Early Prediction of the Need for Orthognathic Surgery in Patients With Repaired Unilateral Cleft Lip and Palate Using Machine Learning and Longitudinal Lateral Cephalometric Analysis Data

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Abstract: The purpose of this study was to determine the cephalometric predictors of the future need for orthognathic surgery in patients with repaired unilateral cleft lip and palate (UCLP) using machine learning. This study included 56 Korean patients with UCLP, who were treated by a single surgeon and a single orthodontist with the same treatment protocol. Lateral cephalograms were obtained before the commencement of orthodontic/orthopedic treatment (T0; mean age, 6.3 years) and at at least of 15 years of age (T1; mean age, 16.7 years). 38 cephalometric variables were measured. At T1 stage, 3 cephalometric criteria (ANB $\leq -3°$; Wits appraisal ≤ -5 mm; Harvold unit difference $\geq$34 mm for surgery group) were used to classify the subjects into the surgery group (n = 10, 17.9%) and non-surgery group (n = 46, 82.1%). Independent *t*-test was used for statistical analyses. The Boruta method and XGBoost algorithm were used to determine the cephalometric variables for the prediction model. At T0 stage, 2 variables exhibited a significant intergroup difference (ANB and facial convexity angle [FCA], all $P < 0.05$). However, 18 cephalometric variables at the T1 stage and 14 variables in the amount of change (ΔT1−T0) exhibited significant intergroup differences (all, more significant than $P < 0.05$). At T0 stage, the ANB, PP-FH, combination factor, and FCA were selected as predictive parameters with a cross-validation accuracy of 87.4%. It was possible to predict the future need for surgery to correct sagittal skeletal discrepancy in UCLP patients at the age of 6 years.

Key Words: Cephalometric predictors, machine learning, orthognathic surgery, unilateral cleft lip and palate

(*J Craniofac Surg* 2021;32: 616–620)

Skeletal Class III malocclusion with restricted maxillary growth is frequently observed in patients with unilateral cleft lip and palate (UCLP), and is related to the intrinsic factors and the scar tissue from surgical intervention.[1–3] A quarter to a half of patients with UCLP are known to need orthognathic surgery or distraction osteogenesis (DO) to obtain a normal intermaxillary relationship and an improved facial esthetics.[4–8]

Although the orthopedic treatment for maxillary protraction using face mask (FM) with bone-anchored mini-plates[9,10] might not fully correct Class III intermaxillary relationship, it would reduce the amount of maxillary advancement in orthognathic surgery or DO. Thus, the postoperative stability of the maxilla can be improved.[11,12] However, orthopedic treatment is usually conducted only when UCLP patients developed moderate sagittal skeletal discrepancy at around 10 years of age.[13–16] Clinicians and parents of cleft patients want to know the future need for the surgical correction of the sagittal skeletal discrepancy. Therefore, early prediction of the maxillofacial growth would be meaningful in determining to start orthopedic treatment or wait for the completion of growth.

Park et al[17] used the feature wrapping method, a kind of machine learning, to determine the cephalometric predictors of the future need for orthognathic surgery to correct the sagittal skeletal discrepancy in Korean male patients with clefts. At the mean age of 9.3, a total of 10 cephalometric variables (APDI, ODI, Harvold unit difference, Wits appraisal, AB to mandibular plane angle, gonial angle, ANB, overjet, A to N perp, and IMPA) were selected as predictors, with a weighted classification accuracy of 77.3%. The study also reported that the frequency of surgical intervention increased with cleft severity from cleft lip and alveolus (CLA) group, UCLP group, to bilateral cleft lip and palate (BCLP) group (8.5%, 21.4%, and 30.0%).[17]

Among the diverse machine learning methods to find the relevant features, several previous studies have used the Boruta method due to its best performance.[18–21] The method is based on a random forest approach that can identify the most important features with high feature-selection stability.[22,23] The XGBoost algorithm[24] is an extendable, cutting-edge application for gradient-boosting machines, and has been proven to push the limits of computing power for boosted tree algorithms. Boosting is an ensemble technique whereby new models are appended to adjust the errors by preexisting models. Gradient boosting is an algorithm whereby new models are created to cover the residuals of prior models and then added together to obtain better predictions.[25] Therefore, this study

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Received May 21, 2020.

Accepted for publication June 30, 2020.

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The authors have no potential conflicts of interest to disclose.

Supplemental digital contents are available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jcraniofacialsurgery.com).

ISSN: 1049-2275

DOI: 10.1097/SCS.0000000000006943

used the Boruta method and the XGBoost algorithm to investigate the cephalometric predictors of the future need for orthognathic surgery or DO in patients with repaired UCLP.

METHODS

Patients

The samples consisted of 56 Korean patients with non-syndromic UCLP (31 males and 25 females), who were treated at the Department of Plastic Surgery, Seoul National University Children's Hospital (SNUCH) and the Department of Orthodontics, Seoul National University Dental Hospitals (SNUDH), Seoul, Republic of Korea. This retrospective study was reviewed and approved by the institutional review board of the SNUDH (ERI20014).

To increase the sample purity for helping the machine learning to obtain better prediction accuracy, we considered three aspects including

1. identical treatment protocol,
2. strict inclusion criteria, and
3. definite grouping criteria in the present study.

Treatment Protocol

The treatment protocol used in SNUCH and SNUDH is summarized as below:

(1) primary cheiloplasty (rotation and advancement flap) was performed between 3 and 5 months of age;
(2) palatoplasty (Furlow double opposing Z-plasty) and late primary gingivoperiosteoplasty were performed between 12 and 18 months of age;
(3) if needed, maxillary arch was expanded before secondary alveolar bone grafting (SABG);
(4) SABG with cancellous bone from the iliac bone was conducted during the mixed dentition stage;
(5) if needed, facemask with bone-anchored mini-plates was used for orthopedic maxillary protraction during the pubertal growth period;
(6) fixed orthodontic treatment was performed during the permanent dentition stage; and
(7) if needed, orthognathic surgery or DO were performed after completion of growth.

Inclusion Criteria

Participants were enrolled on the basis of the following inclusion criteria:

(1) patients who were born before 2002 and whose charts, radiographs, and clinical photographs were available for longitudinal follow-up;
(2) patients who were treated with the same protocol by a single surgeon (SWK) and a single orthodontist (SHB) to eliminate the influences of different surgical and orthodontic treatments;
(3) patients whose initial lateral cephalogram was obtained between 5 and 7 years of age (T0 stage) and who did not undergo orthodontic/orthopedic treatment and alveolar bone grafting to avoid the effects on the skeletodental growth; and
(4) patients whose final lateral cephalogram was obtained at or above 15 years of age (T1 stage) to judge the need for orthognathic surgery or DO. Syndromic patients were excluded.

Grouping

A total of 56 patients with UCLP were recruited. At the T1 stage, patients

(1) who had undergone orthognathic surgery or DO,
(2) who were under presurgical orthodontic treatment, or
(3) who met the cephalometric criteria for orthognathic surgery (ANB ≤ -3 degrees, Wits appraisal ≤ -5 mm, and Harvold unit difference ≥ 34 mm), were classified into the surgery group ($n = 10$, 17.9%).[17]

The remaining patients were allocated into the non-surgery group ($n = 46$, 82.1%).

Cephalometric Analysis

The appendix-1, http://links.lww.com/SCS/B763 and Figure 1 list the definition of cephalometric landmarks and cephalometric variables included in the cephalometric analysis. The cephalometric analysis for all patients at the T0 and T1 stages was assessed twice by a single researcher (GL) by using the V-CEPH (Version 8.4; CyberMed, Seoul, Korea) program. As there was no significant difference between the first and second measurements, the first measurement set was used for further statistical analysis.

Statistical Analysis

The independent *t* test was used to investigate the intergroup differences on the cephalometric variables at the T0 and T1 stages,

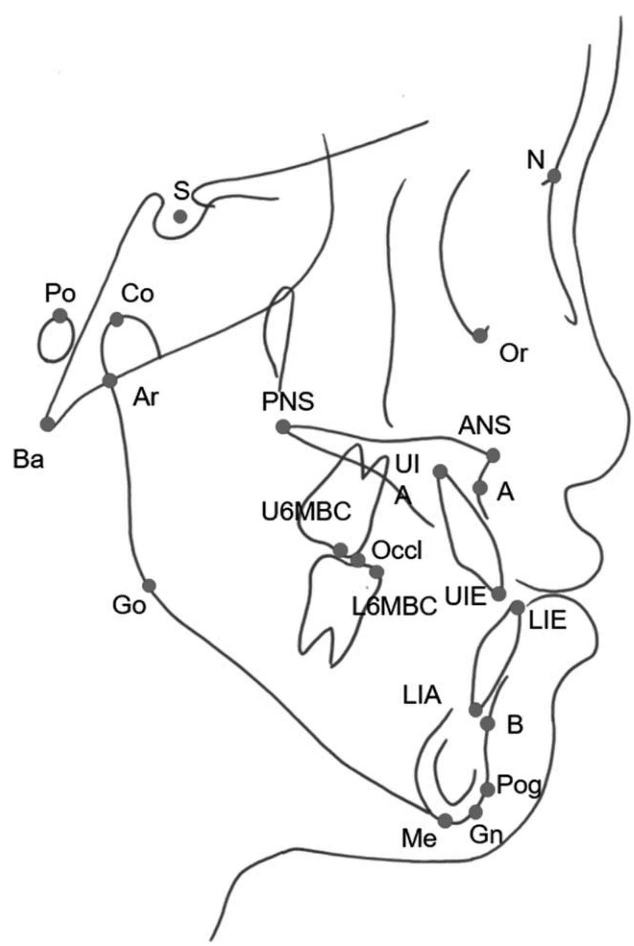

FIGURE 1. Cephalometric landmarks used in this study.

and the amount of change (ΔT1−T0). The SPSS (version 12.0; SPSS, Chicago, IL) software package was used for statistical analysis. P value less than 0.05 was set as an indicator of statistical significance.

Feature Selection (Appendix-2, http://links.lww.com/SCS/B763)

The Boruta method was used to determine the cephalometric predictors at the T0 stage. The XGBoost algorithm was used to generate the machine learning model that classifies the need for surgical correction for each patient, and 10-fold cross-validation accuracy with F1-score were obtained. The prediction model was testified with the confusion matrix without normalization.

RESULTS

Intergroup Differences at Each Stage

The final analysis dataset included 56 patients (T0 stage; mean age, 6.3 years and T1 stage; mean age, 16.7 years). At the T0 stage, only 2 variables exhibited a significant intergroup difference [ANB and FCA, all $P < 0.05$; Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762). At the T1 stage, 18 cephalometric variables showed a significant difference between the two groups (A-N perp, SNB, ODI, articular angle, mandibular body length, IMPA, bisecting occlusal plane to FH plane angle, occlusal plane to SN plane angle, and upper gonial angle, all $P < 0.05$; Pog-N perp, Co-Gn, and AB-MP, all $P < 0.01$; ANB, Wits appraisal, APDI, Harvold unit difference, FCA, and AB to occlusal plane angle, all $P < 0.001$; Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762). For ΔT1−T0, 14 variables (ΔSNB, ΔPog-N perp, ΔCo-Gn, ΔHarvold unit difference, ΔSN-MP, ΔWits appraisal, ΔBjork Sum, Δmandibular body length, and Δbody to anterior cranial base ratio, all $P < 0.05$; ΔANB, ΔAB-MP, ΔFCA, and ΔAB to occlusal plane angle, all $P < 0.01$; ΔAPDI, $P < 0.001$; Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762) exhibited a significant intergroup difference.

Prediction of the Future Need for Orthognathic Surgery or Distraction Osteogenesis

Four cephalometric parameters of the T0 stage including ANB (intermaxillary relationship between the maxilla and mandible; degree of relative protrusion of B point in relation to A point), PP-FH (inclination of the palatal plane in relation to the FH plane), combination factor (CF; sum of ODI and APDI, which means the skeletal size of the maxilla and mandible) and FCA (intermaxillary relationship between the maxilla and mandible; degree of relative protrusion of Pogonion point in relation to A point) were selected as predictors of the future need for orthognathic surgery or DO (Supplementary Digital Content, Table 2, http://links.lww.com/SCS/B762 and Fig. 2). The feature importance of the ANB, PP-FH, CF and FCA were 0.2430162, 0.23951529, 0.24303272 and 0.27443576, respectively (Supplementary Digital Content, Table 2, http://links.lww.com/SCS/B762).

The prediction model has a 10-fold cross-validation accuracy of 87.4% with F1-score of 0.714 (Fig. 3). The sensitivity (the proportion of actual non-surgery patients that was correctly predicted as non-surgery patients) and specificity (the proportion of actual surgery patients that was correctly predicted as surgery patients) of the prediction model were 97.83% and 90.00%, respectively (Fig. 3). This model is uploaded on the following Web site (http://147.47.41.53:8890). The prognosis prediction results for surgery and no surgery are generated when the values of 4 variables (ANB, PP-FH, CF, and FCA) are inserted.

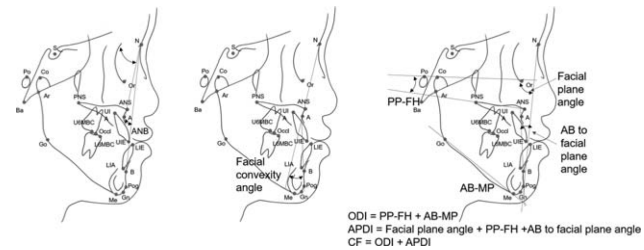

FIGURE 2. Four cephalometric parameters of the initial lateral cephalogram obtained between 5 and 7 years of age (T0 stage). ANB (degree of relative protrusion of B point in relation to A point), intermaxillary relationship between the maxilla and mandible; PP-FH, inclination of the palatal plane (ANS-PNS) in relation to the FH plane; combination factor (CF), sum of overbite depth indicator (ODI) and anteroposterior dysplasia indicator (APDI), which means the skeletal size of the maxilla and mandible; and Facial convexity angle (FCA, degree of relative protrusion of Pogonion point in relation to A point), intermaxillary relationship between the maxilla and mandible.

DISCUSSION

Patients with cleft usually require a long-term multidisciplinary care in order to obtain good facial esthetics and functional occlusion.[26] In this retrospective longitudinal study, 17.9% of the UCLP patients needed orthognathic surgery or DO, which was similar to the results of previous studies (12%–40%).[8,17,27–29]

In the present study, the Boruta method was used to select the predictive features. This method iteratively removes the features which are shown by a statistical test to prove to be less relevant than random probes.[19] Compared to the feature wrapping method used in Park et al’s study,[17] the random forest classification-based Boruta algorithm is relatively quick run without fine tuning of parameters, and gives a numerical estimate of the feature importance.[22]

At the T1 stage, 18 cephalometric parameters exhibited significant differences between the surgery and non-surgery groups (Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762), while at the T0 stage, only 2 variables showed significant intergroup difference (ANB and FCA; Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762). These results

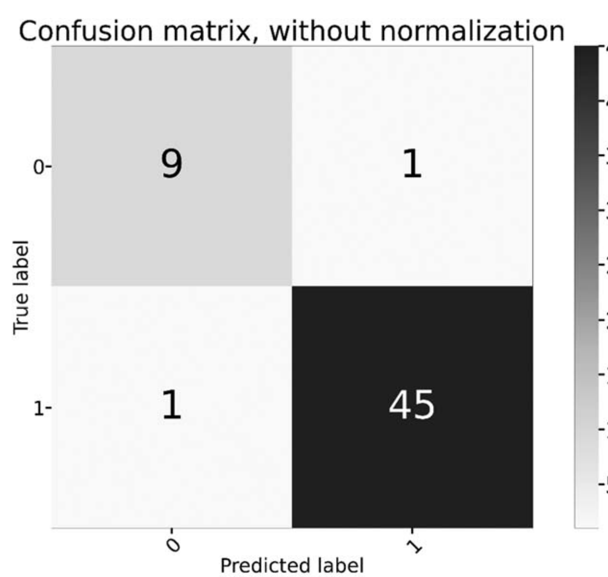

FIGURE 3. The quality of the prediction model. The confusion matrix without normalization was used. 0, surgery patient; 1, non-surgery patient; Sensitivity (the proportion of actual non-surgery patients that was correctly predicted as non-surgery patients), 97.83%; Specificity (the proportion of actual surgery patients that was correctly predicted as surgery patients), 90.00%. 10-fold cross-validation accuracy, 87.4%; F1-score, 0.714.

suggest that most of the unfavorable skeletodental features developed during growth (from age 6.3–16.7 years), which was confirmed by the significant intergroup differences of 14 variables in ΔT1-T0 between the 2 groups (Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762).

When compared to Park et al's study,[17] this study showed four main differences in the composition of subjects; mean age at the T0 stage, number of cephalometric predictors, and weighted classification accuracy (CLA, UCLP and BCLP versus UCLP only; 9.3 year-old versus 6.3 year-old; 10 predictors versus 4 predictors; 77.3% versus 87.4%; Supplementary Digital Content, Table 2, http://links.lww.com/SCS/B762 and Fig. 1). This finding suggests that it is possible to predict the skeletodental growth of UCLP patients using less number of cephalometric variables at earlier age compared to Park et al's study.[17]

Difference in the number of cephalometric predictors was most likely due to the age difference of the subjects between Park et al[17] and this study because the skeletodental growth in 9.3 years of age might be relatively more actively appeared than those in 6.3 years of age.[30–32]

The implications of the 4 cephalometric predictors are enumerated as follows: First, as previously reported in several studies,[8,17,33] the ANB was confirmed as an effective factor to predict the skeletodental growth of UCLP patients in this study (Supplementary Digital Content, Table 2, http://links.lww.com/SCS/B762 Fig. 2). After the evaluation of the lateral cephalograms in UCLP patients at 5 and 10 years of age, Meazzini et al[33] divided their patients into the orthognathic surgery and the non-orthognathic surgery group at the completion of growth. They reported significant differences in the SNA, SN-ANS and ANB between the 2 groups at both 5 and 10 years of age.[33] The present study suggested similar results in terms of the ANB and facial convexity angle (the degree of relative protrusion of the mandible by using B point and Pogonion point in relation to the maxilla, Supplementary Digital Content, Table 2, http://links.lww.com/SCS/B762). Although Meazzini et al[33] investigated participants with different ethnic backgrounds and surgical protocols than in this study, a similar pattern of sagittal skeletal discrepancy (ANB) was observed in the present study. Therefore, it can be stated that the difference in the maxillofacial growth pattern between Asian and Caucasian UCLP patients might be minor.

Second, the finding that PP-FH and CF were selected as predictors (Supplementary Digital Content, Table 2, http://links.lww.com/SCS/B762 Fig. 2) concurs with Park et al's study.[17] The PP-FH indicates the angulation of the palatal plane in relation to the FH plane. If the value of PP-FH is negative, it means an openbite tendency due to upward inclination of the anterior maxilla. If the value of PP-FH is positive, it means a deep bite tendency due to downward inclination of the anterior maxilla. PP-FH can indicate the growth direction of the maxilla, which might be related with possibility of orthognathic surgery. In addition, it is a common component in both APDI [sum of PP-FH angle, facial plane (N-Pog) to FH plane angle, and AB to facial plane angle; Appendix-1, http://links.lww.com/SCS/B763 Fig. 2] and ODI (sum of PP-FH angle and AB to mandibular plane angle; Appendix-1, http://links.lww.com/SCS/B763 Fig. 2), which represent the sagittal and vertical growth patterns, respectively.[34–36] Similarly, as the CF is a sum of the APDI and ODI (Appendix-1, http://links.lww.com/SCS/B763 Fig. 2), it indicates the skeletal size of the maxilla and mandible in the sagittal and vertical aspects.[34–36]

Third, the FCA (the angle between the N-A plane and A-Pog plane; Appendix-1, http://links.lww.com/SCS/B763 Fig. 2) would be a supplementary factor to ANB, which indicates the degree of relative protrusion of the Pogonion point in relation to the A point.

Although Park et al[17] reported that the Wits appraisal and the Harvold unit difference were the crucial cephalometric predictors, these variables were not selected in the present study despite existence of significant difference in the values between the two groups at the T1 stage (Wits appraisal and Harvold unit difference, all $P < 0.001$; Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762) and their amount of change (ΔWits appraisal and ΔHarvold unit difference, all $P < 0.001$; Supplementary Digital Content, Table 1, http://links.lww.com/SCS/B762). The reason for this might be that the eruption of the permanent maxillary incisors is not completed and the growth of the mandible is not prominent at the T0 stage.[37,38] Moreover, the AB to mandibular plane angle, gonial angle, A to N perp, overjet, and IMPA were not selected as cephalometric predictors in the present study. It was also speculated due to the insufficient growth of the maxilla and mandible and eruption of the teeth at the T0 stage.

Compared to previous studies,[8,17,27–29] the present study used the lateral cephalometric data obtained at a younger age (6.3 years) to avoid the effect of orthodontic and orthopedic treatment and alveolar bone grafting on the skeletodental growth, and adopted strict inclusion criteria such as single ethnicity, UCLP patients only, the same treatment protocol with a single surgeon and a single orthodontist to reduce the bias for selection of the subjects. By using machine learning, this study showed a good accuracy in the prediction of the future need for surgery to correct the intermaxillary discrepancy in the patients with UCLP. However, since the relatively small sample size would be the major limitation of the present study, it is necessary to perform the multi-center study with increase of the sample size in the near future.

Early prediction of the future need for orthognathic surgery or DO can help clinicians to setup the proper treatment plan and to adjust the timing and duration of orthodontic/orthopedic treatment for maxillary protraction in cleft patients. Therefore, it is necessary to conduct well-designed case-control studies for the evaluation of the effects of orthodontic/orthopedic treatment for the correction of the maxillary hypoplasia with regard to reducing the frequency of orthognathic surgery or DO in patients with cleft lip and palate.

CONCULSION

At age of 6 years it was possible to predict the future need for surgery to correct their sagittal skeletal discrepancy in patients with UCLP using cephalometric predictors with a good accuracy.

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