European Journal of Orthodontics, 2021, 381–386
doi:10.1093/ejo/cjab007
Advance Access publication 9 March 2021

Original article

Scandcleft randomized trials of primary surgery for unilateral cleft lip and palate: impact of maxillary dental agenesis on craniofacial growth and dental arch relationship in 8 year olds

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Summary

Background: It is suggested that dental agenesis affects maxillary protrusion and dental arch relationship in children with unilateral cleft lip and palate (UCLP). In addition, an association between the need for orthognathic surgery and dental agenesis is reported.

Aim: The aim was to study the impact of maxillary dental agenesis on craniofacial growth and dental arch relationship in 8-year-old children with UCLP.

Subjects and methods: The sample consisted of individuals with UCLP from Scandcleft randomized trials. The participants had available data from diagnosis of maxillary dental agenesis as well as cephalometric measurements (n = 399) and GOSLON assessment (n = 408) at 8 years of age.

Results: A statistically significant difference was found for ANB between individuals with agenesis of two or more maxillary teeth (mean 1.52°) in comparison with those with no or only one missing maxillary tooth (mean 3.30° and 2.70°, respectively). Mean NSL/NL was lower among individuals with agenesis of two or more maxillary teeth (mean 9.90°), in comparison with individuals with no or one missing maxillary tooth (mean 11.46° and 11.45°, respectively). The number of individuals with GOSLON score 4–5 was 47.2% in the group with two or more missing maxillary teeth and 26.1% respectively 26.3% in the groups with no or one missing maxillary tooth. No statistically significant difference was found in the comparison between individuals with no agenesis or with agenesis solely of the cleft-side lateral.

Conclusion: Maxillary dental agenesis impacts on craniofacial growth as well as dental arch relationship and should be considered in orthodontic treatment planning.

Introduction

Children born with unilateral cleft lip and palate (UCLP) exhibit an increased frequency of dental agenesis in comparison with individuals without a cleft (1–5). We know that the cleft lateral is absent in 39–52% and that the number of missing teeth outside the cleft varies (1–3, 6–11). Maxillary growth is reported to be restricted in this group of patients, resulting in a prenormal growth pattern (12–14). However, the current knowledge about the underlying causes for maxillary hypoplasia is still incomplete, even if factors such as surgical method and timing as well as initial cleft width or infant orthopaedics are considered (15–20). An association between dental agenesis and maxillary length as well as protrusion has been suggested for non-cleft individuals (21–23) and is also reported for individuals born with UCLP (15, 24, 25). In addition, the necessity for a Le Fort I has been found to correlate with dental agenesis (26–28). The impact on maxillary growth from especially cleft-side lateral agenesis is discussed but the results are not consistent (15, 25, 29).

The Scandcleft randomized trials were designed to study the impact of the surgical protocol on different outcomes, where the craniofacial growth and dental arch relationship has been evaluated using the GOSLON yardstick, Modified Huddart Bodenham index, and cephalometric measurements (13, 30–34). This extensive and prospectively collected sample offers the possibility to study the effect of other plausible factors on maxillary growth impairment. Therefore, the aim of this project was to study the impact of maxillary dental agenesis on craniofacial growth and dental arch relationship in 8-year-old children with UCLP, included in the Scandcleft randomized trials.

Subjects and methods

The Scandcleft randomized sample includes 448 non-syndromic individuals born with UCLP, who were operated according to four different surgical protocols (35, 36). After the withdrawal from the team in Belfast, nine cleft centres in Denmark, Finland, Norway, Sweden, and Great Britain were enrolled at the time when the participants reached 8 years of age. The participants in this study were collected from the Scandcleft randomized trials, and the sample was pooled independently of which surgical protocol the participants were enrolled in. Maxillary dental agenesis (with the exclusion of third molars) was diagnosed by four independent orthodontists, using panoramic radiographs together with intraoral radiographs or CBCT from the cleft area (2). Extracted teeth were not included in the assessment. Digital or scanned conventional lateral cephalograms obtained at 8 years of age, were analysed by one assessor and the results are previously published (13, 34). In addition, cast models obtained at the same age, were examined by a blinded panel of eleven orthodontists using the GOSLON yardstick to assess dental arch relationship into five categories, from excellent to very poor (33). In the present study, 399 of the participants (261 boys and 138 girls) had available data from both assessment of maxillary dental agenesis and cephalometric measurements, while 408 (267 boys and 141 girls) had available data from assessment of maxillary dental agenesis together with GOSLON scoring. All registrations (panoramic and intraoral radiographs, lateral cephalograms, and cast models) were obtained simultaneously at mean age 8.1 years. According to diagnosed maxillary dental agenesis, the sample was categorized into three groups according to the number of missing maxillary teeth (0, 1, ≥2), including cleft lateral agenesis. In addition, individuals with no maxillary dental agenesis or with agenesis solely of the cleft-side lateral were extracted from the sample for comparison. Three cephalometric angles were chosen to quantify craniofacial growth: 1. SNA describing maxillary prognathism in relation to the anterior skull base, 2. ANB describing the intermaxillary anteroposterior relationship, and 3. NSL/NL illustrating maxillary inclination in relation to the anterior skull base. The GOSLON scoring was categorized into the following three groups; GOSLON 1–2 (excellent and good), GOSLON 3 (fair), and GOSLON 4–5 (poor and very poor).

The Scandcleft study was approved by local ethical committees in the respective centres (Denmark 1997/4121, Finland 4/9/97, Norway S-97152, Sweden R257-97, 97–372, UK 99/197). The principles outlined in the Declaration of Helsinki were followed.

Statistics

ANOVA together with Newman–Keuls test was used for the cephalometric measurements, while Fisher's exact test was used for the distribution of GOSLON scores, when testing for differences between the three groups with different numbers of missing maxillary teeth. Student's *t*-test was used for the cephalometric measurements and Fisher´s exact test for the distribution of GOSLON scores, when comparing the groups with no maxillary dental agenesis or agenesis solely of the cleft-side lateral.

Results

The distribution of maxillary dental agenesis in the present sample is presented in Table 1 and the number of missing maxillary teeth ranged from none to nine. Statistically significant differences were found comparing individuals exhibiting a different number of missing maxillary teeth, with a decreased mean ANB in the group with agenesis of two or more maxillary teeth (mean 1.52°) compared to the groups with agenesis of no or only one maxillary tooth (mean 3.30° and 2.70°, respectively) (Table 2). In addition, the angle NSL/NL was found to be decreased in the group with agenesis of two or more maxillary teeth (mean 9.90°) versus the groups with no or only one missing maxillary tooth (mean 11.46° and 11.45°, respectively) (Table 2). A statistically significant difference was also found for the distribution of GOSLON scores between the groups with agenesis of different numbers of maxillary teeth (Table 2). The group with agenesis of two or more maxillary teeth included an increased number of individuals with GOSLON score 4–5 (47.2%) compared to the groups with agenesis of no or only one maxillary tooth (26.1% and 26.3%, respectively). Correspondingly, the group with agenesis of two or more maxillary teeth exhibited fewer individuals scored in

GOSLON groups 1–2 (24.5%) versus individuals with agenesis of no or only one maxillary tooth (45.2% and 41.7%, respectively) (Table 2).

The groups with no maxillary dental agenesis or agenesis solely of the cleft-side lateral, exhibited no statistically significant differences for either SNA, ANB, NSL/NL, or the distribution of GOSLON scores (Table 3).

Discussion

Individuals born with UCLP together with agenesis of two or more maxillary teeth, were found to display a more unfavourable sagittal intermaxillary relationship at 8 years of age versus the group with full dentition or agenesis of only one maxillary tooth. This finding was illustrated by a lower mean ANB as well as an increased number of individuals with a worse GOSLON score in the group with agenesis of two or more maxillary teeth (Table 2). In addition, the group with the highest number of missing maxillary teeth displayed a decreased anterior maxillary inclination (Table 2). The presence or absence of the cleft-side lateral had no impact on the cephalometric measurements or the distribution of GOSLON scores (Table 3).

The finding of an association between maxillary dental agenesis and a more pronounced maxillary growth restriction in UCLP is in line with previous reports (15, 24–27). In addition, the correlation between a higher number of missing maxillary teeth and a more unfavourable intermaxillary sagittal relation as well as a worse GOSLON score, is supported by a previously published finding, of a decreased overjet with an increased number of missing permanent teeth (37). In our sample, a decreased maxillary inclination was detected in the group with agenesis of two or more maxillary teeth (Table 2). The association between dental agenesis and maxillary inclination is rarely investigated in UCLP. In one single paper, vertical growth in individuals with or without dental agenesis has been evaluated, but no difference was detected (24). To our knowledge, no previous studies have addressed the question of whether the number of missing maxillary teeth is associated with vertical growth.

Agenesis of the cleft-side lateral has been suggested as a factor associated with maxillary hypoplasia and dental arch constriction (15, 24, 25, 38, 39). However, these results are contradicted, as no association between cleft lateral agenesis and maxillary growth could be

Table 1. The distribution of maxillary dental agenesis (including cleft lateral agenesis) for the individuals included in the cephalometric as well as GOSLON assessments is presented.

	Cephalometric assessment	GOSLON assessment
Number of missing maxillary teeth	Individuals (*n*)	Individuals (*n*)
0	197	199
1	153	156
2	34	36
3	8	10
4	4	4
5	1	1
6	0	0
7	1	1
8	0	0
9	1	1
Total	399	408

Table 2. The table displays mean values and SD for SNA, ANB and NSL/NL and the comparison between groups with a different number of missing maxillary teeth (0, 1, ≥2), including cleft lateral agenesis, using ANOVA. Newman–Keuls test was used to test between which groups differences were detected. The distribution of GOSLON scores between the groups with a different number of missing maxillary teeth (0, 1, ≥2) was compared using Fisher´s exact test. A *P*-value < 0.05 was considered statistically significant.

	No maxillary agenesis $n = 197$ (°)		Agenesis of one maxillary tooth $n = 153$ (°)		Agenesis of ≥2 maxillary teeth $n = 49$ (°)			
	Mean	SD	Mean	SD	Mean	SD	*P*	Statistically significant differences
SNA	78.37	4.4	77.79	3.8	77.56	3.6	ns	
ANB	3.30	3.4	2.70	3.2	1.52	3.6	0.004	No versus ≥2 maxillary teeth 1 versus ≥2 maxillary teeth
NL/NSL	11.46	4.0	11.45	4.0	9.90	3.8	0.039	No versus ≥2 maxillary teeth 1 versus ≥2 maxillary teeth
GOSLON	No maxillary agenesis $n = 199$		Agenesis of one maxillary tooth $n = 156$		Agenesis of ≥2 maxillary teeth $n = 53$		*P*	
	(*n*)	(%)	(*n*)	(%)	(*n*)	(%)		
1–2	90	45.23	65	41.67	13	24.53	0.023	
3	57	28.64	50	32.05	15	28.30		
4–5	52	26.13	41	26.28	25	47.17		

Table 3. The table presents mean values and SD for SNA, SNB and NSL/NL as well as the distribution of GOSLON scores for individuals with no agenesis or agenesis solely of the cleft-side lateral, who had available data from both GOSLON and cephalometric analysis. Student's *t*-test and Fischer's exact test showed no statistically significant differences between the two groups. A *P*-value <0.05 was considered statistically significant.

	No maxillary agenesis $n = 193$ (°)		Agenesis of cleft-side lateral $n = 132$ (°)		
	Mean	SD	Mean	SD	*P*
SNA	78.37	4.4	77.72	3.5	ns
ANB	3.28	3.4	2.78	3.1	ns
NSL/NL	11.41	4.0	11.75	4.0	ns
GOSLON	No maxillary agenesis		Agenesis of cleft-side lateral		
	(*n*)	(%)	(*n*)	(%)	
1–2	85	44.04	53	40.15	ns
3	57	29.53	42	31.82	
4–5	51	26.43	37	28.03	

proven neither by Doucet and co-workers nor in the present sample (Table 3) (29). The fact that all the above-mentioned samples are heterogenic regarding a number of individuals, age and cleft-type might contribute to the divergent results (15, 24, 25, 29, 38, 39). In addition, the samples were operated according to a variety of surgical protocols and by surgeons with different level of experience. A severe growth disturbance caused by detrimental palatal surgery might possibly mask the effect from dental agenesis, why agenesis of the cleft-side lateral might be linked to growth impairment in certain samples but not in others. In addition, the impact from cleft-side lateral agenesis on maxillary growth has been studied dividing the sample according to the need for Le Fort I (26–28). This grouping might be biased by treatment preferences from the orthodontist or a subjective treatment desire from the patient. The quality of the present sample collected from the Scandcleft randomized trials, is that it consists of an extensive, homogenous group of participants, operated according to well-defined protocols (however by surgeons with varying level of experience from the surgical methods) and followed with standardized registrations which might be an explanation for diverging results in comparison with other publications. The impact from agenesis of the cleft-side lateral on the dental arch relationship has occasionally been studied using the GOSLON yardstick (38). To date, no publications are found reporting on the effect of the number of congenitally missing teeth on the dental arch relationship.

Several genetic factors have been discussed in association with the development of orofacial clefts and dental agenesis (40–44). In addition, agenesis of maxillary teeth has been proposed to indicate maxillary tissue hypoplasia, resulting from a lack of migration of neural crest cells. It is therefore suggested that agenesis of the cleft-side lateral is a predisposing factor for poor midfacial growth caused by an intrinsic deficiency (24, 38, 39, 45).

A shortcoming of the present study, since evidence for a correlation with dental agenesis has been presented, is the lack of data on maxillary length (24). No linear measurements were chosen as the lateral cephalograms were obtained from multiple centres, using cephalostats with unknown enlargement factors. In addition, only three representative cephalometric angles were selected, to decrease the risk for statistical type 1 errors. In the present sample, only a handful of the individuals exhibited maxillary dental agenesis exceeding two teeth (Table 1). A more extensive sample would thus be required to study the effect on maxillary growth in individuals exhibiting agenesis of multiple teeth, for example, oligodontia. Furthermore, results from non-cleft individuals propose that impact from mandibular dental agenesis on mandibular growth is weak (22, 46). Only a few of the participants in the present sample were diagnosed with mandibular dental agenesis, why this question was not addressed. The participants were only 8 years of age at the time for assessment, with the pubertal growth spurt still due. Continuous monitoring until the cessation of craniofacial growth is required for evaluation of the impact from dental agenesis on the final maxillary protrusion. The future study design will include data on dental agenesis, performed extractions, prosthodontic replacement, dental implants or orthodontic space closure.

Conclusion

The main finding revealed that individuals born with UCLP together with two or more congenitally missing teeth, exhibit a more unfavourable sagittal intermaxillary relationship in comparison with individuals with fewer congenitally missing maxillary teeth, at 8 years of age. This finding contributes to the common knowledgebase, essential for the prediction of craniofacial growth and orthodontic treatment planning. The correlation between surgical protocol and craniofacial growth as well as the dental arch relationship has to date been found weak for the Scandcleft sample (13, 31, 33). However, the impact of maxillary dental agenesis on craniofacial growth as well as a dental arch relationship at the same age, seems to overrule the effect from surgical timing and method in the present sample. The constancy of the results detected in the Scandcleft sample at 8 years of age, will be essential to follow throughout growth.

Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

Data availability

The data underlying this article was provided by the centres participating in the Scandcleft trials. Data will be shared on reasonable request to the corresponding author, with the permission from the participating centres.

References

1. Tortora, C., Meazzini, M.C., Garattini, G. and Brusati, R. (2008) Prevalence of abnormalities in dental structure, position, and eruption pattern in a population of unilateral and bilateral cleft lip and palate patients. *The Cleft Palate-Craniofacial Journal*, 45, 154–162.
2. Rizell, S., et al. (2020) Scandcleft randomized trials of primary surgery for unilateral cleft lip and palate: dental anomalies in 8-year olds. *European Journal of Orthodontics*, 42, 8–14.
3. Bartzela, T.N., Carels, C.E., Bronkhorst, E.M. and Kuijpers-Jagtman, A.M. (2013) Tooth agenesis patterns in unilateral cleft lip and palate in humans. *Archives of Oral Biology*, 58, 596–602.
4. Letra, A., Menezes, R., Granjeiro, J.M. and Vieira, A.R. (2007) Defining subphenotypes for oral clefts based on dental development. *Journal of Dental Research*, 86, 986–991.
5. Menezes, R. and Vieira, A.R. (2008) Dental anomalies as part of the cleft spectrum. *The Cleft Palate-Craniofacial Journal*, 45, 414–419.
6. Pegelow, M., Alqadi, N. and Karsten, A.L. (2012) The prevalence of various dental characteristics in the primary and mixed dentition in patients born with non-syndromic unilateral cleft lip with or without cleft palate. *European Journal of Orthodontics*, 34, 561–570.
7. Tsai, T.P., Huang, C.S., Huang, C.C. and See, L.C. (1998) Distribution patterns of primary and permanent dentition in children with unilateral complete cleft lip and palate. *The Cleft Palate-Craniofacial Journal*, 35, 154–160.
8. Baek, S.H. and Kim, N.Y. (2007) Congenital missing permanent teeth in Korean unilateral cleft lip and alveolus and unilateral cleft lip and palate patients. *The Angle Orthodontist*, 77, 88–93.
9. Bøhn, A. (1950) Anomalies of the lateral incisor in cases of harelip and cleft palate. *Acta Odontologica Scandinavica*, 9, 41–59.
10. Dewinter, G., Quirynen, M., Heidbüchel, K., Verdonck, A., Willems, G. and Carels, C. (2003) Dental abnormalities, bone graft quality, and periodontal conditions in patients with unilateral cleft lip and palate at different phases of orthodontic treatment. *The Cleft Palate-Craniofacial Journal*, 40, 343–350.
11. Ribeiro LL, das Neves LT, Costa B, Gomide MR. (2003) Dental anomalies of the permanent lateral incisors and prevalence of hypodontia outside the cleft area in complete unilateral cleft lip and palate. *The Cleft Palate-Craniofacial Journal*, 40, 172–175.
12. Kappen, I.F.P.M., Bittermann, G.K.P., Schouten, R.M., Bittermann, D., Etty, E., Koole, R., Kon, M., Mink van der Molen, A.B. and Breugem, C.C. (2017) Long-term mid-facial growth of patients with a unilateral complete cleft of lip, alveolus and palate treated by two-stage palatoplasty: cephalometric analysis. *Clinical Oral Investigations*, 21, 1801–1810.
13. Küseler, A., et al. (2020) Scandcleft randomized trials of primary surgery for unilateral cleft lip and palate: maxillary growth at eight years of age. *European Journal of Orthodontics*, 42, 24–29.
14. Semb G. (1991) A study of facial growth in patients with unilateral cleft lip and palate treated by the Oslo CLP Team. *The Cleft Palate-Craniofacial Journal*, 28, 1–21.
15. Meazzini, M.C., Tortora, C., Morabito, A., Garattini, G. and Brusati, R. (2011) Factors that affect variability in impairment of maxillary growth in patients with cleft lip and palate treated using the same surgical protocol. *Journal of Plastic Surgery and Hand Surgery*, 45, 188–193.
16. Liao, Y.F., Prasad, N.K., Chiu, Y.T., Yun, C. and Chen, P.K. (2010) Cleft size at the time of palate repair in complete unilateral cleft lip and palate as an indicator of maxillary growth. *International Journal of Oral and Maxillofacial Surgery*, 39, 956–961.
17. Xu, X., Zheng, Q., Lu, D., Huang, N., Li, J., Li, S., Wang, Y. and Shi, B. (2012) Timing of palate repair affecting growth in complete unilateral cleft lip and palate. *Journal of Cranio-Maxillo-Facial Surgery,* 40, e358–e362.
18. Liao, Y.F., Cole, T.J. and Mars, M. (2006) Hard palate repair timing and facial growth in unilateral cleft lip and palate: a longitudinal study. *The Cleft Palate-Craniofacial Journal,* 43, 547–556.
19. Friede, H., Lohmander, A., Hagberg, C., Elander, A. and Lilja, J. (2006) Maxillary dental arch and occlusion in patients with unilateral cleft lip and palate treated with different delays in closure of the hard palate after early velar repair. *Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery,* 40, 261–266.
20. Bongaarts, C.A., Prahl-Andersen, B., Bronkhorst, E.M., Prahl, C., Ongkosuwito, E.M., Borstlap, W.A. and Kuijpers-Jagtman, A.M. (2009) Infant orthopedics and facial growth in complete unilateral cleft lip and palate until six years of age (Dutchcleft). *The Cleft Palate-Craniofacial Journal,* 46, 654–663.
21. Acharya, P.N., Jones, S.P., Moles, D., Gill, D. and Hunt, N.P. (2010) A cephalometric study to investigate the skeletal relationships in patients with increasing severity of hypodontia. *The Angle Orthodontist,* 80, 511–518.
22. Endo, T., Ozoe, R., Yoshino, S. and Shimooka, S. (2006) Hypodontia patterns and variations in craniofacial morphology in Japanese orthodontic patients. *The Angle Orthodontist,* 76, 996–1003.
23. Sarnäs, K.V. and Rune, B. (1983) The facial profile in advanced hypodontia: a mixed longitudinal study of 141 children. *European Journal of Orthodontics,* 5, 133–143.
24. Antonarakis, G.S. and Fisher, D.M. (2015) Presurgical unilateral cleft lip anthropometrics and the presence of dental anomalies. *The Cleft Palate-Craniofacial Journal,* 52, 395–404.
25. Lai, L.H., Hui, B.K., Nguyen, P.D., Yee, K.S., Martz, M.G., Bradley, J.P. and Lee, J.C. (2015) Lateral incisor agenesis predicts maxillary hypoplasia and Le Fort I advancement surgery in cleft patients. *Plastic and Reconstructive Surgery,* 135, 142e–148e.
26. Oberoi, S., Chigurupati, R. and Vargervik, K. (2008) Morphologic and management characteristics of individuals with unilateral cleft lip and palate who required maxillary advancement. *The Cleft Palate-Craniofacial Journal,* 45, 42–49.
27. Meazzini, M.C., Capello, A.V., Ventrini, F., Autelitano, L., Morabito, A., Garattini, G. and Brusati, R. (2015) Long-term follow-up of UCLP patients: surgical and orthodontic burden of care during growth and final orthognathic surgery need. *The Cleft Palate-Craniofacial Journal,* 52, 688–697.
28. Lee, J.C., Slack, G.C., Walker, R., Graves, L., Yen, S., Woo, J., Ambaram, R., Martz, M.G., Kawamoto, H.K. Jr and Bradley, J.P. (2014) Maxillary hypoplasia in the cleft patient: contribution of orthodontic dental space closure to orthognathic surgery. *Plastic and Reconstructive Surgery,* 133, 355–361.
29. Doucet, J.C., Delestan, C., Montoya, P., Matei, L., Bigorre, M., Herlin, C., Baümler, C., Daures, J.P. and Captier, G. (2014) New neonatal classification of unilateral cleft lip and palate part 2: to predict permanent lateral incisor agenesis and maxillary growth. *The Cleft Palate-Craniofacial Journal,* 51, 533–539.
30. Heliövaara, A., et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate. 6. Dental arch relationships in 5 year-olds. *Journal of Plastic Surgery and Hand Surgery,* 51, 52–57.
31. Karsten, A., et al. (2020) Scandcleft randomized trials of primary surgery for unilateral cleft lip and palate: occlusion in 8-year-olds according to the Modified Huddart and Bodenham index. *European Journal of Orthodontics,* 42, 15–23.
32. Karsten, A., et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 7. Occlusion in 5 year-olds according to the Huddart and Bodenham index. *Journal of Plastic Surgery and Hand Surgery,* 51, 58–63.
33. Heliövaara, A., et al. (2020) Scandcleft randomized trials of primary surgery for unilateral cleft lip and palate. Dental arch relationships in 8 year-olds. *European Journal of Orthodontics,* 42, 1–7.
34. Küseler A, et al. (2020) Scandcleft trial of primary surgery for unilateral cleft lip and palate: craniofacial cephalometrics at 8 years. *European Journal of Orthodontics*, Dec 24. Online ahead of print.
35. Semb, G., et al. (2017) A Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 1. Planning and management. *Journal of Plastic Surgery and Hand Surgery,* 51, 2–13.
36. Rautio, J., et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate. 2. Surgical results. *Journal of Plastic Surgery and Hand Surgery,* 51, 14–20.

37. Wu, T.T., Ko, E.W., Chen, P.K. and Huang, C.S. (2013) Craniofacial characteristics in unilateral complete cleft lip and palate patients with congenitally missing teeth. *American Journal of Orthodontics and Dentofacial Orthopedics,* 144, 381–390.
38. Hardwicke, J., Chhabra, P. and Richard, B. (2015) Absent maxillary lateral incisor as evidence of poor midfacial growth in unilateral cleft lip and palate. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology,* 119, 392–395.
39. Meazzini, M.C., Donati, V., Garattini, G. and Brusati, R. (2008) Maxillary growth impairment in cleft lip and palate patients: a simplified approach in the search for a cause. *The Journal of Craniofacial Surgery,* 19, 1302–1307.
40. Seo, Y.J., Park, J.W., Kim, Y.H. and Baek, S.H. (2013) Associations between the risk of tooth agenesis and single-nucleotide polymorphisms of MSX1 and PAX9 genes in nonsyndromic cleft patients. *The Angle Orthodontist,* 83, 1036–1042.
41. Modesto, A., Moreno, L.M., Krahn, K., King, S. and Lidral, A.C. (2006) MSX1 and orofacial clefting with and without tooth agenesis. *Journal of Dental Research,* 85, 542–546.
42. Vieira, A.R., McHenry, T.G., Daack-Hirsch, S., Murray, J.C. and Marazita, M.L. (2008) A genome wide linkage scan for cleft lip and palate and dental anomalies. *American Journal of Medical Genetics. Part A,* 146A, 1406–1413.
43. Letra, A., et al. (2012) Interaction between IRF6 and TGFA genes contribute to the risk of nonsyndromic cleft lip/palate. *PLoS One,* 7, e45441.
44. Chu, E.Y., Tamasas, B., Fong, H., Foster, B.L., LaCourse, M.R., Tran, A.B., Martin, J.F., Schutte, B.C., Somerman, M.J. and Cox, T.C. (2016) Full spectrum of postnatal tooth phenotypes in a novel Irf6 cleft lip model. *Journal of Dental Research,* 95, 1265–1273.
45. Dentino, K.M., Peck, S. and Garib, D.G. (2012) Is missing maxillary lateral incisor in complete cleft lip and palate a product of genetics or local environment? *The Angle Orthodontist,* 82, 959–963.
46. Ogaard, B. and Krogstad, O. (1995) Craniofacial structure and soft tissue profile in patients with severe hypodontia. *American Journal of Orthodontics and Dentofacial Orthopedics,* 108, 472–477.