Clin Oral Invest (2010) 14:467–477
DOI 10.1007/s00784-009-0308-y

ORIGINAL ARTICLE

Dentofacial characteristics of patients with hypodontia

Marijn Créton · Marco S. Cune · Cornelis de Putter · Jan M. Ruijter · Anne Marie Kuijpers-Jagtman

Received: 10 March 2009 / Accepted: 12 June 2009 / Published online: 10 July 2009

Abstract This study aims to identify distinctive dentofacial characteristics of hypodontia patients. For this purpose, 189 young hypodontia patients (cases) were divided into subgroups, based on criteria from literature. Normalised differences between cases and controls were calculated for various parameters of dentofacial form. Subsequently, cluster analysis was applied to disclose subsets of hypodontia patients with distinctive dentofacial features. The ANB angle, interincisal angle and lower anterior face height were consistently significantly different amongst the subsets. Four clusters of patients with an increasing number of missing teeth and distinctive dentofacial characteristics could be identified. Patients in cluster 1 display a high-angle facial pattern. Patients in clusters 2 and 3 exhibit markable dentoalveolar characteristics (a relatively small and a large interincisal angle, respectively). Patients in cluster 4 exhibited notable sagittal–skeletal discriminative features predominantly because of a retrognathic maxilla. The smallest nasolabial angle and lower anterior face height were seen in this cluster. It is concluded that the anterior–posterior relationship between the jaws, the interincisal angle and the lower anterior face height are discriminative parameters of dentofacial form in hypodontia patients. Patients with hypodontia can be clustered in four groups, each with distinctive vertical–skeletal, dentoalveolar and sagittal–skeletal characteristics. This categorisation of patients with hypodontia into meaningful groups may be useful for treatment planning, interdisciplinary communication and as a means of identifying groups of patients that qualify for reimbursement of costs. Other dental factors should be appreciated as well during restorative clinical decision making in patients with hypodontia.

Keywords Hypodontia · Congenitally missing teeth · Agenesis · Cephalometry · Oligodontia

M. Créton (✉) · M. S. Cune · C. de Putter
Department of Oral–Maxillofacial Surgery, Prosthodontics and Special Dental Care, University Medical Centre Utrecht, P.O. Box 85.060, 3508 AB Utrecht, The Netherlands
e-mail: mcreton@umcutrecht.nl

J. M. Ruijter
Department of Anatomy and Embryology, Academic Medical Center, Amsterdam, The Netherlands

A. M. Kuijpers-Jagtman
Department of Orthodontics and Oral Biology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Introduction

Hypodontia, the congenital absence of one or more permanent teeth, is the most common developmental anomaly in man. It has a prevalence of 5.5% in Europeans, with a preference for women compared to men (1.37:1) [25]. The presentation of severe hypodontia is quite heterogeneous and identical patterns of tooth agenesis are rare when the whole dentition is considered [8]. Tooth size discrepancy and variations in tooth shape are also common findings in severe hypodontia [30]. They constitute additional factors that may complicate orthodontic and restorative decision making. In addition, dentofacial aspects must be taken into account as well.

One could assume a relation between numerical aberrations of permanent teeth and craniofacial development and morphology on several theoretical grounds [2]. There is increasing understanding with respect to the molecular mechanisms during cell and tissues interactions. Some homeobox genes, amongst which the MSX1 gene, bear relevance to the process of both tooth and craniofacial morphogenesis [33, 34]. Recently, a new gene has been identified that, when mutated, causes severe hypodontia, short stature and increased bone density (LTBP3) [22]. It can be hypothesised that dysfunction of such genes may hamper the development of teeth as well as craniofacial structures. In addition, gene mutations can predispose for specific patterns of agenesis and more or less characteristic patterns of absent teeth have been described in patients with severe hypodontia [1, 17]. For example, mutation of the PAX9 gene has been associated with agenesis of posterior teeth [31]. Furthermore, a reduced lower anterior face height could be the result of decreased posterior occlusal support. Finally, completion of crown formation and root development has been considered to be of importance for development of the alveolar process [20]. Hence, tooth agenesis could result in regions with reduced alveolar ridge dimensions.

Several authors investigated whether or not subgroups of hypodontia patients differ on cephalometric measures of dentofacial form or differ from non-hypodontia patients [1, 2, 6, 7, 12, 13, 19, 21, 23, 28, 29, 32, 36, 38]. Grouping of patients was performed on the basis of:

- The location of the missing teeth, e.g. posterior, anterior or anterior/posterior missing teeth [2, 12, 38]. Groups of anterior missing teeth consisted of missing incisors [2] or missing incisors and cuspids [12]. Subdivision in uni- or bilateral anterior as well as uni- or bilateral posterior missing teeth were made [38].
- The jaw in which the teeth are missing, e.g. in the mandible, in the maxilla or both in the mandible and in the maxilla [32]
- The number of missing teeth, e.g. mild (two to five missing teeth), moderate (six to nine missing teeth) or severe (ten or more missing teeth) [2, 12, 23] or five to 12 compared to 13 to 21 missing teeth [21]
- Severe hypodontia associated or not associated with a syndrome, e.g. severe hypodontia (six or more teeth missing) compared to severe hypodontia associated with hypohidrotic ectodermal dysplasia [6]
- The number of missing tooth types (incisors, canines, premolars and molars) [7]
- On the distinction between hypodontia and oligodontia by observation of typically and atypically missing teeth [19]

It is hard to compare these, mostly explorative studies with each other in detail. Different anatomical landmarks, reference planes, angles and distances were used. Patient populations from various racial background and inclusion of cases with different degrees of hypodontia add to the problem. Control groups were occasionally rather small, cases and controls were not always age and gender matched or reference values for adolescents were presumed valid for older patients as well because reference values for adults were not available [2, 12, 38]. An additional problem with previous studies is that preconceived assumptions regarding factors that the authors thought to be of influence on dentofacial form were used to define subgroups of patients. In such an explorative approach, determinants of dentofacial form may be overlooked and the importance of co-existing determining factors may never be fully appreciated. In a more objective approach, preconceived assumptions for grouping of patients should not form the basis for analysis but grouping should result from statistical analysis. So the question is: Can groups of patients who share skeletal features be identified by statistical analysis of the data? Cluster analysis is a useful statistical tool to partition data into subsets (called *clusters*) of subjects who share common traits, i.e. dentofacial characteristics, so that subjects from the same cluster are more similar to each other than subjects from different clusters.

For treatment planning, interdisciplinary communication and as a means of identifying groups of patients that qualify for reimbursement of costs, a useful characterisation of patients with hypodontia is desirable. It should reflect both patterns of absent teeth and skeletal features. The present investigation focuses on the latter one. The purpose of the study is to compare cephalometric measures amongst hypodontia patients with the aim to identify and characterise groups of hypodontia patients that represent distinctive dentofacial features by means of cluster analysis.

Materials and methods

Subjects

Lateral cephalograms of 189 patients (76 boys, 113 girls), who were classified as having ‘hypodontia’, ‘oligodontia’ or ‘tooth agenesis’, were selected from the databases of the Department of Orthodontics and Oral Biology of the Radboud University Nijmegen Medical Center, Nijmegen, the Center for Special Dental Care of the University Medical Center Utrecht, various orthodontic practices and other centres for special dental care in The Netherlands. The mean age at which the cephalograms were taken was 12.1 years (range 7.0–16.9; standard deviation (SD) 2.1) with on average 5.1 missing teeth (range 1–22; SD 4.8).

The following inclusion criteria were applied:

- No previous orthodontic treatment
- Maximum 16 years of age
- Caucasian origin
- Hypodontia is not part of a diagnosed syndrome

– Good quality lateral cephalogram present
– Missing tooth type could be confirmed

The pre-treatment orthodontic records were examined. The number of missing teeth and the tooth type were verified from panoramic radiographs or intra-oral photographs. Hypoplastic and/or radiographically apparent, but not (yet) erupted permanent teeth, were considered as being 'present'. The Fédération Dentaire Internationale tooth numbering system was used [24].

Methods

Lateral cephalometric radiographs were obtained in centric occlusion with the patient positioned in a cephalostat and oriented to the Frankfurt horizontal plane. Analogue radiographs were scanned on a 16-bit scanner (Epson Expression 10000xl, Seiko Epson, Nagano, Japan). All cephalograms were digitised by one observer using a commercially available computer programme for digital cephalometric analysis (Viewbox®, dHAL orthodontic software, Athens, Greece). To assess the intra-observer measurement error, cephalograms of 20 randomly selected patients were digitised twice by the same observer with a time interval of 1 week.

Figure 1 and Table 1 show 18 anatomical landmarks that were identified. Hard and soft tissue reference lines were constructed. Because the radiographs originated from different clinical practices and X-ray devices were replaced over time, reliable magnification factors were not available for all radiographs. Therefore, linear measurements were used for the calculation of ratios only. Consequently, 12 cephalometric angles and ratios were calculated, involving sagittal–skeletal, vertical–skeletal, dentoalveolar and soft tissue measurements for dentofacial form (Fig. 2).

Age- and sex-matched reference values were obtained from a non-treated orthodontic population of skeletally normally developed children as described by Riolo et al. [27], with the exception of the reference value for the nasolabial angle [3]. Normalised differences per subject per parameter were calculated (the difference between the measured and the reference value, divided by the standard deviation of the reference value). The resulting value indicates how many standard deviations an observation is above or below its reference value.

Identification of subgroups and statistical analysis

Dental factors thought to be of influence on cephalometric variables were obtained from previous studies. Subgroups were constructed on the basis of:

– The number of missing teeth (1–5, 6–9, >9)
– The number of missing tooth types (incisors, canines, premolars and molars)

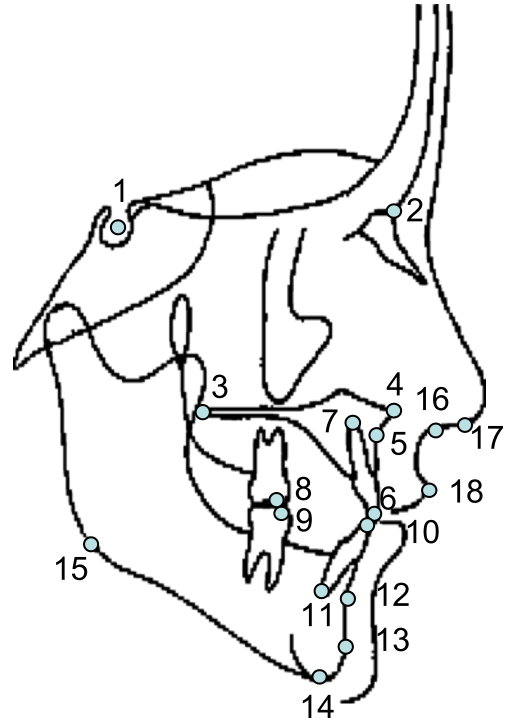

Fig. 1 Anatomical landmarks on the profile cephalometric radiographs. The description of the landmarks is given in Table 1

– The location of the missing teeth (posterior, anterior, both regions). Anterior teeth were defined as central and lateral incisors, as well as canines
– The jaw in which the teeth were missing (mandible, maxilla, both jaws)
– Left/right symmetry with respect to agenesis of teeth (symmetric, for example agenesis of the 12 and 22, asymmetric, for example agenesis of the 12 and 25)
– Symmetry or asymmetry in the upper and opposing lower quadrants, both left and right (symmetric, for example agenesis of the 25 and 35, asymmetric, for example agenesis of the 12 and 45)

Differences in cephalometric normalised values between the groups were tested univariately by means of one-way analysis of variance where appropriate. A significance level of 0.005 was set to compensate for multiple testing. Post hoc tests (Student–Newman–Keuls procedure) were performed to identify homogeneous subsets. These are presented as contrasts.

Cephalometric measures that proved consistently statistically significant in the univariate analyses were introduced in the SPSS TwoStep cluster method to disclose subpopulations of patients with distinctive dentofacial features. Subsequently, like in the univariate analysis, the cephalometric measures were compared amongst the identified clusters (Table 3). A standard

Table 1 Anatomical landmarks

Hard tissues (as seen in norma lateralis)
Sella: centre of the sella turcica (1) [27]
Nasion: most anterior limit of the frontonasal suture (2) [4]
Posterior nasal spine: most posterior point in the sagittal plane on the bony hard palate (3) [27]
Anterior nasal spine: tip of the anterior nasal spine (4) [14]
A-point: deepest point on the contour of the premaxilla (5) [11]
Incision superius: incisal tip of the most anterior maxillary central incisor (6) [27]
Upper incisor apex: root apex of the most prominent upper incisor (7) [3]
Upper molar mesial cusp tip: anterior cusp tip of the maxillary first molar (8)
Lower molar mesial cusp tip: anterior cusp tip of the mandibular first molar (9)
Incision inferior: incisal tip of the most anterior medial mandibular central incisor (10) [27]
Lower incisor apex: root apex of the most prominent lower incisor (11) [3]
B-point: deepest point on the contour of the mandible (12)[11]
Pogonion: most anterior point on the symphysis of the mandible (13) [14]
Menton: most inferior point on the symphysis of the mandible (14)
Gonion: midpoint of the angle of the mandible (15)
Soft tissues (as seen in norma lateralis)
Subnasale: point located at the junction between the lower border of the nose and the beginning of the upper lip at the mid-sagittal plane (16) [3]
Subpronasale: point where the columella tangent through subnasale touches the columella (17)
Labrale superius: most prominent point on the vermilion border of the lower lip in the mid-sagittal plane (18) [3]

statistical programme was used (SPSS version 11.5, SPSS Inc, Chicago, IL, USA). Systematic measurement errors were estimated by means of paired Student t tests and the random error of the method was quantified by means of Dahlberg's formula $Se2=\Sigma d2/2n$, where d is the difference between duplicate measurements and n is the number of double measurements [9, 15].

Results

Error of the method

The random error of the method varied between 0.3° and 0.9° for angles and 0.3% for the ratio ANS-Me/N-Me (ANSMEN). Paired t tests demonstrated no statistically significant intra-observer differences in any of the measurements.

Cephalometric analysis

The mean normalised differences (and their standard deviations) for cephalometric angles and ratios are presented for the various patient subgroups in Table 2. Differences in subpopulations with respect to symmetry between left and right side, as well as upper and lower jaw, proved hardly discriminative and are not presented here.

The anterior–posterior relationship between the jaws (ANB), the interincisal angle (INTERINC), the inclination of the mandibular incisor (ILIML) and anterior lower face height ratio (ANSMEN) were frequently discriminative amongst the various subgroups in the univariate analysis, regardless of the way the subgroups were defined (Table 2). When a statistically significant difference was present, patients who lacked both anterior and posterior teeth, patients with missing teeth in both jaws and patients with an increasing number of missing teeth and missing tooth types presented with the largest differences from their respective subgroups and from their reference values, suggesting that all differences between subgroups are based on similar grouping of these few patients.

Cluster analysis

Because the interincisal angle and the inclination of the lower incisor are strongly related, it was decided to include only angle ANB, the interincisal angle (INTERINC) and the lower anterior face height (ANSMEN) into the TwoStep cluster analysis. This resulted in four clusters of patients with distinctive dentofacial features, all with a substantial number of patients per cluster (Table 3). Table 4 shows the hypodontia features of the subject in these clusters.

Cluster 1— high-angle facial pattern

Cluster 1 was made up of 45 individuals, with an average of 2.6 missing teeth. Their vertical skeletal dimensions were markedly different from the reference values, as well as from the patients of the other three clusters. The group displayed characteristics as seen in high-angle patients.

Cluster 2— proclined lower incisors

Cluster 2 contained 61 individuals, with an average of 4.3 missing teeth. Of all four clusters, this subset most closely mimicked the cephalometric characteristics of the reference group, although there were minor differences with respect to their dentoalveolar features. A more retrusive mandible and a relatively small interincisal angle based upon increasing proclination of the lower incisors were observed.

Fig. 2 Definitions of the hard and soft tissue lines and ratios used in the cephalometric analysis [11, 16, 18, 26]

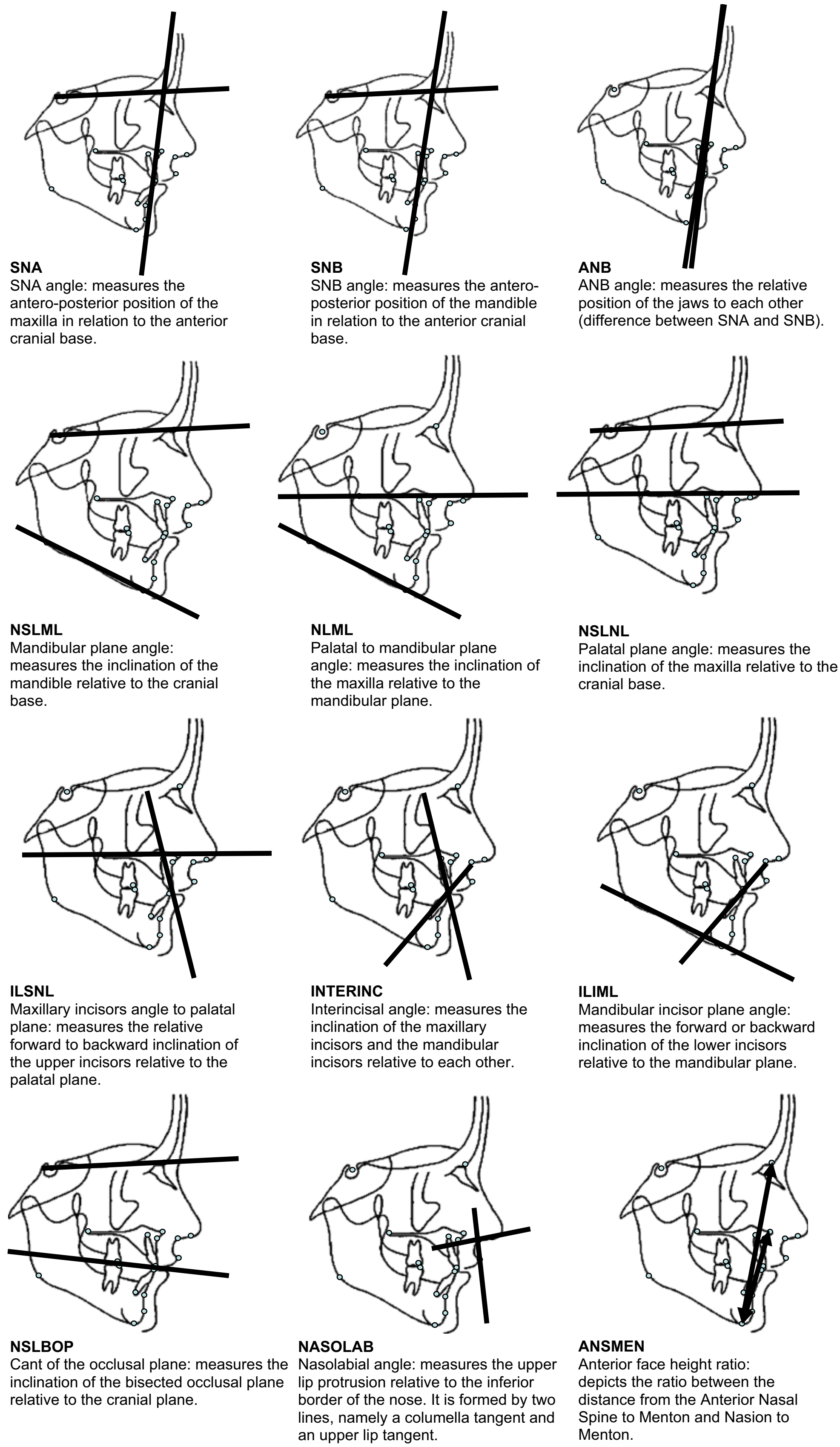

Table 2 One-way analysis of variance and determination of contrasts between subgroups of hypodontia patients

Location of missing teeth

	Posterior (a, n=82)		Anterior (b, n=39)		Posterior and anterior (c, n=68)		Result of one-way ANOVA and SNK comparison of groups	
	Mean	SD	Mean	SD	Mean	SD	p value	Contrasts
SNA	−0.10	1.28	−0.06	1.48	−0.66	1.20		
SNB	−0.19	1.23	0.24	1.10	−0.06	1.19		
ANB	0.14	1.44	−0.36	1.58	−0.93	1.45	0.000	a=b>c
NSLML	0.39	1.21	0.36	1.11	0.00	1.27		
NLML	0.62	1.18	0.39	0.98	0.23	1.17		
NSLNL	−0.51	1.44	−0.16	1.10	−0.55	1.35		
ILSNL	−0.26	1.44	−0.41	1.38	−0.66	1.41		
INTERINC	−0.33	1.33	0.18	0.98	0.54	1.21	0.000	c=b>a
ILIML	0.31	1.47	−0.23	1.04	−0.37	1.32		
NSLBOP	−0.13	1.35	0.01	1.29	−0.03	1.60		
NASOLAB	−0.05	1.24	−0.13	1.15	−0.26	1.22		
ANSMEN	0.05	0.58	−0.05	0.49	−0.14	0.59		

Number of missing teeth

	1–5 (a, n=119)		6–9 (b, n=37)		>9 (c, n=33)		Result of one-way ANOVA and SNK comparison of groups	
	Mean	SD	Mean	SD	Mean	SD	p value	Contrasts
SNA	−0.15	1.34	−0.37	1.34	−0.74	1.11		
SNB	−0.11	1.19	0.18	1.06	−0.11	1.33		
ANB	−0.02	1.50	−0.76	1.52	−1.05	1.37	0.000	a>b=c
NSLML	0.42	1.19	−0.01	0.98	−0.09	1.47		
NLML	0.62	1.10	0.19	1.03	0.04	1.32		
NSLNL	−0.46	1.35	−0.44	1.39	−0.42	1.33		
ILSNL	−0.36	1.35	−0.57	1.45	−0.57	1.64		
INTERINC	−0.25	1.16	0.62	1.34	0.70	1.20	0.000	c=b>a
ILIML	0.24	1.29	−0.50	1.34	−0.56	1.41	0.001	a>b=c
NSLBOP	−0.04	1.32	−0.31	1.20	0.08	1.96		
NASOLAB	−0.08	1.27	−0.03	1.17	−0.49	0.98		
ANSMEN	0.07	0.53	−0.11	0.55	−0.37	0.61	0.000	a=b>c

Jaw of the missing teeth

	Mandible (a, n=57)		Maxilla (b, n=37)		Mandible and maxilla (c, n=95)		Result of one-way ANOVA and SNK comparison of groups	
	Mean	SD	Mean	SD	Mean	SD	p value	Contrasts
SNA	−0.05	1.42	0.07	1.34	−0.58	1.18		
SNB	−0.24	1.28	0.28	1.25	−0.07	1.09		
ANB	0.31	1.29	−0.22	1.59	−0.79	1.52	0.000	a=b>c
NSLML	0.41	1.15	0.34	1.35	0.11	1.20		
NLML	0.72	0.98	0.45	1.18	0.25	1.20		
NSLNL	−0.60	1.32	−0.31	1.54	−0.42	1.28		
ILSNL	−0.27	1.35	−0.28	1.48	−0.59	1.44		
INTERINC	−0.51	1.25	−0.18	1.04	0.55	1.20	0.000	c>b=a
ILIML	0.50	1.23	0.18	1.12	−0.47	1.40	0.000	a=b>c
NSLBOP	−0.14	1.36	−0.08	1.37	−0.02	1.50		
NASOLAB	0.00	1.15	−0.26	1.53	−0.18	1.10		
ANSMEN	0.11	0.51	0.10	0.54	−0.18	0.59	0.002	a=b>c

Number of missing tooth types[a]

	1 (a, n=104)		2 (b, n=42)		3 (c, n=26)		4 (d, n=17)		Result of one-way ANOVA and SNK comparison of groups	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p value	Contrasts
SNA	−0.04	1.34	−0.69	1.33	−0.33	1.18	−0.80	0.99		
SNB	−0.05	1.19	−0.20	1.04	0.33	1.26	−0.31	1.36		
ANB	0.06	1.47	−0.74	1.55	−0.97	1.50	−0.94	1.32	0.001	a>b=d=c
NSLML	0.41	1.20	0.30	0.94	−0.32	1.18	−0.05	1.72		
NLML	0.62	1.11	0.32	1.03	−0.05	1.11	0.34	1.51		
NSLNL	−0.47	1.34	−0.11	1.30	−0.59	1.43	−0.97	1.25		
ILSNL	−0.31	1.37	−0.50	1.39	−0.43	1.36	−1.08	1.84		
INTERINC	−0.27	1.18	0.38	1.26	0.60	1.29	0.78	1.23	0.000	d=b=c>a
ILIML	0.24	1.31	−0.36	1.34	−0.44	1.52	−0.43	1.25		
NSLBOP	−0.10	1.30	0.15	1.21	−0.39	1.53	0.05	2.30		
NASOLAB	−0.12	1.25	0.06	1.24	−0.28	1.16	−0.56	0.87		
ANSMEN	0.06	0.52	−0.16	0.55	−0.13	0.67	−0.24	0.68		

Mean normalised differences with their standard deviations. All units are in degrees, with exception of the anterior face height ratio (ANSMEN). In each of the contrasts, the clusters are ranked from the highest to the lowest value

[a] Four teeth types are distinguished: incisors, cuspids, bicuspids and molars. Groups are subdivided on the basis of the missing number of tooth types

Cluster 3— retroclined upper and lower incisors

Fifty individuals were grouped in cluster 3 with an average of 6.4 absent teeth. Cluster 3 skeletally resembles cluster 2, but from a dental–alveolar perspective, there is a major difference: Their respective normalised values for the interincisal angle differed approximately 2 standard deviations. Subjects in cluster 3 exhibit the largest interincisal angle of all four clusters. A retrusive mandible and retroclined upper and lower incisors were seen.

Cluster 4— retrusive maxillary position

Cluster 4 contains 33 persons with the largest number of missing teeth (7.4 teeth on average). Patients in this group had discriminative sagittal–skeletal characteristics when compared both to reference values and to patients from the other three clusters. There was a relative retruded position of the maxilla compared to the mandible. This retrusive pattern was seen in combination with a small mandibular incisor plane angle, anterior face height ratio and nasolabial angle.

Discussion

Previous studies on craniofacial development and morphology in patients with (severe) hypodontia have produced quite conflicting results. Differences between (subgroups of) patients with hypodontia and controls that have been reported are a smaller more retrognathic maxilla [1, 12, 29, 32, 36, 37] and smaller mandibular length [19], whilst others specifically state that the mandible has a normal length [32]. Earlier studies showed a decreased gonial angle, both mandibular prognatism [12, 19, 21]. Mandibular retrognathism and a more acute chin angle have also been reported. A more counter clockwise rotated occlusal plane [6, 12] was reported as well as reduced upper and lower face height [2, 6, 19, 37]. The latter one was attributed to anterior rotation of the mandible and not the result of skeletal change [23]. Finally, increased frequency in skeletal deep- [10] and normal-bite cases [10, 38], obtuse/blunt nasolabial angle [5], incisor retroinclination [1, 2, 12, 19, 23] causing a larger interincisal angle [12, 19], and in contrast, maxillary protrusion in another study [38] were also mentioned. Confusingly, both anterior and posterior chin positions were observed [1, 19, 23] and both bimaxillary protrusion and bimaxillary retrognathia are seen [1, 38]. Others found only few and small differences in craniofacial features between cases and controls [7, 28, 29]. Some of the variation amongst all these findings is probably caused by different inclusion criteria and patient samples as well as different measurement techniques between the various studies.

In the present study, the more or less arbitrary subgrouping as proposed by others was applied to a single large dataset of hypodontia patients. Detailed cephalometric values of non-orthodontic normals for age groups until 16 years are not available for the Dutch population.

Table 3 One-way analysis of variance and determination of contrasts between the four clusters resulting from the two-step cluster analysis

TwoStep cluster analysis	Cluster 1 (a, *n*=45)		Cluster 2 (b, *n*=61)		Cluster 3 (c, *n*=50)		Cluster 4 (d, *n*=33)		Result of one-way ANOVA and SNK comparison of groups	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*p* value	Contrasts
SNA	0.51	1.37	−0.19	1.29	−0.45	0.94	**−1.32**	1.01	0.000	a>b=c>d
SNB	0.09	1.26	−0.31	1.20	−0.21	0.98	**0.46**	1.23		
ANB	0.72	1.40	0.15	0.84	−0.37	0.96	**−2.68**	0.92	0.000	a>b>c>d
NSLML	**0.54**	1.35	0.25	1.35	0.17	1.05	−0.06	0.96		
NLML	**1.19**	1.00	0.26	1.22	0.42	0.98	−0.26	0.87	0.000	a>c=b>d
NSLNL	**−1.26**	1.47	−0.14	0.97	−0.59	1.18	0.27	1.44	0.000	d=b>b=c>a[a]
ILSNL	−0.37	1.27	**0.02**	1.13	**−1.67**	1.21	0.49	1.16	0.000	d=b>b=a>c[b]
INTERINC	−0.65	0.87	**−0.63**	0.92	**1.38**	0.71	0.46	1.28	0.000	c>d>b=a
ILIML	0.43	1.04	**0.74**	1.18	**−0.78**	1.07	**−1.05**	1.30	0.000	b=a>c=d
NSLBOP	−0.15	1.49	−0.07	1.35	0.20	1.42	−0.36	1.49		
NASOLAB	0.00	1.38	−0.07	1.18	−0.11	1.11	**−0.52**	1.14		
ANSMEN	**0.66**	0.35	−0.30	0.33	−0.01	0.34	**−0.55**	0.54	0.000	a>c>b>d

Mean normalised differences with their standard deviations are given. All units are in degrees, with exception of the anterior face height ratio (ANSMEN). In each of the contrasts, the clusters are ranked from the highest to the lowest value

[a] Cluster b does not differ significantly from clusters d and c, but d and c are in different subsets

[b] Cluster b does not differ significantly from clusters d and a, but d and a are in different subsets

Table 4 Percentage of patients in whom a certain tooth is missing and the mean number of missing teeth per cluster

	Percentage of patients with missing teeth per tooth type																												Number of missing teeth		
Tooth	11	12	13	14	15	16	17	21	22	23	24	25	26	27	31	32	33	34	35	36	37	41	42	43	44	45	46	47	Mean	SD	Range
Cluster 1	0	27	7	7	20	0	7	0	18	4	9	22	0	7	2	4	2	2	51	0	4	2	0	2	0	58	0	4	2.6	2.6	1–15
Cluster 2	2	33	11	20	25	2	10	0	33	10	20	20	2	11	16	8	2	15	61	5	15	21	10	5	10	52	5	16	4.3	4.7	1–22
Cluster 3	0	52	22	28	54	8	22	0	50	28	36	44	8	14	24	14	0	16	62	8	18	20	16	4	12	56	8	20	6.4	4.6	1–18
Cluster 4	0	45	24	27	52	18	36	0	52	27	33	45	18	30	33	12	0	21	52	21	27	27	15	9	21	58	18	27	7.4	5.7	1–20

Therefore, cephalometric measures of subjects from a population of Caucasian, skeletally normal developed children, as described by Riolo et al. served as reference values [27]. Age- and sex-matched *normalised* differences between hypodontia patients and controls were calculated. The use of normalised differences has the advantage that it allows comparison of observations from different normal distributions, despite the fact that there might be differences in skeletal pattern between different populations.

It was observed that patients who lack both anterior and posterior teeth, patients with teeth missing in both jaws and patients with an increasing number of missing teeth and missing tooth types present with the largest cephalometric differences from the other subgroups. With respect to dentofacial form, these subgroups of hypodontia patients can be considered as 'more severe'. The anterior–posterior relationship between the mandible and the maxilla, the interincisal angle and lower face height are the most discriminative in the univariate analysis (Table 2). In general, a smaller ANB angle, a larger interincisal angle and decreasing vertical lower face height are associated with increasing severity of hypodontia. Hence, the population is skeletally different from the reference population but dental compensation is seen as well. The smaller ANB angle seems predominantly determined by a more retrusive maxilla than the reference values and not so much by the position of the mandible in univariate analysis. It appears that the relatively large interincisal angle in groups with 'severe hypodontia' has to be contributed not only to a retroclination of the lower incisors but also to that of the upper incisor, regardless of the subgrouping that is used. This is consistent with many other studies as described above. There is a decrease in lower anterior face height and mandibular plane angle with an increase in severity of hypodontia. However, this was not apparent in the subgrouping that used the number of missing tooth types as criterion. Others could also not confirm the clinical perception that the lower face height decreases with increased severity of hypodontia as reflected by the number of missing tooth types [7].

The hypodontia patients were subsequently clustered on the basis of the observed discriminative cephalometric measures. This is quite a different and possibly more clinically relevant and objective approach than that adopted by others, who subdivided patients on the basis of preconceived assumptions regarding the influence of dental factors on dentofacial form. The applied statistical clustering procedure is descriptive and can only be used to identify subgroups of patients with different patterns of dentofacial characteristics. However, the recognition of these subgroups opens an alee into further research into relations between different (groups of) dentofacial parameters and to the identification of common variables that affect them. So, the clustering can give novel insights into the development of certain dentofacial features in hypodontia patients. Four groups or clusters of hypodontia patients with distinctively different dentoskeletal features could be distinguished.

Cluster 1—high-angle facial pattern—appears different from the other three clusters and their controls with respect to vertical–skeletal characteristics and has the smallest number of missing teeth (2.6 on average). A relatively small angle between the cranial base and the palatal plane and, to a lesser degree, an enlarged mandibular plane angle were observed. The combination of these two features accounts for the mildly increased vertical lower face height and the relatively large palatal to mandibular plane angle. A small palatal to mandibular plane angle was seen by others in a group of hypodontia patients with a large number of missing teeth [7]. The tooth types that are missing in this group are amongst the ones most commonly missing in case of tooth agenesis. From a restorative point of view, this cluster appears the least complex of all clusters.

Although patients from cluster 2—proclined lower incisors—missed an average of 4.3 teeth, their skeletal features did not seem very different from their controls without absent teeth, but there were minor differences with respect to their dental–alveolar features. A relatively small interincisal angle is observed. The latter one is caused by an increased proclination of the lower incisors relative to the mandibular plane. The inclination of the upper incisors was not discriminative.

Cluster 3—retroclined upper and lower incisors—very much resembled cluster 2 from a skeletal perspective, but in contrast, a large interincisal angle was seen as has been reported frequently in association with hypodontia [2, 12, 19, 23]. This is mainly caused by a retroclination of the upper incisors and, to a lesser degree, to that of the lower incisors. Patients in this group missed on average two more teeth than patients from cluster 2 (6.4 on average). These additional missing teeth were usually located in the maxilla, most commonly the second bicuspids (Table 4).

Patients in cluster 4—retrusive maxillary position—are the most challenging from a restorative point of view because generally, a large number of teeth is missing (7.4 on average). Amongst these were teeth whose absence is rather uncommon, such as mandibular and maxillary first and second molars (Table 4) [25]. The most striking dentofacial features of patients in this cluster were their sagittal–skeletal characteristics. Compared to the controls, there was a marked retrusive position of the maxilla compared to the mandible. This is mainly because of a retrognathic maxilla. To a lesser degree, the mandible appeared to be prognathic. In addition, the smallest nasolabial angle and lower face height and largest retroclination of the lower incisors were frequently seen in patients that were clustered in this group. This population of patients needs complex interdisciplinary treatment, which may involve orthodontic treatment and orthognathic surgery and placement of dental implants as part of a comprehensive treatment plan. From both a skeletal and a dental point of view, patients in this cluster suffer from a severe dentoskeletal disorder.

The resulting clusters differ from each other with respect to the a priori variables. However, inspection of the “Contrasts” column of Table 3 learns that not all clusters have different values for those variables and that almost all other variables differ between two for more of the resulting clusters. Moreover, the resulting clusters do not overlap with any of the groupings applied in Table 2. This shows that the clustering based on variables that were selected because they show differences between groups based on hypodontia features can identify clusters of patients with different patterns of dentofacial characteristics.

Although the mean number of absent teeth differs amongst the four clusters that were identified in this study, patients with both a large and a small number of missing teeth were represented in all clusters. Hence, the number of missing teeth by itself cannot fully explain the variation is skeletal patterns amongst hypodontia patients. The preferred dentofacial orthopaedic treatment to cope with patients from the various clusters is subject for debate, but this falls outside the scope of this article. Future studies should further elucidate whether or not specific patterns and locations of missing teeth (and not so much absolute numbers) can be associated with the distinguished clusters.

For treatment planning, interdisciplinary communication and as a means of identifying groups of patients that qualify for reimbursement of costs, a characterisation of patients with hypodontia into meaningful groups is desirable. It should reflect both number and patterns of absent teeth as well as skeletal features. For the former one, the full mouth Tooth Agenesis Code could be a useful measure [8, 35]. It constitutes a unique number that identifies the specific pattern of absent teeth for each individual patient (both number of missing teeth and missing tooth types). For the latter one, the classification in clusters as described in this article may be practical. The usefulness of combining these dental and skeletal methods of characterisation needs to be investigated further, which would require a very large sample size.

Conclusions

The hypodontia population in this study differs from a general orthodontic population on both dental and skeletal aspects. In hypodontia patients, the anterior–posterior relationship between the jaws, the interincisal angle and the lower anterior face height are discriminative parameters of dentofacial form. On the basis of these three cephalometric variables patients with hypodontia can be clustered in four groups, each with distinctive vertical–skeletal, dentoalveolar and sagittal–skeletal characteristics. Cluster 1 is made up of patients with a high-angle facial pattern and patients from cluster 2 exhibit proclined lower incisors. Patients in cluster 3 skeletally resemble those in cluster 2, but are markable because of their retroclined upper and lower incisors. Patients that are grouped in cluster 4 miss the largest number of teeth and stand out because of their retrusive maxillary position. This categorisation of patients with hypodontia into meaningful groups may be useful for treatment planning, interdisciplinary communication and as a means of identifying groups of patients that qualify for reimbursement of costs. Other dental factors such as the distribution of the missing teeth as well as the size and shape of the teeth that are present are important factors to consider during restorative clinical decision making in patients with hypodontia as well.

Acknowledgements The authors are grateful to the following orthodontists J.G. Daggers, L. Kalden, M.T. Wassenaar-te Lintelo, R. A. van Teeseling, S.J.G.A. van 't Veen and the Centers for Special Dental Care of the Isala klinieken Zwolle, The Netherlands (B.J. Polder and P.A.M. Versteegh) and of the Radboud University Nijmegen Medical Center (C. van Heumen) for providing additional patient material. Special thanks to O. van Vlijmen of the Department of Orthodontics and Oral Biology, Radboud University Nijmegen Medical Centre for his help and assistance during the process of data acquisition and radiographic analysis.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Ben-Bassat Y, Brin I (2009) Skeletal and dental patterns in patients with severe congenital absence of teeth. Am J Orthod Dentofacial Orthop 135:349–356
2. Ben-Bassat Y, Brin I (2003) Skeletodental patterns in patients with multiple congenitally missing teeth. Am J Orthod Dentofacial Orthop 124:521–525
3. Bhatia SN, Leighton BC (1993) A manual of facial growth. A computer analysis of longitudinal cephalometric growth data. Oxford University Press, New York
4. Björk A (1947) The face in profile. Svensk Tandlakare Tidschrift 40:No. 40b
5. Bondarets N, Jones RM, McDonald F (2002) Analysis of facial growth in subjects with syndromic ectodermal dysplasia: a longitudinal analysis. Orthod Craniofac Res 5:71–84
6. Bondarets N, McDonald F (2000) Analysis of the vertical facial form in patients with severe hypodontia. Am J Phys Anthropol 111:177–184
7. Chung LK, Hobson RS, Nunn JH, Gordon PH, Carter NE (2000) An analysis of the skeletal relationships in a group of young people with hypodontia. J Orthod 27:315–318
8. Creton MA, Cune MS, Verhoeven JW, Meijer GJ (2007) Patterns of missing teeth in a population of oligodontia patients. Int J Prosthodont 20:409–413
9. Dahlberg G (1940) Statistical methods for medical and biological students. Interscience, New York, pp 100–140
10. Dermaut LR, Goeffers KR, De Smit AA (1986) Prevalence of tooth agenesis correlated with jaw relationship and dental crowding. Am J Orthod Dentofacial Orthop 90:204–210
11. Downs WB (1948) Variations in facial relationships: their significance in treatment and prognosis. Am J Orthod 34:812–840
12. Endo T, Ozoe R, Yoshino S, Shimooka S (2006) Hypodontia patterns and variations in craniofacial morphology in Japanese orthodontic patients. Angle Orthod 76:996–1003
13. Endo T, Yoshino S, Ozoe R, Kojima K, Shimooka S (2004) Association of advanced hypodontia and craniofacial morphology in Japanese orthodontic patients. Odontology 92:48–53
14. Graber TM (1952) New horizons in case analysis-clinical cephalometrics. Am J Orthod 38:603–624
15. Houston WJB (1983) The analysis of errors in orthodontic measurements. Am J Orthod Dentofacial Orthop 83:382–390
16. Jamroz GM, Kuijpers-Jagtman AM, Van't Hof MA, Katsaros C (2006) Dental maturation in short and long facial types. Is there a difference? Angle Orthod 76:768–772
17. Kapadia H, Mues GDSR (2007) Genes affecting tooth morphogenesis. Orthod Craniofac Res 10:237–244
18. Legan HL, Burstone CJ (1980) Soft tissue cephalometric analysis for orthognathic surgery. J Oral Surg 38:744–751
19. Lisson JA, Scholtes S (2005) Investigation of craniofacial morphology in patients with hypo- and oligodontia. J Orofac Orthop 66:197–207
20. Melfi RC (1994) Permar's oral embryology and microscopic anatomy. Lea and Febiger, Philadelphia
21. Nodal M, Kjaer I, Solow B (1994) Craniofacial morphology in patients with multiple congenitally missing permanent teeth. Eur J Orthod 16:104–109
22. Noor A, Windpassinger C, Vitcu I, Orlic M, Rafiq MA, Khalid M, Malik MN, Ayub M, Alman B, Vincent JB (2009) Oligodontia is caused by mutation in LTBP3, the gene encoding latent TGF-beta binding protein 3. Am J Hum Genet 84:519–523
23. Ogaard B, Krogstad O (1995) Craniofacial structure and soft tissue profile in patients with severe hypodontia. Am J Orthod Dentofacial Orthop 108:472–477
24. Peck S, Peck L (1996) Tooth numbering progress. Angle Orthod 66:83–84
25. Polder BJ, Van't Hof MA, van der Linden FP, Kuijpers-Jagtman AM (2004) A meta-analysis of the prevalence of dental agenesis of permanent teeth. Community Dent Oral Epidemiol 32:217–226
26. Riedel RA (1952) The relation of maxillary structures to cranium in malocclusion and in normal occlusion. Angle Orthod 22:142–145
27. Riolo ML, Moyers ME, McNamara JA, Hunter JS (1974) An atlas of craniofacial growth. Center for Human Growth and Development, University of Michigan, Ann Arbor
28. Roald KL, Wisth PJ, Boe OE (1982) Changes in cranio-facial morphology of individuals with hypodontia between the ages of 9 and 16. Acta Odontol Scand 40:65–74
29. Sarnas KV, Rune B (1983) The facial profile in advanced hypodontia: a mixed longitudinal study of 141 children. Eur J Orthod 5:133–143
30. van der Schalk WY, Bosman F (1996) Tooth size in relatives of individuals with oligodontia. Arch Oral Biol 41:469–472

31. Stockton DW, Das P, Goldenberg M, D'Souza RN, Patel PI (2000) Mutation of PAX9 is associated with oligodontia. Nat Genet 24:18–19
32. Tavajohi-Kermani H, Kapur R, Sciote JJ (2002) Tooth agenesis and craniofacial morphology in an orthodontic population. Am J Orthod Dentofacial Orthop 122:39–47
33. Thesleff I (1995) Homeobox genes and growth factors in regulation of craniofacial and tooth morphogenesis. Acta Odontol Scand 53:129–134
34. van den Boogaard MJ, Dorland M, Beemer FA, van Amstel HK (2000) MSX1 mutation is associated with orofacial clefting and tooth agenesis in humans. Nat Genet 24:342–343
35. van Wijk AJ, Tan SP (2006) A numeric code for identifying patterns of human tooth agenesis: a new approach. Eur J Oral Sci 114:97–101
36. Wisth PJ, Thunold K, Boe OE (1974) The craniofacial morphology of individuals with hypodontia. Acta Odontol Scand 32:293–302
37. Woodworth DA, Sinclair PM, Alexander RG (1985) Bilateral congenital absence of maxillary lateral incisors: a craniofacial and dental cast analysis. Am J Orthod 87:280–293
38. Yuksel S, Ucem T (1997) The effect of tooth agenesis on dentofacial structures. Eur J Orthod 19:71–78