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Occlusal characteristics in modern humans with tooth agenesis

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Annahme der Masterthese

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Geme bestätigen wir Ihnen die Annahme Ihrer Masterthese mit dem Titel:

Occlusal characteristics in modern humans with tooth agenesis

Die Anmeldung zur Schlussprüfung ist mit sämtlichen Unterlagen bis zum 17. Februar 2024 im Direktionssekretariat der zmk bern bei Benedicta Gruber einzureichen.

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Freundliche Grüsse



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Occlusal characteristics in modern humans with tooth agenesis

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Abstract

Non-syndromic permanent tooth agenesis affects a significant proportion of the population, especially if third molars are considered. Although tooth agenesis has been linked to a smaller craniofacial size, reduced facial convexity and a shorter skeletal face, the occlusal characteristics of individuals with tooth agenesis remain largely unexplored. Therefore, this study investigated potential associations between tooth agenesis and occlusal traits in 402 modern individuals with permanent tooth agenesis and 404 matched individuals without tooth agenesis, not considering third molars. Dentoskeletal morphology was defined through anatomical landmarks on pre-treatment cephalometric radiographs. Multivariate regression models, adjusted for sex and age, showed that tooth agenesis was significantly associated with a reduced overjet, an increased interincisal angle, and shorter upper and lower dental arch lengths, but not with overbite. Moreover, apart from reduced tooth length and dentoalveolar effects, as the number of missing teeth increased the upper front teeth were progressively retruded according to the craniofacial complex and to the face. Thus, tooth agenesis has a substantial influence on dental and occlusal characteristics, as well as on the sagittal position and inclination of anterior teeth. These findings emphasize the necessity for personalized, multidisciplinary approaches in individuals with multiple agenesis to successfully meet treatment goals.

Keywords: tooth agenesis, dentition, dental occlusion, malocclusion, dental overbite, dental overjet

Introduction

Non syndromic tooth agenesis comprises a common congenital dental anomaly, evident in about 6.4% of the population,^{1,2} without considering the third molars. Racial background and sex have an impact on the prevalence of this dental anomaly, with females showing a higher risk compared to males.¹ Moreover, isolated agenesis of at least one third molar has been reported in 22.6% of the Caucasian population. Here, females are also more affected with a 14% higher prevalence of third molar agenesis compared to males, and the maxilla is more often affected than the mandible.³⁻⁵ Despite the differences in prevalence, recent reports did not detect any sexual differences in the patterns of tooth agenesis, when all teeth were investigated, including the third molars.⁶

Tooth agenesis is related to genetic or epigenetic factors that are also involved in overall craniofacial development.⁷⁻⁹ From an evolutionary viewpoint, it is argued that humans have experienced a reduction in teeth size and number as a response to a reduction in functional needs.^{10,11} This evolutionary mechanism appears to still be active in modern humans, influencing the number of teeth, craniofacial size, and craniofacial shape in a coordinated manner.¹²⁻¹⁴ Isolated third molar agenesis has also been associated to craniofacial size and shape, with the effects being more pronounced, compared to the agenesis of other teeth.^{13,15}

Phenotypically, individuals with tooth agenesis present a less convex craniofacial complex, as well as a shorter lower facial third. These morphological differences become more notable as the severity of tooth agenesis increases¹⁴ and are equally pronounced in males and females.^{14,15} More specifically, tooth agenesis has been shown to result in a more retruded

maxilla, protruded mandible, shorter anterior facial height, and a reduced skeletal profile convexity. The presence of such craniofacial differences between individuals with missing teeth and individuals with a full permanent dentition, allow for speculations regarding the presence of analogous effects on occlusal characteristics, such as overjet and overbite or the position of the incisors relative to the jaws and the face.

Indeed, meta-analytical data of five studies with high geographic variations, which could confound the prevalence of malocclusion as well as agenesis patterns, have shown a higher prevalence of tooth agenesis in CI III malocclusion, compared to CI I or CI II with an odds ratio of 2.15 (95% CI 0.78-5.89), without considering third molars.¹⁶ In agreement with this meta-analysis, a more recent study found a statistically significant association between Class III malocclusion and the prevalence of tooth agenesis (16.2% in Class III malocclusion compared to 2.2% in Class I and 3.6% in CI II malocclusion subgroups).¹⁷ Class II division 2 malocclusion type, which is characterized by reduced overjet, despite the Angle Class II dental relation, has also been associated with an increased prevalence of tooth agenesis.^{18,19} Other studies did not confirm these associations.^{20,21}

The aforementioned research findings could suggest a potential link between tooth agenesis and features of dental occlusion. However, all assessments based on the Angle classification - a somewhat ambiguous categorization that lacks a basis in biological principles.

The primary outcome of the present study was to investigate potential associations between tooth agenesis and occlusal traits in a large sample of modern humans, selected consecutively without considering any malocclusion traits. Furthermore, contrary to previous reports, third molars were also assessed, similarly to all other teeth in the dentition.

Material and methods

2.1 Ethical Approval

The protocol for this observational case control study was reviewed and granted by the Ethics Commission of the Canton of Bern, Switzerland (Project-ID: 2018-01340), and the Research Committee of the School of Dentistry, National and Kapodistrian University of Athens, Greece (Project-ID: 281, 9 February 2016). For reporting, the STROBE criteria were followed. Participants whose information was used in the study provided written informed consent.

2.2. Sample

This study is part of a larger project studying tooth agenesis characteristics and potential associations with the craniofacial form.^{5,6,12-15,24} The study population was derived from consecutive orthodontic patient records archived between 2002 and December 2017, at the following orthodontic clinics: (a) University of Bern, Switzerland; (b) National and Kapodistrian University of Athens, Greece; (c) two private practices in Athens and two in Thessaloniki, Greece; and (d) one private practice in Biel, Switzerland.

Inclusion criteria:

1. Permanent tooth agenesis (congenitally missing) including the third molars.
2. No systemic diseases, craniofacial malformations, syndromes, or any other anomalies affecting craniofacial morphology, as reported in the subjects' medical records.
3. European (White) ancestry.
4. Individuals older than 8 years of age and younger than 40 years of age.
5. Lateral cephalometric radiograph in maximal intercuspation of adequate clinical diagnostic quality and with a reference ruler at the mid-sagittal level.
6. Panoramic radiographs of adequate diagnostic quality.
7. No history of interventions known to influence craniofacial morphology, such as orthodontic treatment.

8. Absence of any other severe dental anomaly regarding tooth number, size, or form in any tooth except from third molars.
9. Individuals where the reason of the absence of any tooth was definite.

Panoramic radiographs obtained at an age older than 12 years were retrieved from all individuals younger than 12 years old at the time of the pre-treatment radiographs.^{25,26}

Data collection was performed by reviewing the medical and dental history, the clinical photographs and the radiographs of each individual. The TAC system was used to record the teeth agenesis patterns.^{5,27}

402 individuals with agenesis (238 females, 164 males; Median age 13.0 years, range: 8.0–38.3 years) including third molars, and 404 control individuals without tooth agenesis, apart from third molars, were included in the present study. The control individuals were matched to the initial agenesis sample for age (within 6 months), sex, and geographic origin.

The total sample size was 806 subjects. Thorough analyses of the patterns of tooth agenesis of a very similar group, excluding third molars,⁵ and those of third molars²⁴ have been published in previous reports.

2.3 Radiograph digitization and measured outcomes

All pre-treatment lateral cephalometric digital images were uploaded on Viewbox 4 software (dHAL software, Kifissia, Greece) for digitization and were scaled to real size, using a reference ruler depicted in the radiographs. One trained operator positioned twelve fixed skeletal and dental anatomical landmarks on each cephalometric image (Figure 1).

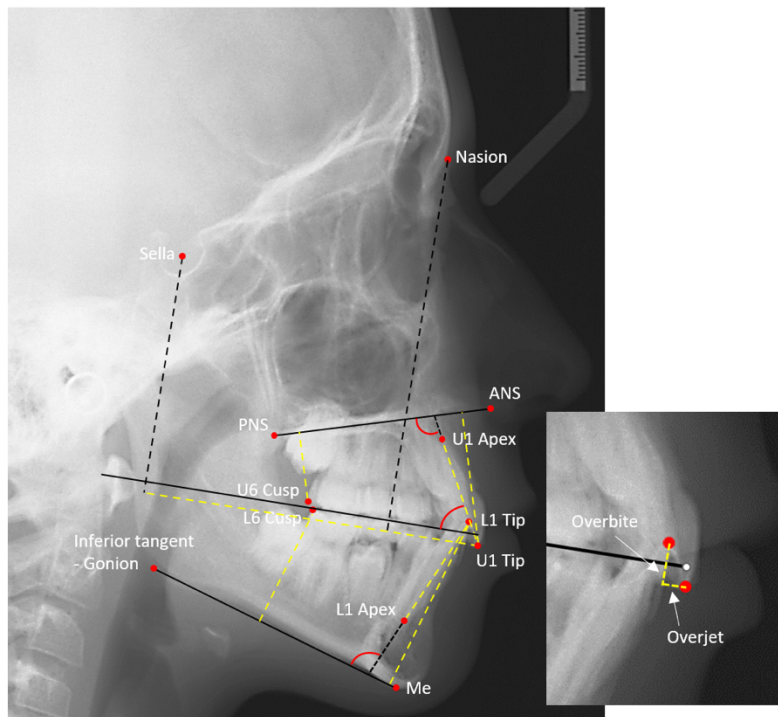


Figure 1. Cephalometric image depicting the twelve fixed landmarks (red circles), the planes (black lines), as well as the linear (yellow lines) and angular (red curves) measurements performed in the study.

Table 1. Definition of the study outcomes.

<i>Occlusal traits (primary outcomes)</i>	
Interincisal angle (°)	The inner angle measured between the long axis of U1 and L1.

Overjet (mm)	Distance of U1 to L1 along the functional occlusal plane.
Overbite (mm)	Distance of U1 to L1 along a line perpendicular to the functional occlusal plane.
Upper functional dental arch length (mm)	Distance of U1 tip to U6 point.
Lower functional dental arch length (mm)	Distance of L1 tip to L6 point.
<i>Dentoalveolar variables (secondary outcomes)</i>	
U1 to palatal plane (°)	The inner angle formed by the U1 and the palatal plane.
U1 to palatal plane (mm)	The vertical distance of U1 incisal tip to palatal plane.
U6 to palatal plane (mm)	The vertical distance of U6 point to palatal plane.
L1 to mand. plane (°)	The inner angle between the long axis of L1 and the mandibular plane.
L1 to mand. plane (mm)	The vertical distance of L1 incisal tip to mandibular plane.
L6 to mand. plane (mm)	The vertical distance of L6 point to mandibular plane.
<i>Dentoskeletal variables (secondary outcomes)</i>	
Sagittal position of U1 to craniofacial complex (mm)	The perpendicular distance of U1 incisal tip from a line passing through Sella and vertical to occlusal plane.
Vertical position of U1 to craniofacial complex (mm)	The perpendicular distance of U1 incisal tip from a line passing through Sella and parallel to occlusal plane.
Sagittal position of U1 to face (mm)	The perpendicular distance of U1 incisal tip from a line passing through Nasion and vertical to occlusal plane.
<i>Dental variables (secondary outcomes)</i>	
U1 length (mm)	The linear distance between the incisal tip and the root apex of the maxillary central incisor (following the root canal, if visible). The most anteriorly positioned lateral incisor was used in case of agenesis.
L1 length (mm)	The linear distance between the incisal tip and the root apex of the mandibular central incisor (following the root canal, if visible). The most anteriorly positioned lateral incisor was used in case of agenesis.

2.4 Statistical analysis

The statistical analysis was conducted with IBM SPSS Statistics for Windows (Version 29.0. Armonk, NY: IBM Corp). A two-sided significance test was carried out at an alpha level of 0.05. A Bonferroni correction was applied on the level of statistical significance, were applicable. Data were tested for normality through the Kolmogorov-Smirnov test and visualization of data distribution histograms, Q-Q and P-P plots and no important deviations were detected. Equality of variances was checked through Levene's test and equality of covariance matrices through Box's test. No significant assumption test violations were noticed, and therefore, following preliminary and exploratory testing, four multivariate regression models were applied to the data (general linear models) to test for the effect of number of missing teeth (including third molars). All models were adjusted for the effects of sex (fixed factor) and age (covariate) factors. The decision to create separate models for the aforementioned dependent variables was chosen to minimize the risk of false positive effects. Observed * predicted * standardized residual plots were visualized to verify the suitability of the applied

models and revealed a good fit across the whole range of data in all cases. Landmark identification was repeated in 30 randomly selected radiographs, one month after the initial process, to test for the intra-operator error in the measured variables. A Wilcoxon signed rank-test was used to assess systematic error and the average and standard deviation of the absolute differences between repeated measurements was indicative of the random error.

Results

There was no systematic error in any of the measured variables ($p > 0.003$, Bonferroni correction applied) and the random error was also negligible. The highest random error was detected for interincisal angle at $0.91 \pm 0.93^\circ$, which is considered acceptable.

Association of occlusal traits to number of missing teeth: after controlling for age and sex, multivariate testing showed that the number of missing teeth had a significant effect on occlusal traits ($P < 0.001$) (Table 2).

Table 2. Results of multivariate regression analysis testing the effects of age, number of missing teeth, and sex on occlusal traits, dentoalveolar, dentoskeletal, and dental variables (n = 331 males and 477 females).

<i>Dependent variables: Occlusal traits (Overjet, Overbite, Interincisal angle, Upper dental arch length, Lower dental arch length)</i>		
Factors	Partial Eta Squared	P-Value*
Age	0.034	<0.001
Number of missing teeth	0.064	<0.001
Sex	0.045	<0.001
<i>Dependent variables: Dentoalveolar variables (U1 to palatal plane distance, U6 to palatal plane distance, L1 to mandibular plane angle and distance, L6 to mandibular plane distance)</i>		
Factors	Partial Eta Squared	P-Value*
Age	0.167	<0.001
Number of missing teeth	0.097	<0.001
Sex	0.095	<0.001
<i>Dependent variables: Dentoskeletal variables (sagittal and vertical position of U1 to craniofacial complex, sagittal position of U1 to face)</i>		
Factors	Partial Eta Squared	P-Value*
Age	0.187	<0.001
Number of missing teeth	0.075	<0.001
Sex	0.150	<0.001
<i>Dependent variables: Dental variables (U1 length, L1 length)</i>		
Factors	Partial Eta Squared	P-Value*
Age	0.022	<0.001
Number of missing teeth	0.041	<0.001
Sex	0.074	<0.001

*Wilks' Lambda Test

Table 3. Parameter estimates indicating the effect of tested factors on each occlusal trait variable (dependent variable).

Dependent Variable	Parameter	β coefficient	95% Confidence Interval		P-value
			Lower Bound	Upper Bound	
Overjet	Intercept	5.10	4.49	5.71	<0.001
	Age	-0.02	-0.05	0.01	0.134
	Number of missing teeth	-0.10	-0.16	-0.04	0.001
	Female (Ref.: male)	0.07	-0.33	0.47	0.727
Overbite	Intercept	2.63	2.10	3.17	<0.001
	Age	0.02	0.01	0.05	0.080
	Number of missing teeth	0.03	-0.02	0.08	0.256
	Female (Ref.: male)	-0.25	-0.59	0.10	0.161
Interincisal angle	Intercept	123.93	121.19	126.68	<0.001
	Age	0.10	-0.04	0.23	0.151
	Number of missing teeth	0.80	0.54	1.07	<0.001
	Female (Ref.: male)	0.59	-1.20	2.37	0.519
Dental arch length upper	Intercept	40.28	39.24	41.31	<0.001
	Age	0.08	0.03	0.13	0.002
	Number of missing teeth	-0.32	-0.42	-0.22	<0.001
	Female (Ref.: male)	-1.70	-2.37	-1.03	<0.001
Dental arch length lower	Intercept	34.95	33.90	35.99	<0.001
	Age	0.10	0.05	0.15	<0.001
	Number of missing teeth	-0.27	-0.37	-0.16	<0.001
	Female (Ref.: male)	-1.49	-2.17	-0.81	<0.001

The number of missing teeth showed a significant association with overjet, interincisal angle, upper arch length, and lower arch length ($P \leq 0.001$). Specifically, as the number of missing teeth increased, overjet decreased by 0.10 mm per tooth unit (95% CI = -0.16 to -0.04), while the interincisal angle increased by 0.80° per tooth unit (95% CI = 0.54 to 1.07). Additionally, both upper and lower dental arch lengths decreased by 0.32 and 0.27 mm per tooth unit, respectively, with an increasing number of missing teeth (95% CI = -0.42 to -0.22; -0.37 to -0.16). However, the association between the number of missing teeth and overbite was not statistically significant ($P > 0.05$) (Table 3)

Table 4. Marginal estimates for occlusal traits in the different sex groups.

Dependent Variable	Sex	Mean ^a	Std. Error	95% Confidence Interval		P-value
				Lower Bound	Upper Bound	
Overjet	F	4.5	0.1	4.3	4.8	0.727
	M	4.5	0.2	4.1	4.8	
Overbite	F	2.9	0.1	2.7	3.1	0.161
	M	3.1	0.1	2.9	3.4	
Interincisal angle	F	128.3	0.6	127.1	129.4	0.519
	M	127.7	0.7	126.3	129.1	
Dental arch length upper	F	39.2	0.2	38.8	39.7	<0.001
	M	40.9	0.3	40.4	41.4	
Dental arch length lower	F	34.7	0.2	34.3	35.1	<0.001
	M	36.2	0.3	35.7	36.7	

^aCovariates appearing in the model are evaluated at the following values: Age = 18.2 years, Number of missing teeth = 2.47.

Association of dentoalveolar variables to number of missing teeth:

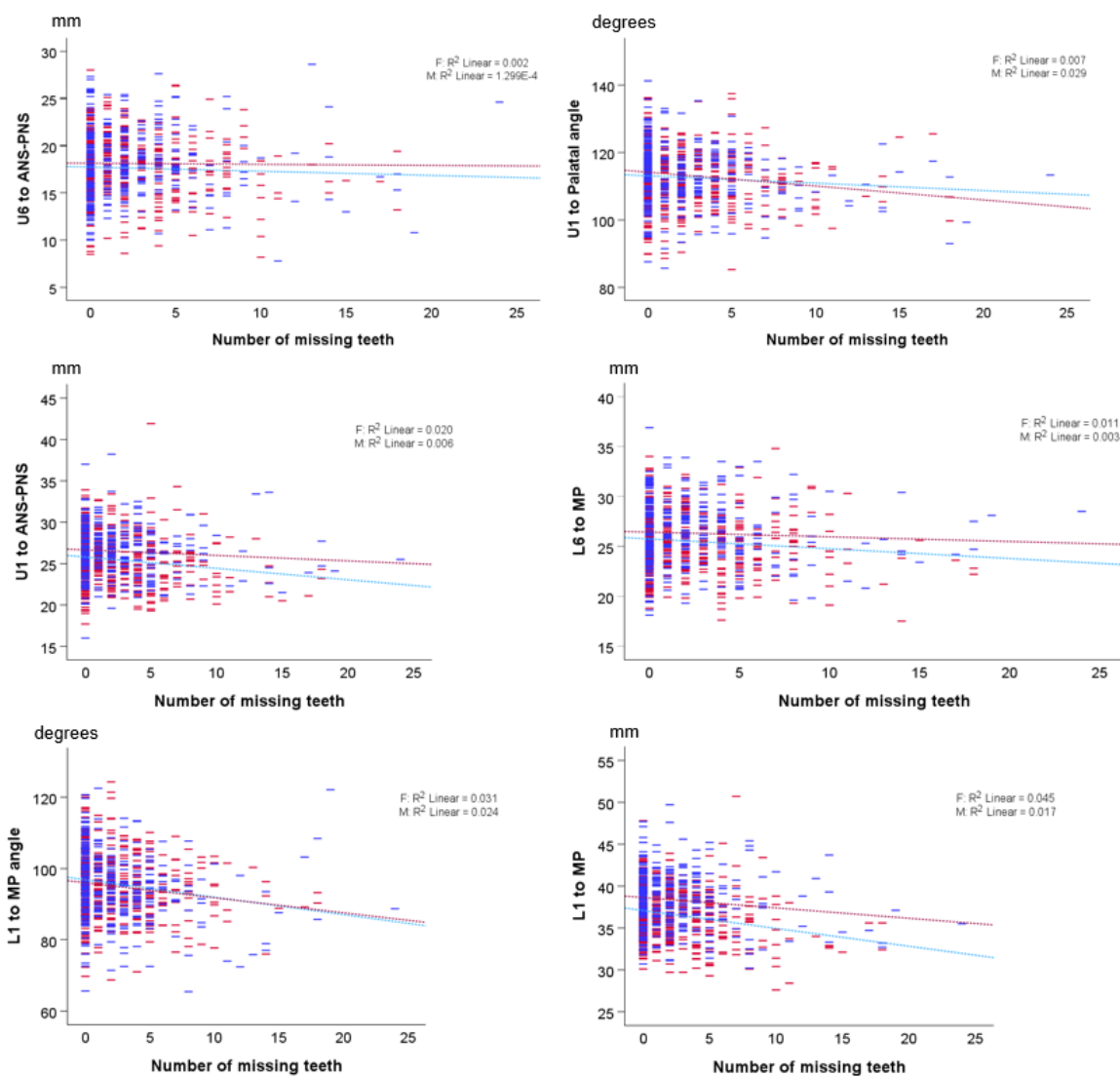


Figure 2. Scatter plots showing the association of the six dentoalveolar variables to the number of missing teeth in males (blue) and females (red). The dashed lines represent the linear regression lines fitted to each group.

The number of missing teeth shows a significant association with all tested dentoalveolar variables ($P < 0.003$). Parameter testing showed that U1 to palatal plane angle decreases by 0.29° for every tooth that is missing (95% CI = -0.46 to -0.11) and U1 to palatal plane distance decreases by 0.14 mm per missing tooth (95% CI = -0.20 to -0.08). Additionally, U6 to palatal plane distance decreases by 0.08 mm (95% CI = -0.15 to -0.01), and L6 to mandibular plane distance decreases by 0.12 mm for every missing tooth (95% CI = -0.18 to -0.06). Finally, L1 to mandibular plane angle and L1 to mandibular plane distance decrease by 0.49° and 0.22 mm per missing tooth, respectively (95% CI = -0.68 to -0.30; -0.28 to -0.16).

Association of dentoskeletal variables to number of missing teeth

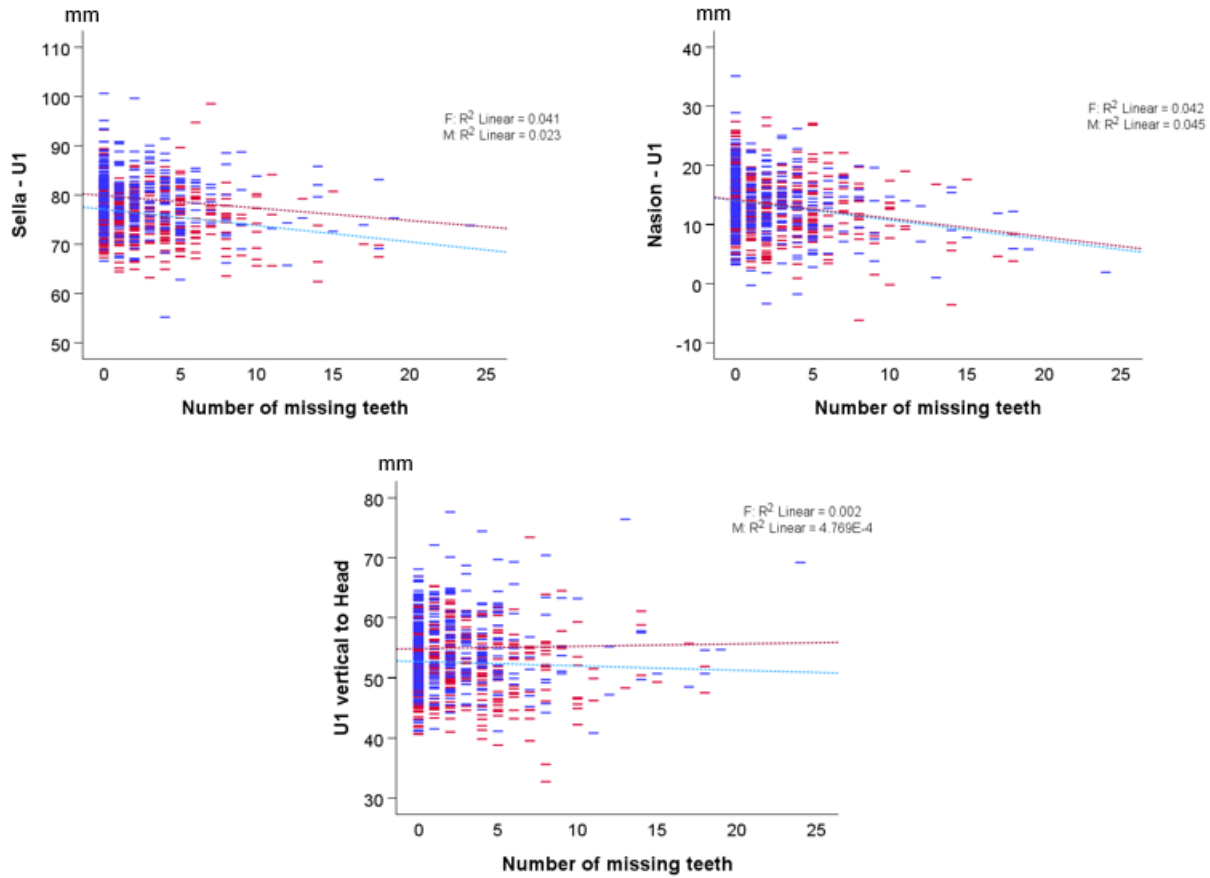


Figure 3. Scatter plots showing the association of the three dentoskeletal variables to the number of missing teeth in males (blue) and females (red). The dashed lines represent the linear regression lines fitted to each group.

The number of missing teeth showed a significant association with the sagittal position of U1 to craniofacial complex and to the face ($P < 0.001$). Specifically, as the number of missing teeth increased, the sagittal position of U1 to craniofacial complex decreased by 0.35 mm per missing tooth (95% CI = -0.45 to -0.24) and the sagittal position of U1 to the face decreased by 0.32 mm per missing tooth (95% CI = -0.43 to -0.22). There was no association between the number of missing teeth and the vertical position of U1 to craniofacial complex ($P > 0.05$).

Association of dental variables to number of missing teeth

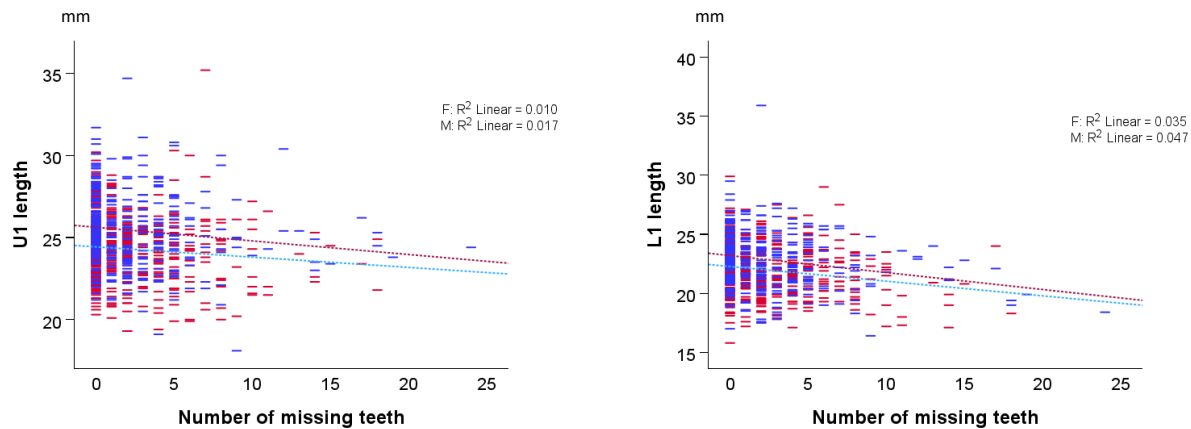


Figure 4. Scatter plots showing the association of both dental variables to the number of missing teeth per sexual group. The dashed lines represent the linear regression lines fitted to each group.

Discussion

The present study investigated the association between non-syndromic tooth agenesis and occlusal traits, dentoalveolar variables, dentoskeletal characteristics, as well as anterior tooth length in a large sample. Tooth agenesis is the most prevalent congenital dental anomaly in the population, impacting a little less than one-third of individuals, when third molars are taken into consideration.^{16,28} In this study, the third molars were included in the analyses, as third molar agenesis relates to the agenesis of other teeth²⁴ and also has a more profound impact on human craniofacial morphology, than the agenesis of other teeth.^{13,15}

The results show that the number of missing teeth is significantly associated with various occlusal traits except overbite. Similarly, the number of missing teeth was also associated to the corresponding sagittal, dentoalveolar, and dentoskeletal variables examined in this study. Specifically, an increased number of missing teeth was linked to a reduction in the upper incisor to palatal plane angle and the lower incisor to mandibular plane angle. Additionally, a more retruded sagittal position of the upper incisors was observed relative to both the craniofacial complex and the anterior facial structures. These findings are supported by recent reports regarding the interincisal angle, the overjet, and the incisor inclinations in individuals with maxillary lateral incisor agenesis.²⁹ Hence, tooth agenesis appears to affect the sagittal position of the incisors, and subsequently impacts sagittal occlusal traits, with potential impact on facial esthetics.³⁰⁻³²

In the vertical dimension, the upper and lower incisors and first molars showed significant reduction to their respective skeletal bases as the number of missing teeth increased. A reduction in the vertical distance of the upper central incisor from the palatal plane has been reported in the literature in adults with maxillary lateral incisors agenesis.³³ A reduction in the dentoalveolar and dentoskeletal linear variables might be attributed to the effects of tooth agenesis on craniofacial morphology, namely the smaller facial size and the shorter anterior facial height.^{12-15,34}

Sexual dimorphism was investigated in all multivariate models and its effects were statistically significant. However, post-hoc analysis revealed that both sexes were similarly affected by tooth agenesis. The vertical position of U1 to palatal plane, the vertical distance of L6 to mandibular plane as well as the sagittal and vertical distances of U1 to the craniofacial complex were also reduced in females, which was expected due to the smaller craniofacial size compared to males.^{12,35} Thus, despite the potential difficulties associated with evaluating certain dental parameters on cephalometric radiographs, mainly due to the overlapping of various anatomical structures in the apical region, the results affirmed the precision of the measurements.

As the number of missing teeth increased, the vertical position of the upper and lower incisors relative to the palatal plane or mandibular plane, as well as the inclination of the upper incisors to the palatal plane, decreased. This suggests that tooth agenesis can have a negative impact on dental and dentofacial aesthetics, as well as on smile attractiveness, not only due to missing teeth per se, but also through the effects on incisor position and angulation.³⁶⁻³⁸ For instance, the sagittal position of the upper incisor in relation to the face is strongly related to upper lip position,³⁹ and thus an increased retral angulation of the upper incisors will probably lead to a more retro positioned upper lip and affecting facial and dental aesthetics⁴⁰

The argument that the dental effects exceed the skeletal effects is also supported by the association of the tested variables with the number of missing third molars, investigated on a subsample including exclusively individuals with all other teeth present (females: 237, males: 167). These analyses showed that after controlling for age and sex, the number of missing third molars did not have a significant effect on occlusal traits ($P = 0.215$), as well as on dentoalveolar variables ($P = 0.285$). When considering that the third molar agenesis has a more profound impact on craniofacial morphology than the agenesis of other teeth,¹⁵ along with the present findings, it becomes evident that the detected impact of tooth agenesis on occlusal traits can be attributed partially to localized dental effects. These might occur as part of a dental compensation mechanism in response to missing teeth within the dental arches.

The robustness of the present results is strengthened by the large sample size and the inclusion of third molars, which are often overlooked in similar studies, despite their significant association to tooth agenesis and craniofacial morphology.^{13,15,24} Additionally, The study population consisted of well documented individuals over a certain period of time, enhancing the diagnostic ability and reducing the chances of misdiagnosis. However, the sample population was restricted to individuals with white-European ancestry, limiting the generalizability of the findings to other populations.¹⁶ Also, the analyzed lateral cephalometric radiographs provide valuable information, but have inherent limitations in capturing three-dimensional craniofacial features.⁴⁰

Conclusion

The outcomes of this study suggest that after controlling for age and sex, tooth agenesis has a significant impact on various dental and occlusal traits. Tooth agenesis also had a notable influence on sagittal dentoalveolar and dentoskeletal variables, resulting in a more retruded sagittal position and reduced labial inclination of the anterior teeth. Addressing these challenges is particularly crucial when treating orthodontic patients with multiple teeth agenesis, highlighting the need for personalized, multidisciplinary treatment approaches for such individuals.

The observed associations contribute to our understanding of the broader implications of tooth agenesis, which extends its influence to encompass dental and occlusal features.

Conflicts of interest

None.

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