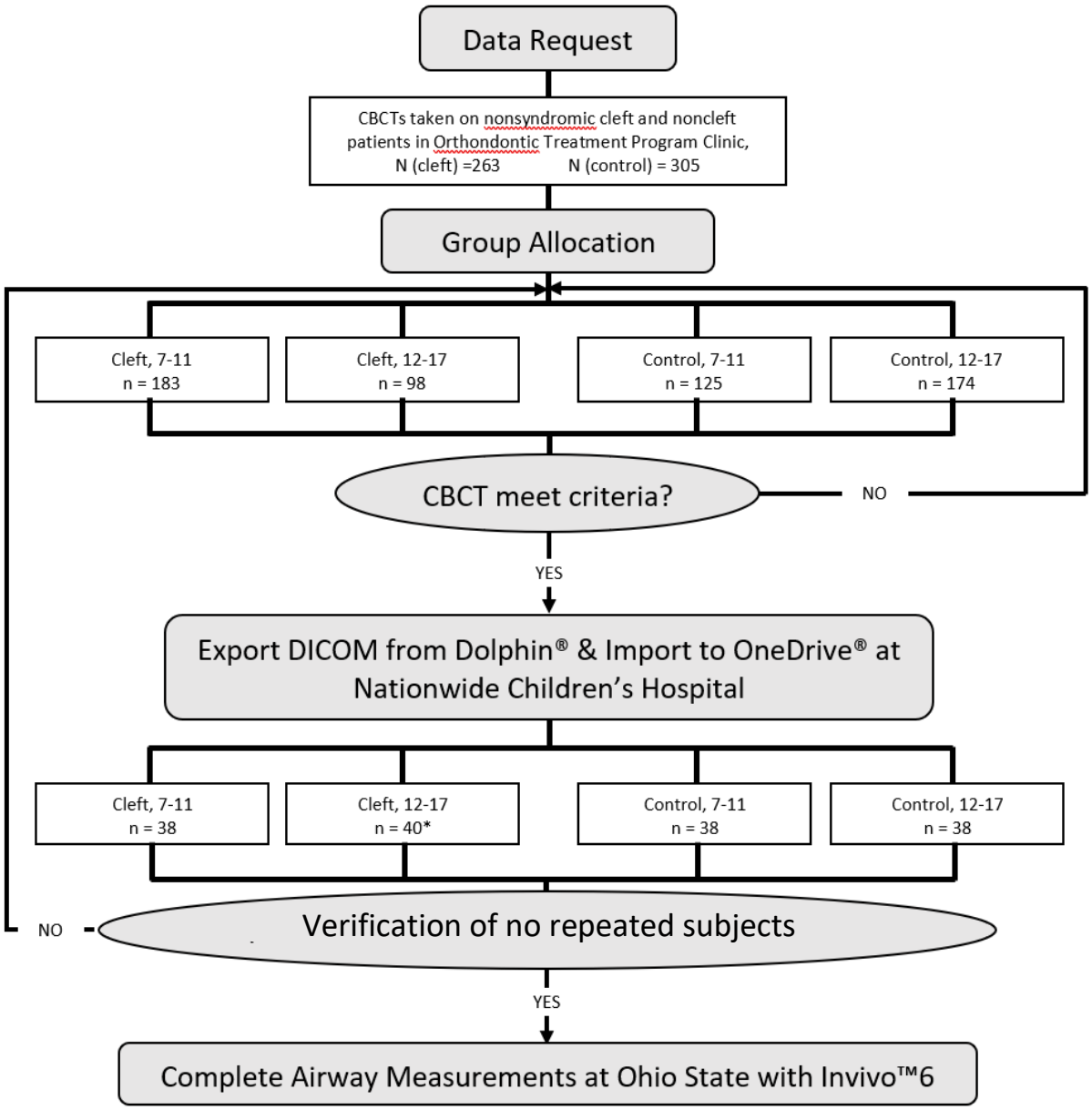

Figure 1: Workflow from initial data query to airway analysis.

B. CBCT Exposure Technique

All scans were taken using the same CBCT machine (iCAT FLX Imaging System, Imaging Sciences International, Hatfield, PA) with a standardized protocol

("Expanded 3D Ceph", 23cm x 17cm volume size, 0.3mm voxel size, 17.8s scan time, 877.6mGy cm^2). During the year of 2020, adjustments were made to reduce ionizing radiation exposure in the OTP and thus the new standardized protocol was adopted, affecting a small number of CBCTs assessed ("3D Ceph", 16cm x 13cm volume size, 0.3mm voxel size, 8.96s scan time, 623.96mGy cm^2). Proper positioning was consistent between patients to minimize movement and maximize image quality. Images were acquired with patients seated and feet stabilized with a footstool, if indicated. Head stabilization was obtained with a head support, head strap, and/or chin cup. Proper three-dimensional orientation was obtained through integrated red laser lights. The horizontal beam was parallel to the ala-tragus and positioned at the occlusal plane horizontally (between the lips). The vertical beam was positioned 1.5 inches anterior to the condyles. The sagittal beam was positioned through the center of the patient's face and chin support. Patients were instructed to close their eyes, stay as still as possible, breathe slowly, keep their teeth together gently, and not swallow during the scan. A lead apron was used for every scan.

C. Data Collection

CBCT assessment and data collection was standardized for every patient. Invivo6 was the software program utilized for data collection. A board certified oral and maxillofacial radiologist trained and calibrated the investigator on proper CBCT image orientation and airway measurement techniques with Invivo6. The same trained investigator completed all imaging assessment and data acquisition. All images were

analyzed in the same computer in the radiological assessment room in Postle Hall at The Ohio State University. Room lighting was turned off during CBCT examination.

Invivo6 was set to use a fixed threshold technique, making the airway analysis less time consuming. Parameters were standardized for each patient (50 mm^2 color minimum, 50mm^2 color increment, -550 Hounsfield units (H.U.) threshold). Initial image orientation was completed prior to data collection in all three planes as shown below in Table 2. Figure 2 shows proper orientation of the CBCTs with landmarks identified.

Image Orientation Criteria	
Coronal	Image was aligned vertically with a line passing through the inferior border of the orbit bilaterally
Sagittal	Image was aligned sagittally with a line passing through the palatal plane, or anterior nasal spine (ANS) to posterior nasal spine (PNS)
Axial	Image was aligned mediolaterally with the midpalatal suture

Table 1: CBCT image positioning completed for each patient prior to data collection.

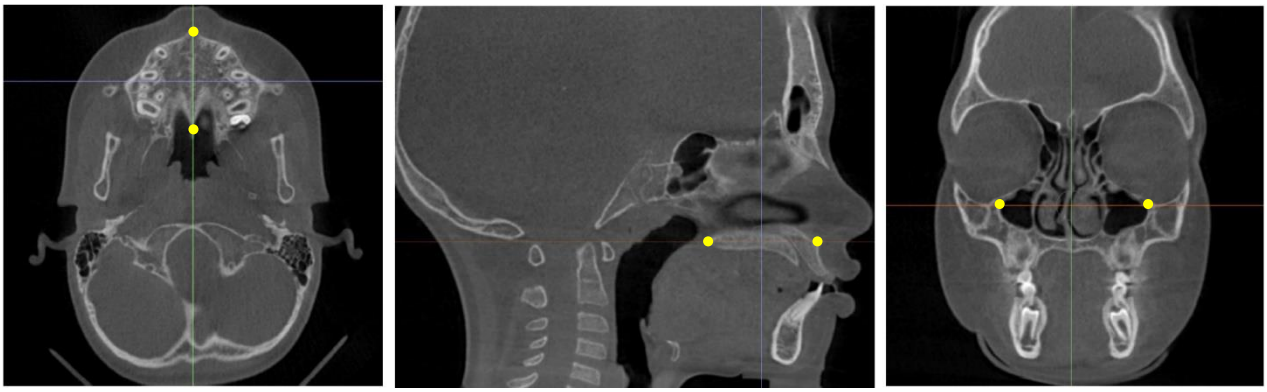

Figure 2: CBCT images with axial (left), sagittal (middle) and coronal (right) sections positioned according to criteria in Table 1.

Once the scans were oriented, the airway was defined using criteria in Table 2. The airway was assessed from the most superior border of the nasopharynx (line passing through the postero-inferior point of vomer and the PNS) to the inferior border of the hypopharynx (base of the epiglottis) and from the pharyngeal wall posteriorly to the PNS anteriorly. The landmark point of the vomer was identified by the dorsal projection point. Airway segmentation was completed semi-automatically by placing points along the airway using the technical limits defined in Table 1. If the airway extended beyond the desired region, the snipping tool was used for section removal. Readings for volume, minimum cross-sectional area (MCSA), anterior-posterior (AP) dimension of MCSA, and transverse (Tr) dimension of MCSA were automatically generated. Volume measures were taken from the nasopharynx (NP), oropharynx (OP), velopharynx (VP) and hypopharynx (HP) and the total volume was determined by adding NP, OP, and HP. MCSA measures were taken for NP, OP, VP, and HP with the region of the total airway MCSA recorded as well as the AP and Tr dimensions. Table 2 shows the criteria defining upper and lower limits of each airway segment. Figure 3 demonstrates the parameters of Table 2 on CBCT scan in sagittal section on a noncleft patient, with yellow dots signifying section limit landmarks.

Airway Section Limits	
Nasopharynx	**Upper limit** = Transverse plane formed by line passing from Posterior Nasal Spine (PNS) to dorsal projection of vomer in sagittal view **Lower limit** = Transverse plane parallel to the palatal plane passing through PNS in sagittal view
Oropharynx	**Upper limit** = Transverse plane parallel to palatal plane passing through PNS in sagittal view **Lower limit** = Transverse plane parallel to palatal passing through anterior inferior of body of C3
Velopharynx	**Upper limit** = Line from PNS and the posterior pharyngeal wall (PPW) at the height of the upper limit of the atlas (C1) **Lower limit** = Transverse plane from the end of the soft palate to the posterior pharyngeal wall at the same height
Hypopharynx	**Upper limit** = Transverse plane parallel to palatal plane passing through anterior inferior of body of C3 **Lower limit** = Transverse plane parallel to palatal plane passing though inferior border of epiglottis

Table 2: Defined upper and lower limits for segments of pharyngeal airway.

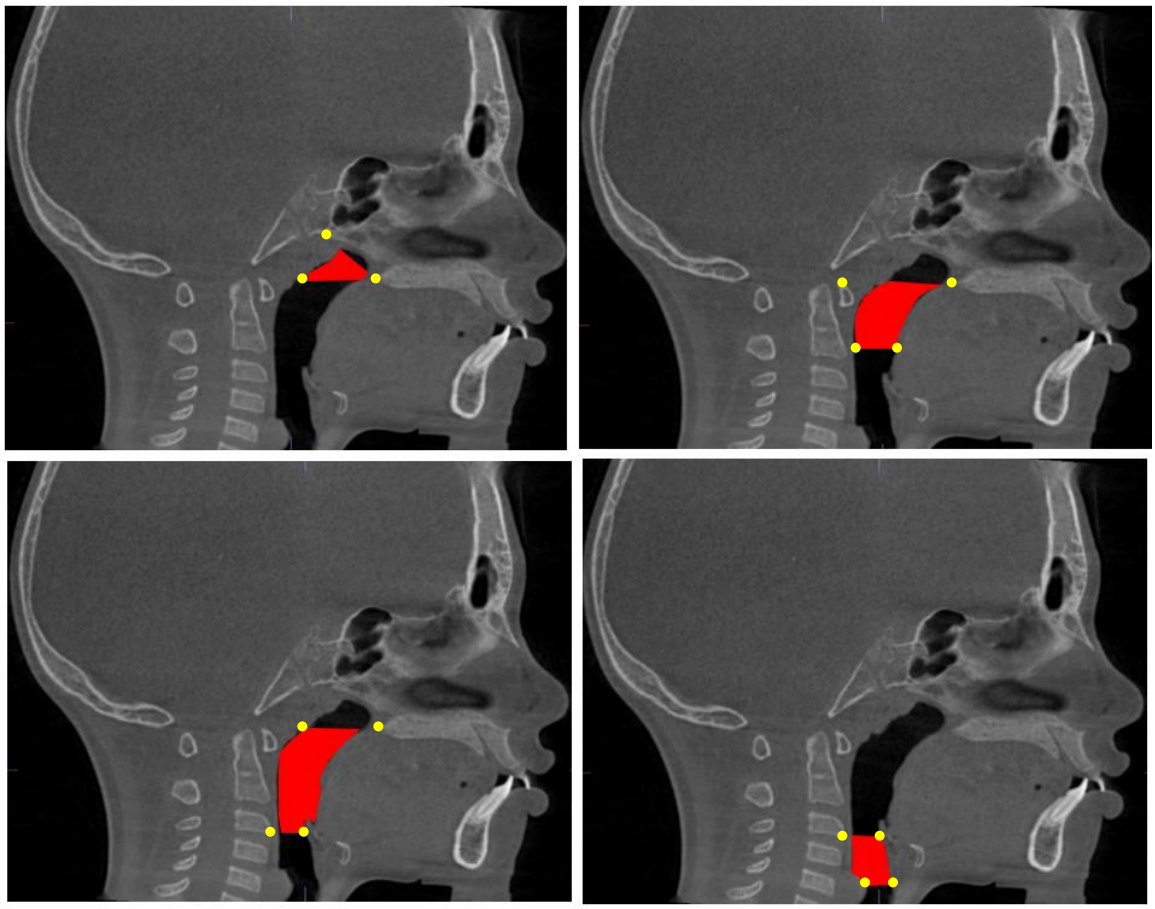

Figure 3: Sections of the airway in sagittal section shown as nasopharynx (top left), oropharynx (bottom left), velopharynx (top right) and hypopharynx (bottom right)

The following parameters were also analyzed for each CBCT, based on recent literature, as they provide thorough quantification of the velopharynx in multiple dimensions:[53]

- Airway area cranial velopharynx (mm2) – area at most cranial slice of VP volume
- Airway area caudal velopharynx (mm2) – area at most caudal slice of VP volume

- Total airway length (mm) – measure taken perpendicular to palatal plane from the vomer superiorly to the inferior border of hypopharynx
- Distance PNS-PPW (mm) – measures distance from posterior nasal spine (PNS) to posterior pharyngeal wall (PPW) at the level of the atlas (C1)
- Distance Velum-PPW (mm) – measures distance from velum to posterior pharyngeal wall at the same height
- Length of PPW (mm) – measures distance from posterior pharyngeal wall at the level of atlas (C1) to the posterior pharyngeal wall at the level of the inferior border of the velum
- Length of APW (mm) – measures distance from anterior pharyngeal wall at the level of the posterior nasal spine (PNS) to the anterior pharyngeal wall at the inferior border of the velum

The initial data query provided demographic data (date of birth, date of CBCT, and gender) and quantitative data (patient height, weight, and BMI). Chart review using the NCH Epic Hyperspace eChart Software (Epic Systems Corporation, WI, USA) was used to obtain specific cleft or orthodontic diagnoses with ICD-10 code, assess additional relevant diagnoses, and verify no previous history of sleep disorder was present.

D. Statistical Analysis

Data was analyzed with the assistance from NCH Research Information Solutions and Innovation (RISI). All analyses were performed using R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria). Patient characteristics were tabulated by

presence of cleft diagnosis. Comparisons of airway measurements between the cleft group and the control group were performed using Welch's two sample t-test. Effect sizes were reported using Cohen's d standardized mean differences. A P-value of < 0.05 was considered as statistically significant. The chi square test was used to compare categorical outcomes. Six multiple linear regression models were developed to examine whether the six airway measurements remained significantly different between cases and controls after adjusting for age, gender, BMI, and presence of other medical diagnoses. Assumptions for all statistical models (including approximate normality, equal variance, constant variance, and linearity) were verified using Shapiro-Wilk tests, qq-plots, and residual plots.

Chapter 3. Results

When compared as a whole (*n*=154), patients in both the cleft (*n*=78, 51%) and noncleft (*n*=76, 49%) groupings showed similarities in demographic and qualitative data. The average age of the noncleft group was 12.0 years (median: 12.0 years) and the average age of the cleft group was 11.6 years (median: 12.1 years). The noncleft group has 39 females (51%) and 37 males (49%) and the cleft group had 37 females (47%) and 41 males (53%). The average BMI for the noncleft group was 23.7 (median: 23) and for the cleft group was 22.6 (median: 19.7). The most frequent orthodontic diagnosis in the noncleft group was malocclusion (ICD-10 Code:M26.4). The most frequent diagnosis in the cleft population was cleft lip and palate (ICD-10 Code: Q37.9). Additional relevant diagnoses were recorded if they were determined to possibly either produce or be a product of airway changes, OSA, of VPI. Of the 76 noncleft patients, only 12 (16%) had recorded relevant diagnoses, which included obesity (*n*=4), tonsillar and adenoid hypertrophy (*n*=2), micrognathism (*n*=1), maxillomandibular skeletal deficiency (*n*=1), open bite (*n*=1), jaw size anomaly (*n*=1), oligodontia (*n*=2), microcephaly (*n*=1), and maxillary excess (*n*=1). For the cleft population, 30 patients (38%) showed additional relevant diagnoses, including speech disturbance (*n*=3), developmental speech or language disorder (*n*=1), speech delay (*n*=2), hypernasality (*n*=2), articulation disorder (*n*=3), dysphonia (*n*=1), other voice and resonance disorders (*n*=2), oral-nasal fistula

(*n*=1), fistula of hard palate (*n*=1), adenotonsillar hypertrophy (*n*=1), tonsillar hypertrophy (*n*=1), nasal deformity (*n*=3), nasal obstruction (*n*=4), nasal septal deviation (*n*=3), hypertrophy of nasal turbinate (*n*=1), chronic rhinitis (*n*=1), velopharyngeal incompetence (n=2), snoring (*n*=1), overweight (*n*=1), obesity (*n*=1), and morbid obesity (*n*=1). Findings for demographics and diagnoses are summarized in Table 3.

	Control Group	Cleft Group
Total, n (%)	76 (49)	78 (51)
Demographics, Age in years		
Mean	12.0	11.6
Standard Deviation (SD)	2.8	3.1
Median	12.0	12.1
Min, Max	7.2, 17.4	7.0, 17.6
Gender, n (%)		
Female	39 (51)	37 (47)
Male	37 (49)	41 (53)
BMI		
Mean	23.7	22.6
Standard Deviation (SD)	7.9	11.1
Median	23	19.7
Min, Max	14.9, 62.8	13.7, 96.1
Medical diagnoses		
Most frequent diagnosis	malocclusion	cleft lip and/or palate
Other diagnoses, n (%)		
Yes	12 (16)	30 (38)
No	64 (84)	48 (62)

Table 3: Demographic and quantitative comparison between cleft and noncleft groups.

Airway volume measurements were similar between cleft and noncleft groups for NP, OP, HP, and total airway. VP volumes were significantly lower in cleft patients when compared to control patients for age 7-11 cohort (P=0.03), 12-17 age cohort (P=0.002), as well as the combined grouping (P=0.004). Figure 4 shows variation in shape of

velopharynx between cleft and noncleft patients, with the white line representative of the palatal plane and the yellow line showing the superior VP border. Figure 5 shows the sizes of each component of the airway in bar chart form. Note that total volume is equal to NP + OP + HP. VP was not considered in total volume calculation.

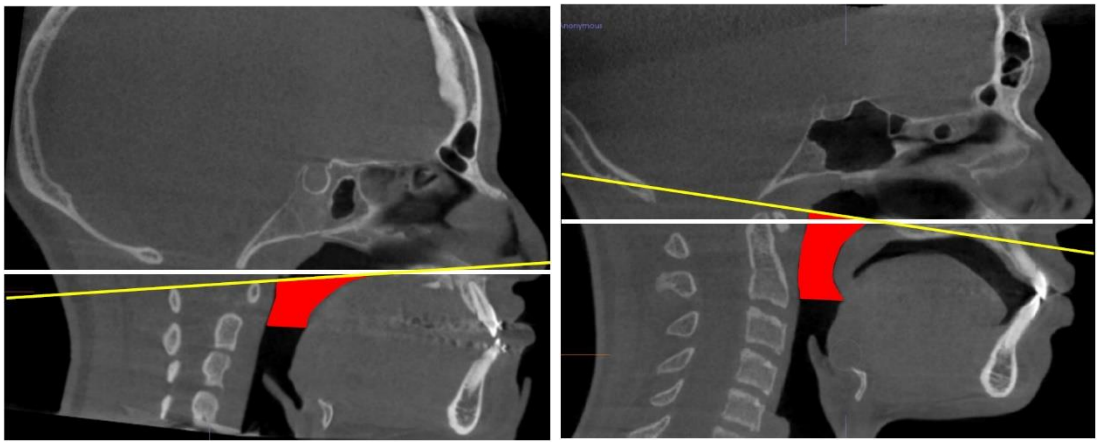

Figure 4: Variation in velopharynx shape for cleft (left) and noncleft (right) patients.

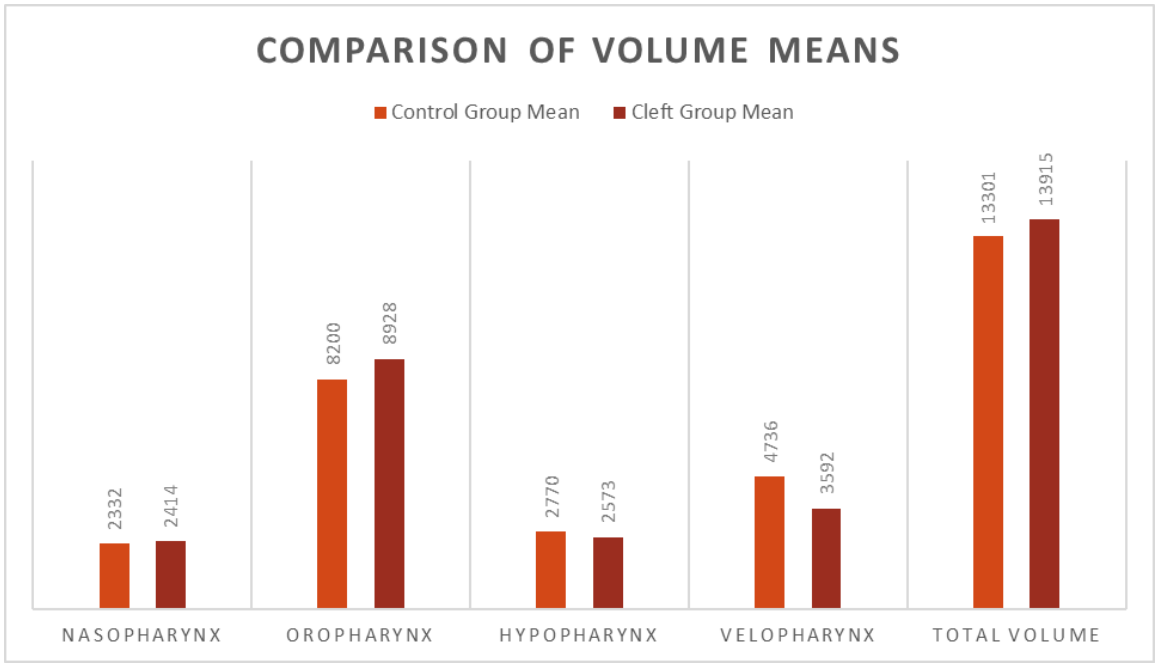

Figure 5: Segmented airway volume means (mm^3) for cleft and control patients.

MCSA measures were similar between cleft and noncleft groups for the 7-11 age cohort for the OP, HP, VP, and total MCSA. For the 12-17 age cohort, the MCSA measures for the OP (P=0.001), the VP (P=0.03), and the total MCSA (P=0.001) were all significantly lower in cleft patients when compared to control patients. Figure 6 shows a sample MCSA measurement with 3D modeling, skeletal airway superimposition, AP and RL (transverse) distance measures, and cross section area. The MCSA values for the NP were not analyzed, as it has a triangular prism shape unlike the other portions of the airway (OP, HP, VP, total airway) that are cylindrical in shape. For the anterior-posterior (AP) and transverse (Tr) dimensions of the MCSA, the Tr dimension of MCSA was significantly smaller in cleft patients when compared to control in the 12-17 age cohort (P<0.001). The Tr MCSA measure is represented in Figure 7, with yellow arrows spanning the dimension. These values were automatically generated by Invivo6. The AP-MCSA measure was similar between cleft and control patients in both age cohorts. Means and standard deviations for each group, as well as statistical analysis, were shown in Table 4 and 5. Welch's two sample t-test with P-value <0.05 was considered statistically significant. Standard categories for Cohen's d (standardized mean differences) were as follows: small (0.2), medium (0.5), large (0.8). Cohen's d values >0.5 and/or P <0.05 are denoted in red. Cohen’s d values approximating 0.5 were denoted in blue.

The chi square test was completed to compare MCSA location values, as these were either OP or HP. For the 7-11 age group, the cleft patients were more likely to have the MCSA in the oropharynx, whereas the control patients were more likely to have the

MCSA in the hypopharynx. This result was significant (P=0.04). For the 12-17 age cohort, both cleft and control patients were more likely to have the MCSA in the oropharynx, however differences between groups were not significant.

7-11	Cleft	Control		
	Mean (SD)	Mean (SD)	Cohen's d	p-value
Volume				
NP (mm^3)	1774 (1288)	1784 (1074)	0.01	0.97
OP (mm^3)	7934 (3784)	6684 (3196)	-0.36	0.12
HP (mm^3)	1787 (1088)	1839 (991)	0.05	0.83
VP (mm^3)	3053 (1479)	3882 (1733)	**0.51**	**0.03***
Total (mm^3)	11495 (4996)	10308 (4162)	-0.26	0.26
Area				
MCSA-OP (mm^2)	68.56 (54.97)	78.92 (56.23)	0.19	0.42
MCSA-HP (mm^2)	89.66 (63.82)	72.80 (57.94)	-0.28	0.23
MCSA-VP (mm^2)	103.93 (79.89)	113.17 (67.62)	0.12	0.59
MCSA (mm^2)	52.36 (39.54)	50.58 (37.33)	-0.05	0.84
VP Caudal (mm^2)	139.59 (72.62)	141.17 (76.12)	0.02	0.93
VP Cranial (mm^2)	233.62 (124.57)	248.15 (93.94)	0.13	0.57
Linear				
MCSA AP (mm)	5.03 (2.18)	5.11 (2.81)	0.03	0.89
MCSA Tr (mm)	11.67 (6.08)	12.44 (5.98)	0.13	0.58
Airway Length (mm)	72.93 (6.81)	73.02 (5.51)	0.01	0.95
PNS-PPW (mm)	25.45 (7.63)	19.58 (4.83)	**-0.92**	**1.7E-04**
Vel-PPW (mm)	8.58 (3.00)	9.42 (3.21)	0.27	0.24
VP-PPW (mm)	19.30 (4.75)	25.50 (3.96)	**1.42**	**3.4E-08**
VP-APW (mm)	25.60 (7.15)	27.11 (2.68)	0.28	0.23

Table 4: Volumetric, area, and linear measures for cleft and control patients in the 7-11 age group.

12-17	Cleft	Control		
	Mean (SD)	Mean (SD)	Cohen's d	p-value
Volume				
NP (mm^3)	3023 (1593)	2879 (1230)	-0.10	0.66
OP (mm^3)	9873 (4278)	9716 (4914)	-0.03	0.88
HP (mm^3)	3320 (1843)	3700 (1915)	0.20	0.38
VP (mm^3)	4105 (1915)	5589 (2154)	**0.73**	**2.0E-03**
Total (mm^3)	16215 (5638)	16295 (7014)	0.01	0.96
Area				
MCSA-OP (mm^2)	67.65 (53.70)	122.47 (83.34)	**0.79**	**1.1E-03**
MCSA-HP (mm^2)	131.98 (83.16)	158.98 (91.58)	0.31	0.18
MCSA-VP (mm^2)	109.71 (86.86)	151.17 (83.05)	**0.49**	**0.03**
MCSA (mm^2)	59.87 (48.81)	105.09 (66.54)	**0.78**	**1.1E-03**
VP Caudal (mm^2)	144.27 (82.34)	174.44 (88.41)	0.35	0.12
VP Cranial (mm^2)	321.32 (133.55)	315.24 (112.60)	-0.05	0.83
Linear				
MCSA AP (mm)	5.94 (3.04)	6.35 (3.31)	0.13	0.57
MCSA Tr (mm)	11.92 (6.52)	17.00 (6.41)	**0.79**	**8.6E-04**
Airway Length (mm)	86.14 (8.58)	83.01 (6.44)	-0.41	0.07
PNS-PPW (mm)	29.53 (10.72)	22.09 (4.86)	**-0.89**	**2.0E-04**
Vel-PPW (mm)	8.81 (3.04)	9.05 (3.29)	0.07	0.74
VP-PPW (mm)	22.00 (5.46)	29.31 (4.85)	**1.41**	**2.2E-08**
VP-APW (mm)	31.05 (7.44)	32.40 (4.23)	0.22	0.33

Table 5: Volumetric, area, and linear measures for cleft and control patients in the 12-17 age group.

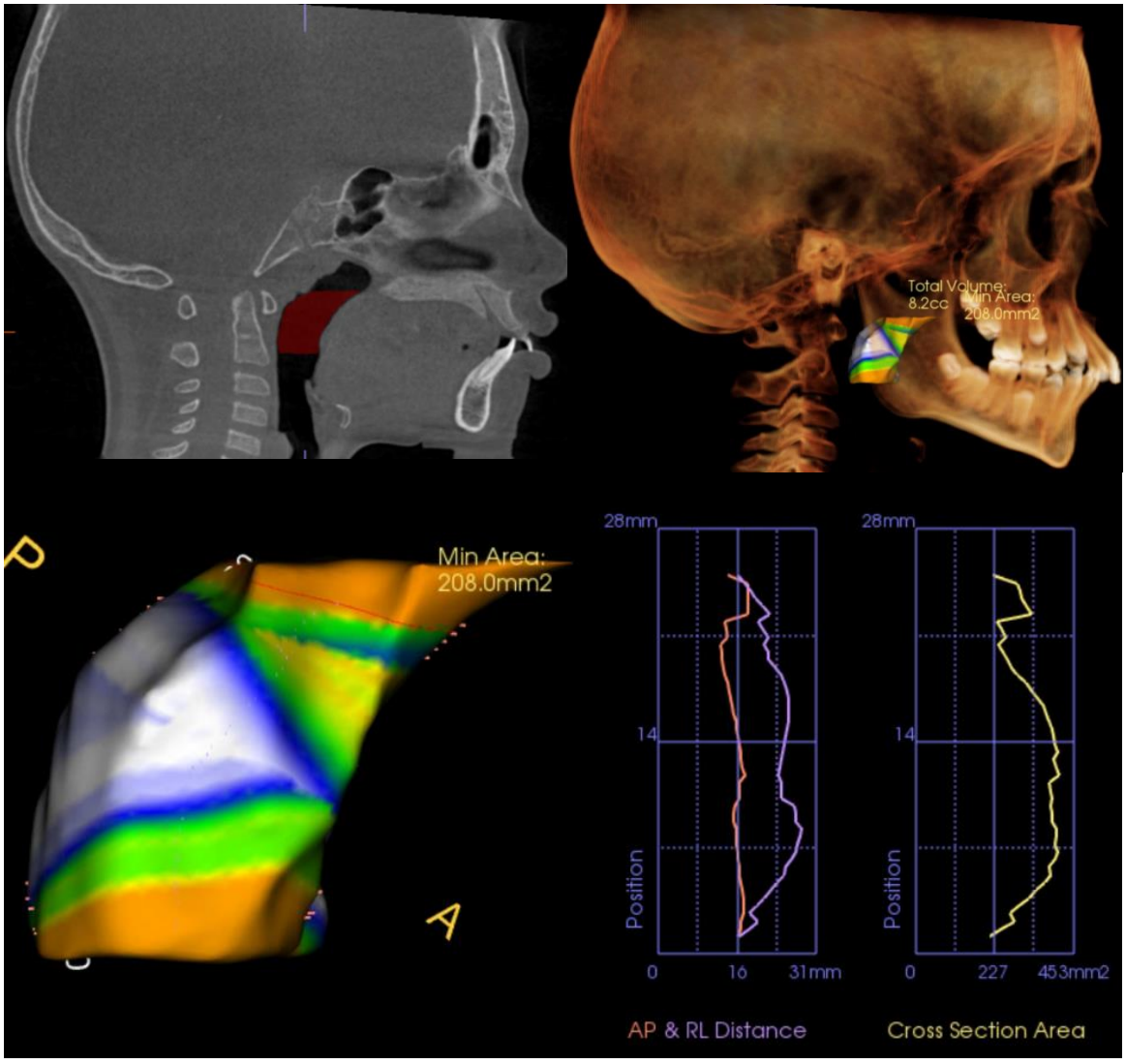

Figure 6: Sample MCSA measurements for velopharynx in noncleft patient.

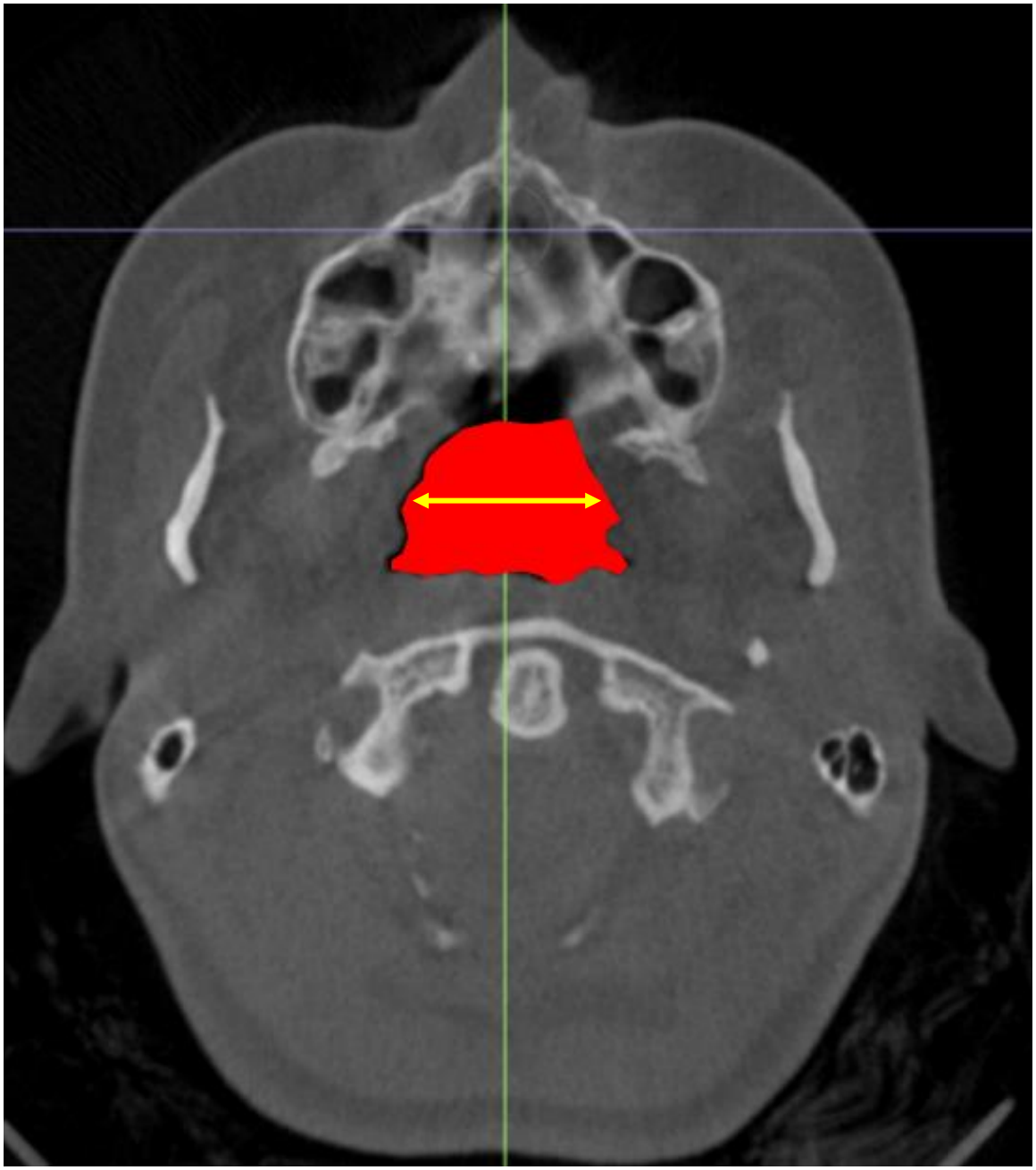

Figure 7: Sample transverse measure at MCSA in OP for noncleft patient.

Within the velopharynx, both the most cranial and most caudal area measures were similar between cleft and noncleft for both age cohorts. The distance measure between the PNS and the PPW was significantly larger in the cleft population when compared to the noncleft population in both the 7-11 ($P<0.001$) and 12-17 age groups ($P<0.001$). A comparison of PNS to PPW measures in shown in Figure 8, with yellow line portraying the linear measurement from PNS to PPW at the level of the atlas (C1).

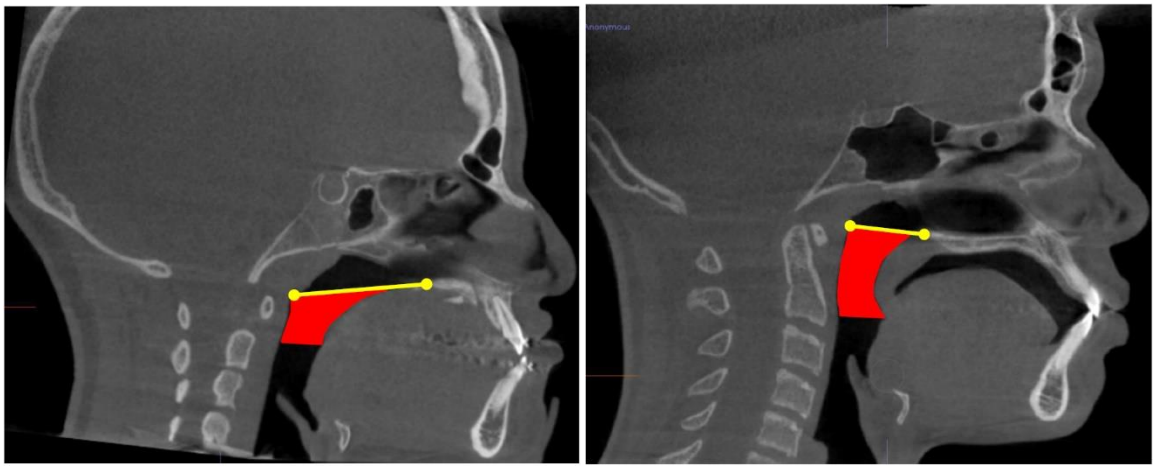

Figure 8: PNS to PPW distance for cleft (left) and noncleft (right) patients.

The distance measure between the inferior point of the velum and the PPW were similar for both cleft and control patients in both age cohorts. The APW length measures were similar for both the cleft and control patients in both age cohorts. The PPW length was significantly shorter in cleft patients when compared to noncleft patients in both the 7-11 ($P<0.001$) and 12-17 ($P<0.001$) age cohorts. PPW length difference is shown in Figure 9, with the yellow line portraying the PPW measurement. The total airway length measures were similar between cleft and noncleft patients in both age groups. These findings are all listed in Table 4 and 5.

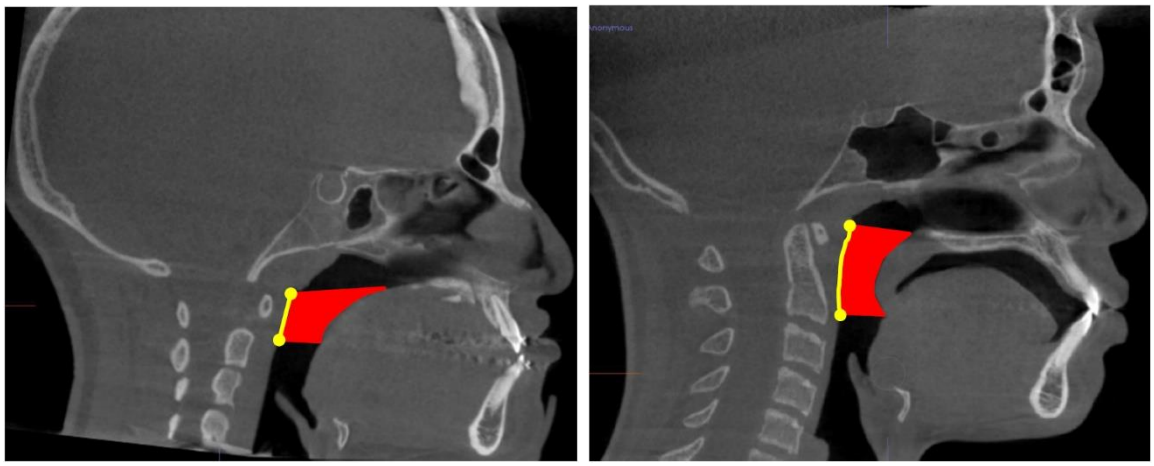

Figure 9: PPW length for cleft (left) and noncleft (right) patients.

Diagnostic group comparisons for airway measurements were completed, only considering cleft or noncleft status not age group allocation. NP, OP, HP, and total airway volume measures were similar between cleft and noncleft groups. VP volume was significantly smaller in the cleft group ($P<0.001$). OP, HP, VP and total MCSA measures were all smaller for the cleft group when compared to the control group. However, only the OP-MCSA ($P=0.002$) and total MCSA ($P=0.01$) were significant. The VP caudal and cranial areas were smaller in the cleft group, but this result was not significant. The AP and Tr dimensions for the MCSA were smaller in the cleft group compared to the control, but this was only significant for the Tr-MCSA ($P=0.005$). Total airway length was similar between cleft and noncleft groups. PNS to PPW at level of C1 was significantly larger for the cleft patients when compared to controls ($P<0.001$) and the PPW length was significantly shorter for cleft patients compared to controls ($P<0.001$). APW length and Velum-PPW distance were similar between groups. These findings are in Table 6, displaying Welch's two sample t-test results with P-value <0.05 considered as statistically

significant. Standard categories for Cohen's d (standardized mean differences) were as follows: small (0.2), medium (0.5), large (0.8). Cohen's d values >0.5 and/or P <0.05 are denoted in red. Cohen's d values approximating 0.5 denoted in blue.

	Control group (n=76)	Cleft group (n=78)		
Volume	Mean	Mean	Cohen's d	p-value[1]
NP (mm^3)	2332	2414	-0.06	0.72
OP (mm^3)	8200	8928	-0.17	0.29
HP (mm^3)	2770	2573	0.11	0.48
VP (mm^3)	4736	3592	**0.58**	**0.0004**
Total (mm^3)	13301	13915	-0.1	0.54
Area				
MCSA-OP (mm^2)	101	68	**0.50**	**0.002**
MCSA-HP (mm^2)	116	111	0.05	0.73
MCSA-VP (mm^2)	132	107	0.31	**0.05**
MCSA (mm^2)	78	56	**0.41**	**0.01**
VP Caudal (mm^2)	158	142	0.20	0.23
VP Cranial (mm^2)	282	279	0.03	0.88
Linear				
MCSA AP (mm)	5.7	5.5	0.08	0.62
MCSA Tr (mm)	14.7	11.8	**0.45**	**0.005**
Airway Length (mm)	78	79.7	-0.19	0.25
PNS-PPW (mm)	20.8	27.5	**-0.88**	**<0.0001**
Vel-PPW (mm)	9.2	8.7	0.17	0.29
VP-PPW (mm)	27.4	20.7	**1.33**	**<0.0001**
VP-APW (mm)	29.8	28.4	0.21	0.18

Table 6: Volumetric, area, and linear measures for cleft and control groups.

Multiple linear regression was performed to examine whether the selected outcome measurements remain significantly different between cleft group and control group after adjusting for age, gender, BMI, and presence of other diagnoses. Estimated mean differences were calculated with 95% confidence interval with P-value <0.05 considered as statistically significant and denoted in red. After adjustment, VP volume, OP-MCSA, MCSA transverse, and PPW length were significantly smaller for cleft patients when compared to noncleft patients. PNS-PPW distance was significantly higher after adjustment for cleft patients when compared to control patients. The MCSA value was smaller in cleft patients when compared to controls, but not significant after adjustment. These findings are summarized in Table 7.

	Estimated mean difference between cleft group and control group	95% Confidence Interval	P-value
Airway Volume Measurements			
Velopharyngeal Volume (mm3)	-938	(-1540, -337)	**0.003**
Airway Area Measurements			
Oropharyngeal MCSA (mm2)	-28	(-49, -7)	**0.01**
MCSA (mm2)	-15	(-31, 1)	**0.07**
Airway Linear Measurements			
Tr Dimension of MCSA (mm)	-2	(-5, -0.4)	**0.02**
PNS-PPW (mm)	7	(5, 9)	**<0.0001**
PPW Length (mm)	-7	(-8, -5)	**<0.0001**

Table 7: Multiple linear regression outcomes for significant differences.

Chapter 4. Discussion

This study aimed to compare pharyngeal airway measurements between nonsyndromic pediatric CP and CLP patients with nonsyndromic, noncleft controls. Traditionally, airway measurements were taken using acoustic rhinometry, bronchoscopy, or conventional 2D imaging modalities. However, upper airway structures are complex and 2D views do not give an accurate indication of true volume and morphology. For this study, CBCT was selected as it is a simple, effective, and accessible means for accurate 3D airway evaluation.[54,55,56,57] Though CBCT imaging is not usually indicated explicitly for soft tissue imaging,[54] it has been shown to provide accurate airway volume measurements due to significant contrast gradient allowing segmentation in areas bordered by soft or hard tissues.[57] One of the major benefits of CBCT and reasons why it is increasingly used as part of diagnostic imaging for patients with craniofacial anomalies is its significant reduction in radiation dose compared to multislice CT. When compared to multislice CT, CBCT overall radiation dose is more than 12 times lower.[58] Although the effective CBCT dose is dependent on field of view, resolution, and patient size, reducing exposure is critically important for any patient, especially children.[59]

The orthodontic patients selected for each group showed no significant difference in age, sex, and BMI data, reducing confounding effects. Fewer patients from the control

group reported additional diagnoses or medical problems when compared to the cleft population. For those control patients, the most common additional diagnoses were obesity and tonsillar and adenoid hypertrophy. However, the two noncleft patients with tonsillar and adenoid hypertrophy both had adenoidectomy and tonsillectomy completed before the CBCT was acquired, thus suggesting that these may have been pre-surgical diagnoses. Conversely, more of the cleft patients had additional medical findings relevant to the airway. Fourteen of the cleft patients had diagnosed speech issues and twelve had comorbid nasal conditions. The additional nasal diagnoses would be expected to have an impact on the nasal airway, not the nasopharynx. Additionally, the speech issues are a product of the airway morphology, not a causative factor. One cleft patient had a diagnosis of adenotonsillar hypertrophy, but adenoidectomy had been completed prior to CBCT, further suggestive of a pre-surgical diagnosis. There was only one cleft patient who had a diagnosis of tonsillar hypertrophy with no surgical intervention. According to the patient's otolaryngologist, there was no indication for removal. As patients with OSA and SDB were ruled out with the exclusion criteria, this study controlled for many factors that could interfere with the airway measurements, increasing study validity.

Both the 7-11 and 12-17 age cohorts in the cleft patient group showed decreased velopharynx volumes when compared to control patients. After multiple linear regression analysis with adjustment for possible confounding factors, velopharynx volumes remained significantly smaller than control patients. Several authors have reported similar findings. Al-Fahdawi et al.[51] found that pediatric unilateral CLP patients showed significantly smaller superior oropharyngeal airway volumes than controls. Yoshihara et

al.[60] similarly noted that both unilateral and bilateral CLP adolescents had significantly smaller superior oropharyngeal airway volumes compared to controls. Though not explicitly termed the "velopharynx," the measurement techniques cited in these studies were similar to the present study. Generally, the control patients in this study exhibited velopharynx shapes that were longer and narrower, as opposed to the velopharynx in cleft subjects being shorter and wider, similar to previous literature.[53] Nevertheless, volume measurements for the nasopharynx, oropharynx, hypopharynx, and total airway were similar between groups in the present study. Previous studies have shown varying findings regarding segmented airway volumes. Pimenta et al.[61] assessed nasopharynx volumes on children with unilateral CLP compared to controls using CBCT and found no significant difference between groups. Using rhinomanometry, Fukushiro and Trindade[62] found that bilateral cleft lip and palate patients had smaller nasal airways than control patients, but unilateral cleft lip and palate and isolated cleft palate patients showed no difference in nasal airway. Celikoglu et al.[63] assessed adolescent patients with unilateral CLP and found lower oropharyngeal airway volumes, but no difference in nasopharyngeal or total airway volume. In another publication, Celikoglu et al.[52] again found lower oropharyngeal airway volumes in adolescent bilateral CLP patients, but no significant difference between nasopharyngeal and total airway volumes. Cheung and Oberoi[64] studied nonsyndromic CLP patients and found no significant differences in pharyngeal airway volumes when compared to controls. When looking at adolescents with cleft palate, Diwakar et al.[65] found no difference in oropharyngeal or oronasal airway volumes when compared to controls. Though specific study methodology varies

for each study, the findings are suggestive of variability in pharyngeal airway volumes for cleft patients compared to controls as well as differences within the cleft samples based on diagnosis.

In terms of cross-sectional area, cleft patients in the 12-17 age group had significantly smaller MCSA values in the oropharynx, velopharynx, and total airway when compared to controls. The anterior-posterior and transverse dimension of the MCSA were found to be smaller in cleft patients when compared to controls in that age group, but only the transverse dimension was significant. After multiple linear regression comparing the entire cleft and control population with adjustment for confounding, the oropharyngeal MCSA and the transverse dimension of MCSA remained significantly smaller in the cleft population. Similar to the findings in this study, Agarwal and Marwah[66] found that children with cleft lip and palate have reduced oropharyngeal airway widths and smaller area measures when compared to noncleft controls. Trindade-Suedam et al.[67] also found smaller upper pharyngeal cross-sectional area measurements in unilateral cleft palate patients compared to controls. In the present study, the MCSA could have been in either the oropharynx or hypopharynx, which is important to consider when interpreting the significant reduction in transverse dimension. Since there was no significant inter-group difference in hypopharynx MCSA measures, it is likely that the dimensional differences existed mostly in the oropharynx. One possible explanation for this difference may be increased adenoid or tonsillar tissue in the cleft population. Unlike their noncleft counterparts, cleft patients have a unique challenge to surgical management of the adenotonsillar tissues. Adenoidectomy is almost entirely contraindicated in cleft

patients due to risk of unveiling a palatal problem and precipitating VPI.[68] The adenoid acts as a pad for the soft palate to contact to form the velopharyngeal closure. Enlarged adenoid tissues may compensate for a short or poorly mobile soft palate in cleft patients.[69] Some have suggested performing partial adenoidectomy to prevent an inadequate mass of adenoid tissue that may lead to VPI.[70] Tonsillectomy has been cited to have possibility for both deleterious effects on the velopharyngeal closure leading to VPI[71] and beneficial effects by eliminating an interfering tissue if the superior pole obstructs velopharynx closure.[72] The patients in the current study were not evaluated for history of adenotonsillectomy, as the study design was retrospective and only would include operative records from NCH, not capturing procedures done at outside institutions. As mentioned previously, patients were not evaluated for other surgical procedures, such as pharyngeal flap or palatoplasty. Further evaluation of these differences would require a more extensive understanding of medical and surgical history as well as adjunctive nasopharyngoscopy to supplement the 3D imaging studies.

Linear measures of the velopharynx showed significantly larger distances between the PNS and PPW and significantly decreased lengths of the PPW for cleft patients when compared to controls. This result was anticipated, as cleft patients have a more anteriorly positioned PNS. PNS to PPW distances were representative of pharyngeal depth and the PPW length, in combination with APW length, represented pharyngeal height. Similar to the findings of this study, Xu et al.[73] found increased pharyngeal diameter at the level of the palatal plane in isolated cleft palate patients compared with controls. In a study on adults, Miller et al.[53] found significantly increased

distance measures for PNS to PPW and decreased measures for PPW for cleft palate patients when compared with controls. Their study also measured significantly smaller distances from velum to PPW in cleft palate patients. The cleft palate patients in our study had smaller distance measures from velum to PPW, but this result was not significant. Additionally, using lateral cephalometric films, Wu et al.[74] found increased measures from PNS to the pharyngeal wall in isolated cleft palate patients when compared to controls. Interestingly, the previous two studies both found a significant decrease in anterior pharyngeal wall length for cleft patients. The APW length values in the current study were smaller in the cleft patients when compared to controls in both age cohorts, but the difference was not significant.

A restricted upper airway is a known anatomic feature for the cleft palate population.[75] Through morphological analysis, studies have shown that cleft patients tend to exhibit maxillary and mandibular retrognathia, reduced maxillary length and height at the posterior nasal spine, antero-inferior positioning of the hyoid bone, and reduced pharyngeal depth, height, and area.[76,77,78] Though controversial in the literature, previous well-controlled research into pediatric cleft patients has shown reduced airway volumes in the nasopharynx, oropharynx, and total pharyngeal space.[79] Functional impairment of the oropharyngeal musculature, in addition to the morphological changes, limits the ability for cleft patients to maintain airway patency.[80] These hard and soft tissue alterations compromise the airway, leading to inadequate ventilation and obstruction, ultimately resulting in increased risk in OSA and SDB. It is estimated that risk of SDB in cleft lip and palate patients is between 22% and 65%, with 28% of those patients

suffering from severe SDB.[81] OSA can result in serious systemic effects, such as failure to thrive, behavioral problems, neurocognitive impairment, and systemic or pulmonary hypertension.[50] It has even been suggested that cognitive differences cleft and noncleft patients found in the literature may be attributable to the effects of disordered breathing.[81] Early and accurate diagnoses of a sleep disorder could be critical for the overall health and development of a child with a cleft. The present study showed reduction in velopharynx volume and smaller oropharyngeal MCSA in cleft children compared to noncleft controls, suggesting a narrower airway and thus an increase in risk for sleep disorders among the pediatric cleft population. This study also showed no difference between cleft and noncleft patients in the hypopharynx volume or MCSA. This result makes sense, as the major morphologic changes in cleft patients occur superior to the hypopharynx. The similarities in nasopharynx volumes could be a consequence of having multiple cleft palate conditions (ex. unilateral CLP, bilateral CLP, cleft palate, etc) with varying severities in the inclusion criteria. It is important to note the results suggest an increased risk for OSA, not necessarily a predictive factor. Further research is needed to determine relationships between sleep studies and three-dimensional factors in OSA.

Velopharyngeal sufficiency and competence are directly related to the soft and hard tissues structures of the velopharynx. Impairment of velopharynx function is often found in individuals with cleft lip and palate, commonly leading to hypernasal resonance with nasal air emission and compensatory articulation disorders.[82] Velopharyngeal closure is obtained by anterior movement of the posterior pharyngeal wall, posterior displacement of the velum, and medial movement of the lateral pharyngeal walls. These

movements, in combination with the appropriate depth and width of the nasopharynx and adequate length and function of the velum, contribute to a normal functioning velopharyngeal closure.[83] Thus, ideal velopharyngeal architecture would include narrow pharyngeal depth and long velar length. Though it may be possible for lateral pharyngeal walls to compensate for structural or functional deficiencies in some cleft patients, unfavorable relationships between velar length and distance from PNS to the posterior pharynx have been shown to be suggestive of increased risk for velopharyngeal insufficiency.[74] The cleft patients in this study showed shorter velar lengths, as represented by lower APW lengths, and larger pharyngeal wall depths. This suggests an increase in VPI risk. These measurements closely resemble those used in calculating the VP ratio, which compared velar length to pharyngeal depth. For noncleft pediatric patients, VP ratios have been estimated to be between 1.2 - 1.7. When VP ratios are lower than normal, as seen in many cleft patients, VPI risk and likelihood of future surgery is higher. Multiple previous studies have used the VP ratio as a tool to stratify risk for VPI as it represents lack of harmony between the velum and pharyngeal depth.[84,85,86,87,88] Ma et al.[89] additionally suggested that pharyngeal height should be included in evaluation for VPI. Nevertheless, VP ratio alone cannot explain velopharyngeal function. Though outside of the scope of the present study, future research should be done to assess relationships between specific CBCT acquired measurements, such as those in the present study, with VP ratio scores and VPI diagnosis.

When speech concerns are identified during developmental years, timing of each surgical procedure for a child with cleft palate becomes increasingly important. Early

surgery can assist in correction of resonance issues but can result in an increased rate of adverse effects on development of velopharyngeal structures when compared to later surgery. Hard palate repair performed earlier on cleft patients has been associated with maxillary hypoplasia due to interferences with maxillary growth sites and scar formation.[90,91] After palate repair, residual velopharyngeal dysfunction is estimated to occur between 10% to 20% of the time, requiring secondary surgical management.[92] Even with highly successful conventional techniques, up to 19.4% of primary palatoplasties have been shown to require revision, whether due to fistula or residual speech issues.[93,94] Additionally, SDB and OSA are known complications from palatoplasty surgery.[81,95] The risk for sleep disorders from surgical procedures in the velopharynx is highly dependent on the surgical technique, with as high as a 40% incidence of OSA 3-months after surgery.[96,97] Surgical intervention must simultaneously aim to correct or prevent speech impairment and limit harmful effects. Three-dimensional assessment of the velopharynx, as shown in the present study, can help describe the structural relationships and provide quantitative indications for surgical intervention as well as guidance during post-operative monitoring. It is important to specify that CBCT images are static and cannot describe functional capacity of airway structures. These movements are complex and are best investigated with other modalities, such as nasopharyngoscopy or other real-time techniques. Nevertheless, the use of CBCT as an adjunct diagnostic tool continues to prove tremendously beneficial for cleft palate patients. More research in the area of 3D imaging and its implications for sleep medicine and reconstructive surgery is needed.

There were several limitations for this retrospective study. For the cleft population, surgeries for speech, adenoidectomy, tonsillectomy, and orthodontic treatment completed was unknown, resulting in a treatment effect that is unaccounted-for. Though patients were pre-screened for diagnosed sleep disorders, questionnaires and/or polysomnography were not completed on all patients to rule out a sleep condition. Patients were additionally not excluded for specific nasal diagnoses, such as nasal septal deviation or turbinate hypertrophy. Although these nasal structures are more supero-anteriorly positioned to the areas measured in this study, abnormalities therein can have an impact on the airway. Cleft patients inherently have higher incidence of cervical vertebral anomalies, particularly in C1.[98] Additionally, variation in palatal morphology made some palatal structures, such as ANS, PNS, and midpalatal suture, more difficult to identify. As image orientation and measurements were completed using these structures as landmarks, anatomical variations could have led to measurement error. Additionally, this study evaluated all clefting conditions affecting the palate as opposed to more precise cleft types (bilateral, unilateral, hard palate cleft, soft palate cleft, submucous cleft). This decision was made in an effort to increase sample size for adequate power, but this ignores diagnosis-specific conclusions. Having a single, trained individual complete measurements on a large sample size was protective from inter-rater issues from multiple researchers. However, the individual measuring was not blinded to subjects being measured, e.g. cleft versus noncleft. Even though multiple measurements were repeated throughout data collection to verify precision, formal intra-rater reliability was not evaluated. As with many retrospective studies, patient selection was prone to bias. Lastly,

changes to NCH protocol for CBCT acquisition in 2020 may have affected data collection for a small number of patients, as modifications were made to dosing parameters.

Chapter 5. Conclusion

Children with nonsyndromic palatal cleft diagnoses have distinct deficiencies in pharyngeal airway and associated tissues when compared to noncleft controls. Cleft patients showed smaller velopharyngeal volumes with smaller minimum cross-sectional area in the oropharynx. Cleft patients also showed increase in distance from the posterior hard palate to the pharyngeal wall with shortened velopharynx height. This narrowed, abnormal airway may result in impairment in respiration and velopharyngeal closure. As CBCT can provide detailed, quantitative data on airway structures, multidisciplinary care teams should consider its application as an adjunct in treatment planning for cleft patients, together with speech evaluations and studies such as polysomnography and nasopharyngoscopy. Further studies are required to validate these results based on individual cleft diagnoses and to apply them to specific risk factors for OSA and VPI.

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