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Persistent Craniofacial and Airway Alterations in Young Adults with Isolated Robin Sequence: A CBCT- Based Analysis

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Short Report

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Abstract

Objectives:

To assess craniofacial and upper airway morphological characteristics in young adults with isolated Robin sequence (IRS) using cone-beam computed tomography (CBCT), compared with matched controls.

Materials and Methods:

This cross-sectional study included CBCT scans from 12 individuals: six with IRS and six controls matched by sex and craniofacial skeletal pattern. Morphometric analyses of the tongue, oral cavity, mandible, hyoid bone, and oropharyngeal airway were performed using two- and three-dimensional computational approaches. Group comparisons were conducted using Student's t-test, and effect sizes were calculated using Cohen's *d*.

Results:

Individuals with IRS exhibited significantly reduced tongue area, tongue length, oral cavity area, and oropharyngeal airway depth compared with controls ($p \leq 0.05$), with large effect sizes ($d \geq 1.7$). Mandibular body length, total length, and mandibular angle were also significantly reduced. Hyoid bone volume and positional parameters differed significantly between groups. Several variables demonstrated moderate to large effect sizes despite non-significant p-values.

Conclusions:

Craniofacial and airway-related morphological alterations appear to persist into adulthood in individuals with IRS and may contribute to impaired aerodigestive function.

Clinical Relevance:

These findings highlight the importance of long-term structural assessment in individuals with IRS, particularly regarding potential airway compromise and associated functional outcomes.

INTRODUCTION

Robin sequence affects approximately one in 14,000 to 24,500 live births, with the isolated form accounting for nearly 36% of cases [1, 2]. It is characterized by a triad of mandibular dysmorphology, glossoptosis, and upper airway obstruction, frequently associated with cleft palate [3, 4]. Functional

impairments, including breathing, feeding, and sleep disturbances, may occur depending on clinical severity [5].

The structural basis of airway compromise in infants with isolated Robin sequence (IRS) has been extensively described, including reduced mandibular dimensions, altered tongue morphology, and hyoid bone abnormalities [6–8]. However, the persistence of these craniofacial and airway-related alterations into adulthood remains insufficiently understood. Previous studies suggest that micrognathia, altered hyoid position, and reduced pharyngeal dimensions may persist despite craniofacial growth [9–11], although findings are heterogeneous and often lack comparison with matched controls.

Clarifying whether these morphological alterations persist into adulthood is clinically relevant, particularly given their potential association with obstructive sleep apnea and other aerodigestive dysfunctions [12, 13]. Therefore, this study aimed to assess craniofacial and upper airway morphological characteristics in young adults with IRS using cone-beam computed tomography, compared with matched controls.

METHODS

This cross-sectional study included cone-beam computed tomography (CBCT) scans from 12 individuals: six with isolated Robin sequence (IRS) and six controls (CON), matched by sex and craniofacial skeletal pattern. All scans had been previously obtained for clinical purposes and met inclusion criteria regarding image quality and visualization of anatomical structures of interest. Individuals with a history of orthognathic surgery, adenoidectomy, tonsillectomy, or craniofacial syndromes were excluded.

CBCT images were acquired using an i-CAT Next Generation scanner (Imaging Sciences International, Hatfield, PA, USA), following standardized acquisition protocols. The study was approved by the Institutional Review Board (protocol no. 87275618.0.0000.5441).

Morphometric analyses were performed using ITK-SNAP (version 3.8.0) and Ansys® SpaceClaim software. The following structures were evaluated: tongue (area, length, height, and shape index), oral cavity area, mandible (linear and volumetric measurements), hyoid bone (volume and position), and oropharyngeal airway depth at the retroglossal level. Measurements were obtained using two- and three-dimensional approaches based on standardized anatomical landmarks. All measurements were performed by two calibrated examiners at two time points, demonstrating high intra- and interobserver reliability (intraclass correlation coefficient ≥ 0.90). Mean values were used for analysis.

Statistical analyses were conducted using Student's t-test for group comparisons and Pearson's correlation coefficient for association analyses, with significance set at $p \leq 0.05$.

RESULTS

Both groups had similar sex distribution, with four women and two men in each group. The mean age was 18.7 ± 4.9 years in the IRS group and 25.2 ± 6.3 years in controls ($p > 0.05$).

Compared with controls, individuals with IRS exhibited significantly reduced tongue area, tongue length, and oral cavity area ($p \leq 0.05$), with large effect sizes ($d \geq 1.7$). Oropharyngeal airway depth was also significantly reduced in the IRS group (4.66 ± 2.45 mm vs. 9.22 ± 2.61 mm; $p = 0.01$; $d = 1.80$), indicating decreased retroglossal airway space.

Mandibular measurements demonstrated significantly reduced body length, total length, and mandibular angle in individuals with IRS ($p \leq 0.05$), with large effect sizes observed for body and total length ($d = 1.43$ and $d = 2.04$, respectively). Although mandibular volume did not differ significantly between groups ($p > 0.05$), moderate effect sizes were identified ($d = 0.7$).

The hyoid bone showed significantly reduced volume and differences in positional parameters ($p \leq 0.05$), with large effect sizes ($d > 1.0$). Notably, some variables did not reach statistical significance but demonstrated moderate to large effect sizes, including hyoid position relative to the cervical spine ($d = 1.42$).

Correlation analyses revealed that reduced mandibular dimensions were associated with decreased tongue measurements. Additionally, tongue shape index was negatively correlated with oropharyngeal airway depth ($r = -0.817$; $p \leq 0.05$).

All morphometric findings are summarized in Table 1 and Fig. 1 shows representative sagittal CBCT-based reconstructions of craniofacial structures in an individual with IRS (A) and a control subject (B).

Table 1
Morphometric characteristics of craniofacial and airway-related structures in individuals with isolated Robin sequence (IRS) and controls (CON), including effect size (Cohen's d).

Variable	IRS (n = 6) Mean ± SD	CON (n = 6) Mean ± SD	p-value	Effect size (d)
Tongue				
Area (cm²)	30.04 ± 11.48	48.71 ± 9.56	0.01	1.78
Length (mm)	62.88 ± 6.51	78.32 ± 7.54	< 0.001	2.19
Height (mm)	56.53 ± 6.56	66.89 ± 13.61	0.03	0.97
Shape index (%)	0.90 ± 0.08	0.85 ± 0.11	0.29	0.53
Apex–ANS (mm)	9.45 ± 6.72	5.27 ± 5.57	0.22	0.68
Dorsum–palatal plane (mm)	8.90 ± 5.01	7.85 ± 5.44	0.68	0.20
Oral cavity				
Area (cm²)	33.49 ± 12.29	54.91 ± 6.11	0.01	2.20
Tongue/oral cavity ratio	0.88 ± 0.07	0.85 ± 0.10	0.47	0.35
Airway				
Oropharyngeal depth (mm)	4.66 ± 2.45	9.22 ± 2.61	0.01	1.80
Mandible				
Volume with teeth (cm³)	40.31 ± 12.73	47.61 ± 6.91	0.18	0.70
Volume without teeth (cm³)	27.46 ± 8.33	32.34 ± 4.11	0.17	0.72
Ramus height (mm)	50.83 ± 5.96	53.68 ± 4.61	0.29	0.53
Body length (mm)	62.22 ± 10.11	73.43 ± 3.69	0.02	1.43
Total length (mm)	102.30 ± 11.17	121.60 ± 7.08	< 0.001	2.04
Mandibular angle (°)	111.80 ± 25.18	128.10 ± 11.19	0.04	0.83
Hyoid bone				
Volume (cm³)	0.81 ± 0.30	1.29 ± 0.40	0.02	1.36
H–CIII (mm)	30.47 ± 1.28	33.42 ± 2.59	0.06	1.42
H–RGn (mm)	30.71 ± 4.16	36.26 ± 4.43	0.02	1.28
CIII–RGn (mm)	58.45 ± 8.06	65.46 ± 5.39	0.04	1.02

Variable	IRS (n = 6) Mean ± SD	CON (n = 6) Mean ± SD	p-value	Effect size (d)
H–H’ (mm)	6.38 ± 4.66	9.69 ± 4.02	0.21	0.76
H–Go.Me (mm)	13.38 ± 5.03	18.80 ± 9.99	0.19	0.66

DISCUSSION

The present findings demonstrate that craniofacial and airway-related morphological alterations associated with isolated Robin sequence persist into adulthood. Reduced tongue and oral cavity dimensions, combined with mandibular deficiencies, appear to contribute to decreased oropharyngeal airway space, suggesting a persistent structural predisposition to airway compromise.

These results are consistent with previous studies describing the structural basis of airway compromise in individuals with Robin sequence, including mandibular hypoplasia, altered tongue morphology, and hyoid positioning [6–8]. Importantly, longitudinal observations indicate that these alterations may persist despite craniofacial growth, particularly in relation to mandibular dimensions and pharyngeal airway space [9–11]. The magnitude of differences observed in the present study further supports the biological relevance of these persistent structural characteristics.

The association between mandibular dimensions and tongue morphology reinforces the interdependence between skeletal and soft tissue structures. Reduced mandibular dimensions may limit oral cavity space, influencing tongue position and reducing airway patency. This interpretation is consistent with previous studies demonstrating that the relationship between tongue volume and oral cavity capacity plays a critical role in upper airway morphology [12–15]. In this context, the findings suggest that airway compromise is more strongly related to morphological imbalance than to absolute tongue size alone.

The reduced oropharyngeal airway dimensions observed in the IRS group are also consistent with structural risk factors associated with obstructive sleep apnea and related conditions [16, 17]. Although clinical outcomes were not assessed in the present study, these findings reinforce the potential long-term functional implications of craniofacial alterations in this population.

Alterations in hyoid morphology and position were also identified, although their clinical significance remains uncertain. Previous studies suggest that hyoid characteristics may reflect both structural and functional adaptations and are not exclusively associated with pathological conditions [18, 19].

From a clinical perspective, the persistence of these morphological characteristics supports the need for long-term monitoring of individuals with isolated Robin sequence. Even in the absence of overt clinical symptoms, structural features associated with airway compromise may remain present into adulthood.

This study has limitations, particularly the small sample size and cross-sectional design, which may restrict generalizability. However, the consistency of findings across multiple anatomical structures and their magnitude support the relevance of these results. Future studies with larger samples and longitudinal designs are warranted.

Declarations

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Funding Declaration

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Data Availability

The datasets generated and/or analyzed during the current study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author on reasonable request.

Author Contribution

M.N.M.-R. contributed to the study conception and design, data analysis, interpretation of results, and drafting of the manuscript.
L.L.S.B. contributed to data collection, image processing, and methodological development.
A.B.G.A. contributed to data analysis and manuscript preparation.
I.K.T.-S. contributed to study supervision, critical revision of the manuscript, and final approval of the version to be published.

All authors reviewed and approved the final manuscript.

Competing Interest

The authors declare that they have no conflict of interest.

Ethics declaration

This study was approved by the Institutional Review Board of the Catholic University of Pelotas (protocol no. 87275618.0.0000.5441). All procedures performed were in accordance with the ethical standards of

the institutional and national research committees and with the 1964 Helsinki Declaration and its later amendments. Informed consent was obtained from all individual participants included in the study.

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Figures

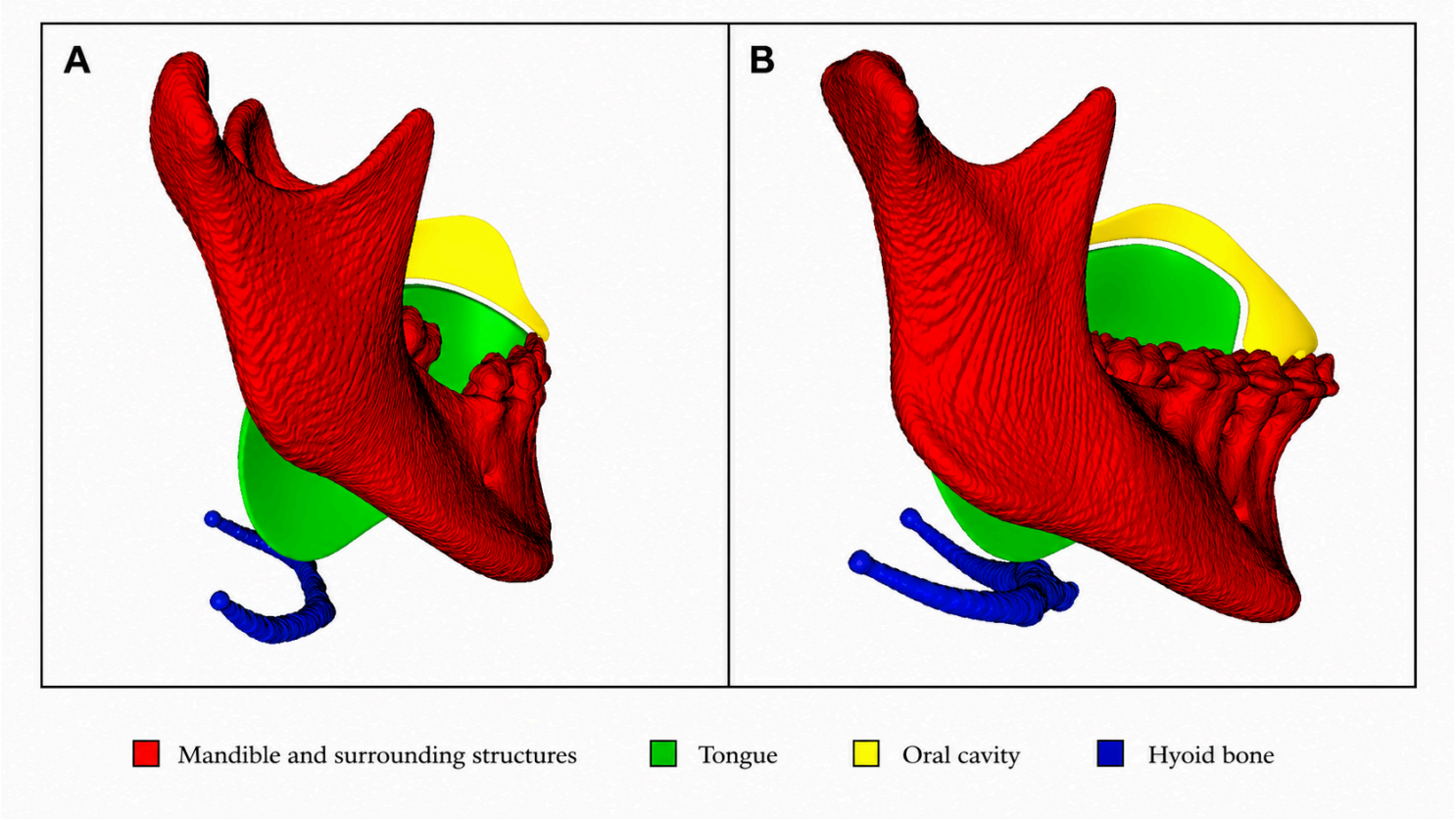


Figure 1

Representative sagittal CBCT-based reconstructions of craniofacial structures in an individual with isolated Robin sequence (IRS) (A) and a control subject (B). The IRS case demonstrates reduced tongue and oral cavity dimensions and decreased posterior airway space compared with the control. The mandible, tongue, oral cavity, and hyoid bone are depicted.