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Tooth agenesis patterns in Japanese orthodontic patients with nonsyndromic oligodontia

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Introduction: Tooth agenesis is the most common dental anomaly in humans and is often found in orthodontic patients. However, severe tooth agenesis (oligodontia) is rare and its characteristics are poorly understood. This study aimed to investigate tooth agenesis patterns of Japanese orthodontic patients with nonsyndromic oligodontia. **Methods:** Panoramic radiographs of 228 orthodontic patients (141 females, 87 males) with nonsyndromic oligodontia were selected and permanent tooth agenesis excluding third molars was evaluated. Influence of cutoff age was tested, tooth agenesis patterns for each quadrant were calculated, and antagonistic maxillary and mandibular quadrants were merged as the occluding tooth agenesis pattern. Full-mouth tooth agenesis patterns were also evaluated. **Results:** The highest prevalence of tooth agenesis was observed in maxillary and mandibular second premolars, followed by maxillary first premolars. Prevalence of a symmetric pattern between right and left quadrants was significantly higher than matched patterns between maxillary and mandibular antagonistic quadrants. Among 456 possible tooth agenesis patterns, 51 and 49 patterns were observed for the maxillary and mandibular quadrants, respectively, but 215 patterns for the occluding patterns were observed. In addition, 180 full-mouth tooth agenesis patterns were observed in the 228 patients. **Conclusions:** Distinct characteristics in highly ranked patterns were observed compared with studies from other geographic areas, especially in the maxillary arch. Occluding and full-mouth tooth agenesis patterns showed wide variation, suggesting difficulty in orthodontic diagnosis. (Am J Orthod Dentofacial Orthop 2019;156:238-47)

Permanent tooth agenesis is one of the most common developmental anomalies in humans[1] and is often found in orthodontic patients. It has been clinically classified into 3 categories—hypodontia, oligodontia, and anodontia—based on the number of undeveloped teeth. Severe hypodontia or oligodontia defines agenesis of 6 or more permanent teeth, excluding third molars.[2-4] The reported prevalence of oligodontia has ranged from 0.08% to 0.16% in the general population,[5-7] and higher prevalence rates were reported for orthodontic patients.[8,9] Environmental factors known to interfere with tooth development include trauma, infection, smoking,[10] surgical intervention, hematopoietic stem cell transplantation, radiotherapy, and combination chemotherapy for childhood cancer.[11,12] Oligodontia is often associated with genetic syndromes, such as ectodermal dysplasia,[13] Klinefelter syndrome, incontinentia pigmenti, and Asperger syndrome.[14] Oligodontia may also occur as an isolated nonsyndromic condition, referred to as nonsyndromic oligodontia.[15]

Severity of nonsyndromic oligodontia is usually related to the number of missing teeth, but the location of the missing tooth or agenesis "pattern" can be another important aspect in orthodontic diagnosis for individual cases.[16] For example, agenesis of anterior teeth mainly affects esthetics,[17] whereas that of posterior teeth influences skeletal growth pattern,[18] masticatory function, and orthodontic anchorage. The primary motivation of orthodontic treatment for nonsyndromic oligodontia is that of esthetics,[18] but functional and psychologic problems of such young patients are also serious.[19] However, because of the low prevalence of oligodontia, the number of case reports is limited. Accordingly, diagnosis and treatment planning are often difficult even for experienced orthodontists. The management of such patients usually requires multidisciplinary treatment that frequently includes

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orthodontics[20] to mainly improve coordination of dental arches and obtain sufficient space for dental implants,[21] which usually requires costly long-term care.[22] Therefore, epidemiologic studies on the prevalence of tooth agenesis patterns in nonsyndromic oligodontia are important to estimate health care costs to support patients and their families.[23]

Tooth development is a multifactorial phenomenon, with more than 200 genes expressed during the process.[24] Among them, relationships between specific genetic mutations and tooth agenesis patterns have been suggested for nonsyndromic oligodontia.[25,26] Currently hypothesized genotype-phenotype relationships included a missense mutation in the *MSX1* gene, which results in agenesis of second premolars, maxillary first premolars, and mandibular first molars.[1] The *PAX9* region also is associated with variable forms of oligodontia that mainly affect the molars,[27,28] and *AXIN2* mutations[29] have been shown to affect a wider range of tooth types. However, to date, it has been unclear precisely how genetic mutations are related to specific tooth agenesis patterns,[30] and interaction between these candidate genes[31] and epigenetic and environmental factors have also been suggested.[30,32]

Ethnic differences[33] and the influence of genetic background in different geographic areas[34,35] on tooth agenesis patterns also have been suggested. For example, studies on hypodontia have shown a higher prevalence of mandibular incisor agenesis in East Asian countries,[33,34] although oligodontia is not well studied.[30] Therefore, to expand current knowledge on hereditary factors of oligodontia, documenting the characteristics of tooth agenesis patterns in orthodontic patients with nonsyndromic oligodontia in different geographic areas may contribute to investigations of the influence of genetic background.[30,34]

The minimum cutoff age as an inclusion criterion of patients may also affect the results of tooth agenesis frequency in epidemiologic studies,[35] especially in patients with mandibular second premolar agenesis caused by delayed dental development.[36,37] Recent meta-analyses[38,39] on hypodontia confirmed the possibility of misdiagnosis of tooth agenesis in patients younger than 13 years. Although patients with oligodontia showed a tendency for delayed tooth formation,[4] minimum cutoff ages for previous epidemiologic studies on oligodontia have varied.[40] Clinically, a delay in orthodontic treatment or treatment planning until the patient is 13 years of age or older may be too late for most patients.

I hypothesized that East Asian nonsyndromic oligodontia patients exhibit unique tooth agenesis patterns compared with European nonsyndromic oligodontia patients. The purposes of the present study were to investigate the characteristics of permanent tooth agenesis patterns in orthodontic patients with nonsyndromic oligodontia in Japan and confirm the influence of evaluation cutoff age on analyses.

MATERIAL AND METHODS

The study protocol was reviewed and approved by the Research Ethics Committee of Nippon Dental University, School of Life Dentistry at Tokyo (NDU-T2013-26). The need for informed consent from individual patients was waived by the Ethics Committee owing to the retrospective and observational design of the epidemiologic study.

To estimate the number of hypodontia and oligodontia patients, a preliminary questionnaire survey was conducted, which included 433 exclusive orthodontic clinics of members of the Japanese Association of Orthodontists. Completed questionnaires were returned from 119 clinics (27.5%). According to the survey, 740 patients (508 female and 232 male) with hypodontia (excluding oligodontia) and 58 patients (31 female and 27 male) with oligodontia were found among 11,195 new patients (7253 female and 3942 male) in 2012.

Consequently, we again surveyed all members by mail to select and send panoramic radiographs of orthodontic patients with oligodontia. Initial inclusion criteria were as follows: patients with agenesis of 6 or more permanent teeth, excluding third molars, diagnosed by means of an orthodontic clinical examination, with diagnostic records including panoramic radiographic examinations, cephalometric evaluation, and dental cast analysis. Exclusion criteria were cleft lip or palate, ectodermal dysplasia, or other congenital anomalies.

Digital images of panoramic radiographs with age, sex, dental anomalies, including tooth agenesis according to the results of intra- and extraoral clinical examinations and evaluation of diagnostic records, and family history on tooth agenesis were sent to the author by mail on CD-ROMs. Before mailing, patients' personal information (name and address) was removed.

A total of 252 panoramic radiographs were collected from 71 clinics. Because we asked orthodontic clinics to send information on all former and current patients, we could not obtain the total number of patients in the population. Agenesis of permanent teeth, excluding third molars, was independently evaluated by 2 orthodontists of the Department of Orthodontics, Nippon Dental University, Tokyo, Japan, using panoramic radiographs displayed on the same 40-inch computer screen. Third molars were excluded from the evaluation because orthodontic treatment rarely includes these teeth.

During the evaluation process, 1 image was excluded because of poor image quality. Disagreement between the 2 evaluators occurred for 3 patients, whose images were excluded from the analyses (agreement rate 248/251 patients, 98.8%). Twenty patients were also excluded based on age for the following reasons: age unknown (n = 2), age younger than 7 years (n = 17), and age older than 25 years (n = 1). Finally, 228 patients (141 female and 87 male, mean age 12.63 ± 3.79 years, range 7 years 2 months to 24 years 3 months) were selected. Among them, single images were obtained for 217 patients and additional images were obtained for 11 patients. In these 11 patients, the following numbers of additional images taken during the observational period or during and after orthodontic treatment were obtained: 2 images (n = 4), 3 images (n = 5), 4 images (n = 1), and 5 images (n = 1). For patients with more than 1 image available, the image taken at the oldest age was used for analysis. The number of missing teeth was counted for each patient, and medians and interquartile ranges (IQRs) for female and male patients were calculated and compared by means of the Mann-Whitney U test. The number of missing teeth was the same for both sex groups (median 7.0, IQR 4.0, range for females was 6-18, and for males was 6-19 teeth) and a sex difference was not observed (z = 0.406; $P > 0.05$). Therefore, data in the groups were pooled for subsequent analyses.

Tooth agenesis in other family members was reported for 48 patients (21.0%). Four pairs of family members were included in this study: sister-sister (n = 2), mother-daughter (n = 1), and sister-brother (n = 1). No family history was reported for 156 patients (68.4%), and no answer or family history unknown was reported for 24 patients (10.5%).

Analysis

The number of missing teeth was counted for each patient. Patients were then grouped according to age as the younger or older group based on cutoff ages from 8 to 14 years. The mean, standard deviation (SD), median, and IQR were then calculated for younger and older age groups. Distributions of the number of missing teeth per patient in each group were evaluated by means of the Shapiro-Wilk test. No group showed normal distribution; therefore, medians were compared between certain age groups older and younger than each cutoff age by means of the nonparametric Mann-Whitney U test. This statistical comparison was repeated for the 7 different cutoff ages.

Frequency distribution of the number of missing teeth per patient was counted. The number of missing teeth and prevalence (%) of tooth agenesis for each tooth type in maxillary and mandibular arches excluding third molars were calculated. To evaluate the prevalence of tooth agenesis patterns, dental status was evaluated and the Tooth Agenesis Code (TAC) value, excluding third molars, was calculated for each quadrant.[41]

Numbers of patients with symmetric and asymmetric patterns and prevalence (%) were calculated for maxillary and mandibular arches and then pooled.

Numbers of patients with matched and unmatched number and prevalence (%) of patterns between antagonistic maxillary and mandibular quadrants were calculated and then pooled.

Symmetric and asymmetric tooth agenesis patterns between right and left quadrants and matched and unmatched tooth agenesis patterns between maxillary and mandibular antagonistic quadrants were compared by means of chi-square test at a significance level of 0.05.

Numbers of patients with matched and unmatched tooth agenesis patterns in all 4 quadrants and prevalence (%) also were calculated.

Tooth agenesis patterns in right and left quadrants were pooled and rankings of the prevalence of tooth agenesis patterns for maxillary and mandibular arches were created by the pivot table function of Microsoft Office Excel 2013 (Microsoft, Redmond, Wash).

Tooth agenesis patterns between antagonistic maxillary and mandibular quadrants were merged as the occluding tooth agenesis pattern and the prevalence was calculated for right and left sides separately and then pooled. A ranking of the prevalence of occluding tooth agenesis patterns was also calculated.

Tooth agenesis patterns of the 4 quadrants were merged as the full-mouth tooth agenesis pattern of each patient.[16] Then the prevalence and ranking of the prevalence of full-mouth tooth agenesis patterns were calculated.

The 50% cumulative frequency was calculated for maxillary, mandibular, occluding, and full-mouth tooth agenesis patterns to evaluate the variation among this cohort. Wider individual variation is indicated when a larger number of patterns is required to reach 50% total variation of the sample.[13]

RESULTS

There was no significant difference in the median numbers of missing teeth per patient between older and younger groups according to cutoff ages set from 8 to 14 years (Table 1). A decay curve tendency was observed in the frequency distribution of numbers of missing teeth per patient (Fig 1). The greatest number of missing teeth was observed for maxillary and

Table I. Comparison of means, SDs, medians, and IQRs of numbers of missing teeth per patient according to different cutoff ages

	≥ Cutoff age (older group)					< Cutoff age (younger group)					
		Missing teeth per patient					Missing teeth per patient				
Cutoff age (y)	*n*	*Mean*	*SD*	*Median*	*IQR*	*n*	*Mean*	*SD*	*Median*	*IQR*	*P value (Mann-Whitney U test)*
8	216	8.30	2.71	7	4	12	8.25	2.38	8	4	0.976[NS]
9	198	8.31	2.75	7	4	30	8.20	2.28	8	4	0.898[NS]
10	170	8.38	2.86	7	4	58	8.07	2.10	8	4	0.985[NS]
11	141	8.27	2.94	7	3	87	8.34	2.22	8	4	0.184[NS]
12	109	8.30	2.96	7	3	119	8.29	2.43	8	4	0.478[NS]
13	84	8.31	2.82	7	3.25	144	8.29	2.61	7.5	4	0.686[NS]
14	63	8.52	3.06	7	4	165	8.21	2.54	7	4	0.887[NS]

IQR, interquartile range; *NS*, not significant.

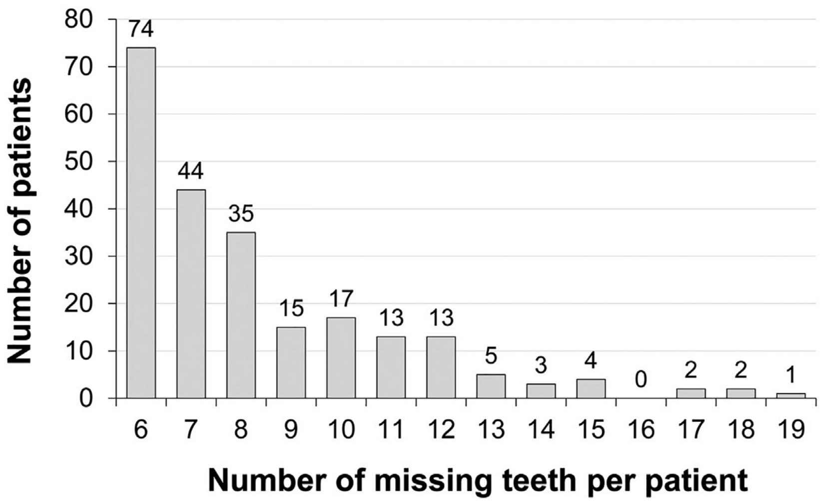


Fig 1. Frequency distribution of the numbers of missing teeth per patient. A decay curve tendency was observed.

mandibular second premolars, followed by the maxillary first premolar (Table II).

Tooth agenesis patterns in right and left quadrants for the maxillary arch were pooled and 51 patterns were observed. Tooth agenesis patterns with higher prevalence included maxillary first and second premolars (24.8%), followed by maxillary second premolar only (10.3%). The top 10 ranked patterns included second premolars. The 50% cumulative frequency was reached with 5 patterns (Fig 2). Forty-nine patterns were observed for the mandibular arch. Agenesis of second premolar only (25.0%) and first and second premolars (20.2%) was prominently higher than other patterns. The 50% cumulative frequency was reached with only 3 patterns (Fig 3).

When tooth agenesis patterns between antagonistic maxillary and mandibular quadrants were merged as the occluding tooth agenesis pattern, 215 patterns were observed. The 50% cumulative frequency was reached with 27 patterns. Higher-ranked patterns included premolars (Fig 4). For the full-mouth tooth agenesis pattern, 180 patterns were observed for the 228 patients. Among them, 164 patients showed a unique pattern. Sixty-six patterns were required to reach the 50% cumulative frequency (Fig 5).

Symmetric tooth agenesis patterns between right and left quadrants were observed in ~50% of patients for both maxillary and mandibular arches, however, only 30% of patients showed a symmetric pattern in both arches (Table III). Matching tooth agenesis patterns between antagonistic maxillary and mandibular quadrants were observed in ~13% of patients. Twelve patients had the same pattern for all 4 quadrants. Affected teeth for 11 patients were first and second premolars, and 1

Table II. Number of patients and prevalence (%) of agenesis for each tooth in the maxillary and mandibular arches for the 228 orthodontic patients with nonsyndromic oligodontia

Arch	*Right side*							*Left side*						
	M2	*M1*	*P2*	*P1*	*C*	*I2*	*I1*	*I1*	*I2*	*C*	*P1*	*P2*	*M1*	*M2*
Maxilla	55 (24.1%)	23 (10.1%)	187 (82.0%)	126 (55.3%)	56 (24.6%)	79 (34.6%)	3 (1.3%)	3 (1.3%)	76 (33.3%)	59 (25.9%)	113 (49.6%)	184 (80.7%)	25 (11.0%)	56 (24.6%)
Mandible	51 (22.4%)	13 (5.7%)	177 (77.6%)	82 (36.0%)	18 (7.9%)	36 (15.8%)	45 (19.7%)	48 (21.1%)	41 (18.0%)	14 (6.1%)	72 (31.6%)	185 (81.1%)	12 (5.3%)	53 (23.2%)

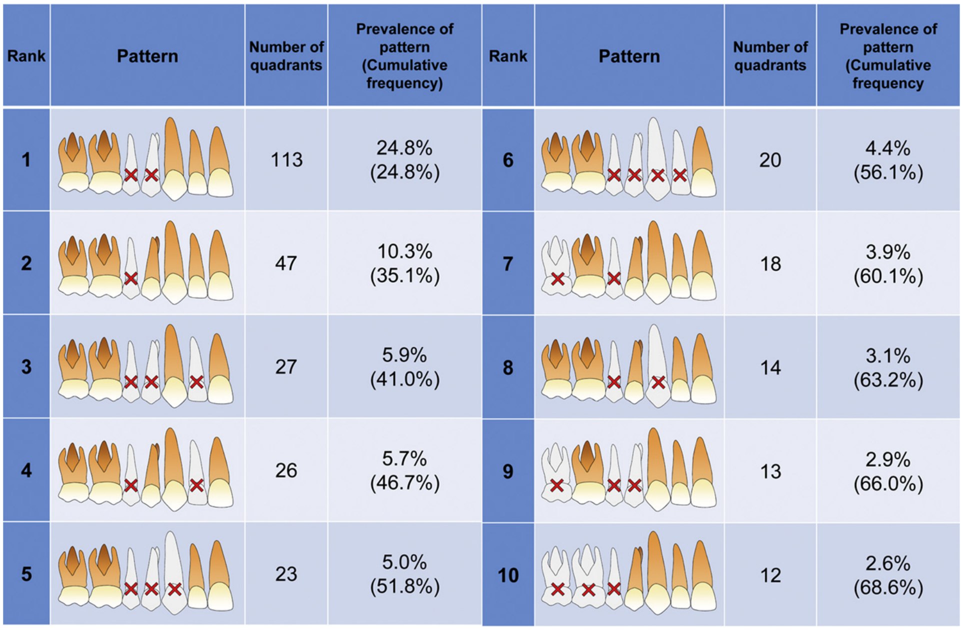
C, canine; *I1*, central incisor; I2, lateral incisor; *M1*, first molar; *M2*, second molar; *P1*, first premolar; *P2*, second premolar.

patient exhibited first and second premolar and second molar agenesis in every quadrant (Table IV). A significant difference was found between the prevalence of tooth agenesis patterns between symmetric right and left quadrants and matched antagonistic maxillary and mandibular quadrants ($\chi^2 = 179.13$; $P < 0.01$).

DISCUSSION

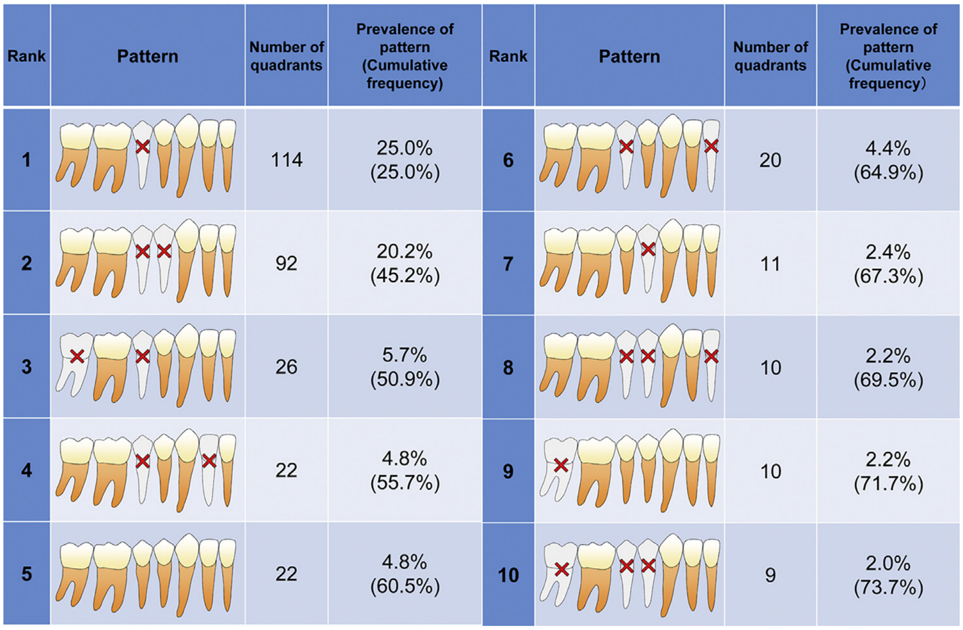
According to meta-analyses of epidemiologic studies on hypodontia, there is a possibility of misdiagnosis of tooth agenesis in patients younger than 13 years,[38,39] but it is clinically difficult to wait for the orthodontic diagnosis until such an age. Therefore, in the present study, the effect of cutoff age in nonsyndromic oligodontia patients was evaluated. However, no significant difference in medians was observed between older and younger groups with cutoff ages ranging from 8 to 14 years. One reason for this observation may be attributed to the finding that the greatest number of missing teeth (~80% of cases) was observed for mandibular second premolars, which has a relatively higher possibility of delayed formation than other permanent teeth, excluding third molars.[2] However, great individual variations in timing of tooth formation in patients with nonsyndromic oligodontia were also observed.[4,42] Therefore, further longitudinal investigation on nonsyndromic oligodontia is required to confirm the results of the present study. Until a deeper understanding of the mechanisms of tooth development is established, clinicians should pay attention to the possibility of delayed permanent tooth formation in orthodontic patients with nonsyndromic oligodontia on an individual basis.

Symmetric tooth agenesis patterns between right and left quadrants for the maxillary and mandibular arches in ~50% of the cases were demonstrated. This finding supports those of previous studies.[16,25] In the literature, a tendency of symmetric tooth agenesis has been observed in hypodontia and oligodontia patients, suggesting the involvement of possible nonlocal[25] and genetic[30] factors. These findings also indicate that it is rational to plan and apply symmetric treatment mechanics for the majority of orthodontic patients with nonsyndromic oligodontia. In previous studies conducted in Europe,[16,25] tooth agenesis patterns in each quadrant were independently evaluated for right and left sides. Similar patterns were observed for both sides, with no specific pattern for the right or left side. In the present study, more than 50% of patients showed symmetric tooth agenesis patterns in the right and left quadrants; therefore, we pooled the data to identify tooth agenesis pattern specific for East Asian



Rank	Pattern	Number of quadrants	Prevalence of pattern (Cumulative frequency)	Rank	Pattern	Number of quadrants	Prevalence of pattern (Cumulative frequency
1		113	24.8% (24.8%)	6		20	4.4% (56.1%)
2		47	10.3% (35.1%)	7		18	3.9% (60.1%)
3		27	5.9% (41.0%)	8		14	3.1% (63.2%)
4		26	5.7% (46.7%)	9		13	2.9% (66.0%)
5		23	5.0% (51.8%)	10		12	2.6% (68.6%)

Fig 2. Ranking of tooth agenesis patterns in the maxillary arch. The top 10 of 51 patterns observed are shown. Five patterns were required to reach 50% cumulative frequency.



Rank	Pattern	Number of quadrants	Prevalence of pattern (Cumulative frequency)	Rank	Pattern	Number of quadrants	Prevalence of pattern (Cumulative frequency)
1		114	25.0% (25.0%)	6		20	4.4% (64.9%)
2		92	20.2% (45.2%)	7		11	2.4% (67.3%)
3		26	5.7% (50.9%)	8		10	2.2% (69.5%)
4		22	4.8% (55.7%)	9		10	2.2% (71.7%)
5		22	4.8% (60.5%)	10		9	2.0% (73.7%)

Fig 3. Ranking of tooth agenesis patterns in the mandibular arch. The top 10 of 49 patterns observed are shown. Three patterns were required to reach 50% cumulative frequency.

populations. However, the remaining 45% of patients showed asymmetric tooth agenesis patterns, suggesting the influence of genetic or environmental factors. Therefore, further studies on factors that control the symmetricity of tooth agenesis should be conducted.

In the present study, a higher prevalence of tooth agenesis of individual teeth was found in maxillary

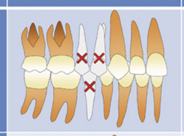
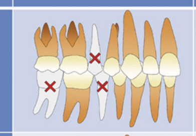
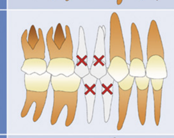
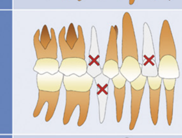
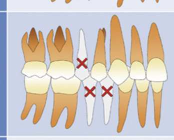
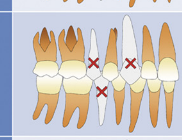
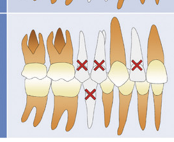
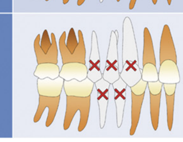
Rank	Pattern	Number of quadrants	Prevalence of pattern (Cumulative frequency)	Rank	Pattern	Number of quadrants	Prevalence of pattern (Cumulative frequency)
1		46	10.1% (10.1%)	5		9	2.0% (27.4%)
2		40	8.8% (18.9%)	5		9	2.0% (29.4%)
3		20	4.4% (23.2%)	5		9	2.0% (31.4%)
4		10	2.2% (25.4%)	5		9	2.0% (33.3%)

Fig 4. Ranking of the occluding tooth agenesis pattern in both maxillary and mandibular arches. Twenty-seven patterns were required to reach 50% cumulative frequency.

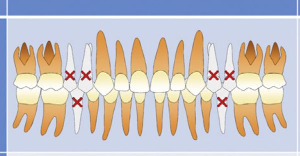
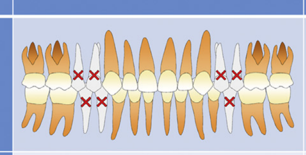
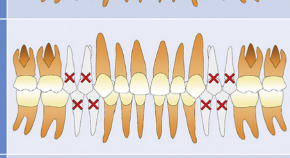
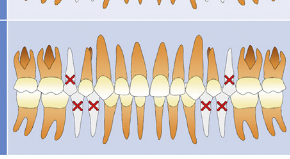
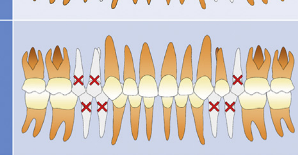
Rank	Pattern	Number of patients	Prevalence of pattern (Cumulative frequency)	Rank	Pattern	Number of patients	Prevalence of pattern (Cumulative frequency)
1		17	7.5% (7.5%)	4		4	1.8% (16.7%)
2		11	4.8% (12.3%)	5		3	1.3% (18.0%)
3		6	2.6% (14.9%)	5		3	1.3% (19.3%)

Fig 5. Ranking of the full-mouth tooth agenesis pattern. Sixty-six patterns were required to reach 50% cumulative frequency.

and mandibular second premolars, followed by maxillary first molar, mandibular first premolar, maxillary lateral incisor, and maxillary and mandibular second molars. This finding supports Butler's field theory,[43] similarly to previous European studies.[3,6] However, the frequencies of lateral incisor agenesis and mandibular central incisor agenesis were lower than those observed in The Netherlands[16] and England,[44] respectively.

Moreover, tooth agenesis patterns including premolars were more frequent in the maxillary arch, and the highest pattern of maxillary lateral incisor agenesis was ranked third with only 6% of patients. These findings could be attributed to the higher prevalence of tooth agenesis found in maxillary and mandibular second molars (∼80%) and maxillary first premolar (∼50%). These findings support previous studies on severe hypodontia patients with 5 or more missing teeth

Table III. Number and prevalence (%) of patients with symmetric and asymmetric tooth agenesis patterns between right and left quadrants in maxillary and mandibular arches

	Tooth agenesis pattern between right and left quadrants	
Arch	*Symmetric*	*Asymmetric*
Maxilla	126 (55.3%)	102 (44.7%)
Mandible	123 (53.9%)	105 (46.1%)
Total	249 (54.6%)	207 (45.4%)
Both arches	73 (32.0%)	155 (68.0%)

Table IV. Number and prevalence (%) of matched and unmatched tooth agenesis patterns of quadrants between maxillary and mandibular arches on right and left sides

	Tooth agenesis pattern between maxillary and mandibular quadrants	
Side	*Matched*	*Unmatched*
Right side	31 (13.6%)	197 (86.4%)
Left side	27 (11.8%)	201 (88.2%)
Total	58 (12.7%)	398 (87.3%)
Both sides (4 quadrants)	12 (5.3%)	216 (94.7%)

in Japan,[34,45] the United States,[46] northern Europe,[5,7,47] and England.[44] In contrast, a similarly higher prevalence of tooth agenesis of both lateral incisors and premolars has been observed in patients with nonsyndromic oligodontia in Belgium[14] and The Netherlands.[3,16,30] Therefore, the nonsignificant increase in agenesis of the maxillary lateral incisor may be a reflection of geographic background, including genetic variation. However, a similar discrepancy in the prevalence of agenesis of the maxillary lateral incisor was also observed between patients with and without ectodermal dysplasia in Norway,[6] suggesting the influence of genetic mutations. In addition, significant increases in the prevalence of tooth agenesis were observed in premolars and molars in patients who underwent hematopoietic stem cell transplantation in The Netherlands,[48] indicating the importance of environmental and epigenetic factors on tooth agenesis pattern.

In this study, 49 tooth agenesis patterns were observed in the mandibular arch, and patterns including the second premolar only or first and second premolars were most common. Only 3 patterns were required to reach 50% cumulative frequency, in contrast to 5 patterns required for the maxillary arch. These results support those of a previous study[30] and were similar to previous European studies.[14,16,30] In previous studies on hypodontia in Japan, agenesis of mandibular incisors was the second most frequently observed pattern after mandibular second premolars.[34,49] However, in the present study, tooth agenesis patterns in the mandible arch including lateral incisors ranked fourth, sixth, and eighth. This result supports clinical epidemiologic studies on hypodontia conducted in Japan,[34,45] which described a higher possibility of mandibular lateral incisor agenesis in orthodontic patients with 1 or 2 missing teeth than with more than 3 missing teeth. However, observations that the etiology of mandibular incisor agenesis may be influenced by the development of mandibular innervation[50] and *PAX9* mutations in East Asian cohorts[51,52] underscore the necessity of future biologic studies.

Occlusal relationship is an essential factor not only for orthodontic diagnosis but also treatment mechanics. Therefore, the occluding tooth agenesis pattern was also evaluated and 215 patterns were observed in 456 sides of 228 orthodontic patients with nonsyndromic oligodontia. In addition, 180 full-mouth patterns were observed among the 228 patients. Highly ranked patterns included maxillary and mandibular second premolars, which were also independently observed in highly ranked patterns in maxillary and mandibular quadrants. These findings suggest the possibility of *MSX1* mutations,[25] but such genotype-phenotype relationship is not always observed.[49,53] Because pattern variation was wider than that in each quadrant, 27 and 66 patterns were required to reach 50% cumulative frequency for the occluding and full-mouth patterns, respectively. Unique tooth agenesis patterns were found in 153 of 456 sides (33.6%) and in 167 of 228 patients (73.2%) for the occluding and full-mouth patterns, respectively. This wide variation in occluding and full-mouth tooth agenesis patterns reinforces the difficulty of establishing a standard orthodontic diagnostic protocol[30] based on skeletal[54] and dental[55] morphologic analyses to improve esthetic and functional occlusion for individual patients with nonsyndromic oligodontia. Furthermore, the experience of 1 orthodontist may be limited; therefore, a database including multidisciplinary treatment results might be proposed as a possible solution. This wide variation could be attributed to the lower possibility of matching between antagonistic maxillary and mandibular quadrants. Consequently, this finding supports Butler's field theory[43,56] and differences in origins between maxilla and mandible from early embryonic developmental phases controlled by genetic, epigenetic, and environmental factors.[25,56]

There are some limitations associated with the present study. First, patients were diagnosed by pediatric or general dentists before visiting orthodontic clinics. In addition, socioeconomic factors may have influenced whether patients visited dental professionals or received treatment. Therefore, the results of the present study may not adequately reflect biologic variation in the general population. Second, although a sex difference in tooth agenesis has been reported, another bias may be a sex discrepancy because of the general tendency of orthodontic patients with hypodontia.[38,57,58] There was no significant sex difference in the number of missing teeth per patient between female and male oligodontia patients in the present study; this finding led us to pool the sexes for evaluation. However, differences in tooth agenesis patterns between males and females may exist. Therefore, tooth agenesis patterns should be compared according to sex, and further study on this issue with the use of a larger sample size is necessary.[58] Finally, it was not possible to obtain precise family dental and medical histories of the patients, including history of exposure to teratogens or surgical, radiographic, and chemical therapies for childhood cancer.[7,11-13]

CONCLUSIONS

The present study is thought to be the first epidemiologic investigation of permanent tooth agenesis patterns in East Asian orthodontic patients with nonsyndromic oligodontia with the use of panoramic radiographs. Within the limitations of this study, the following conclusions were reached:

1. Compared with previous European studies, higher ranked tooth agenesis patterns including maxillary first and second and mandibular second premolars were observed.
2. The prevalence of symmetric patterns between right and left quadrants was significantly higher than unmatched patterns observed between maxillary and mandibular antagonistic quadrants.
3. Among 456 possible tooth agenesis patterns, 51 and 49 patterns were observed for the maxillary and mandibular quadrants, respectively.
4. In contrast, 215 patterns among 456 possible patterns for occluding tooth agenesis pattern and 180 patterns for full-mouth tooth agenesis patterns among 228 patients were observed, suggesting large individual variations.

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