Anatomical analysis of zygomatic bone in ectodermal dysplasia patients with oligodontia

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Abstract
Background: Abnormalities of some facial bones derived from the ectomesenchyme have been found in ectodermal dysplasia (ED) patients, but the characteristics of the zygoma are unknown.
Purpose: Comparison between ED patients and normal individuals to understand the anatomical features of the zygoma in ED patients.
Materials and Methods: Thirty patients diagnosed with ED based on clinical features and/or gene sequence tests and 80 normal individuals were recruited from 2016 to 2018. The thickness of the zygomatic body at 12 points on the superior, middle, and inferior areas and the length of four lines were measured on a three-dimensional cone beam computed tomography image. Differences between ED patients and normal individuals were then compared.
Results: The zygomatic thicknesses and lengths were smaller in ED patients than in normal individuals. For ED patients, the largest thicknesses on the superior, middle, and inferior areas of the zygoma were 8.47 ± 1.49, 7.03 ± 1.56, and 5.99 ± 1.22 mm.
Conclusion: The development of zygomatic thickness on the inferior area and the zygomatic length were insufficient in ED patients with oligodontia. Consequently, zygomatic hypoplasia presented difficulties for the "quad approach" to zygomatic implants in this group of patients.

KEYWORDS
ectodermal dysplasia, hypodontia, zygomatic bone, zygomatic implant

1 INTRODUCTION

Ectodermal dysplasia (ED) is a congenital disorder characterized by the abnormal development of two or more ectoderm-derived structures, at least two of which involve pathological abnormalities in hair, sweat glands, nails, or teeth. ED can be X-linked recessive (MIM#305100), autosomal dominant (MIM#129490), and autosomal recessive (MIM#224900).³ Hypohidrotic ectodermal dysplasia is the...
most common form, with an incidence of 1-7 individuals per 10,000 live births.2

There are some structural and functional abnormalities in tissues derived from the ectoderm in ED patients. The facial bones include the maxilla, mandible, alveolar bone, nasal bone, and zygomatic bone derived from the ectomesenchyme during embryological development. The clinical dento-craniofacial features are maxillary hypoplasia, mandibular protrusion, midface depression, reduced facial height, a wide and prominent forehead, abnormal or missing sweat glands, sparse hair, dry skin, protuberant lips, saddle nose, oligodontia or hypodontia, abnormal conical teeth, and severe developmental defects of the alveolar ridges.1,3 However, it is unclear whether the development of the zygomatic bone is affected in those patients.

Prosthodontic treatment of ED includes tooth-supported fixed dentures, removable partial protheses, overdentures, and implant-supported prostheses.4 Due to severe developmental defects of the alveolar ridges and salivary gland hypoplasia, the use of traditional overdentures makes it difficult to reconstruct oral function for ED patients. In most cases, especially for oligodontia patients, undeveloped alveolar bone could not provide sufficient bone volume to contain the conventional implant, so patients frequently need to undergo additional bone augmentation before implant placement.3,5,6 Obvious disadvantages of extensive bone grafting exist, such as donor site morbidity, unpredictable resorption of grafting, staged placement of implant, and prolonged therapy.7–9 Zygomatic implant (ZI) was a suitable approach to save treatment time and avoid grafting of the severely atrophic maxilla, with a long-term survival rate from 95.1% to 100% in ED patients.10–15 The bone volume of the zygoma is the key for the placement of the ZI. However, there is no information regarding the evaluation of the characteristics of the zygoma in ED patients. Therefore, this study aimed to evaluate the thickness and length in different areas of the zygoma and the relationships between thickness and length and gender in ED patients; and the difference between ED patients and normal individuals by measurement of three-dimensional reconstruction computed tomography images.

2 | MATERIALS AND METHODS

2.1 | Patients

The study was approved by the Ethical Committee of the Shanghai Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine. All patients provided written informed consent.

Patients who underwent cone beam computed tomography (CBCT) examinations for treatment planning in the Department of Second Dental Clinic and Department of Oral Implantology, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine, between February 2016 and February 2018 were enrolled in the study. For ED patients, the inclusion criteria were as follows: (1) diagnosis of ED according to the method defined by Freire-Maisa16 in that the features of patients exhibited at least two of the following characteristics: abnormal hair, abnormal dentition, abnormal nails, and abnormal sweat glands; (2) diagnosis of ED through genetic screening (Table 1); (3) patient age older than 18 years; and (4) presentation with congenital absence of multiple permanent teeth (≥10, excluding the third molar). For normal individuals, the inclusion criteria were as follows: (1) age similar to that of the ED patients; (2) not toothless in the maxilla; and (3) no anatomical abnormalities in the maxilla or zygoma.

2.2 | CBCT standardization

All cases were scanned with CBCT (i-Cat: Imaging Sciences International, LLC, Hatfield, Pennsylvania) with a standard x-ray tube (80 kV, 5 mA) and an amorphous silicon flat panel detector (19.2 × 23.8 cm). The exposure volume was set at 0.4 mm. The voxel dimension in the reconstructed image was 0.2 × 0.2 × 0.2 mm3. All DICOM files were imported and measured with the planning software NobelClinician (Nobel Biocare AB, Goteborg, Sweden).

2.3 | CBCT analysis

2.3.1 | Landmark designation

All points and lines were designed according to a previous study (Figures 1 and 2).17

1. LM: a line passed through the most lateral margin of the orbital socket parallel to the midsagittal plane (Figure 1A).
2. IM: a line connected the two lowermost points of the bilateral infraorbital margin (Figure 1A).
3. Point E: the point of intersection between LM and IM (Figure 1B).
4. Point O: the point of intersection between angular bisector of LM and IM and orbital margin (Figure 1B).
5. L1: a line passed through Point O and Point E (Figure 1C).
6. L3: a line located anteriorly at a distance of 5 mm was parallel to L1 (Figure 1D).
7. L2: a line located posteriorly at a distance of 5 mm was parallel to L1 (Figure 1D).
8. L4: a line located posteriorly at a distance of 5 mm was parallel to L2 (Figure 1D).
9. Point A0, B0, and C0: three points quartered the L0 from the top to the bottom (Figure 1D).
10. Point A3, B3, and C3: three points quartered the L3 from the top to the bottom (Figure 1D).
11. L0, L1, and L2: three lines connected points A0 and B0, points B0 and C0, and points C0 and C3, respectively (Figure 1D).
12. Points A1, A2, B1, B2, C1, and C2: six points of intersection between the L0, L1, and L2 (Figure 1D).

2.3.2 | Measurement of the thickness and length of the zygoma

The thickness of the zygoma at 12 points on the inferior, middle, and superior regions and the length of zygoma at L0–L3 lines was measured on the bilateral zygoma in all ED patients and normal individuals (Figure 3). All the measurements were performed by one oral surgeon twice with a 1-month interval, and the difference between the two measurements was determined by intraclass correlation.
coefficient (=0.985). The mean values were expressed as the dates with two measurements.

2.4 | Statistical analysis

All dates were performed with SPSS (SPSS, Inc, Chicago, Illinois). The Shapiro-Wilk test was used to assess whether dates were normally distributed. The mean ± standard deviation (SD) or the median and interquartile range expressed the data for parametric variables and nonparametric variables, respectively. Differences in the thickness and length of the zygoma between males and females were compared by independent Student's t-test. Differences in the thickness of the inferior, middle, and superior areas and the length at the L0-L3 lines were compared by ANOVA. A P value of <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Patients

Thirty oligodontia ED patients (male = 17, female = 13; age range: 18-36 years; mean age = 22.5 ± 4.3 years) and 80 normal individuals (male = 40, female = 40; age range: 18-36 years; mean age = 23.1 ±
4.4 years) were enrolled in the study. The ED patients presented congenital absence of multiple teeth (Figure 4), and the average number of permanent teeth lost was 22.1 ± 3.9 (range: 16-28). The average number of teeth lost in the maxilla was 11.5 ± 1.5 (range: 10-14; Table 1).

3.2 | The thickness of the zygoma at points and length at lines in ED patients

A total of 60 zygomata were measured. The mean ± SD were used to express all dates that were normally distributed. Tables 2 and 3 show the thickness of the zygoma at each point and the length of the zygoma at each line, respectively. Differences in thickness at points on the superior, middle, and inferior regions of the zygoma were significant (P < 0.001). Differences in length of the lines were also significant (P < 0.001). The largest thicknesses on the superior, middle, and inferior areas were at point A1 (8.47 ± 1.49 mm), point B1 (7.03 ± 1.56 mm), and point C0 (5.99 ± 1.22 mm), respectively. The thickness of the zygoma decreased from point C0 to point C3 in the inferior area; the thickness of the zygoma decreased from point B1 to point B0 and point B3 in the middle area; and the thickness of the zygoma decreased from point A1 to point A0 and point A3 in the superior area (Table 2 and Figure 2). The length of the lines gradually increased from L0 (21.39 ± 3.13 mm) to L3 (29.25 ± 3.14 mm) (Table 3).

3.3 | Correlation of the thickness and length of the zygoma with gender in ED patients

The thickness of the zygoma at the designated points and length of the lines were compared between males and females. The results revealed that the thickness at all points excluding point A3 was significantly larger in males than in females (Table 4). The length at all lines was significantly longer in males than in females (Table 4).

3.4 | Differences in the thickness and length of zygoma between ED patients and normal individuals

The thickness of the zygoma at the designated points and length of the lines was compared between ED patients and normal individuals. For normal individuals, the thickness of the zygoma decreased from point C0 to point C3 in the inferior area; the thickness of the zygoma decreased from point B1 to point B0 and point B3 in the middle area; and the thickness of the zygoma decreased from point A1 to point A0 and point A3 in the superior area, and the length of the lines gradually increased from L0 to L3 (Table 5). Table 5 proves that for males, females, and total patients, the difference in the thickness of the superior and middle regions was not significant between ED patients and normal individuals; the thickness in the inferior region was significantly lower in ED patients than in normal individuals; and the length at all lines was shorter in ED patients than in normal individuals (P < 0.001).
4 | DISCUSSION

Facial bones, such as the maxilla, mandible, alveolar bone, and nasal bone, derived from the ectomesenchyme present abnormalities in ED patients. Additionally, double or quadruple ZIs were used to restore oral function with the advantage of a reduced total treatment time and to avoid complex bone grafting for ED patients with a congenital, edentulous, and severely atrophic maxilla. However, it is unclear whether the development of the zygomatic bone and the placement of ZIs are affected in those patients. Therefore, this study evaluated the thickness and length of different areas of the zygoma so that dentists can better understand the characteristics of the zygoma in ED patients.

The results of this study showed that the thicknesses of the zygoma ranged from 3.54 ± 0.83 to 8.48 ± 1.49 mm, and the lengths ranged from 21.39 ± 3.13 to 29.25 ± 3.14 mm in ED patients. The thicknesses of the zygoma ranged from 4.30 ± 1.09 to 8.88 ± 1.99 mm, and the lengths ranged from 25.54 ± 3.25 to 32.53 ± 2.88 mm in normal individuals. The thickness and length of the zygoma were smaller in ED patients than in normal individuals. Regarding ED patients, this study also revealed that the thickness and length of the zygoma were larger in males than in females, which is consistent with previous reports in normal individuals.

The study proved that the largest thicknesses in the superior, middle, and inferior areas were at point A1, point B1, and point C0, respectively, and that there was a changing trend in the thickness and length of the zygoma in ED patients; this trend is the same as that found for zygomatic characteristics in normal individuals from this study and the previous study. The thicknesses of the zygoma in the superior area and in the middle area in this study were similar to the thickness of the zygoma in normal individuals. However, compared to normal individuals, the thicknesses of zygoma at point C0 (5.99 ± 1.22 mm), point C1 (5.40 ± 1.12 mm), point C2 (4.49 ± 0.98 mm), and point C3 (3.54 ± 0.83 mm) in the inferior area and the lengths of zygoma at L0 (21.39 ± 3.13 mm), L1 (22.27 ± 2.09 mm), L2 (24.58 ± 3.14 mm), and L3 (29.25 ± 3.14 mm) in ED patients were smaller than the thicknesses of the zygoma at point C0 (6.59 ± 1.75 mm), point C1 (6.10 ± 1.35 mm), point C2 (5.31 ± 1.30 mm), and point C3 (4.30 ± 1.30 mm) in the inferior area and the lengths of zygoma at L0 (25.54 ± 3.25 mm), L1 (26.39 ± 3.03 mm), L2 (28.31 ± 2.78 mm), and L3 (32.53 ± 2.88 mm) in normal individuals. Therefore, the author suggested that the development of zygomatic thickness in the inferior area and the zygomatic length were insufficient in ED patients with oligodontia.

### TABLE 2 Difference of zygomatic thicknesses at points on the superior, middle, and inferior regions in ectodermal dysplasia patients

| Region     | Point | Mean ± SD  | P value |
|------------|-------|------------|---------|
| Thickness  |       |            |         |
| Superior   | A0    | 7.04 ± 1.71| <0.001  |
|            | A1    | 8.47 ± 1.49|         |
|            | A2    | 8.17 ± 1.66|         |
|            | A3    | 5.86 ± 2.01|         |
| Middle     | B0    | 5.98 ± 1.21| <0.001  |
|            | B1    | 7.03 ± 1.56|         |
|            | B2    | 5.62 ± 1.46|         |
|            | B3    | 3.92 ± 1.25|         |
| Inferior   | C0    | 5.99 ± 1.22| <0.001  |
|            | C1    | 5.40 ± 1.12|         |
|            | C2    | 4.49 ± 0.98|         |
|            | C3    | 3.54 ± 0.83|         |

### TABLE 3 Difference of zygomatic lengths at lines in ectodermal dysplasia patients

| Line | Mean ± SD  | P value |
|------|------------|---------|
| L0   | 21.39 ± 3.13| <0.001  |
| L1   | 22.27 ± 2.09|         |
| L2   | 24.58 ± 3.14|         |
| L3   | 29.25 ± 3.14|         |
Presented dento-craniofacial features of ED patients included maxillary hypoplasia, mandibular protrusion, midface depression, and severe developmental defects of the alveolar ridges.1,2,20 Although most abnormalities of craniofacial morphology and bone structural anomalies can be attributed to molecular etiologies, some studies have proposed that the congenital absence of teeth could also be responsible.1,2,21 Molecular etiologies of ED consisted of changes in the signaling pathways that modulate NK-κB activity, such as the ectodysplasin (EDA)-EDAR-EDARRADD signaling pathway and the NEMO regulatory pathway that modulates NK-κB activity, such as the ectodysplasin (EDA)-EDAR-EDARRADD signaling pathway and the NEMO regulatory pathway that modulates NK-κB signaling pathway resulted in abnormal skeletogenetic neural crest cell differentiation, migration, and osteoclastic differentiation such that craniofacial abnormalities presented clinical signs in ED patients.20,22 Mutation of the p63 gene also caused disorders in facial development because the transcription and expression of the p63 gene played an essential role in epidermal differentiation and proliferation during embryogenesis.1,2,23,24 Additionally, other authors suggested that craniofacial features, such as reduced maxilla length and prognathism, retroclined nasal bone, short nose, and reduced facial height, also resulted from the absence of teeth.1,2,21 However, there was no information about the study of zygomatic morphology and reports of zygomatic hypoplasia in ED patients in the literature. Furthermore, the study showed that the development of the zygoma was insufficient in ED patients with molecular etiologies and oligodontia. ED is a congenital disease characterized by structural and functional abnormalities in tissues derived from the ectoderm. All facial bones include the maxilla, mandible, alveolar bone, and zygomatic bone derived from the ectomesenchyme. As mentioned earlier, the author suggested that molecular etiologies and congenital absence of multiple teeth possibly resulted in zygomatic hypoplasia in ED patients.

Some studies proposed that the bone thickness placed at the apex of the ZI should be at least 5.75 mm,25,26 and this study showed that the thicknesses of the zygoma at point C1 (5.40 mm), point C2 (4.49 mm), and point C3 (3.54 mm) in the inferior area were smaller than 5.75 mm, except for point C0 (5.99 mm); in addition, the length of the zygoma was significantly shorter in ED patients than in normal individuals. Therefore, when the distal implant of quadruple ZIs was designed for placement on the inferior areas in ED patients, dentists should not only be careful to place the implant in the proper regions but also avoid damaging important anatomical structures in the infratemporal fossa. Based on the above characteristics of the zygoma in ED patients, the use of computer-assisted navigation technology for the placement of ZIs is more necessary than it is for normal individuals.

### Table 5
**Difference of zygomatic thicknesses at points and zygomatic lengths at lines between ectodermal dysplasia (ED) patients and normal individuals**

| Point/line (mm) | ED Male | ED Female | ED Total | Normal individuals Male | Normal individuals Female | Normal individuals Total | P values |
|-----------------|---------|-----------|----------|-------------------------|---------------------------|-------------------------|----------|
| A0              | 7.49 ± 1.39 | 6.46 ± 1.91 | 7.04 ± 1.71 | 7.75 ± 2.10 | 6.50 ± 2.30 | 7.09 ± 2.29 | 0.870    |
| A1              | 8.85 ± 1.65 | 7.96 ± 1.09 | 8.47 ± 1.49 | 9.52 ± 1.89 | 8.10 ± 1.72 | 8.88 ± 1.99 | 0.057    |
| A2              | 8.53 ± 1.56 | 7.70 ± 1.57 | 8.17 ± 1.66 | 6.75 ± 2.73 | 6.22 ± 3.11 | 6.17 ± 2.93 | 0.355    |
| A3              | 6.15 ± 1.56 | 5.48 ± 2.46 | 5.86 ± 2.01 | 9.08 ± 2.29 | 7.74 ± 1.94 | 8.37 ± 2.21 | 0.400    |
| B0              | 6.53 ± 1.27 | 5.26 ± 1.78 | 5.98 ± 1.21 | 6.72 ± 2.03 | 5.29 ± 1.84 | 5.96 ± 2.05 | 0.787    |
| B1              | 7.59 ± 1.23 | 6.30 ± 1.67 | 7.03 ± 1.56 | 7.83 ± 2.31 | 7.04 ± 1.89 | 7.41 ± 2.13 | 0.672    |
| B2              | 6.13 ± 1.16 | 4.93 ± 1.55 | 5.62 ± 1.46 | 6.64 ± 2.17 | 5.63 ± 1.40 | 6.01 ± 1.86 | 0.287    |
| B3              | 4.55 ± 1.02 | 3.09 ± 1.02 | 3.92 ± 1.25 | 4.92 ± 1.42 | 3.50 ± 0.84 | 4.17 ± 1.35 | 0.850    |
| C0              | 6.28 ± 1.09 | 5.62 ± 1.30 | 5.99 ± 1.22 | 6.91 ± 1.86 | 6.30 ± 1.57 | 6.59 ± 1.75 | 0.021    |
| C1              | 5.66 ± 1.09 | 5.05 ± 1.10 | 5.40 ± 1.12 | 6.30 ± 1.53 | 5.74 ± 1.13 | 6.10 ± 1.35 | 0.008    |
| C2              | 4.76 ± 0.97 | 4.13 ± 0.89 | 4.49 ± 0.98 | 5.78 ± 1.46 | 4.80 ± 0.99 | 5.31 ± 1.30 | <0.001   |
| C3              | 3.73 ± 0.76 | 3.30 ± 0.87 | 3.54 ± 0.83 | 4.75 ± 1.17 | 3.80 ± 0.84 | 4.30 ± 1.09 | <0.001   |
| L0              | 22.20 ± 3.51 | 20.33 ± 2.19 | 21.39 ± 3.13 | 27.13 ± 3.26 | 24.12 ± 2.33 | 25.54 ± 3.25 | <0.001   |
| L1              | 22.99 ± 3.59 | 21.33 ± 1.96 | 22.27 ± 2.09 | 27.85 ± 3.09 | 25.08 ± 2.32 | 26.39 ± 3.03 | <0.001   |
| L2              | 25.34 ± 3.47 | 23.57 ± 2.36 | 24.58 ± 3.14 | 29.59 ± 2.78 | 27.17 ± 2.08 | 28.31 ± 2.78 | <0.001   |
| L3              | 30.14 ± 3.38 | 28.09 ± 2.38 | 29.25 ± 3.14 | 33.59 ± 2.84 | 31.58 ± 2.23 | 32.53 ± 2.88 | <0.001   |

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To the best of our knowledge, this study was the first to evaluate anatomical characteristics of zygomatic bone by measuring the thickness and length of the zygoma based on CBCT images and to propose that the development of zygomatic thickness on the inferior area and zygomatic length in ED patients with oligodontia was insufficient. However, the sample of ED patients was limited, and it is difficult to distinguish the relationship among zygomatic hypoplasia, the mutation of genes, and the absence of teeth with the limited evidence presented here. Furthermore, the author will study whether zygomatic hypoplasia affects the placement of ZIs by placing implants on the CBCT images.

5 | CONCLUSION

The limitations of the study suggest that the development of zygomatic thickness and length in ED patients with oligodontia was insufficient. The largest thickness of the zygoma in ED patients with oligodontia existed in the center of the zygoma close to the infraorbital area, which provided the optimal region for ZI apex anchorage. However, the length of the zygoma in this group of patients was limited, and it presented difficulties for the “quad approach” in ZIs.

CONFLICT OF INTEREST

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