Effects of Mandibular Distraction Osteogenesis on Three-Dimensional Upper Airway Anatomy in Newborns Affected by Isolated Pierre Robin Sequence

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Background: Effective airway management is critical to Pierre Robin Sequence treatment. The goal of this study is to assess the three-dimensional changes in airway size and shape in 117 newborns with isolated Pierre Robin sequence who underwent mandibular distraction osteogenesis.

Methods: During the study period (11/29/2016 to 11/26/2019), 117 newborns affected by isolated Pierre Robin sequence met the inclusion criteria for the present study. All 117 included patients underwent linear distraction. Demographic variables were recorded and analyzed. Cone-beam computed tomography were performed before and after mandibular distraction osteogenesis. A systemic quantitative three-dimensional analysis of size and shape of upper airway was performed.

Results: The mean age was 71 day (range 12 to 213). The mean weight was 3.9 kg (range 2.3–6.8). A total of 53 patients are female and 64 are male. When the distraction device was removed, the upper and lower jaws were symmetrically aligned. Pre- and post-distraction comparison clearly showed osteogenesis. For the size of the upper airway, airway volume, anteroposterior dimension of the retroglossal airway, lateral dimension of retrolingual airway, minimum retropalatal area, minimum retroglossal area, average cross-sectional area and minimum cross-sectional area increased significantly after mandibular distraction osteogenesis (P < 0.001). However, the airway length did not change significantly (P > 0.05). For the shape of the upper airway, the lateral/anteroposterior ratio in the retroglossal region and the ratio of the retropalatal airway diameter to the retroglossal airway diameter significantly decreased after mandibular distraction osteogenesis (P < 0.001). The airway uniformity significantly increased after mandibular distraction osteogenesis (P < 0.001).

Conclusion: Mandibular distraction osteogenesis for isolated Pierre Robin sequence improved size and shape of the upper airway, further confirming mandibular osteogenesis distraction as an effective surgical modality to address the airway obstruction in newborns affected by isolated Pierre Robin sequence. Cone-beam computed tomography scanning and analysis can serve as a safe and effective examination modality for upper airway applications of PRS newborns.

Key Words: Airway obstruction, isolated Pierre Robin sequence, Mandibular distraction osteogenesis, micrognathia, Pierre Robin sequence

(P < 0.001). The airway uniformity significantly increased after mandibular distraction osteogenesis (P < 0.001).

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Cone-beam computed tomography (CBCT) has emerged as a useful imaging technique owing to significantly low radiation exposure as compared to conventional CT and high quality of three-dimensional images. Very few studies, till date have used CBCT data to evaluate airways volume for newborns with PRS. In our present study, we adopted CBCT to realize a systematic quantitative three-dimensional analysis of the pre and post distraction airway anatomy for PRS newborns. With small radiation dose that largely reduces the danger of radiation overexposure to newborns, we believe CBCT scanning and analysis can serve as a safe and effective examination modality for PRS newborns.

Pierre Robin sequence (PRS) may occur alone (isolated) or be associated with a variety of other signs and symptoms (syndromic) such as Stickler syndrome or campomelic dysplasia. In about 20% to 50% of cases, the condition occurs alone. The clinical phenotype is highly variable in terms of craniofacial, airway and neurological anomalies, which collectively increase the potential for upper and lower airway obstruction. Isolated PRS and syndromic PRS such as Treacher Collins syndrome show distinctly different patterns of mandibular hypoplasia relative to normal controls, underscoring distinct considerations which must be made in surgical planning for reconstruction. Unlike previously reported research, our study is able to look at isolated PRS and syndromic PRS separately, since we have relatively large number of cases, resulting in a higher accuracy of result and conclusion.

METHODS

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. During 3 years from 11/29/2016 to 11/26/2019, 117 isolated PRS patients were included in the Department of Oral and Maxillofacial Surgery of Guangzhou Women and Children’s Medical Center. Diagnosis of PRS was made on the basis of the clinical consensus report. Two doctors, Dr Zhe Mao and Dr Yingqiu Cui were on the job at the same time for the diagnosis of any single case. Patients showing micrognathia, glossoptosis and airway obstruction established the initial diagnosis of PRS. A fiberoptic nasopharyngoscopy examination was conducted in all patients to further confirm glossoptosis and airway obstruction, resulting in the final diagnosis.

Exclusion criteria for the study were as follows:
1. severe cardiopulmonary disease;
2. head and neck tumors or trauma leading to changes in the local anatomical structure;
3. laryngomalacia, brain-induced central apnoea, or mixed apnoea;
4. other anomalies causing airway obstruction;
5. syndromic PRS.

Surgical Procedure
Mandibular Distraction Osteogenesis (MDO) were performed on all 117 included patients as described previously. A sub-mandibular incision was given, running 1.5 cm below and parallel to the inferior border of the mandible (Fig. 1). CBCT images were referred for the osteotomy line. A “walking-stick” shaped osteotomy line passing through the mandibular angle was utilized to avoid the tooth bud and condylar neck (Fig. 1). A non-absorbable distraction device was implanted (Fig. 1). After 48 hours, the patient underwent mandibular distraction at a speed of 1.2 mm per day. Distraction was performed until the upper and lower jaws were symmetrically aligned or a slight underbite was achieved.

Image Acquisition, Three-Dimensional Reconstruction, and Parameters Analysis
All included 117 patients underwent a CBCT (NewTom, Verona, Italy) scan before and after distraction. Scans were reconstructed into a digital 3D model of the upper airways using NNT (NewTom, Verona, Italy). Parameters for upper airway size including volume (V), length (L), minimum retropalatal area (RP), minimum retro-glossal area (RG), average cross-sectional area (avgCSA), minimum cross-sectional area (minCSA), lateral dimension of retroglossal airway (LAT) and anteroposterior dimension of the retroglossal airway (AP), and parameters for shape including the lateral/anteroposterior ratio in the retroglossal region (LAT/AP), the ratio of the retropalatal airway diameter to the retroglossal airway diameter (RG/RP) and the airway uniformity (U) have been defined. These parameters for evaluation of airway size and shape were assessed and recorded. Three-dimensional craniofacial reconstruction and three-dimensional model of upper airway were performed.

Statistical Analysis
The airway parameters before and after MDO were compared by using Wilcoxon signed-rank test. P < 0.05 was considered statistically significant.

RESULTS

Characteristics of Subjects
During the study period (11/29/2016 to 11/26/2019), 177 newborns were diagnosed with PRS (Fig. 2). Of these patients, 117 met the inclusion criteria for the present study (Fig. 2). Of those excluded, 1 had tracheomalacia, 1 had laryngomalacia, 1 had subglottic tracheal stenosis, 1 had brain-induced central apnoea, 2 had Bronchial epithelial hyperplasia, and 53 had syndromic PRS (Fig. 2). 1 isolated PRS who met the inclusion criteria refused treatment (Fig. 2). For 117 included patients, the mean age was 71 day (range 12–213) (Supplemental Table 1, http://links.lww.com/SCS/C159). The mean weight was 3.9 kg (range 2.3–6.8) (Supplemental Table 1, http://links.lww.com/SCS/C159). A total of 53 patients are female and 64 are male (Supplemental Table 1, http://links.lww.com/SCS/C159). No subject was tracheostomy dependent after MDO.

Osteogenesis
All included 117 patients underwent linear distraction. The magnitude of advancement ranges 13 to 15 mm. Pre and post MDO comparison clearly shows osteogenesis (Fig. 3). Distraction was performed until a slight underbite was achieved (Fig. 3). When the distraction device was removed, the upper and lower jaws were symmetrically aligned (Fig. 3).

Changes in Airway Size
The airway volume increased 114.7% (P < 0.001) after MDO. The retroglossal anteroposterior and lateral diameters increased 155.1% (P < 0.001) and 17.9% (P < 0.001), respectively. The minimal retro-palatal area (RP) and minimum retro-glossal area (RG) increased 245.9% and 60.2% (P < 0.001), respectively.
The airway length didn’t change significantly after MDO ($P > 0.05$). (Supplemental Table 2, http://links.lww.com/SCS/C160) The above results demonstrated the size of upper airway increased after MDO, while the length didn’t change significantly, indicating a wider upper airway was achieved.

Changes in Airway Shape

The RP/RG ratio decreased 89.8% (from 15.728 ± 47.462 before MDO to 1.601 ± 1.045 after MDO, $P < 0.001$). LAT/AP ratio decreased 61.4% (from 3.543 ± 2.757 before MDO to 1.367 ± 0.676 after MDO, $P < 0.001$). The uniformity increased 96.3% (from 0.241 ± 0.176 before MDO to 0.473 ± 0.180 after MDO, $P < 0.001$). (Supplemental Table 3, http://links.lww.com/SCS/C161) Thus, the upper airway became more uniform in shape after MDO.

Three-Dimensional Model of Upper Airway

Pre and post MDO comparison shows the three dimensional CBCT scans of the newborn with isolated PRS and the 3D airway models. Before MDO, the airway was narrow (Fig. 4). After MDO, the airway has become wider (Fig. 4).

**DISCUSSION**

Some people have the features of PRS as part of a syndrome that affects other organs and tissues, such as Stickler syndrome, Velo-cardiofacial syndrome, Treacher Collins syndrome, Kabuki syndrome, DiGeorge syndrome or campomelic dysplasia. These instances are described as syndromic PRS. When PRS occurs by itself, it is described as isolated PRS. In about 20% to 50% of cases, the condition occurs alone in an isolated form, while 35% to 70% of cases are syndromic.2,14,24–27 Stickler syndrome and velocardiofacial syndrome (also called Shprintzen syndrome) are the most common syndromes that are associated with Robin sequence. In addition to Stickler syndrome and velocardiofacial syndrome, there are other syndromes associated with Robin sequence such as Treacher Collins syndrome and Kabuki syndrome. Mandibles are differentially affected in these various manifestations of Robin sequence. Mandibular body length was found to be significantly shorter for children with Pierre Robin sequence while ramus height was significantly shorter for children with Treacher Collins syndrome, resulting in distinctly different ramus height/mandibular body length ratios.17 For patients with deletion 22q11.2 syndrome, the mandible is essentially normal in size, but retrognathic in position because the cranial base angle is larger than normal.28 These findings underscore distinct considerations which must be made in surgical planning for reconstruction among Robin sequence patients. For the current study, our goal is to study effect of MDO on three-dimensional airway anatomy in patients with isolated Robin sequence. This is different from previous studies subjects of which are a mixed group comprising not only isolated PRS but also syndromic PRS. From 11/29/2016 to 11/26/2019, we included 117 isolated PRS patients in this study.

The mortality rate of children with Pierre Robin sequence ranged from 1.7% to 65%.29–32 The cause of death is mainly attributed to respiratory obstruction and/or failure to thrive.33 Before tongue hyoid suspension and skeletal expansion such were applied for the first time in patients with obstructive sleep apnea,34 medical modalities including positive pressure mask ventilation, supplemental oxygen, temporary nasopharyngeal airways and oropharyngeal airway placement, and surgical modalities including tonsillectomy, adenoidectomy, uvulopalatopharyngoplasty and relief of nasal septal obstruction were widely adopted treatments for this condition. But, they were not effective for severe cases in children. Permanent tracheostomy became the only solution for those severely affected children. But, this will result in morbidity and mortality. Long hospital stays, increased costs and potential...
problems outside hospital are also concerns. Fortunately, as a relatively new treatment option for PRS newborns, MDO has proven to be a cost-effective alternative to tracheostomy and tongue-lip adhesion.35–37 Publications show MDO can gradually lengthen the mandible, achieving correction of the posterior tongue base position and relieving of pharyngeal airway obstruction in the patients with PRS.38–40 Nowadays MDO has become a preferable surgical modality for addressing the underlying cause of obstruction for PRS newborns.

Several authors have proved the three-dimensional rendering of airway is an useful method to evaluate and quantify the upper airway condition.41,10,11 The parameters for three-dimensional rendering of airway were developed and defined, including parameters for airway size and parameters for airway shape.41,10,11,21–23 For the current study we performed a systemic quantitative three-dimensional analysis of the pre and post distraction airway anatomy for isolated PRS newborns with using a comparatively large sample size. Also, smaller radiation dose was achieved since we adopted CBCT. For length of upper airway, our result is different from data of previous study on PRS patients who undergo MDO. Some researchers reported a decreased value for length of upper airway after MDO.10,11 Abramson et al showed the length of upper airway decreased from 57.1 ± 16.5 mm to 53.1 ± 13.9 mm after MDO.10 Ramieri et al reported a decrease from a pre distraction value of 36.7 ± 61.65 mm to a post distraction value of 5.00 ± 15.05 mm.11 However, Humphries LS et al reported an increase for the length of upper airway after MDO (29.39 ± 3.89 mm versus 32.99 ± 3.89 mm).41 In our present study, airway length did not change significantly after MDO (27.650 ± 4.924 mm before MDO versus 29.697 ± 4.978 mm after MDO, \( P > 0.05 \)). Several reasons could explain this. The subjects of previous studies were from a mixed group that comprised both syndromic and nonsyndromic patients. Our subjects are only isolated PRS patients. Also, we have a much larger sample size compared to previous studies. 11 patients were included in Abramson’s study, 4 included in Ramieri’s,10,11 and 43 included in Humphries’.54 Our present study included 117 patients. In terms of the value for airway length, we saw the difference between the data of Abramson’s study and Ramieri’s.10,11 Ramieri et al got 5 mm for the mean length of the airway after MDO while Abramson et al got 53.1 mm.10,11 This might be mainly attributed to the age difference of subjects two studies adopted. The mean age of subjects of Abramson’s study was 6.8 years (range 1.3 to 20.6 years) while the oldest among subjects of Ramieri’s study was 24 days.10,11 The value for airway length in our present study (27.650 ± 4.924 mm before MDO versus 29.697 ± 4.978 mm after MDO) and in Humphries’ study (29.39 ± 6.24 mm versus 32.99 ± 3.89 mm) are in the

FIGURE 3. Three-dimensional CBCT scan & craniofacial skeletal reconstruction of newborn affected by isolated PRS shows osteogenesis (new bone formation) after MDO. (A) Three-dimensional CBCT scan & craniofacial skeletal reconstruction of newborn affected by isolated PRS before MDO. (B) Three-dimensional CBCT scan & craniofacial skeletal reconstruction of newborn affected by isolated PRS 10 days after MDO. (C) Three-dimensional CBCT scan and craniofacial skeletal reconstruction of newborn affected by isolated PRS 4 months after MDO.

FIGURE 4. Three-dimensional CBCT scan & airways study of newborn affected by isolated PRS shows improved size and shape of the upper airway after MDO. (A) Three-dimensional CBCT scan & airways study of newborn affected by isolated PRS before MDO (Sagittal). (B) Three-dimensional CBCT scan & airways study of newborn affected by isolated PRS before MDO (Coronal). (C) Three-dimensional CBCT scan and airways study of newborn affected by isolated PRS 4 months after MDO (Sagittal). (D) Three-dimensional CBCT scan and airways study of newborn affected by isolated PRS 4 months after MDO (Coronal).
same range since both studies have a larger sample size compared to Abramson’s and Ramieri’s, and adopted subjects at a similar age range.

CONCLUSION

In conclusion, we provide compelling evidence to show that both size and shape of upper airway of patients with isolated PRS were largely improved after MDO. MDO can serve as an effective surgical modality to address the underlying causes of airway obstruction in newborns with isolated PRS. Also, CBCT scanning as a surgical modality to address the underlying causes of airway obstruction in newborns with isolated PRS. Also, CBCT scanning and analysis can serve as a safe and effective examination modality for upper airway applications of PRS newborns.

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REFERENCES


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