Original Article

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Evaluating the impact of mandibular developmental abnormalities and distraction osteogenesis on swallowing function in Pierre Robin Sequence

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SUMMARY: This study aims to evaluate the relationship between mandibular developmental abnormalities and swallowing function in children with Pierre Robin Sequence (PRS). Swallowing function was assessed by a Modified Kubota Drinking Test (MKDT). Pre- and postoperative CT scans of PRS patients who underwent Mandibular Distraction Osteogenesis (MDO) were analyzed through three-dimensional (3D) digital reconstruction technology. Mandibular and airway evaluation parameters were measured, including the distance between bilateral mandibular angular, the length of bilateral mandibular ramus, mandibular notch angle (α), mandibular angle (β), mandibular body angle (γ), and the lateral and longitudinal dimensions of the posterior lingual airway. Results showed that the length of the bilateral mandibular rami and posterior lingual airway dimensions were significantly reduced postoperatively compared to controls ($p < 0.01$). After MDO, the length of mandibular rami and lateral retroglossal airway dimensions increased, α and β angles increased, while γ angle decreased ($p < 0.05$). Notably, the distance between bilateral mandibular angles, mandibular rami length, and lateral retroglossal airway dimensions had the strongest impact on swallowing score. In conclusion, mandibular width, length, and airway dimensions were closely linked to swallowing function in PRS patients. MDO effectively improved mandibular hypoplasia, improved swallowing dysfunction, and significantly enhanced quality of life for the patients.

Keywords: Pierre Robin Sequence, swallowing function, Mandibular Distraction Osteogenesis

1. Introduction

Despite China's declining fertility rate (*1*), the increasing recognition of the complex causes of rare diseases and their frequent association with other intricate conditions has brought heightened attention to these medical challenges (*2*). Pierre Robin Sequence (PRS) is a congenital disorder characterized by micrognathia, glossoptosis, and cleft palate, which collectively contribute to upper airway obstruction and feeding difficulties. According to the European guidelines, the diagnostic triad includes micrognathia, glossoptosis, and respiratory distress (*3*). Due to mandibular hypoplasia, PRS patients often experience posterior displacement of the tongue base, leading to airway obstruction, which can be life-threatening in severe cases (*4*). While progress has been made in understanding the mechanisms of airway obstruction and surgical interventions offer partial relief, the relationship between PRS and swallowing dysfunction remains poorly understood (*5*).

Children with PRS often face feeding challenges primarily due to airway obstruction caused by glossoptosis and micrognathia, which disrupt normal swallowing mechanics. Research highlights significant abnormalities in both oral and esophageal motility, including sucking-swallowing discoordination, incomplete lower esophageal sphincter (LES) relaxation, and abnormal esophageal wave patterns (*6*). These dysfunctions may elevate the risk of aspiration pneumonia. Additionally, elevated LES tone and gastroesophageal reflux further impair swallowing and respiratory function (*7*). These abnormalities in esophageal dynamics are potentially associated with gastroesophageal reflux, which exacerbates swallowing difficulties and respiratory problems. Early palatoplasty combined with submucosal release procedures has been shown to effectively reduce the incidence of upper respiratory infections and gastroesophageal reflux, thereby improving swallowing function (*8*). However, since cleft palate repair is usually performed after the age of 8 months, persistent swallowing difficulties in the interim can result in malnutrition, which may delay neurological and overall physical development, significantly impacting the child's health. Thus, PRS patients experience multiple factors that impair swallowing function, including abnormalities in oral and esophageal motility as well as gastroesophageal reflux. Comprehensive treatment should address airway and swallowing issues to reduce complications and improve quality of life (*9*).

Mandibular Distraction Osteogenesis (MDO) is widely recognized as an effective treatment for PRS, promoting mandibular growth to alleviate airway obstruction and feeding difficulties (*10*). MDO improves health-related quality of life, particularly physiological outcomes (*11*). The use of distraction devices enables rapid mandibular advancement, which can effectively expand the airway and relieve respiratory distress within a short period (*12*). The application of 3D printing technology in MDO has demonstrated promising outcomes, facilitating surgical planning and reducing complications. While MDO has been extensively studied for alleviating airway obstruction, its effects on swallowing dysfunction remains unclear. Mandibular advancement is thought to indirectly benefit swallowing function by mitigating glossoptosis and improving airway patency (*13*). However, the precise relationship between mandibular morphological changes in the mandible and swallowing remains unclear. Despite these gaps, MDO is regarded as an effective treatment option that significantly improves PRS patients' physical health, emotional well-being, and quality of life (*14*).

This study aims to evaluate mandibular morphology following MDO and examine how these morphological changes influence swallowing function. The ultimate objective is to optimize surgical treatment strategies and lay the groundwork for integrating digital-assisted MDO to simultaneously address airway obstruction and swallowing disorders in PRS patients. By achieving these goals, the study seeks to enhance long-term quality of life for affected individuals.

2. Patients and Methods

2.1. Study population

The study was approved by the Ethics Committee at Guangzhou Women and Children's Medical Center and written informed consent was obtained from all parents or other guardians prior to enrollment (approve #: 2024307A01). Additionally, the conduct of the research complies with the Declaration of Helsinki. In this study, 15 cases of isolated Pierre Robin Sequence were randomly enrolled from patients treated at the Department of Oral and Maxillofacial Surgery. Diagnosis of PRS was made based on the clinical consensus report. Ten cases with cleft palate were randomly selected as the control group. Exclusion criteria for the study were as follows: *i*) syndromic PRS; *ii*) severe cardiopulmonary disease; *iii*) head and neck tumors or trauma leading to changes in the local anatomical structure; *iv*) laryngomalacia, brain-induced central apnoea, or mixed apnoea; and *v*) other anomalies causing airway obstruction. MDO was performed on all 30 included patients according to previously described methods (*15*), and the mandibular distraction devices were removed six months later.

2.2. Swallowing function assessment, imaging acquisition, three-dimensional reconstruction and parameters analysis

First, the swallowing function of patients was assessed preoperatively and postoperatively using a quantitative swallowing function scale, primarily based on the Modified Kubota Drinking Test (MKDT). MKDT is a clinical assessment tool used to evaluate swallowing function, particularly in pediatric patients.

Second, after computed tomography (CT) scanning, the images of preoperative and 6-month postoperative patients with PRS were collected. Mimics 21.0 image analysis software was used for reconstruction and analysis. The measurement parameters were as follows: *i*) distance between bilateral mandibular angular; *ii*) the length of bilateral mandibular ramus; *iii*) mandibular notch angle (α) formed by the anterior border of the mandibular ramus and the superior border of the mandibular body; *iv*) mandibular angle (β) formed by the posterior border of the mandibular ramus and the inferior border of the mandibular body; *v*) mandibular body angle (γ) formed by the bilateral mandibular bodies; *vi*) lateral and Longitudinal dimensions of the posterior lingual airway.

2.3. Statistical analysis

In this study, statistical analyses were conducted using SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). A two-sample *t*-test was employed to assess the differences in various indices between the normal group and the preoperative group. A paired *t*-test was used to compare the indices between the preoperative and postoperative groups.

Subsequently, variables that exhibited statistically significant differences were further analyzed using multiple linear regression. A stepwise regression analysis was performed to explore the impact of the selected covariates on the swallowing score. For all statistical tests, a significance level of $p < 0.05$ was considered to indicate statistical significance. SHapley Additive exPlanations (SHAP) algorithm (*16*) and multivariate logistic regression models were also used to assess the correlation between anatomical factors and the swallowing score before and after MDO.

3. Results

3.1. Imaging of the mandible with PRS using 3D reconstruction

Imaging results reveal that children with PRS often present with a shortened and small mandible (Figure 1A, B and C), along with mandibular retraction, a significant posterior drop of the tongue base (Figure 1D), and narrowing of the posterior lingual airway (Figure 1E).

Mandibular lengthening is achieved through MDO, where a traction device is fixed at the mandibular angle to extend the length of the mandible (Figure 2A). Over six months, the device guides bone growth (Figure 2B) and helps reconstruct the jaw morphology using mimics software. It can be visually observed that the mandible is significantly elongated, improving mandibular retrognathia and alleviating tongue prolapse (Figure 2).

3.2. Assessment of swallowing dysfunction in PRS patients

Preoperative assessments using the MKDT and clinical swallowing examinations revealed moderate to severe swallowing dysfunction in PRS patients (Figure 3). Symptoms included the need for nasogastric tube feeding, frequent choking during oral feeding, and

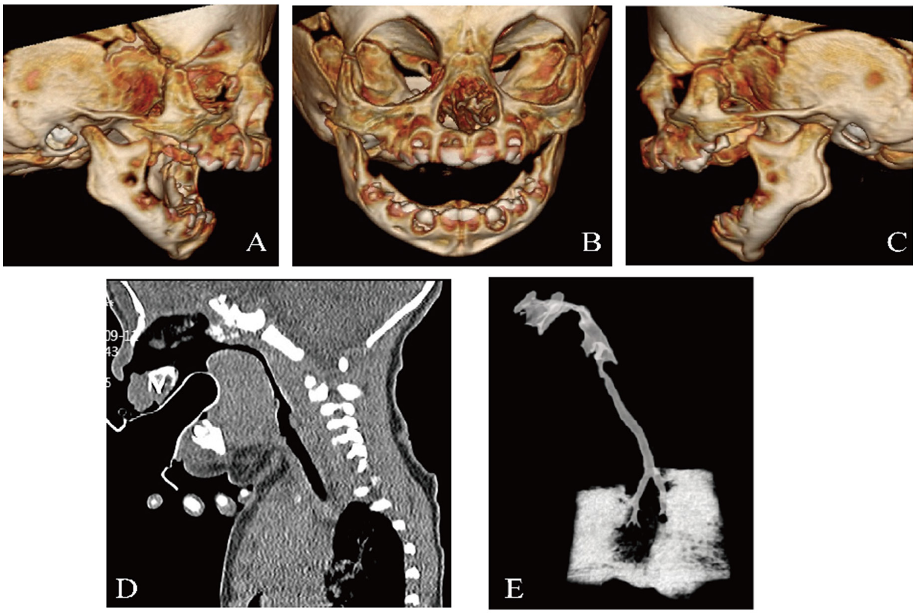

Figure 1. Imaging data collection of patients with PRS, including reconstruction of the mandible and airway. (A) Lateral view of the mandible (right side); **(B)** Frontal view of the mandible; **(C)** Lateral view of the mandible (left side); **(D)** Lateral view of the airway; **(E)** Airway reconstruction. PRS, Pierre Robin Sequence.

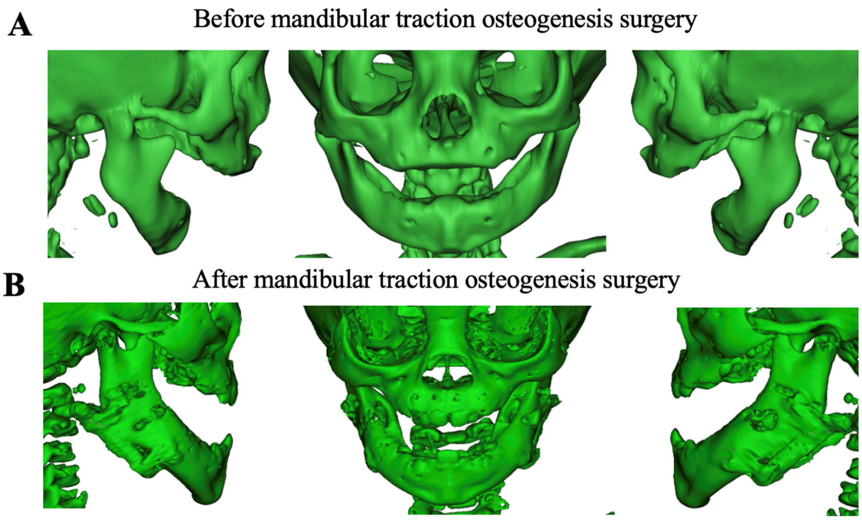

Figure 2. Changes of mandibular morphology before and after traction osteogenesis in PRS. (A) Lateral and frontal view of the mandible before MDO; **(B)** Lateral and frontal view of the mandible after MDO. PRS, Pierre Robin Sequence; MDO, Mandibular Distraction Osteogenesis.

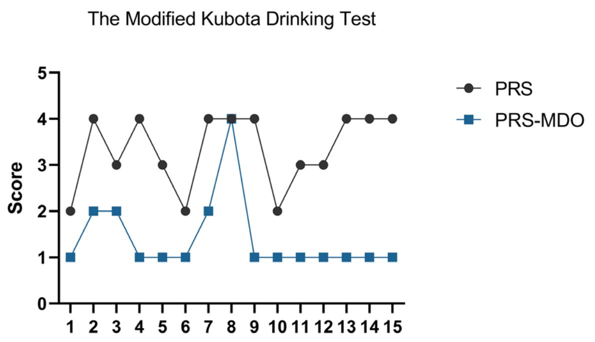

Figure 3. Modified Kubota Drinking Test Scale. Score 1: normal swallowing function, no choking or coughing observed, no changes in respiration during drinking; Score 2: mild difficulty swallowing, occasional choking or coughing observed, but no significant changes in respiration; Score 3: moderate difficulty, frequent choking or coughing, noticeable changes in respiration during drinking; Score 4: severe swallowing difficulty, inability to drink without aspiration, significant changes in respiration, often requiring interventions such as nasogastric tube feeding; Score 5: unable to swallow safely, complete dependence on alternative feeding methods (*e.g.*, nasogastric or gastrostomy tube). Each level is determined based on the child's ability to drink a specified amount of water (often 3 mL or 30 mL) in one go, while observing for symptoms like choking, coughing, or changes in breathing patterns. PRS-MDO, PRS after MDO.

weakened tongue and soft palate elevation strength, although masticatory muscle function was generally preserved. Postoperative assessments after MDO surgery demonstrated significant improvement in these symptoms.

3.3. Evaluation of mandibular morphology with PRS

The results showed that both the bilateral mandibular angular length and mandibular ramus lengths were significantly smaller in the PRS group compared to the control group ($p < 0.01$). This suggest that PRS mandibles are not only shorter in ramus length but also narrower in mandibular body width, which may contribute to airway stenosis (Figure 4A).

Furthermore, the mandibular angle in the PRS group was smaller than in controls, likely due to the shorter ramus and body, while the relatively increased angle of the mandibular body might be linked to tongue retraction (Figure 4B).

After MDO surgery, there was a significant increase in the bilateral mandibular angular and ramus lengths compared to the preoperative PRS group, indicating

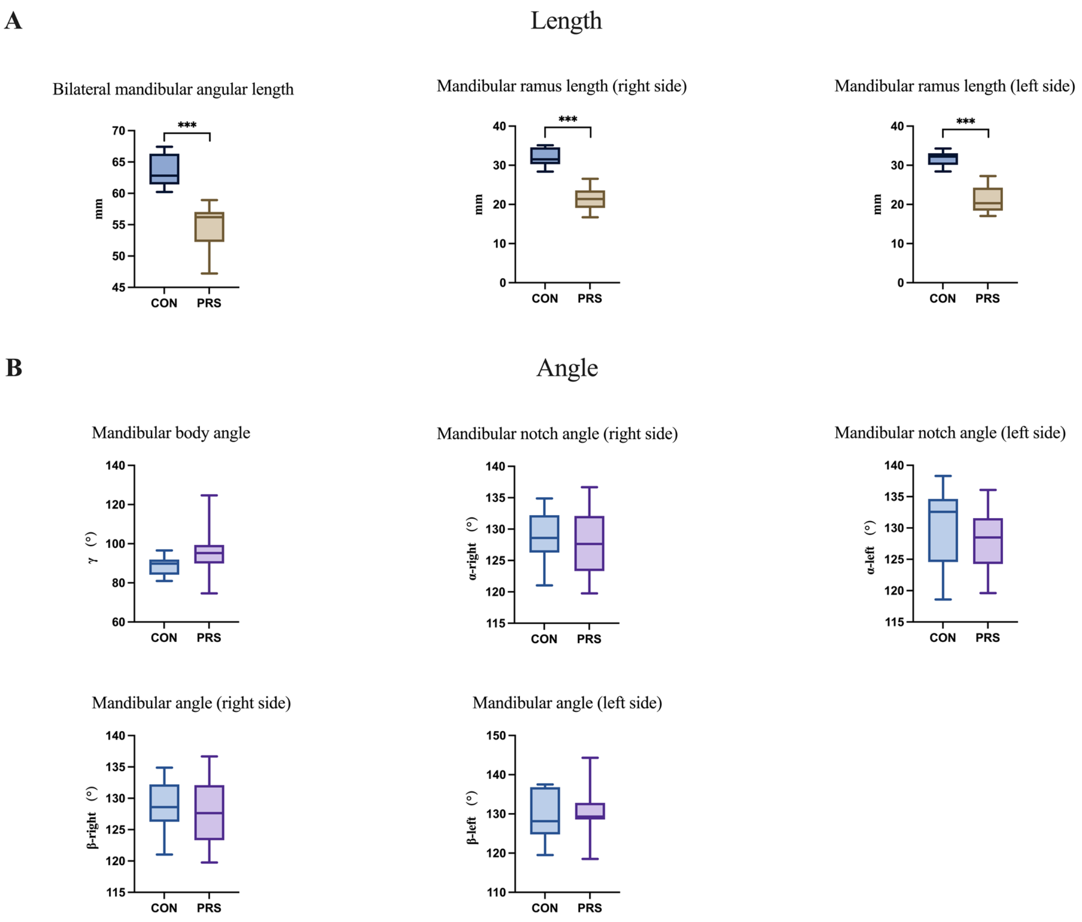

Figure 4. (A) Differences in mandibular length, including distance of bilateral mandibular angular and mandibular ramus (right side and left side) measurements between PRS and control groups following 3D reconstruction; **(B)** Differences in mandibular angle, including mandibular body, mandibular notch angle (right side and left side) and mandibular angle (right side, left side) measurements between PRS and control groups following 3D reconstruction. CON, control group; PRS, Pierre Robin Sequence group. $^{**}p < 0.01$ *vs.* CON group.

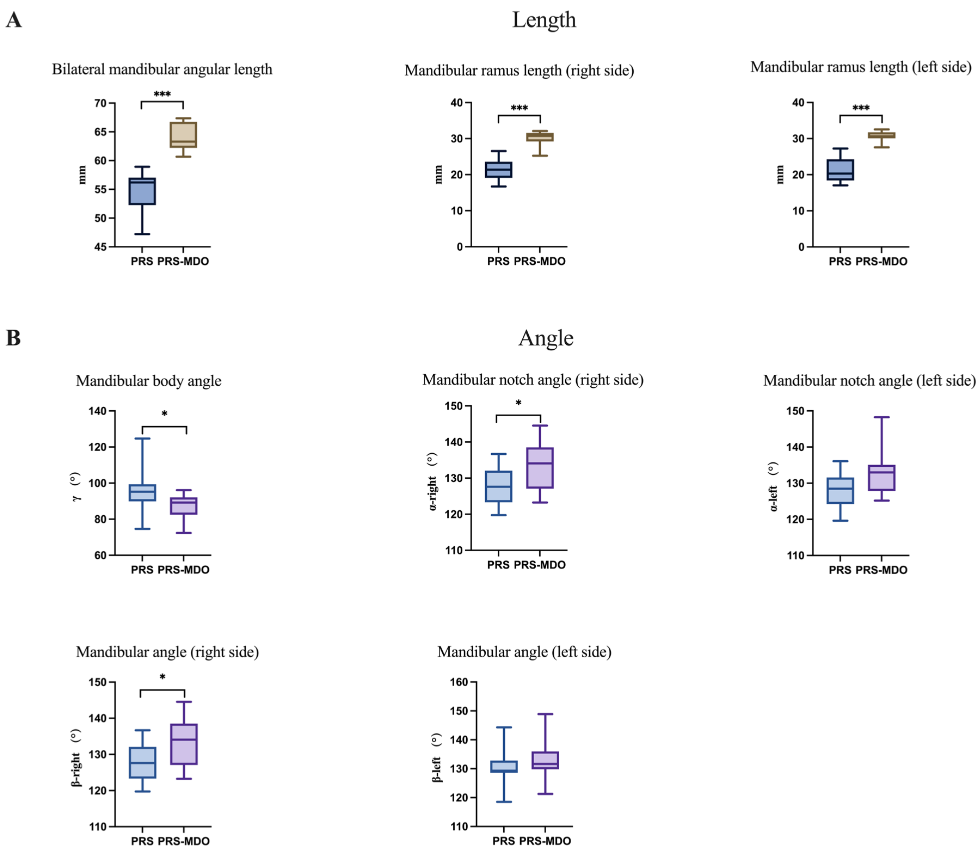

Figure 5. (A) Differences in mandibular length, including distance of bilateral mandibular angular and mandibular ramus (right side and left side) measurements between PRS and after MDO groups following 3D reconstruction. **(B)** Differences in mandibular angle, including mandibular body, mandibular notch angle (right side and left side) and mandibular angle (right side, left side) measurements between PRS and after MDO following 3D reconstruction. ***p < 0.01 *vs.* PRS group, *p < 0.05 *vs.* PRS group.

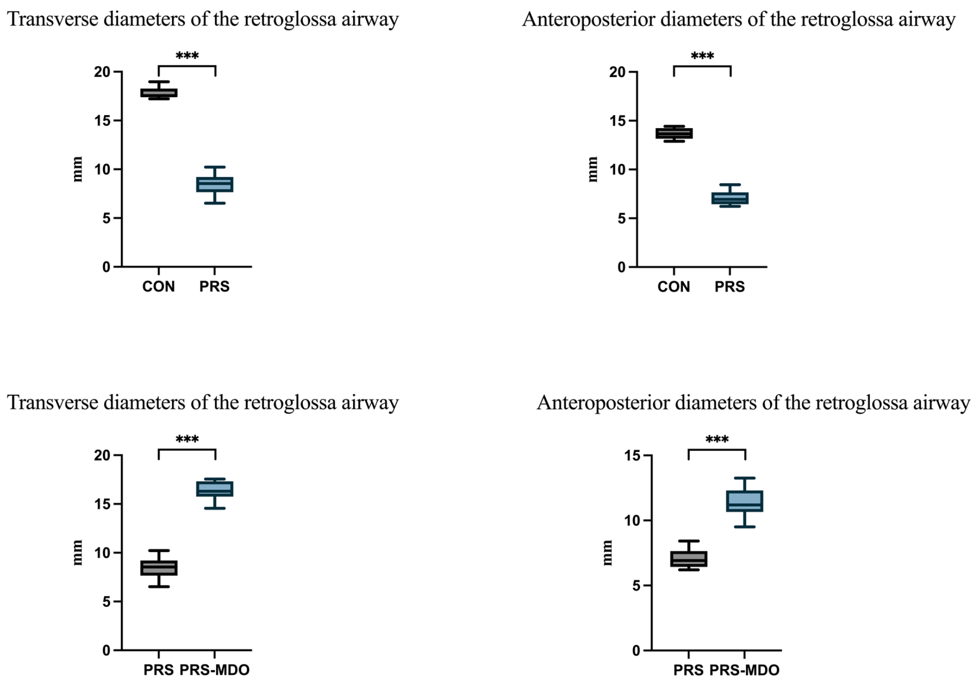

Figure 6. Differences in diameters of the retroglossal airway, including transverse and anteroposterior measurements among control, PRS and after MDO group following 3D reconstruction. Statistical significance is indicated by ***p < 0.01. PRS, Pierre Robin Sequence; MDO, Mandibular Distraction Osteogenesis.

that MDO effectively improves mandibular morphology (Figure 5A). Additionally, the angle of the mandibular ramus increased, while the angle of the mandibular body decreased compared to the PRS group ($p < 0.05$) (Figure 5B).

The transverse and anterior diameter of the posterior lingual airway, which are indicative of airway stenosis, were significantly smaller in the PRS group — almost half the size of the control group ($p < 0.01$). After MDO surgery, these diameters increased significantly ($p < 0.01$) (Figure 6).

3.4. Multiple linear regression analysis of mandibular and airway morphology with swallowing function

A stepwise regression analysis was conducted to examine the impact of various anatomical factors on the swallowing score. Based on differential analysis, five covariates with statistically significant differences were identified: distance between bilateral mandibular angular, mandibular ramus (right side), mandibular ramus (left side), transverse diameters of the retroglossal airway, and anteroposterior dimension of the retroglossal airway. The result was consistent with multivariate logistic regression models (Figure 7A) and SHAP algorithm (Figure 7B). To address potential multicollinearity, a correlation analysis was performed. A strong positive correlation was observed between the distance between bilateral mandibular angular and the mandibular ramus (left side) ($r = 0.864$, $p < 0.01$).

To minimize the impact of multicollinearity on the regression model, stepwise regression analysis was conducted in two approaches. First, using the distance between bilateral mandibular angular, after excluding the mandibular ramus (left side), stepwise regression analysis was performed with the distance between bilateral mandibular angular and the other covariates. The results indicated that the transverse diameters of the retroglossal airway (B = -0.246, $t = -9.600$, $p < 0.001$) and mandibular ramus (right side) (B = -0.088, $t = -2.077$, $p = 0.046$) were significant predictors of the swallowing score (dependent variable). Then using mandibular ramus (left side), after excluding distance between bilateral mandibular angular, stepwise regression analysis was performed with the mandibular ramus (left side) and the other covariates. The results showed that the mandibular ramus (left side) significantly influenced the swallowing score, with an unstandardized coefficient of B = -0.200 ($t = -10.195$, $p < 0.001$).

By including either distance between bilateral mandibular angular or the mandibular ramus (left side) in separate models, multicollinearity was reduced, and the relationship between the covariates and the dependent variable was clarified. These findings highlight the importance of careful selection and evaluation of covariates in regression modeling.

4. Discussion

PRS is a congenital condition characterized by mandibular hypoplasia, glossopteris, which often leads to respiratory distress, feeding difficulties, and various other complications, all of which significantly impact patient survival rates (*3*). PRS has an incidence of 1 in 8,500 to 1 in 30,000 live births. Mortality rates are significant, with an average of 16% across cases, but rising to 41.4% in severe forms. Reports indicate early infant mortality rates of 30% to 65%, driven by airway obstruction and feeding difficulties (*5,17,18*). Timely interventions, such as MDO, are crucial to improving

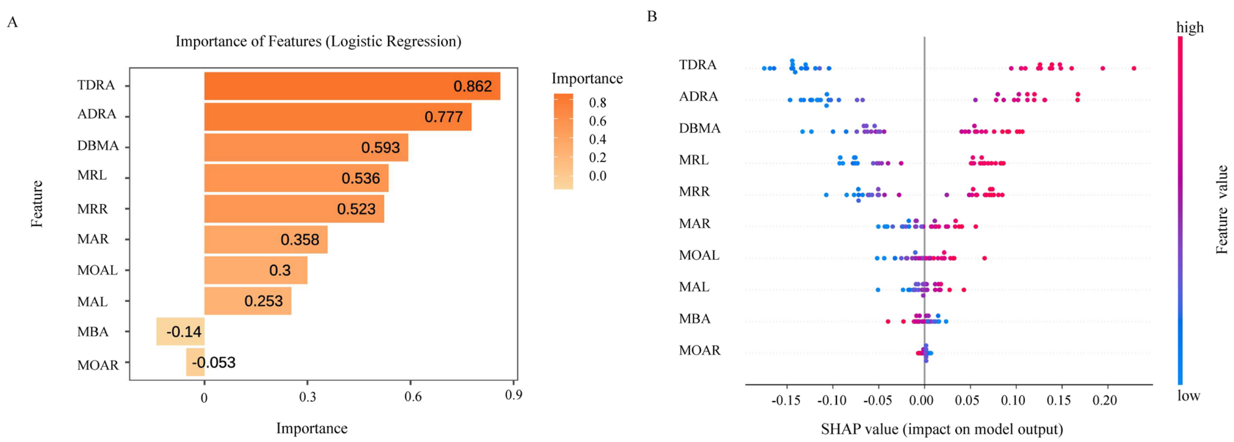

Figure 7. Feature importance evaluation using the logistic regression (LR) model and SHAP algorithm. (A) The Importance (coefficients of features) ranking of features in LR model; **(B)** SHAP honeycomb diagram of the LR model. Each point represents a feature value, and different colors represent the final influence of the feature on the LR model output results, where red represents a larger SHAP value and blue represents a smaller SHAP value. TDRA, Transverse diameters of the retroglossal airway; ADRA, Anteroposterior diameters of the retroglossal airway; DBMA, Distance between bilateral mandibular angular; MRL, Mandibular ramus (left side); MRR, Mandibular ramus (right side); MAR, Mandibular angle (right side); MOAL, Mandibular notch angle (left side); MAL, Mandibular angle (left side); MBA, Mandibular body angle; MOAR, Mandibular notch angle (right side).

outcomes.

The findings of this study confirm that MDO effectively increases mandibular length and adjusts the mandibular angle, bringing it closer to normal. Studies using 3D morphological analysis reveal that different types of PRS patients exhibit distinct mandibular characteristics compared to normal children. These differences may be associated with factors such as condylar rotation direction, rotation angle, and mandibular body elongation (*12*). Furthermore, research shows that MDO may affect the temporomandibular joint (TMJ). Following unilateral mandibular distraction, anatomical changes and mild degenerative alterations in the TMJ may occur, but these changes generally resolve over time, indicating that the short-term effects of MDO on the TMJ are largely reversible (*19*). Studies on adult patients with hemifacial microsomia have shown that MDO effectively reduces recurrence rates, as demonstrated by improvements in the ratio of ramus length, body length, and the distance from the chin point to the facial midline (*20,21*). These findings underscore the significant impact even minor variations in mandibular length and angle can have on mandibular development in PRS patients, highlighting the critical importance of precise preoperative planning, surgical strategy, and postoperative evaluation to achieve optimal therapeutic outcomes. Furthermore, the use of Mimics 3D reconstruction technology in this study enhances the accuracy of mandibular measurements (*22*). Scholars such as Chelsea L Reighard, have demonstrated that 3D printing technology allows for precise prediction of postoperative mandibular changes, facilitating surgical planning, improving outcomes, and reducing complications (*23*).

Mandibular morphology plays a critical role in swallowing function. As a key component of the oral system, the mandible directly influences essential oral functions like mastication and swallowing (*24*). Mandibular morphological features, such as the mandibular angle and ramus shape, are closely associated with masticatory muscle strength (*25*). In PRS patients, who typically present symptoms in the neonatal period before the establishment of dental arches, the position and shape of the mandible significantly impact the size of the oropharyngeal airway. For instance, mandibular retrognathia can reduce the size of the oropharyngeal airway and alter the hyoid bone's position, moving it upward and backward (*26,27*). This suggests that mandibular morphological abnormalities in PRS patients directly affect swallowing function. Our study results indicate that the lateral dimension of the retroglossal airway and the distance between bilateral mandibular angles are closely related to swallowing function.

In PRS patients, mandibular shortening and retrognathia commonly result in glossoptosis and upper airway narrowing, which subsequently impair swallowing function (*28*). Accurate evaluation of swallowing dysfunction in these patients is essential. For mild cases, intermittent oral feeding paired with perioral stimulation can improve swallowing (*28-31*). In severe cases where swallowing difficulties compromise growth and development, MDO surgery is necessary. This procedure effectively elongates the mandible, increases the oropharyngeal airway volume, and improves swallowing function (*32*). Treatment strategies for PRS patients should consider both mandibular morphology and swallowing needs to ensure the most suitable approach (*28*). This study underscores MDO as one of the most effective treatments, improving airway patency and alleviating respiratory and swallowing dysfunction by lengthening the mandible.

In summary, PRS is a congenital condition with a relatively low incidence but a high mortality rate. Early diagnosis and comprehensive treatment are essential for improving the survival rates of affected newborns. Treatment strategies should not only focus on alleviating airway obstruction but also address the impacts of swallowing dysfunction. Future research should aim to refine surgical indications for MDO, optimize preoperative planning, improve surgical techniques, and enhance postoperative care. Additionally, genetic testing plays a crucial role in personalized diagnosis and precision treatment (*33*). These advancements will help manage airway obstruction and swallowing issues more effectively, minimize secondary mandibular deformities, reduce surgical complications, and improve bone regeneration quality.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Chen Z, Wang Y, Lan F, Li S, Wang J. An expanded view of infertility: The challenge of the changing profiling of major birth defects in China. Biosci Trends. 2023; 17:318-321.
2. Chen Z, Gao Y, Lu L, Li N, Liu P, Peng R, Liu L, Huang H, Fu Q, Hong H, Zhang J, Wang H. Rare loss-of-function variants reveal threshold and multifactorial inheritance of dextrocardia. Sci Bull (Beijing). 2023; 68:1993-1998.
3. By the Working Group on Writing a European Guideline on Robin Sequence. European Guideline Robin Sequence An Initiative From the European Reference Network for Rare Craniofacial Anomalies and Ear, Nose and Throat Disorders (ERN-CRANIO). J Craniofac Surg. 2024; 35:279-361.
4. Bütow KW, Naidoo S, Zwahlen RA, Morkel JA. Pierre Robin sequence: Subdivision, data, theories, and

treatment - Part 4: Recommended management and treatment of Pierre Robin sequence and its application. Ann Maxillofac Surg. 2016; 6:44-49.
5. Gasparin M, Barth FL, Pauletti LF, Simon MISDS, da Nóbrega Figueiredo RI, Schweiger C, Levy DS, Marostica PJC. Therapeutic management with airway clearance in children with Robin Sequence and association with swallowing outcomes: A systematic review and meta-analysis. Dysphagia. 2023; 38:1267-1276.
6. Baujat G, Faure C, Zaouche A, Viarme F, Couly G, Abadie V. Oroesophageal motor disorders in Pierre Robin syndrome. J Pediatr Gastroenterol Nutr. 2001; 32:297-302.
7. Abadie V, Morisseau-Durand MP, Beyler C, Manach Y, Couly G. Brainstem dysfunction: A possible neuroembryological pathogenesis of isolated Pierre Robin sequence. Eur J Pediatr. 2002; 161:275-280.
8. Haas J, Yuen K, Farrokhyar F, Aminnejad M, Williams C, Choi M. Non-operative interventions for Pierre-Robin sequence: A systematic review and meta-analysis. J Craniomaxillofac Surg. 2024; 52:1422-1427.
9. Hong P, Brake MK, Cavanagh JP, Bezuhly M, Magit AE. Feeding and mandibular distraction osteogenesis in children with Pierre Robin sequence: A case series of functional outcomes. Int J Pediatr Otorhinolaryngol. 2012; 76:414-418.
10. Goza SD, Brown MI, Hopper SJ, Phillips J, Sink MC, Brown KW, Fernstrum CJ, Friel MT, Humphries LS, Hoppe IC. Mandibular distraction in patients with Pierre Robin Sequence: A multisurgeon experience. Ann Plast Surg. 2024; 92(6S Suppl 4):S382-S386.
11. Mao Z, Battaglino R, Zhou J, Cui Y, Shrivastava M, Tian G, Sahebdel F, Ye L. The effect of timing of mandibular distraction osteogenesis on weight velocity in infants affected by severe Robin Sequence. Children (Basel). 2022; 9:319.
12. Reina-Romo E, Gómez-Benito MJ, Sampietro-Fuentes A, Domínguez J, García-Aznar JM. Three-dimensional simulation of mandibular distraction osteogenesis: Mechanobiological analysis. Ann Biomed Eng. 2011; 39:35-43.
13. Liu Z, Gong B, Li X, Zhao C, Chen Y, Li S, Abduwali R, Bai Y, Teng L, Lu J. Global Research Trends and Focuses on Pierre Robin Sequence From 1992 to 2023: A Bibliometric Analysis of the Past 3 Decades. J Craniofac Surg. 2024. doi: 10.1097/SCS.0000000000010186. Epub ahead of print.
14. Meazzini MC, Piza A, Giorgio N, Sozzi D, de Ponti E, Mazzoleni F. Long-term mandibular growth in patients with airway obstruction treated with mandibular distraction. J Craniomaxillofac Surg. 2024; 52:792-797.
15. Mao Z, Ye L. Effects of mandibular distraction osteogenesis on three-dimensional upper airway anatomy in newborns affected by isolated Pierre Robin Sequence. J Craniofac Surg. 2021; 32:1459-1463.
16. Ejiyi CJ, Qin Z, Ukwuoma CC, Nneji GU, Monday HN, Ejiyi MB, Ejiyi TU, Okechukwu U, Bamisile OO. Comparative performance analysis of Boruta, SHAP, and Borutashap for disease diagnosis: A study with multiple machine learning algorithms. Network. 2024:1-38.
17. Pendem S, Jayakumar NK, Gopalakrishnan S, Arakeri G. Systematic review and meta-analysis of surgical approaches for improving airway stability in infants with Robin sequence: Evaluating complications and outcomes. Br J Oral Maxillofac Surg. 2024; 62:511-522.
18. Gomez OJ, Lopez A, Gutierrez E. Pierre Robin Sequence: An updated evidence-based treatment proposal. J Craniofac Surg. 2024. doi: 10.1097/SCS.0000000000010240. Epub ahead of print.
19. Xia L, Zhang Y, An J, Chen S, He Y. Evaluating the remodeling of condyles reconstructed by transport distraction osteogenesis in the treatment of temporomandibular joint ankylosis. J Craniomaxillofac Surg. 2020; 48:494-500.
20. Han W, Kim BS, Zhang Z, Chen X, Yan Y, Lin L, Zhang Y, Chai G. Changes of masseter muscle after mandible distraction osteogenesis in patients with Hemifacial microsomia: A retrospective study. Front Pediatr. 2024; 12:1453270.
21. Li X, Xia S, Li Z, Zhang Z. Evaluation of post-activation mandibular remodelling in children with craniofacial microsomia treated with distraction osteogenesis. Orthod Craniofac Res. 2024; 27:860-867.
22. Bianchi A, Betti E, Badiali G, Ricotta F, Marchetti C, Tarsitano A. 3D computed tomographic evaluation of the upper airway space of patients undergoing mandibular distraction osteogenesis for micrognathia. Acta Otorhinolaryngol Ital. 2015; 35:350-354.
23. Reighard CL, Powell AR, Zurawski TY, Rooney DM, Keilin CA, Zopf DA. Development of a novel mandibular distraction osteogenesis simulator using Computer Aided Design and 3D printing. Int J Pediatr Otorhinolaryngol. 2021; 142:110616.
24. Harris JA, Caprio RM, Resnick CM. Do infants with Robin Sequence have improved feeding and weight gain after mandibular distraction? J Oral Maxillofac Surg. 2021; 79:1331-1338.
25. Shen YF, Wei MC, Li HP, Pan YH, Hong HH, Chen CC, Kuo SB, Ho CY, Chang CT, Huang YF. Vertical dimension of occlusion related to mandibular movement during swallowing. Biomed J. 2021; 44:217-222.
26. Renault F, Baudon JJ, Galliani E, Flores-Guevara R, Marlin S, Garabedian EN, Vazquez MP. Facial, lingual, and pharyngeal electromyography in infants with Pierre Robin sequence. Muscle Nerve. 2011; 43:866-871.
27. Marques IL, Prado-Oliveira R, Leirião VH, Jorge JC, de Souza L. Clinical and fiberoptic endoscopic evaluation of swallowing in Robin sequence treated with nasopharyngeal intubation: the importance of feeding facilitating techniques. Cleft Palate Craniofac J. 2010; 47:523-529.
28. Yao CT, Wang JN, Tai YT, Tsai TY, Wu JM. Successful management of a neonate with Pierre-Robin syndrome and severe upper airway obstruction by long term placement of a laryngeal mask airway. Resuscitation. 2004; 61:97-99.
29. Mace EL, Krishnapura SG, Golinko M, Phillips JD, Belcher RH. Pre-operative characteristics helping to avoid gastrostomy tube after mandibular distraction in neonates with Pierre-Robin Sequence: A institutional case-series and review of the literature. Ann Otol Rhinol Laryngol. 2024; 133:679-685.
30. Gasparin M, Barth FL, Schweiger C, Collares MVM, Levy DS, Marostica PJC. Sensory-motor-oral stimulation combined with early sucking during the mandibular distraction osteogenesis process in children with Robin Sequence. Cleft Palate Craniofac J. 2024. doi: 10.1177/10556656241264710. Epub ahead of print.
31. Radhakrishnan J, Sharma A. Feeding plate for a neonate

with Pierre Robin sequence. J Indian Soc Pedod Prev Dent. 2011; 29:239-243.
32. Ai JB, McQueen RG, McCarty RM, Sharda M, Zagloul M, Shakir S, Yi C, Klement K, Lin KY. A comparative assessment of outcomes following mandibular distraction osteogenesis and tongue-lip adhesion in Pierre Robin Sequence. J Craniofac Surg. 2024. doi: 10.1097/SCS.0000000000010287. Epub ahead of print.
33. Chen Z, Finnell RH, Lei Y, Wang H. Progress and clinical prospect of genomic structural variants investigation. Sci Bull (Beijing). 2024; 69:705-708.

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