Three-Dimensional Assessment of Facial Development in Children With Pierre Robin Sequence

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Abstract: Newborns with Pierre Robin sequence (PRS) have mandibular hypoplasia, glossoptosis, and possibly cleft palate. Their facial appearance is characteristic. The further facial development is controversial. The aim of this study was to analyze the facial development of children with PRS.

In a prospective, cross-sectional study, 344 healthy children and 37 children with PRS and cleft palate younger than 8 years were scanned three-dimensionally. Twenty-one standard anthropometric landmarks were identified, and the images were superimposed. Growth curves for normal facial development were calculated. The facial morphology of children with PRS was compared with that of healthy children.

The facial growth of children with PRS in the transversal and vertical direction was normal. In the sagittal direction, the mandibular deficit was confirmed. Except for the orbital landmarks and nasion, all landmarks of the midface demonstrated a significant sagittal deficit. This difference to healthy children remained constant for all ages.

Our study cannot support the theory of mandibular catch-up growth. The sagittal deficit of the midface could be observed in all ages. This indicates that children with PRS have a very early, severe, and persistent underdevelopment of this part of the face. We conclude that this disturbance must be addressed in early childhood with orthodontic and speech therapy.

Key Words: Pierre robin sequence, facial growth, photogrammetry

Patients

Thirty-seven children with PRS and cleft palate aged 0 to 7 years were examined in a cross-sectional study. The median age was 28 months (range, 5–85 months). Twenty-one patients were girls, and 16 were boys. After birth, all children had severe respiratory distress that was quantified via oxycardiorespirogram. All newborns were treated with an orthodontic appliance with a velar extension to reduce upper airway obstruction. The cleft palate was closed in the technique of intravelar veloplasty postponed at a median age of 8.4 months (range, 4.5–27.8 months).

Control Persons

Three hundred forty-four healthy white children at the age of 0 to 7 years were evaluated as controls. The median age at the time of examination was 35 months (range, 0–94 months). One hundred sixty-eight children were girls; 176 were boys. The control and patient group did not differ significantly in the aspects of age and sex distribution (Wilcoxon test $P = 0.2$; Fisher exact test $P = 0.4$).

There was a positive vote of the ethical committee of the Medical Faculty of the University of Tübingen to conduct the presented study.

Digital Surface Photogrammetry

The system 3dMDface (3dMD, London, UK) was used for three-dimensional surface imaging. Data capture was performed with 6 synchronized video cameras (4 geometry and 2 texture cameras) and took 2 milliseconds per capture. Approximately 60,000 polygons were calculated from each image set by stereo triangulation. With this image resolution, a geometrical accuracy better than 0.5 mm could be achieved. The children were asked to maintain a neutral facial expression (no smile, no grimace) for imaging and
wore a yellow cap to avoid capturing the hair. Three-dimensional data sets with color were exported in VRML format and imported for landmark placement in the software 3ds Max (Autodesk, San Rafael, CA) for landmark placement.

### Anthropometrical Landmarks and Analysis of the Three-Dimensional Coordinates

Twenty-one anthropometric landmarks (9 bilateral, 3 median) according to the definition of Farkas\(^\text{14}\) were manually identified on the surface (Table 1).

To analyze the spatial development of the landmarks with growth, correspondence was established between the three-dimensional images. Any rigid rotation or translation offsets between the individual scans were removed using the method of singular value decomposition on the three-dimensional positions of the exocanthion (ex), endocanthion (en), otobasion inferius (obi), and nasion (n) landmarks.\(^\text{15}\) In a first step, the center of gravity for the points ex, en, and obi was calculated for each face and then subtracted from each landmark position, centering all faces on this point. Next, the singular value decomposition method computed the optimal rotation for the three-dimensional images for a best fit in a least squares sense for the points ex, en, n, and obi.

The coordinate system was defined as follows: the x axis was defined by the axis ex-ex (transverse axis). The median sagittal plane was defined as the vertical plane to the midpoint of the x axis. The transversal plane was constructed as defined by the Frankfurt horizontal.

### Statistical Analysis

In a first step, normal growth curves of healthy children were estimated for the selected landmarks in the 3 dimensions. Then, the measurements of the children with PRS were compared with the established reference values for the facial growth of the healthy children. The global level of significance was set at 0.05. For

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<thead>
<tr>
<th>Abbreviation</th>
<th>Landmark</th>
<th>Definition</th>
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<tr>
<td>ac</td>
<td>Alar curvature</td>
<td>Most lateral point in the curved base line of each ala</td>
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<tr>
<td>c</td>
<td>Columella</td>
<td>Point on each columella crest, level with the top of the corresponding nostril</td>
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<tr>
<td>ch</td>
<td>Cheilion</td>
<td>Point located at each labial commissure</td>
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<tr>
<td>en</td>
<td>Endocanthion</td>
<td>Point at the inner commissure of the eye fissure</td>
</tr>
<tr>
<td>ex</td>
<td>Exocanthion</td>
<td>Point at the outer commissure of the eye fissure</td>
</tr>
<tr>
<td>ls</td>
<td>Labiale superius</td>
<td>Midpoint of the upper vermillion line</td>
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<tr>
<td>n</td>
<td>Nasion</td>
<td>Point in the midline of both the nasal root and the nasofrontal suture</td>
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<tr>
<td>obi</td>
<td>Otobasion inferius</td>
<td>Point of attachment of the ear lobe to the cheek</td>
</tr>
<tr>
<td>pgn</td>
<td>Pogonion</td>
<td>Most anterior midpoint of the chin</td>
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<tr>
<td>prn</td>
<td>Pronasale</td>
<td>Most protruded point of the apex nasi</td>
</tr>
<tr>
<td>sbal</td>
<td>Subalare</td>
<td>Labial insertion point of the alar base</td>
</tr>
<tr>
<td>sn</td>
<td>Subnasale</td>
<td>Midpoint of the angle at the columella point base</td>
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**FIGURE 1.** Frontal view of facial development and morphology in PRS and cleft palate (age in months is color coded).
multiple testing of 21 landmarks, an adjustment according to the Bonferroni rule was applied. We calculated the proportion of patients outside the reference limits and determined their exact 99.8% binomial confidence limits.

**RESULTS**

The three-dimensional development of the face in the examined 37 children with PRS is shown color coded in Figures 1–3.

**Transversal Direction**

Facial morphology and growth in the transversal direction do not differ significantly from healthy children (Fig. 4).

**Sagittal Direction**

In the sagittal direction, the landmarks on the orbit (ex and en) and ear (obi) have normal values. Also the point n on the nasal root is in a normal position.

All other studied facial landmarks in PRS children differ significantly in their sagittal position from healthy children. They indicate a severe sagittal deficit of the midface and the mandible (Fig. 5).

This sagittal deficit of the midface and the mandible remains stable throughout the observed age intervals. The position of the examined landmarks does not change with respect to the estimated growth curves.

**Vertical Direction**

The vertical dimensions of the face in PRS children are not statistically significantly different compared with healthy children (Fig. 6).

The results, however, might indicate a vertical growth deficit of the mandible.

**DISCUSSION**

Newborns with PRS have mandibular hypoplasia, glossoptosis, and possibly cleft palate. Respiratory distress is the leading clinical symptom after birth. The facial appearance of the newborns

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**FIGURE 2.** Sagittal view of facial development and morphology in PRS and cleft palate (age in months is color coded).

**FIGURE 3.** Axial view of facial development and morphology in PRS and cleft palate (age in months is color coded).
is characteristic with a severely retruded chin. The further development of the face, however, is controversial in the literature. Most studies concentrate on the development of the mandible. There is a frequent discussion whether the mandible has a normal potential of anterior growth to compensate partially or completely for the neonatal deficit.\textsuperscript{4,16,17}

The morphology of the complete face and its growth, however, is rarely addressed and discussed controversially. Anthropometric studies and indirect three-dimensional surface measurements of children with PRS are not described in the literature.

Landmarks close to the skull base (en, ex, obi, n) demonstrated a normal spatial position compared with healthy children in the current study. This result is in accordance with the study of Hirschfeld and Aduss,\textsuperscript{18} who found a normal to slightly decreased interorbital distance in these patients. With 3-projection cephalometry, Hermann et al\textsuperscript{19} described a retruded lateral orbital rim and a significantly smaller interorbital distance in children with PRS. This result, however, must be viewed with caution, as the control group consisted of children with unilateral cleft lip.

The most striking and possibly the least expected result of the current study is the observed development of the midfacial landmarks. In transversal and vertical direction, there is no difference in the normal population. But all landmarks on the tip of the nose, the alar wing, and the upper lip demonstrate a significant posterior position. This deficit can be seen from the youngest to the oldest examined children. By visual analysis of the position of the

**FIGURE 4.** A, Observed measurements of 37 children together with the age-specific reference limits for 21 landmarks in the transversal direction. B, Proportion of children outside the reference limits together with their 99.8% exact binomial confidence limits.

**FIGURE 5.** A, Observed measurements of 37 children together with the age-specific reference limits for 21 landmarks in the sagittal direction. B, Proportion of children outside the reference limits together with their 99.8% exact binomial confidence limits.
landmarks in relation to the normal growth curves, no change over time can be seen. This result indicates that there is a very early and persistent hypoplasia of the midface.

Laitinen and Ranta\(^6\) have reported some maxillary retrusion compared with healthy Scandinavian children using cephalometry. More precise information, however, is missing. A significant difference in children with isolated cleft palate could not be demonstrated. Using three-dimensional plaster casts, Bacher et al\(^23\) studied the position of the maxilla already in newborns with PRS. They found a shortening of the maxilla in the sagittal direction compared with healthy babies. And also, Hermann et al\(^21\) described a significant retrognathic position of the maxilla in 2- and 22-month-old infants with PRS using 3-projection cephalometry. In summary, these studies, using more invasive and more elaborate techniques, demonstrated similar results concerning the position of the midface.

The shortened and retrognathic mandible is a distinct feature of PRS and was already frequently described. The postnatal development of the mandible, however, is discussed controversially. Figueroa et al\(^4\), Pruzansky and Richmond\(^5\) and others support the hypothesis that the mandible has a catch-up growth during the first year of life and a normal size thereafter. Our study cannot support this hypothesis. With the limitation of a cross-sectional study, a catch-up growth cannot be assumed up to the age of 3 years. After this age, the number of examined children is far less, and therefore, statements are less reliable. But still there is a tendency for a retrognathic mandible. Our observation is supported by the cephalometric examination of Hermann et al\(^21\) who could also not demonstrate a mandibular catch-up growth up to the age of 2 years. Daskalogiannakis et al\(^12\) could not find a compensatory increased growth of the mandible after the fifth year of life. The size and the retrognathic position of the mandible persisted. Also, the studies of Marcovic\(^5\), Stellmach and Schettler\(^2\), Veger et al\(^24\) and Eriksen et al\(^25\) are in agreement with the presented results.

**CONCLUSIONS**

The facial morphology of children with PRS differs significantly from healthy children. Not only the mandible but also the midface is highly affected by the deformity. The sagittal growth deficit of the entire face necessitates early orthodontic treatment and speech therapy.

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