Effect of Alveolar Bone Graft Surgery Timing on Maxillary Size and Position in Non-syndromic Unilateral Cleft Lip and Palate

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Abstract

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Background:
Unilateral cleft lip and/or palate (UCLP) is a congenital condition resulting from incomplete or lack of fusion between orofacial tissues and leads to both functional and aesthetic concerns. Surgical reconstruction of the cleft involves the following procedures: Lip closure, primary palate closure, lip and palate revisions as needed, and alveolar bone grafting (ABG). This study aims to describe the maxillary growth of patients with UCLP, quantify the effect that ABG timing has on maxillary size, and determine the total surgical impact patients with UCLP patients undergo.

Materials and Methods:
124 patients with UCLP who received ABG from Seattle Children's Hospital were evaluated in this retrospective study. Electronic health records were reviewed to assess patient demographic data, time of ABG, cephalometric values before and after ABG, and surgical details, including quantity of surgeries each patient received. T tests were used to quantify maxillary growth compared to age adjusted norms. Logistic regression analysis and ANOVA were used to assess any associations on maxillary growth based on timing of ABG and number of surgeries received.

Results:
The mean (SD) age of ABG was 9.3 (1.3) years. The mean (SD) growth period evaluated was 8.3 (2.7) years. The average (SD) age of T1 was 7.6 (1.3) years, and T2 was 15.8 (2.6) years (Table 3). All cephalometric measurements of patients were statistically smaller compared to respective age adjusted normal measurements. Patients in this sample had significantly less growth compared to age adjusted norms. Chronologic age and canine development at time of ABG had no significant association with cephalometric changes measured. No association was observed between total number of surgeries and any of the cephalometric measurements.

Conclusion:
Early ABG for improved outcomes can be performed without significant concern for maxillary growth and development. Palatal revision surgeries needed to improve patients' function and quality of life should not be postponed due to concerns about maxillary growth.

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Introduction

Surgical reconstruction of a unilateral cleft lip and palate (UCLP) involves multiple staged procedures addressing both the soft tissue and hard tissue deficits. At Seattle Children's Hospital, a typical sequence includes lip and nose closure between 3-6 months, hard and soft palate repair between 9-15 months, and alveolar bone grafting (ABG) between 7-11 years in advance of the eruption of the maxillary permanent canine. Additional surgeries in the perioral area may include lip/nose revision, palate revision due to fistula, and/or soft palate surgery to support speech.

Children and adolescents with CLP generally follow normal somatic growth and maturation when compared to non-cleft control peers.(Marques et al., 2015) In the typically developing child without UCLP, rapid maxillary growth occurs during the first five years with continued size increase in the transverse, anterior-posterior (AP), and vertical dimensions until about age 16 years.(Laowansiri et al., 2013)

Cephalometric measurements have been used to study maxillary growth in patient with UCLP. Early studies of maxillary growth for these patients were retrospective cohort studies with low patient numbers. A study of 20 patients receiving no surgical interventions for UCLP reported normal maxillary growth. (Bishara et al., 1976) In a study of 22 patients with UCLP who had received only lip repair, the maxilla was shorter and retrusive compared to population norms. The authors suggested maxillary retrusion in patients with UCLP may be independent of palatal closure and ABG. (Yoshida et al., 1992) In 24 patients with UCLP who never had surgery, the maxillae were generally smaller, but more protruded than the norm. (Capelozza Júnior et al., 1993) In a review article of surgical closure of palatal clefts with and without alveolar clefts, progressive maxillary sagittal hypoplasia was reported in some studies, suggesting that surgery can potentially decrease maxillary growth.(Shi & Losee, 2015)

The timing of ABG has also been implicated in maxillary growth restriction. A reduced maxillary unit length was reported for 21 patients with UCLP grafted between the ages of 8.4 to 12.9 years as compared to 37 non-grafted patients with UCLP. (Daskalogiannakis & Ross, 1997) A study of maxillary growth in patients with CLP compared ABG at mean age 2.5 years (n=79) to ABG mean age 9.8 years (n=67). While both groups were retrusive compared to norms, a more significant maxillary deficiency was found those grafted at the younger age. (Brudnicki et al., 2017) A multi-center study compared 33 patients grafted at age six years to 148 patients grafted between eight and eleven years. ABG surgery at age six years did not significantly impact maxillary position as measured by SNA.(Doucet et al., 2019) A single center study of 128 patients with UCLP grafted between 1.4 and 11.5 years, identified that ABG performed before age eight years inhibited maxillary growth, and one year delay of ABG resulted in maxillary length increase of 0.52 mm. (Brudnicki et al., 2020)

The association between surgical interventions in the perioral area for UCLP and subsequent maxillary growth and development is not completely understood. Surgery and growth data from more craniofacial centers is needed to provide clearer understanding of potential associations between ABG timing, overall surgical burden, and ultimate maxillary growth outcomes.

This single center, retrospective study of non-syndromic patients with UCLP examined:

1) maxillary length and position prior to and following ABG,

2) association between timing of ABG and maxillary size and position, and

3) association between the number of lip and palate surgeries prior to ABG and maxillary size and position.

Methods

Patient data was collected from Seattle Children's Hospital's (SCH) Craniofacial Center. Lateral cephalometric radiographs and intraoral photographs were collected at time points before and after ABG. Time 1 (T1) was defined as date of imaging prior to ABG and Time 2 (T2) was date of imaging at least 2 years following ABG. When multiple T2 images were available, the latest date after ABG was used.

Inclusion criteria included non-syndromic UCLP, ABG completed at SCH Craniofacial Center, adequate imaging before and after ABG, and documentation in the electronic health record of all variables of interest. Exclusion criteria were incomplete or nondiagnostic imaging, history of treatment with protraction facemask or facial orthopedic therapy prior to post-ABG image, and history of multiple ABGs.

Demographic, medical, and surgical data was collected from electronic health records. Lateral cephalometric radiographs were imported, traced, and measured using Dolphin Imaging™. Intraoral photographs were used to assess posterior crossbite. All data was entered into REDCap hosted at the University of Washington. REDCap is an online, secure database that manages and analyzes electronic health record information. (Harris et al., 2009, 2019)

Patient Variables

- Birthdate, gender, race/ethnicity, surgery dates (primary lip closure, primary palate closure, palate revision(s), speech surgery involving soft palate [Furlow palatoplasty], ABG).

Clinical photograph variables

- Transverse presentation: Posterior crossbite (none, unilateral, bilateral)
- Anterior-Posterior presentation: Anterior crossbite (none, partial, complete)

Radiographic Variables

- Image dates
- Cephalometric measurements

Table 1: Cephalometric measurements: collected pre-ABG and post-ABG

Measurement	***Description***
SNA	Angle formed by sella-nasion and nasion-point A lines
N-A	Distance between nasion and point A
ANS-Ptm	Distance between anterior nasal spine and pterygomaxillary fissure
ANS-PNS	Distance between anterior nasal spine and posterior nasal spine
N-ANS	Distance between nasion and anterior nasal spine
Co-A	Distance between condylion and point A
Ba-A	Distance between basion and point A
Co-ANS	Distance between condylion and anterior nasal spine
Ba-ANS	Distance between basion and anterior nasal spine

Age adjusted normative sample

The Michigan Growth Study cephalometric radiograph archive was used as a historic age- and gender-matched normative sample. Age- and gender-matched normative sample measurements from this collection included the following: SNA (Variable 2), ANS-PNS (Variable 116), ANS-Ptm (Variable 120), N-ANS (Variable 130), Ba-ANS (Variable 181), and Ba-A (Variable 182). (Riolo et al., 1974)

Data Analysis

Descriptive summaries including the frequency and percent for categorical variables and mean, standard deviation and range for quantitative variables were created to describe the study patients.

To determine the reliability of the cephalometric measurements, 10 patients were randomly selected and their cephalometric radiographs at T1 and T2 were measured twice 4 weeks apart. To summarize the reliability of the cephalometric measurements the mean and standard deviation (SD) were computed for each set of measurements, as well as the mean (SD) of the differences and 95% confidence interval (CI) for the mean difference, the intraclass correlation coefficient (ICC) and 95% CI for the ICC (Cicchetti, 1994), Dahlberg's error (Kim, 2013), and the minimum and maximum for the absolute value of the difference between the repeated measurements.

Mean values and 95% confidence intervals were used to compare the cephalometric values at T1 and T2 and the change from T1 to T2. The paired t-test was used to test for change from T1 to T2. The patient cephalometric values were compared to age adjusted normal values using a one-sample t test. McNemar's test was used to assess trends in anterior and posterior crossbite between T1 and T2. Welch's two-sample t-test was used to determine any differences in cephalometric changes (T2-T1) by sex.

Linear regression with heteroskedisticity-robust standard errors and scatter plots with a loess smooth were used to determine if there was any association between the cephalometric changes (T2-T1) and age. (White, 1980) Linear regression was also used to test for an association between cephalometric changes (T2-T1) and canine development at time of ABG. The assessment of the association between cephalometric changes (T2-T1) and number of surgeries was restricted to patients with lip surgery performed at SCH. Due to the small number of patients with multiple surgeries, the total number of surgeries was grouped into 3 categories (1-2, 3 or 4+) and the number of palate surgeries was grouped into 2 categories (1, or 2-3 and 0-1 or 2+, respectively). Welch's one-way analysis of variance (ANOVA) and two-sample t-test were used to compare the change in cephalometric values versus the total number of surgeries, number of lip surgeries, number of palate surgeries and number of speech surgeries. Analyses were performed with R version 4.3.0. (R Core Team, 2023)

Sample Size

A total of 223 patient records were screened for inclusion in the study. All patient records meeting criteria were included in the study. To achieve 80% power at a 0.05 significance level to detect a correlation as small as 0.25 requires 125 subjects.

Table 2: Level of correlation detectable with 80% power at 0.05 significance level

Total number of subjects	Correlation
50	0.38
75	0.31
100	0.27
125	0.25
150	0.23

Results

In total, 223 patients who received ABGs at SCH were screened for this study and 124 patients met criteria of inclusion. Reasons for exclusion were: inadequate imaging (70), multiple ABGs (28), and overly delayed ABG beyond typical timing for this surgery (1 at age 16).

Dahlberg's error gives the absolute error for each measurement based on the single investigator. The error for each measurement was less than one degree for SNA or less than one mm for most other measurements, but always 2 mm or less. The interclass correlation coefficient (ICC) gives the relative measurement of agreement. All measurements had excellent agreement (ICC >=0.82). See Appendix 1 for a full summary of the measurement reliability.

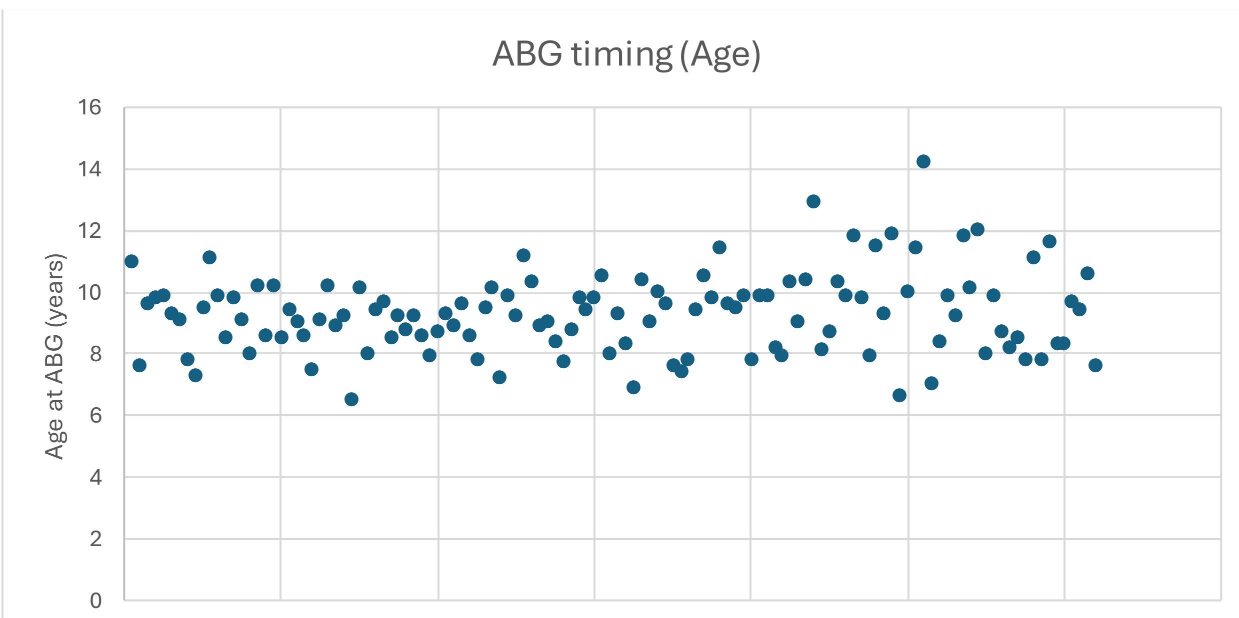
Slightly more patients were female (52%). Most of the patients had complete clefts extending into the alveolus and palate (94%). The mean (standard deviation, SD) age of ABG was 9.3 (1.3) years. The mean (SD) growth period evaluated was 8.3 (2.7) years. The average (SD) age of T1 was 7.6 (1.3) years, and T2 was 15.8 (2.6) years (Table 3). Figure 1 shows the timing (age) of ABG for each patient.

Table 3: Patient sex, cleft type, age at imaging and age at ABG

Variable	**N = 124**
Sex, n (%)	
Male	60 (48%)
Female	64 (52%)
Extent of cleft, n (%)	
Alveolus only	8 (6.5%)
Alveolus and Palate	116 (94%)
Age at Pre ABG image (T1) (Years)	
Mean (SD)	7.6 (1.3)

Variable	N = 124
Min, Max	4.9, 12.7
Age at ABG (Years)	
Mean (SD)	9.3 (1.3)
Min, Max	6.5, 14.2
Age at Post ABG image (T2)(Years)	
Mean (SD)	15.8 (2.6)
Min, Max	10.5, 24.1
Growth Period (Years)	
Mean (SD)	8.3 (2.7)
Min, Max	3.3, 19.0

Figure 1: Patient age (Years) at time of ABG



Aim 1: Describe maxillary length and position prior to and following ABG and quantify the change in maxillary length and position prior to and following ABG

At T1, all measurements were significantly smaller as compared to gender matched, age adjusted normal values (AA norms). Maxillary position was retrusive as reflected by SNA angle decrease of 4.8 degrees. Mean maxillary unit length (ANS-PNS) was decreased by 6.4mm compared to AA norms (Table 4).

Table 4: T1 Cephalometric measurements of patients with UCLP compared to gender matched, age-adjusted normal values (AA Norms) prior to ABG

Variable	UCLP N = 124[1]	95% CI[2]	AA Norms	p-value[3]
SNA (degrees)	76.3 (4.6)	(75.4, 77.1)	81.1	<0.001
ANS-PTM (mm)	43.7 (4.1)	(42.9, 44.4)	54.2	<0.001
N-ANS (mm)	42.2 (3.9)	(41.5, 42.9)	47.7	<0.001
ANS-PNS (mm)	44.3 (4.3)	(43.5, 45.0)	50.7	<0.001
Ba-A (mm)	75.8 (5.9)	(74.8, 76.9)	92.9	<0.001
Ba-ANS (mm)	79.4 (6.0)	(78.4, 80.5)	97.0	<0.001

[1]Mean (SD)
[2]CI = Confidence Interval
[3]One-sample t-test

Presence of crossbite for 122 patients was assessed at T1 using clinical photographs. Prevalence of anterior crossbite at T1 was: 54.8 % complete (N=68), 35.5% partial (N=44) and 8.1% no anterior crossbite (N=10). Prevalence of posterior crossbite at T1 was: 47.6% no posterior crossbite (N=59), 31.5% unilateral (N=39), and 19.4% bilateral (N=24).

At T2, all measurements were significantly smaller as compared to AA norms. Compared to AA norms, mean maxillary position was retrusive as reflected by SNA angle decrease of 9.3 degrees and mean maxillary unit length (ANS-PNS) was shorter by 13 mm (Table 5).

Table 5: T2 Cephalometric measurements of patients compared to age-adjusted normal values (AA Norms)

Variable	**UCLP**, N = 124[1]	95% CI[2]	AA Norms	p-value[3]
SNA (Degrees)	72.1 (5.1)	(71.2, 73.0)	81.4	<0.001
ANS-PTM (mm)	45.0 (4.8)	(44.1, 45.8)	61.7	<0.001
N-ANS (mm)	49.4 (4.2)	(48.7, 50.2)	56.7	<0.001
ANS-PNS (mm)	45.2 (5.4)	(44.2, 46.1)	58.2	<0.001
Ba-A (mm)	78.5 (6.7)	(77.3, 79.7)	102.7	<0.001
Ba-ANS (mm)	83.5 (7.1)	(82.2, 84.7)	107.9	<0.001

[1]Mean (SD)
[2]CI = Confidence Interval
[3]One-sample t-test

Presence of crossbite for 123 patients was assessed at T2 using clinical photographs. Presence of anterior crossbite at T2 was: 59.7% complete (N=74), 21.8% no anterior crossbite (N=27), and 17.7% partial (N=22). Prevalence of posterior crossbite at T2 was: 49.2% no posterior crossbite (N=61), 29.0% bilateral (N=36), and 21.0% unilateral (N=26).

Cephalometric changes between T1 and T2

There was a statistically significant change from T1 to T2 in all cephalometric measurements. All linear measurements increased. Mean maxillary unit length (ANS-PNS) increased by 5.1 mm. Maxillary retrusion increased. The mean SNA angle decreased 4.2 degrees (Table 6).

Table: 6: Cephalometric measurements of patients at T1 and T2

Variable	**T1**, N = 124[1]	95% CI[2]	**T2**, N = 124[1]	95% CI[2]	Difference (SD)	95% CI[2]	p-value[3]
SNA (degrees)	76.3 (4.6)	(75.4, 77.1)	72.1 (5.1)	(71.2, 73.0)	-4.2 (3.3)	(-4.7, -3.6)	<0.001
N-A (mm)	48.3 (4.9)	(47.4, 49.1)	55.8 (4.9)	(54.9, 56.6)	7.5 (4.7)	(6.7, 8.4)	<0.001
ANS-PTM (mm)	43.7 (4.1)	(42.9, 44.4)	45.0 (4.8)	(44.1, 45.8)	1.3 (3.7)	(0.64, 1.9)	<0.001
N-ANS (mm)	42.2 (3.9)	(41.5, 42.9)	49.4 (4.2)	(48.7, 50.2)	7.2 (4.3)	(6.4, 8.0)	<0.001
ANS-PNS (mm)	44.3 (4.3)	(43.5, 45.0)	49.4 (4.2)	(48.7, 50.2)	5.2 (4.4)	(4.2, 6.1)	<0.001
Co-A (mm)	67.8 (5.8)	(66.8, 68.9)	71.4 (6.2)	(70.3, 72.5)	3.5 (4.6)	(2.7, 4.3)	<0.001
Ba-A (mm)	75.8 (5.9)	(74.8, 76.9)	78.5 (6.7)	(77.3, 79.7)	2.7 (4.7)	(1.9, 3.5)	<0.001
Co-ANS (mm)	70.0 (5.8)	(68.9, 71.0)	74.7 (6.5)	(73.5, 75.9)	4.7 (4.7)	(3.9, 5.6)	<0.001
Ba-ANS (mm)	79.4 (6.0)	(78.4, 80.5)	83.5 (7.1)	(82.2, 84.7)	4.0 (4.9)	(3.2, 4.9)	<0.001

[1]Mean (SD)

[2]CI = Confidence Interval

[3]Paired t-test

During growth period, for the patients with UCLP, all linear measurements increased and angular measurement (SNA) decreased. For AA norms, all cephalometric measurements, both linear and angular, increased. Patients with UCLP had maxillary unit length growth (ANS-PNS) of 6.5mm less than the AA norms. Patients with UCLP had a 4.2 degree decrease in maxillary position (SNA), in contrast to the 0.3 degree increase for AA norms (Table 7).

Table 7: Change in Cephalometric measurements (T2-T1) of patients compared to age-adjusted normal values (AA Norms)

Variable	**UCLP**, N = 124[1]	**95% CI**[2]	**AA Norms**	**p-value**[3]
SNA (degrees)	-4.2 (3.3)	(-4.7, -3.6)	0.3	<0.001
ANS-PTM (mm)	1.3 (3.7)	(0.64, 1.9)	7.4	<0.001
N-ANS (mm)	7.2 (4.3)	(6.4, 8.0)	9.1	<0.001
ANS-PNS (mm)	0.9 (4.4)	(0.15, 1.7)	7.4	<0.001
Ba-A (mm)	2.7 (4.7)	(1.9, 3.5)	9.7	<0.001
Ba-ANS (mm)	4.0 (4.9)	(3.2, 4.9)	10.8	<0.001

[1]Mean (SD)
[2]CI = Confidence Interval
[3]One-sample t-test

Two measurements were found to differ significantly between sexes. Both related to maxillary linear measurements. Males had more vertical growth (N-ANS) by 1.6mm and more horizontal growth (Co-ANS) by 1.9mm (Table 8).

Table 8: Change in cephalometric measurements (T2-T1) of patients by sex

Variable	**Male**, N = 60[1]	**Female**, N = 64[1]	**Difference**[2]	**95% CI**[2,3]	**p-value**[2]
SNA (degrees)	-4.1 (3.6)	-4.2 (3.1)	0.11	(-1.1, 1.3)	0.860
N-A (mm)	8.2 (5.4)	6.8 (3.8)	1.4	(-0.27, 3.1)	0.098
ANS-PTM (mm)	1.9 (3.8)	0.8 (3.5)	1.1	(-0.18, 2.4)	0.091
N-ANS (mm)	8.0 (4.8)	6.4 (3.5)	1.6	(0.07, 3.1)	0.041
ANS-PNS (mm)	1.2 (4.6)	0.7 (4.1)	0.55	(-1.0, 2.1)	0.490
Co-A (mm)	4.3 (4.5)	2.8 (4.6)	1.5	(-0.13, 3.1)	0.072
Ba-A (mm)	3.3 (4.9)	2.2 (4.5)	1.1	(-0.57, 2.8)	0.195
Co-ANS (mm)	5.7 (4.3)	3.8 (5.0)	1.9	(0.26, 3.5)	0.024
Ba-ANS (mm)	4.8 (4.7)	3.3 (5.1)	1.5	(-0.28, 3.2)	0.100

[1]Mean (SD)
[2]Welch Two Sample t-test
[3]CI = Confidence Interval

Aim 2: Describe the association between chronologic and dental age at ABG with maxillary size and position following ABG

There was no significant association between chronologic age at ABG and the change in cephalometric values measured before and after the growth period (Table 9).

Table 9: Relationship of change in cephalometric measurements and chronologic age of patient at time of ABG

Measurement	Characteristic	Beta N=124	95% CI[1]	p-value
SNA (Degrees)	Age at 1st graft, y	0.32	(-0.11, 0.75)	0.144
	R^2	0.014		
N-A (mm)	Age at 1st graft, y	-0.11	(-0.93, 0.71)	0.795
	R^2	0.001		
ANS-PTM (mm)	Age at 1st graft, y	0.04	(-0.55, 0.62)	0.903
	R^2	0.000		
N-ANS (mm)	Age at 1st graft, y	-0.07	(-0.77, 0.63)	0.844
	R^2	0.000		
ANS-PNS (mm)	Age at 1st graft, y	-0.28	(-0.93, 0.36)	0.386
	R^2	0.006		
Co-A (mm)	Age at 1st graft, y	0.11	(-0.52, 0.75)	0.722
	R^2	0.001		
Ba-A (mm)	Age at 1st graft, y	0.08	(-0.56, 0.71)	0.812
	R^2	0.000		
Co-ANS (mm)	Age at 1st graft, y	0.03	(-0.62, 0.67)	0.937
	R^2	0.000		
Ba-ANS (mm)	Age at 1st graft, y	-0.01	(-0.69, 0.66)	0.968
	R^2	0.000		

[1]CI = Confidence Interval

Canine development at the time of ABG was used as a proxy for dental age. There was no significant association between dental age at ABG and the change in cephalometric values measured before and after the growth period (Table 10).

Table 10: Relationship of change in cephalometric measurements and canine development of patient at time of ABG

Measurement	Canine Development	Beta	95% CI[1]	p-value
SNA (Degrees)				0.526
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	0.89	(-0.74, 2.52)	0.282
	2/3 - Full Root development	1.03	(-1.12, 3.18)	0.343
	R^2	0.015		
N-A (mm)				0.682
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	-0.92	(-3.13, 1.30)	0.415
	2/3 - Full Root development	-1.08	(-3.97, 1.80)	0.458
	R^2	0.008		
ANS-PTM (mm)				0.968
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	0.11	(-1.57, 1.79)	0.896
	2/3 - Full Root development	-0.13	(-2.44, 2.19)	0.913
	R^2	0.001		
N-ANS (mm)				0.316
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	-1.51	(-3.48, 0.45)	0.130
	2/3 - Full Root development	-1.14	(-3.89, 1.61)	0.414
	R^2	0.023		
ANS-PNS (mm)				0.877
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	-0.31	(-2.23, 1.60)	0.746
	2/3 - Full Root development	0.25	(-2.53, 3.03)	0.858
	R^2	0.002		
Co-A (mm)				0.161
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	-1.71	(-3.54, 0.11)	0.065
	2/3 - Full Root development	-0.50	(-3.17, 2.17)	0.711
	R^2	0.028		
Ba-A (mm)				0.031
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	-2.65	(-4.71, -0.59)	0.012
	2/3 - Full Root development	-2.85	(-5.47, -0.22)	0.034
	R^2	0.062		
Co-ANS (mm)				0.160
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	-1.73	(-3.77, 0.30)	0.095

Measurement	**Canine Development**	**Beta**	**95% CI[1]**	**p-value**
	2/3 - Full Root development	-0.08	(-2.96, 2.80)	0.955
	R^2	0.031		
Ba-ANS (mm)				0.059
	< 1/3 Root Development	—	—	
	1/3 - 2/3 Root Development	-2.63	(-4.85, -0.42)	0.020
	2/3 - Full Root development	-2.61	(-5.54, 0.31)	0.079
	R^2	0.054		

[1]CI = Confidence Interval

Aim 3: Describe the association between the number of lip and palate surgeries prior to ABG with maxillary size and position

Of the 124 patients, 75 had all surgeries (lip, palate, speech) completed at SCH. This subgroup of patients with all surgeries at SCH were evaluated for association between number of surgeries and change in maxillary size and position between T1 and T2. Surgical association was evaluated by using these categories: 1-2 surgeries (N=24), 3 surgeries (N=30) and 4 or more surgeries(N=20) performed on patients. No association was observed between the total number of surgeries and linear and angular cephalometric changes during the growth period (Table 11).

Table 11: Number of perioral surgeries prior to ABG for patients who received all surgical care at SCH

	Number of surgeries (Lip, palate, speech)			
Variable	**1-2**, N = 25	**3**, N = 30	**4+**, N = 20	**p-value**[1]
SNA (Degrees)				0.606
Mean (SD)	-5.0 (4.3)	-4.0 (2.4)	-4.1 (2.7)	
Range	-17.0, 2.5	-8.2, 0.4	-9.6, 1.4	
N-A (mm)				0.737
Mean (SD)	7.2 (4.1)	7.6 (4.0)	6.7 (4.4)	
Range	-1.9, 15.0	1.0, 15.2	0.4, 18.8	
ANS-PTM (mm)				0.921
Mean (SD)	1.6 (3.7)	1.8 (4.2)	2.0 (3.4)	
Range	-5.7, 8.4	-7.0, 11.4	-3.6, 7.2	
N-ANS (mm)				0.094
Mean (SD)	7.8 (4.3)	7.6 (3.6)	5.4 (3.8)	
Range	-3.0, 16.5	1.0, 13.7	-0.9, 15.6	
ANS-PNS (mm)				0.565
Mean (SD)	2.1 (4.5)	1.4 (4.2)	0.7 (4.2)	
Range	-7.7, 9.8	-5.4, 10.2	-6.0, 7.6	

	Number of surgeries (Lip, palate, speech)			
Variable	**1-2**, N = 25	**3**, N = 30	**4+**, N = 20	**p-value**[1]
Co-A (mm)				0.476
Mean (SD)	4.3 (4.5)	3.3 (4.5)	2.5 (5.7)	
Range	-5.2, 12.2	-7.5, 11.1	-8.1, 12.3	
Ba-A (mm)				0.365
Mean (SD)	3.7 (3.5)	2.6 (5.5)	1.8 (5.5)	
Range	-2.3, 11.5	-10.8, 14.9	-9.5, 11.5	
Co-ANS (mm)				0.183
Mean (SD)	6.4 (5.0)	4.3 (4.6)	4.0 (4.6)	
Range	-1.4, 15.3	-6.0, 12.5	-4.6, 12.0	
Ba-ANS (mm)				0.173
Mean (SD)	5.7 (4.0)	3.8 (5.7)	3.5 (4.6)	
Range	-1.5, 14.8	-10.1, 16.6	-6.0, 12.5	

[1]One-way analysis of means (not assuming equal variances)

The effect of increasing exposure to palatal surgeries was evaluated by dividing the sample into categories: 0-1 surgeries (N=56) or 2 or more surgeries (N=19). Only 4 patients included in the sample had no palatal surgery at all and they were combined with the low exposure (single surgery) group. No significant effect from high exposure to palatal surgery was seen on linear and angular cephalometric changes during the growth period (Table 12).

Table 12: Number of Palatal surgeries for patients who received all surgical care at SCH

	Number of surgeries (Palate)		
Variable	**0-1**, N = 56	**2+**, N = 19	**p-value**[1]
SNA (degrees)			0.139
Mean (SD)	-4.7 (3.3)	-3.5 (2.9)	
Range	-17.0, 2.5	-9.6, 1.4	
N-A (mm)			0.888
Mean (SD)	7.3 (4.0)	7.1 (4.5)	
Range	-1.9, 15.2	0.8, 18.8	
ANS-PTM (mm)			0.807
Mean (SD)	1.7 (4.0)	1.9 (3.0)	

Number of surgeries (Palate)			
Variable	**0-1**, N = 56	**2+**, N = 19	**p-value**[1]
Range	-7.0, 11.4	-3.6, 7.2	
N-ANS (mm)			0.105
Mean (SD)	7.5 (3.8)	5.7 (4.3)	
Range	-3.0, 16.5	-0.9, 15.6	
ANS-PNS (mm)			0.373
Mean (SD)	1.7 (4.4)	0.7 (4.0)	
Range	-7.7, 10.2	-6.0, 7.6	
Co-A (mm)			0.767
Mean (SD)	3.3 (4.6)	3.7 (5.6)	
Range	-7.5, 12.2	-8.1, 12.3	
Ba-A (mm)			0.900
Mean (SD)	2.8 (4.8)	2.6 (5.4)	
Range	-10.8, 14.9	-9.5, 11.5	
Co-ANS (mm)			0.793
Mean (SD)	5.0 (4.9)	4.7 (4.6)	
Range	-6.0, 15.3	-4.6, 12.5	
Ba-ANS (mm)			0.664
Mean (SD)	4.5 (5.0)	3.9 (4.8)	
Range	-10.1, 16.6	-6.0, 13.1	

[1]Welch Two Sample t-test

Fourteen patients received surgeries to support speech goals–these were 11 Furlow palatoplasties, 2 sphincter palatoplasties, and 1 combined sphincter and pharyngeal flap. The effect of speech surgery on cephalometric measurements was assessed in a binary fashion based on exposure (Table 13). Patients who received a speech surgery had a noted decreased change in the following cephalometric measurements: N-A (p=0.019), N-ANS (p<0.001), and Ba-ANS (p=0.048), indicating these patients had less AP growth in those measurements.

Table 13: Cephalometric changes during the growth period for patients that did or did not receive speech surgeries

	Speech surgery		
Variable	**No**, N = 61	**Yes**, N = 14	**p-value**[1]
SNA (Angle)			0.595
Mean (SD)	-4.4 (3.5)	-4.1 (1.9)	
Range	-17.0, 2.5	-7.0, -0.6	
N-A			0.019
Mean (SD)	7.7 (4.1)	5.0 (3.5)	
Range	-1.9, 18.8	0.8, 11.1	
ANS-PTM			0.253
Mean (SD)	2.0 (3.9)	0.9 (3.1)	
Range	-7.0, 11.4	-3.6, 5.5	
N-ANS			<0.001
Mean (SD)	7.8 (3.9)	4.1 (3.0)	
Range	-3.0, 16.5	-0.9, 8.7	
ANS-PNS			0.099
Mean (SD)	1.8 (4.3)	-0.3 (4.0)	
Range	-7.7, 10.2	-5.7, 7.6	
Co-A			0.113
Mean (SD)	3.9 (4.5)	1.2 (5.8)	
Range	-8.1, 12.2	-7.7, 12.3	
Ba-A			0.082
Mean (SD)	3.3 (4.8)	0.5 (5.0)	
Range	-10.8, 14.9	-7.2, 8.3	
Co-ANS			0.075
Mean (SD)	5.5 (4.6)	2.6 (5.3)	
Range	-4.3, 15.3	-6.0, 12.0	
Ba-ANS			0.048
Mean (SD)	4.9 (5.0)	2.1 (4.3)	
Range	-10.1, 16.6	-3.6, 8.4	

[1]Welch Two Sample t-test

Discussion

Patients with UCLP undergo many surgical procedures as part of their longitudinal care including lip closure, primary palate closure, alveolar bone grafting, and surgeries to support speech. All procedures aim to improve the patients' quality of life and it is not uncommon for patients to have multiple lip and palate revision surgeries. Patients at Seattle Children's Hospital Craniofacial Center generally have at least two maxillary surgeries (primary palate closure and ABG) within the first decade of life.

Orthodontists have historically believed that cleft related perioral surgeries may have significant negative impact upon maxillary growth. This belief may stem from influential work describing normal maxillary growth in 20 untreated patients with UCLP receiving no surgical interventions. (Bishara et al., 1976) Authors of a more recent review paper concluded that early palate closure inhibited maxillary sagittal, vertical, and transverse growth (Shi & Losee, 2015) and contributed to concern that early and repeated surgical exposures for the palate and maxilla have long-term detrimental growth effects. Hesitation to perform early surgeries may be partially attributed to this literature and clinical experience with poor maxillary development in this patient population.

Counterpoint to concerns about decreased maxillary growth with early ABG, there are important reasons to consider grafting during the growth period. Improved outcomes of early grafting may be seen in radiographic evaluations, decreased maxillary permanent canine impaction rate, and surgical complications. (Fahradyan et al., 2019) Earlier ABG has improved outcomes for bone graft longevity and decreased need for re-grafting. Patients with earlier grafting are reported to have improved psychosocial outcomes, including reduced anxiety and depression as teenagers and adults. (Hu et al., 2022)

It is critical to establish if earlier surgery will adversely affect maxillary growth as many craniofacial centers and providers advocate for earlier ABG placement to improve periodontal, functional, and psychological outcomes. The present study found no significant differences in maxillary growth outcomes based on patient chronological or dental age at the time of ABG.

The subset of 75 patients receiving all cleft-related surgeries at Seattle Children's Hospital were examined to address concerns that each surgical trauma to the maxilla may contribute to maxillary growth deficiency with a cumulative negative effect. This study assessed each patient's perioral surgical burden including surgeries to support speech. Surprisingly, no association was found between the number of surgeries and maxillary size and position. Only 14 patients received speech surgeries, and most were Furlow palatoplasties. The 2-3mm statistically significant decrease in three linear measurements (N-A, N-ANS, Ba-ANS) found in these patients may be a clinical concern, but the small numbers of included patients with speech surgery should be interpreted with caution. These findings should be corroborated by other studies.

The key findings of this study support the view that individuals with UCLP have less maxillary growth potential than those without UCLP. Prior to ABG, the 124 patients in this study had retrusive, short maxillae and a slim majority had posterior crossbite. A second assessment after a growth period of at least two years following ABG and prior to comprehensive orthodontic treatment (with or without planned orthognathic surgery) demonstrated that maxillae became more retrusive and exhibited less vertical and horizontal change than normally seen during this growth period in patients without UCLP.

Limitations

This is a retrospective study using available images for patients undergoing treatment at one center. Inclusion bias for patients with severe maxillary deficiency may be present since these individuals receive more imaging. Patients with more favorable maxillary growth may have been excluded because of reduced or inadequate imaging because they lacked clinical indications for additional imaging. This study included only patients with successful ABG on the first attempt, minimizing the number of patients with higher surgery burdens. Accuracy bias may be present from a single examiner involved in collecting cephalometric measurements. Somatic growth information was not collected, which could give more insight on patients' overall growth.

Conclusions

- Patients with UCLP have significantly smaller and more retrusive maxillae in comparison to gender and age matched norms.
- Timing of ABG did not have any significant impact on maxillary growth, and an earlier graft may be indicated for improved clinical outcomes such as periodontal support for erupting teeth or psycho-social wellness.
- The number of plate revision surgeries did not have a significant impact on maxillary growth.
- Further studies with more patients will be needed to understand the association between speech surgeries and maxillary growth.

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Appendix 1: Reliability summary of cephalometric measurements

Measure	n	1st Mean (SD)	2nd Mean (SD)	Diff. (SD) [95% CI)]	Diff % [95% CI)]	ICC (95% CI)	D. Error % (Min, Max)
SNA T1	10	75.8 (5.6)	75.8 (5.5)	0.0 (0.8) [-0.6, 0.5]	0.0% (-0.8, 0.7%)	0.99 (0.97, 1.00)	0.5 0.7% (0.1, 1.4)
T2	10	73.0 (4.3)	72.5 (4.5)	0.5 (0.9) [-0.2, 1.2]	0.7% (-0.3, 1.6%)	0.97 (0.90, 0.99)	0.7 1.0% (0.0, 2.6)
T1&T2	20	74.4 (5.1)	74.2 (5.2)	0.2 (0.9) [-0.2, 0.6]	0.3% (-0.2, 0.9%)	0.98 (0.96, 0.99)	0.6 0.8% (0.0, 2.6)
T2-T1	10	-2.8 (3.7)	-3.4 (3.4)	0.5 (1.3) [-0.4, 1.4]	-16.7% (12.2, -45.7%)	0.93 (0.76, 0.98)	0.9 29.6% (0.0, 2.9)
NA T1	10	46.7 (3.3)	46.6 (3.9)	0.1 (1.2) [-0.8, 0.9]	0.1% (-1.7, 1.9%)	0.95 (0.83, 0.99)	0.8 1.7% (0.0, 2.6)
T2	10	54.7 (3.3)	54.3 (3.2)	0.4 (1.5) [-0.6, 1.5]	0.8% (-1.1, 2.8%)	0.90 (0.66, 0.97)	1.1 1.9% (0.0, 2.8)
T1&T2	20	50.7 (5.2)	50.4 (5.2)	0.3 (1.3) [-0.4, 0.9]	0.5% (-0.7, 1.7%)	0.97 (0.92, 0.99)	0.9 1.8% (0.0, 2.8)
T2-T1	10	8.1 (4.3)	7.7 (4.4)	0.4 (1.7) [-0.8, 1.6]	5.0% (-10.8, 20.7%)	0.92 (0.74, 0.98)	1.2 15.2% (0.0, 3.3)
ANS-PTM T1	10	42.7 (5.1)	43.4 (5.4)	-0.6 (0.7) [-1.2, -0.1]	-1.5% (-2.7, -0.2%)	0.98 (0.94, 1.00)	0.7 1.6% (0.0, 2.2)

Measure	n	1st Mean (SD)	2nd Mean (SD)	Diff. (SD) [95% CI)]	Diff % [95% CI)]	ICC (95% CI)	D. Error % (Min, Max)
T2	10	45.5 (4.8)	45.9 (5.0)	-0.4 (0.7) [-1.0, 0.1]	-1.0% (-2.1, 0.1%)	0.99 (0.95, 1.00)	0.6 1.2% (0.0, 2.0)
T1&T2	20	44.1 (5.0)	44.6 (5.2)	-0.5 (0.7) [-0.9, -0.2]	-1.2% (-2.0, -0.5%)	0.99 (0.96, 0.99)	0.6 1.4% (0.0, 2.2)
T2-T1	10	2.8 (5.2)	2.6 (5.1)	0.2 (0.9) [-0.5, 0.9]	7.1% (-17.8, 32.0%)	0.98 (0.94, 1.00)	0.6 23.9% (0.0, 2.1)
N-ANS T1	10	42.0 (3.0)	41.9 (2.9)	0.1 (0.4) [-0.2, 0.4]	0.3% (-0.4, 0.9%)	0.99 (0.97, 1.00)	0.3 0.7% (0.0, 0.7)
T2	10	48.3 (4.1)	48.8 (4.2)	-0.5 (0.8) [-1.0, 0.1]	-1.0% (-2.1, 0.2%)	0.98 (0.92, 0.99)	0.6 1.3% (0.0, 2.4)
T1&T2	20	45.2 (4.7)	45.4 (5.0)	-0.2 (0.7) [-0.5, 0.1]	-0.4% (-1.1, 0.3%)	0.99 (0.98, 1.00)	0.5 1.0% (0.0, 2.4)
T2-T1	10	6.3 (3.6)	6.9 (3.4)	-0.6 (0.7) [-1.1, -0.1]	-8.8% (-16.8, -0.9%)	0.97 (0.88, 0.99)	0.6 9.7% (0.0, 2.1)
ANS-PNS T1	10	43.8 (4.4)	44.8 (4.6)	-1.0 (0.9) [-1.7, -0.3]	-2.2% (-3.7, -0.7%)	0.96 (0.85, 0.99)	0.9 2.1% (0.0, 2.3)
T2	10	44.7 (4.7)	45.7 (5.0)	-1.0 (1.0) [-1.8, -0.3]	-2.3% (-4.0, -0.7%)	0.96 (0.84, 0.99)	1.0 2.3% (0.0, 3.1)
T1&T2	20	44.2 (4.4)	45.3 (4.7)	-1.0 (1.0) [-1.5, -0.6]	-2.3% (-3.3, -1.3%)	0.95 (0.89, 0.98)	1.0 2.2% (0.0, 3.1)

Measure	n	1st Mean (SD)	2nd Mean (SD)	Diff. (SD) [95% CI)]	Diff % [95% CI)]	ICC (95% CI)	D. Error % (Min, Max)
T2-T1	10	0.9 (5.1)	0.9 (5.0)	-0.1 (1.2) [-0.9, 0.8]	-7.7% (-102.0, 86.7%)	0.97 (0.91, 0.99)	0.8 88.6% (0.2, 2.7)
Co-A T1	10	68.8 (5.1)	68.4 (4.9)	0.4 (0.8) [-0.2, 1.0]	0.6% (-0.2, 1.4%)	0.99 (0.95, 1.00)	0.6 0.9% (0.0, 1.6)
T2	10	73.5 (4.5)	71.7 (5.2)	1.8 (2.3) [0.1, 3.5]	2.5% (0.2, 4.8%)	0.83 (0.48, 0.95)	2.0 2.8% (1.0, 6.1)
T1&T2	20	71.1 (5.2)	70.0 (5.2)	1.1 (1.9) [0.2, 2.0]	1.6% (0.3, 2.8%)	0.92 (0.81, 0.97)	1.5 2.1% (0.0, 6.1)
T2-T1	10	4.7 (5.0)	3.3 (4.3)	1.4 (2.6) [-0.4, 3.3]	35.6% (-10.7, 81.8%)	0.82 (0.45, 0.95)	2.0 50.2% (0.4, 6.1)
Ba-A T1	10	77.0 (4.4)	77.1 (4.6)	-0.1 (1.2) [-1.0, 0.8]	-0.1% (-1.3, 1.0%)	0.97 (0.88, 0.99)	0.8 1.1% (0.0, 2.5)
T2	10	79.9 (6.7)	79.5 (6.7)	0.4 (1.1) [-0.4, 1.2]	0.5% (-0.5, 1.5%)	0.99 (0.95, 1.00)	0.8 1.0% (0.0, 2.9)
T1&T2	20	78.4 (5.7)	78.3 (5.7)	0.1 (1.2) [-0.4, 0.7]	0.2% (-0.5, 0.9%)	0.98 (0.95, 0.99)	0.8 1.0% (0.0, 2.9)
T2-T1	10	2.9 (5.5)	2.4 (4.9)	0.5 (1.7) [-0.8, 1.7]	17.6% (-28.6, 63.8%)	0.95 (0.81, 0.99)	1.2 45.1% (0.0, 3.0)
Co-ANS T1	10	71.0 (4.7)	70.9 (4.9)	0.1 (0.9) [-0.6, 0.8]	0.2% (-0.8, 1.1%)	0.98 (0.93, 1.00)	0.6 0.9% (0.3, 1.8)

Measure	n	1st Mean (SD)	2nd Mean (SD)	Diff. (SD) [95% CI)]	Diff % [95% CI)]	ICC (95% CI)	D. Error % (Min, Max)
T2	10	76.6 (4.5)	75.6 (5.6)	1.1 (2.2) [-0.5, 2.7]	1.4% (-0.7, 3.5%)	0.89 (0.65, 0.97)	1.7 2.2% (0.5, 5.6)
T1&T2	20	73.8 (5.4)	73.2 (5.7)	0.6 (1.7) [-0.2, 1.4]	0.8% (-0.3, 1.9%)	0.95 (0.87, 0.98)	1.3 1.7% (0.3, 5.6)
T2-T1	10	5.6 (5.6)	4.7 (5.5)	0.9 (2.3) [-0.7, 2.6]	18.5% (-14.1, 51.2%)	0.91 (0.68, 0.98)	1.7 33.3% (0.0, 5.3)
Ba-ANS T1	10	80.4 (4.2)	80.9 (4.3)	-0.5 (1.4) [-1.5, 0.5]	-0.6% (-1.9, 0.6%)	0.94 (0.81, 0.99)	1.0 1.2% (0.2, 2.6)
T2	10	84.6 (6.5)	84.8 (6.5)	-0.2 (0.6) [-0.7, 0.2]	-0.3% (-0.8, 0.2%)	1.00 (0.98, 1.00)	0.4 0.5% (0.0, 1.2)
T1&T2	20	82.5 (5.7)	82.9 (5.8)	-0.4 (1.1) [-0.9, 0.1]	-0.4% (-1.0, 0.2%)	0.98 (0.96, 0.99)	0.8 0.9% (0.0, 2.6)
T2-T1	10	4.2 (6.8)	3.9 (6.0)	0.3 (1.4) [-0.8, 1.3]	7.0% (-18.7, 32.6%)	0.98 (0.91, 0.99)	1.0 24.6% (0.1, 2.6)