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RESEARCH PAPER

Epidemiological Analysis of Cleft Lip and/or Palate by Cleft Pattern

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Abstract
Objectives To analyze gender differences in cleft pattern by the clinical statistical study of Japanese patients with cleft lip and/or cleft palate.
Study design Cleft pattern modeling was used to analyze 782 patients with cleft lip and/or cleft palate (417 males and 365 females) who had been examined at the Cleft Lip and Palate Center, Aichi-Gakuin University Hospital, and whose details could be confirmed. Relationships between gender and cleft type were analyzed with chi-squared test.
Results A comparison of gender differences by cleft type revealed that a greater percentage of males had milder cleft lip, cleft lip and palate, or cleft palate, whereas the percentage of females tended to be greater as cleft severity increased.
Conclusions Modeling of cleft patterns enables more detailed classification of cleft lip and palate, and can lead to a greater understanding of pathology.

Keywords Cleft lip · Cleft palate · Clinical statistics · Congenital malformation

Introduction

Epidemiological research is indispensable for treatment, therefore periodical clinical reports with clinical statistics are essential for error free diagnosis. Methods of classification represent an important factor in clinical statistics, and we think that systemic classification of diseases is necessary to improve the provision of treatment. However, no consensus criteria have been reached regarding underlying diagnoses, and criteria have yet to be established for each institution or diagnostician. Detailed epidemiological analyses carried out on the basis of the existing classifications are thus inadequate. The present study is a clinical statistical analysis and tabulation of patients with cleft lip/cleft palate who were examined at the Center during a 12-year period beginning from 1997 and for whom details could be confirmed. On that basis, in this cleft pattern modeling, a clinical statistical study was conducted on orofacial cleft type using pattern models composed of 16 codes, and gender differences in patterns of cleft lip/cleft palate were analyzed.

Materials and Methods

Data from 782 patients with cleft lip/cleft palate (417 males, 365 females) who were examined at the Center during the 12-year period from April 1, 1997 to March 31, 2009 and for whom details could be confirmed were tabulated. This was performed on the basis of an epidemiological data protocol as well as outpatient and surgical records and interview forms. To achieve more effective classification, we undertook a preliminary study in which we performed classification using a cleft pattern model comprising 17 codes as reported by Natsume et al. in 1984 [1]. By means of repeated trial and error, we were able to achieve clearer determinations. This was because the number of codes for cleft soft palate, which tend to be unclear, was reduced from 3 to 2, enabling clearer

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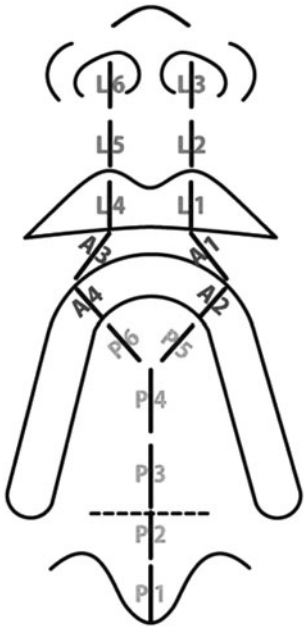


Fig. 1 The model for cleft lip and/or palate divided into 16 regions

Table 1 Classification of cleft type

	CL	CLP	CP	Total
Male	111	182	104	397
	28.0%	45.8%	26.2%	100%
Female	99	123	128	350
	28.3%	35.1%	36.6%	100%
Total	210	305	232	747
	28.1%	40.8%	31.1%	100%

Table 2 Cleft laterality

	Right side		Left aide		Bilateral		Total	
CL	63 (31.7%)		110 (55.3%)		26 (13.1%)		199 (100%)	
	M.34	F.29	M.56	F.54	M.17	F.9	M.105	F.94
CLP	65 (21.8%)		151 (50.7%)		82 (27.5%)		298 (100%)	
	M.35	F.30	M.91	F.60	M.49	F.33	M.175	F.123
CP	–		–		–		230 (100%)	
							M.104	F.126

M Male, *F* Female

determination of codes during diagnosis. We thus prepared a new cleft pattern model composed of a total 16 codes, with 6 codes for cleft lip, 4 codes for cleft jaw and 6 codes for cleft palate (4 codes for the soft palate and 2 codes for the hard palate) (Fig. 1). In regard to this reduction, Natsume et al. [2] reported that gender differences became even clearer in epidemiological analysis of cleft palate when the number of data codes was reduced. The incidence of each cleft pattern was therefore investigated using pattern models composed of 16 codes. Gender differences in cleft type were also analyzed. The χ^2 test was conducted to identify significant differences.

Results

Classification of Cleft Type

The most frequent type was cleft lip and palate, accounting for 40.8% overall. Analysis of cleft type by gender revealed that cleft lip and palate occurred more often in males, whereas cleft palate occurred more often in females (Table 1).

Cleft Laterality

In cleft lip, the majority of cases were left-sided (55.3%). In cleft lip and palate, the majority of cases were again left-sided (50.7%). Cleft lip and palate thus occurred more often on the left side than on the right (Table 2).

Classification by Cleft Pattern

In cases with ≥2 types of cleft pattern, a total of 35 patterns were ascertained (Fig. 2). These could be broken down into 21 patterns of cleft lip, 10 patterns of cleft lip and palate, and 4 patterns of cleft palate, representing a sufficient number of patterns for epidemiological analysis. Nine patterns included only a single case.

Overall, the most common cleft patterns were left complete cleft lip and palate (L123. A12. P12345.) (20.2%), incomplete cleft palate (L̄. Ā. P123.) (11.6%) and bilateral complete cleft lip and palate (L123. A1234. P123456.) (9.6%). In addition, the most common cleft patterns included many cases of cleft lip and palate, accounting for close to 40% of the total. However, the results showed that the cleft pattern of cleft palate occurred at the second highest incidence within that most common cleft-lip and palate cleft pattern. Conversely, using a simple cleft classification, even though cleft lip and palate were the most common, it was also confirmed that among them there was a cleft pattern of cleft lip and palate that occurred at low incidence.

Gender Differences in Cleft Pattern of Cleft Lip

The incidence of cleft pattern was analyzed in 183 patients with cleft lip in whom the cleft type was obvious. The most common cleft pattern in cleft lip was left cleft lip, wherein left complete cleft lip (L123. A12. P.12345.) was clearly

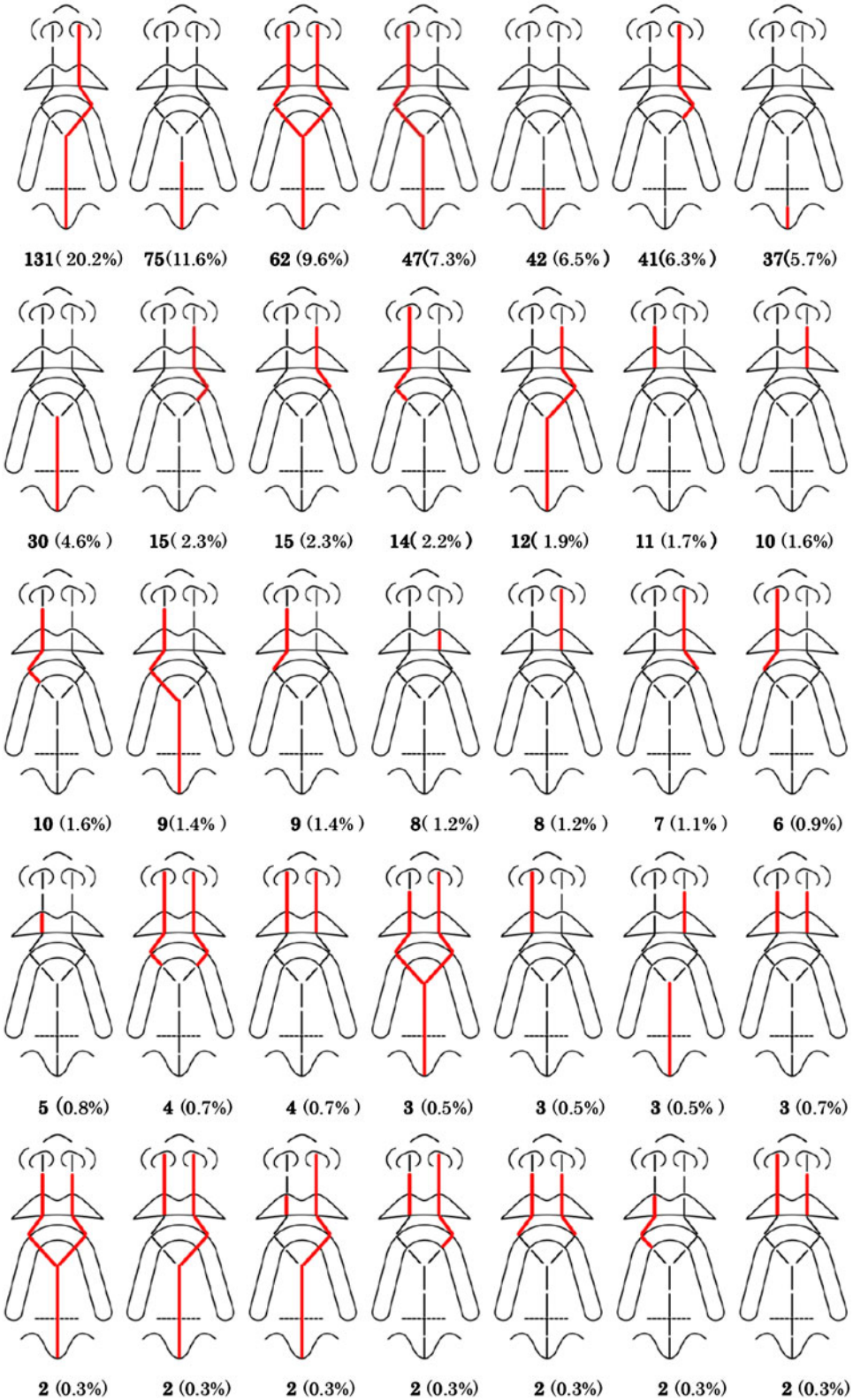
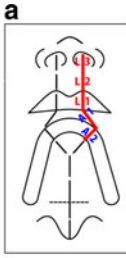


Fig. 2 The model for cleft of cleft lip and/or palate divided into 35 regions

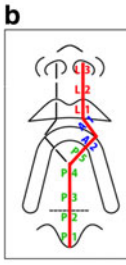
the most common (Fig. 3a). In terms of cleft laterality, cleft lip was generally more frequent in males and was often found on the left side. However, comparison of gender differences by cleft type by applying the cleft pattern method to unilateral cleft lip found that the incidence of mild cleft type cleft pattern was similar to the

a



	Cleft pattern			Male	Female	Total
1	L123.	A12.	P–.	19	22	41(22.4%)
2	L12.	A12.	P–.	8	7	15(8.2%)
3	L12.	A1.	P–.	9	6	15(8.2%)

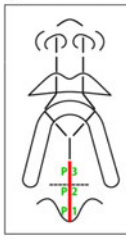
b



	Cleft pattern			Male	Female	Total
1	L123.	A12.	P12345.	74	57	131(46.8%)
2	L123456.	A1234.	P123456.	35	27	62(22.1%)
3	L456.	A34.	P12346.	24	23	47(16.8%)

Total Patients:280(male166,female114)

c



	Cleft pattern			Male	Female	Total
1	L–.	A–.	P123.	24	51	75(40.8%)
2	L–.	A–.	P12.	20	22	42(23.3%)
3	L–.	A–.	P1.	26	11	37(20.1%)

Total Patients:184(male78,female106)

Fig. 3 **a** Sexual difference (cleft lip). **b** Sexual difference (cleft lip and palate). **c** Sexual difference (cleft palate)

classification of the cleft type, i.e., more common in males, whereas slight gender differences emerged as cleft severity increased, with complete cleft lip conversely being more common in females than in males. On the basis of the cleft incidence, the results showed a reversal in gender differences (Tables 3a, b). In contrast, in the case of bilateral cleft lip, complete cleft was more common in males, whereas incomplete cleft showed no difference between the sexes.

Gender Differences in Cleft Pattern of Cleft Lip and Palate

The incidence of cleft pattern was analyzed in 280 patients with cleft lip and palate in whom the cleft type was obvious. The most common cleft pattern in cleft lip and palate was left complete cleft lip and palate (L123. A12. P12345.), followed by bilateral complete cleft lip and palate (L123. A1234. P12345.) and then by right complete cleft lip and palate (L456. A34. P12346.) (Fig. 3b). More males than females were seen among the total number of cases of cleft lip and palate ($P < 0.01$). However, comparison of gender differences for each cleft pattern in cleft lip and palate revealed a greater percentage of males in all types of incomplete cleft patterns, including left incomplete cleft lip and palate ($P < 0.01$). In cases where the cleft pattern was incomplete cleft, such as bilateral incomplete cleft lip and palate ($P < 0.05$), the percentage of males was markedly higher. In the case of complete cleft, the percentage of males was only slightly higher, and no gender difference was apparent in the case of right cleft lip and palate. Characteristics of the gender differences in cleft-lip and palate patterns were able to be confirmed not only in regard to complete and incomplete cleft, but also for laterality of the deformity (Table 4).

Gender Differences in Cleft Pattern of Cleft Palate

The incidence of cleft pattern was analyzed in 184 patients with cleft palate in whom the cleft type was obvious. The most common cleft pattern in cleft palate was incomplete cleft palate (L̄. Ā. P123.) (Fig. 3b). The cleft pattern of cleft palate was investigated for gender differences. In the cleft type classification, the percentage of females was greater than that of males. In contrast, analysis of gender differences by the cleft pattern method found that mild cleft patterns in cleft palate were more common in males ($P < 0.05$), whereas severe cleft patterns were more common in females ($P < 0.05$). The percentages of males and females were thus reversed (Table 5).

Discussion

Classification of Cleft Type

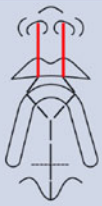
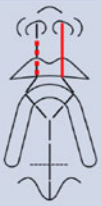
In past reports on cleft type classification by Natsume [3] and Aragaki [4], cleft lip and palate was the most common, followed by cleft lip and cleft palate. However, cleft lip and palate was the most common in the present study, accounting for 40.8% overall, followed by cleft palate. The results of a report by Ootsuki et al. [5] were similar to ours, indicating that cleft lip and palate was the most common, followed by cleft palate. Gender differences were also similar to past reports, with cleft lip and cleft lip/palate found more often in males and cleft palate found more often in females. Similar findings have been reported from other countries [6–8]. These results resemble those reported previously, and can be considered to approximate distributions in the general population.

Cleft Laterality

Cleft lip (55.3%) and cleft lip and palate (50.7%) occurred more often on the left side, similar to previous reports. According to Hirayama [9], one reason for the greater

Table 3 (a) Cleft patterns and gender differences for cleft lip (Lateral model). (b) Cleft patterns and gender differences for cleft lip (Bilateral model)

	A	B	C	D	E	F	Total
Pattern							
Male	5	16	10	25	22	6	84
Female	3	14	13	31	18	3	82
Total	8	30	23	56	40	9	166

	A	B	C	D	Total
Pattern					
Male	6	2	1	1	10
Female	2	3	1	1	7
Total	8	5	2	2	17

---- Shows the totals for each type of incomplete cleft pattern.

incidence on the left side is that facial artery development is slower on the left side compared to the right; however, this has not been fully confirmed. In addition, differences in cleft laterality and gender differences were similar to those with cleft classification, and the results show that both cleft lip and cleft palate are more common in males. Classification based on cleft laterality did not reveal any idiosyncrasies.

Classification by Cleft Pattern

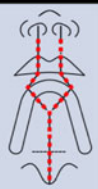
A total of 44 cleft patterns were diagnosed, including 9 patterns that were seen in only 1 patient each. The most common cleft pattern was cleft lip and cleft palate, and the results showed that within those, the pattern seen at the second highest incidence was cleft palate. In addition, although cleft lip and palate were found to be the most common by cleft classification, a cleft pattern of cleft lip and palate was confirmed to occur at low incidence. These are interesting results that should help us to investigate possible correlations between these phenomena and various factors, such as environmental and genetic factors. In the future, we hope to increase the number of analyzed cases to further our understanding of these rare cleft patterns as well as cleft patterns that were not detected in the present series.

Gender Differences in Cleft Pattern

Gender Differences in Cleft Lip

In terms of cleft laterality, cleft lip generally occurred more often on the left side. However, a comparison of gender differences by cleft type in unilateral cleft lip revealed that, as reported by Natsume et al. [10], mild cleft types clearly occurred more often in males, whereas slight gender differences emerged as cleft severity increased, with complete cleft lip being more common in females than in males. By performing analysis on the basis of the cleft pattern model, we confirmed a difference compared with information provided to date regarding gender differences. These findings are similar to those of Natsume et al. [10] Meskin et al. [11] have also reported a higher incidence of

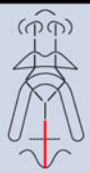
Table 4 Cleft pattern and gender differences for cleft tip and palate

	A	B	C	D	E	F	Total
Pattern							
Male	5	24	8	35	20	74	166
Female	4	23	1 *	27	2 **	57	114 **
Total	9	47	9	62	22	131	280

---- Shows the totals for each type of incomplete cleft pattern.

* $P < 0.05$, ** $P < 0.001$

Table 5 Cleft patterns gender differences for cleft palate

	A	B	C	D	Total
Pattern					
Male	8	24	20	26	78
Female	22 *	51 *	22	11 *	106 *
Total	30	75	42	37	184

* $P < 0.05$

complete cleft lip, which is characterized by greater cleft severity, in females. This suggests that gender may be related to the development of this condition and that developmental stage differences, hormones, or similar factors are involved. Although no conclusion can be reached on the basis of the present data alone, confirmation of similar phenomena in future studies would suggest the possibility of new knowledge that in the case of unilateral cleft lip, complete cleft occurs more commonly in females, while incomplete cleft is more common in males.

Gender Differences in Cleft Lip and Palate

The most common cleft patterns in cleft lip and palate were all the complete types. However, a detailed comparison of gender differences for each cleft pattern yielded the following results. Whereas the percentage of males in whom the cleft pattern was incomplete was markedly higher for left incomplete cleft lip and palate ($P < 0.01$) and bilateral incomplete cleft lip and palate ($P < 0.05$), gender differences were less pronounced in the case of complete cleft. In addition, no gender differences existed in the case of right cleft lip and palate, and the characteristics of gender differences in relation to laterality were also confirmed. As in the case of cleft lip, the cleft pattern method allowed us to confirm the characteristics of gender differences that have not previously been reported. In the future, we plan to increase the number of patients and further elucidate these characteristics. In addition, left complete cleft lip and palate was the most common of all cleft patterns and was found more often in males, which may be of interest in future considerations of genetic factors.

Gender Differences in Cleft Palate

In terms of cleft classification, cleft palate is generally found more often in females. However, comparison of gender differences by the cleft pattern method revealed that milder cleft patterns are more common in males, whereas the percentage of females tended to exceed that of males with increasing cleft severity. These new findings were generated using the cleft pattern method, and can be thought to validate the significance of this classification method. Also, these results agree with those reported by Natsume et al. [10] and Meskin et al. [11]. In contrast, Ueda et al. [12] reported no differences in cleft severity between males and females. This may have been because the use of our coded cleft pattern classifications resulted in more detailed analysis, once again suggesting the need for classification based on cleft pattern.

With regard to the reasons for gender-related differences in cleft patterns, Miura et al. [13] from the Center suggested the involvement of female sex hormones, and Ross et al. [14] suggested a relationship between female sex hormones and the palatine process.

Accordingly, the timing of initial movement of bilateral palatine processes in the course of palate development occurs earlier in males and later in females, and this difference affects the degree of cleft. Here, we applied the cleft pattern method for analyses, allowing us to demonstrate in detail the effects of that difference in relation to each cleft pattern. We analogize that it was because we elucidate the characteristics of new gender differences in each stage.

Conclusions

Cleft lip and cleft palate are common surface malformations, and also often occur with other congenital anomalies. Cleft lip and cleft palate can lead to a wide range of disorders, such as neonatal feeding disorders, eating disorders, and language disorders due to maxillary undergrowth, dental deficiencies, and malocclusion. In addition, these anomalies present as conspicuous facial malformations, and can thus be considered cosmetic disturbances that can result in profound mental and psychological disorders in individuals and families. Modeling (assigning numerical values to) cleft patterns to analyze cleft severity not only enables more objective diagnosis, but also allows more detailed classification of cleft lip/cleft palate and may lead to a better understanding of pathology based on cleft severity. The cleft patterns and gender differences suggest the possibility of new knowledge that has not therefore been discovered with conventional classification methods. In addition, this cleft pattern method has potential for effective application in preventive medicine by elucidating pathologies and facilitating genetic counseling by allowing the investigation of possible correlations between cleft patterns and various factors, such as environmental and genetic factors. We hope to continue examining correlations between cleft pattern and various other factors via rapid computer analysis of accumulated data using these systems in the future. The present system of analysis may also be useful in the development of comprehensive therapeutic systems for each and every cleft pattern. We also hope to continue our studies to understand the pathogenesis of this condition.

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