Three-Dimensional Airway Changes after Le Fort III Advancement in Syndromic Craniosynostosis Patients

Erik Nout, M.D., D.D.S.
Frederik P. Bouw, M.D.
Jifke F. Veenland, Ph.D.
Wim C. J. Hop, Ph.D.
Karel G. H. van der Wal, M.D., D.D.S., Ph.D.
Irene M. J. Mathijssen, M.D., Ph.D.
Eppo B. Wolvius, M.D., D.D.S., Ph.D.

Rotterdam, The Netherlands

Background: To investigate the changes of upper airway volume in syndromic craniosynostosis patients following Le Fort III advancement, computed tomographic scans were analyzed and related to the amount of advancement.
Methods: In this retrospective study, the preoperative and postoperative computed tomographic scans of 19 patients with syndromic craniosynostosis who underwent Le Fort III advancement were analyzed. In four cases, preoperative polysomnography demonstrated obstructive sleep apnea. The airway was segmented using a semiautomatic region growing method with a fixed Hounsfield threshold value. Airway volumes of hypopharynx and oropharynx (compartment A) and nasopharynx and nasal cavity (compartment B) were analyzed separately, as was the total airway volume. Advancement of the midface was recorded using lateral skull radiographs. Data were analyzed for all patients together and for patients with Crouzon/Pfeiffer and Apert syndromes separately.
Results: Airway volume increased significantly in compartment A (20 percent; $p = 0.044$) and compartment B (48 percent; $p < 0.001$), as did total airway volume in (37 percent; $p < 0.001$) in the total study group. No significant differences in volume changes were found comparing Apert with Crouzon/Pfeiffer patients. No distinct relation could be found between advancement of the midface and volume gain either in the total study group or in Apert and Crouzon/Pfeiffer patient groups separately. Postoperative polysomnography showed significant improvement of obstructive sleep apnea in all four patients.
Conclusions: A significant improvement of the upper airway after Le Fort III advancement in syndromic craniosynostosis patients is demonstrated. No distinct relation could be observed between advancement and airway volume changes. (*Plast. Reconstr. Surg.* 126: 564, 2010.)

Midface hypoplasia is an important three-dimensional skeletal defect that is commonly seen in patients with syndromic craniosynostosis, such as Crouzon, Apert, and Pfeiffer syndromes. This midface hypoplasia may give rise to obstructive sleep apnea, ocular proptosis, and class III malocclusion including a transverse maxillary hypoplasia and aesthetic facial disharmony. In addition, there is strong evidence for an association between obstructive sleep apnea and raised intracranial pressure in these syndromic craniosynostosis patients.[1] Although the primary aim of midface advancement for syndromic craniosynostosis patients with obstructive sleep apnea is to create airway volume, it remains unclear to what extent the Le Fort III advancement increases the airway volume on the nasopharyngeal, oropharyngeal, and hypopharyngeal levels.

Traditionally, in nonsyndromic orthognathic patients, airway measurements were conducted using plain lateral skull radiographs.[2–9] By identifying anatomical landmarks, distances were calculated and used to describe pharyngeal depth and posterior airway space in the anteroposterior di-

From the Departments of Oral and Maxillofacial Surgery, Radiology, and Plastic and Reconstructive Surgery, and the Departments of Medical Informatics and Biostatistics, Faculty of Medicine, Erasmus MC University Medical Center.
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mension. By this means, changes in both upper and lower airway spaces have been investigated extensively and correlated with the outcome of obstructive sleep apnea measurements after orthognathic surgery.[6–8] Using the same method, Ishii et al. reported an improvement of nasopharyngeal airway volume after Le Fort III advancement in syndromic craniosynostosis patients.[10] Commensurable results were obtained by Flores et al., who found a significant increase in nasopharyngeal and velopharyngeal airway after Le Fort III distraction osteogenesis.[11] Recently, Degerliyurt et al. and Fairburn et al. have used both sagittal and transversal slices of computed tomographic scans to enhance accuracy in nonsyndromic patients.[12–14] With the progression of digital postprocessing techniques, three-dimensional segmentation of the airway has become possible, enhancing accuracy even further.[15]

The purpose of the current study was to evaluate the changes of airway volume in syndromic craniosynostosis patients after Le Fort III advancement by analyzing preoperative and postoperative computed tomographic scans with an airway volume segmentation technique. In addition, preoperative and postoperative cephalograms of all these patients were analyzed to evaluate a possible correlation between the amount of horizontal and vertical advancement and the changes of the upper airway volume.

PATIENTS AND METHODS

In this retrospective study, 19 patients were reviewed (10 female patients and nine male patients) with Apert syndrome (five female patients and two male patients), Crouzon syndrome (six female patients and three male patients), and Pfeiffer syndrome (three male patients). Because of genetic similarity between Crouzon and Pfeiffer patients, we chose to consider these patients with proven non-Apert *FGFR2* mutations as one entity and refer to these patients as Crouzon/Pfeiffer. Indications for Le Fort III osteotomy in this study group were obstructive sleep apnea (four patients: two moderate obstructive sleep apnea and two severe obstructive sleep apnea based on preoperative polysomnography), exorbitism (four patients), and class III malocclusion (all patients). Patients were included when both preoperative and postoperative computed tomographic scans (after completion of distraction and consolidation period) and lateral skull radiographs were available. Patients who required endotracheal intubation during the scanning process were excluded. Between 2003 and 2008, 18 patients underwent Le Fort III distraction osteogenesis with external (16 patients) or internal distractors (two patients), and one patient underwent a conventional Le Fort III osteotomy. The average age at time of surgery was 14.6 ± 4.3 years. Postoperatively, all patients were seen in an outpatient clinic on a weekly basis.

Le Fort III Distraction Protocol

A latency period of 7 days postoperatively was applied to all patients irrespective of age or degree of advancement. Distraction rate was 1 mm/day. Distraction was continued for a varying period depending on the desired correction. Vector modifications took place during distraction when necessary. After distraction, a consolidation period of 3 months was respected in all patients, during which the distractors were retained.

Computed Tomographic Scans and Lateral Skull Radiographs

Preoperative scans were obtained on average 7 ± 5 months before surgery. Postoperative scans were obtained on average 6 ± 3 months after surgery. All scans were obtained in Sophia Children's Hospital using the same scanner (Emotion 6; Siemens, Munich, Germany) with a fixed slice thickness of 1.25 mm. Sedation was indicated in some cases during scanning and depended on the patient's cooperation and age. All scans were obtained in supine position.

Preoperative lateral skull radiographs were obtained on average 4 ± 4 months before surgery. Postoperative lateral skull radiographs were obtained on average 7 ± 4 months after surgery. All lateral skull radiographs were obtained in Sophia Children's Hospital in the upright position with the jaws in centric occlusion using the same calibrated device (Orthophos Plus DS; Sirona, Salzburg, Austria).

The software program MevisLab (MeVis Medical Solutions AG, Bremen, Germany) was used to import and analyze the computed tomographic scans by means of a custom-designed tool. First, by manually masking for each scan in each slice the maxillary, ethmoidal, frontal, and sphenoidal sinuses and the oral cavity (posterior boundary defined by a transversal plane from the uvula to the tongue base), the inactive respiratory airways were excluded (Fig. 1). Hereafter, two compartments were marked according to predefined strict anatomical boundaries (Fig. 2). Compartment A, containing the hypopharynx and oropharynx, was defined to range from the lower part of the hyoid bone to half the length of the uvula visualized in midsagittal view. Compartment B, containing the nasopharynx and nasal

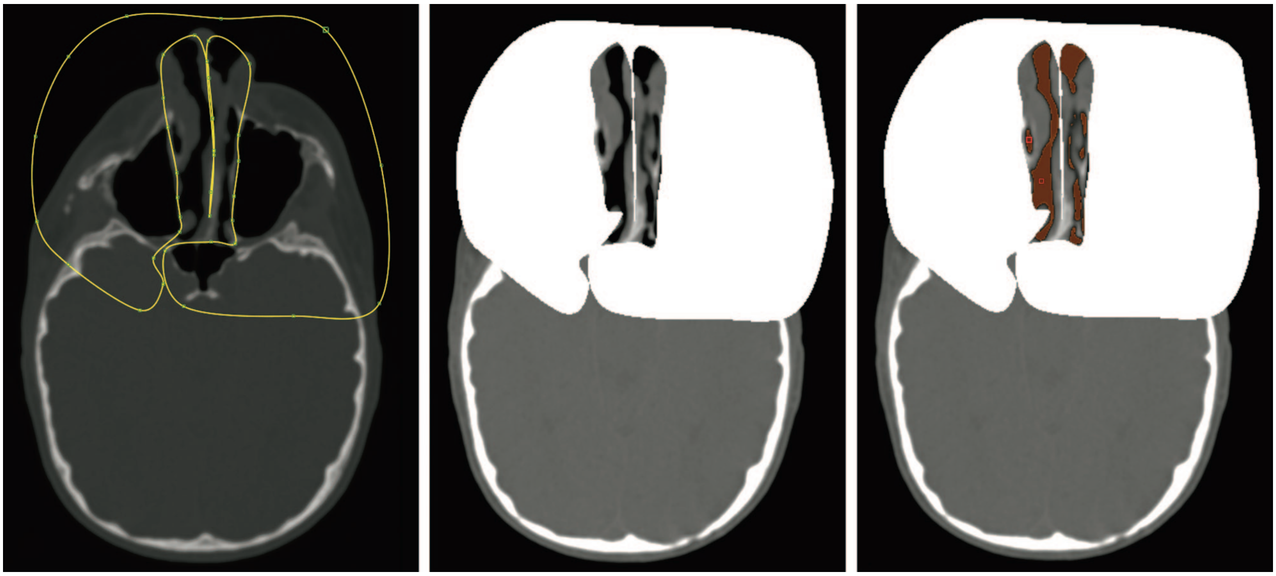

Fig. 1. Example of the step-by-step exclusion of paranasal sinuses. By manually creating a contour in each slice (*left*), a mask can be computed (*center*). By segmentation of the selected areas, indicated by placing seeding points (*right*), and use of a semiautomatic region growing method with a fixed Hounsfield threshold value, volumes can be computed for areas of interest. Exclusion of the oral cavity took place in a similar way.

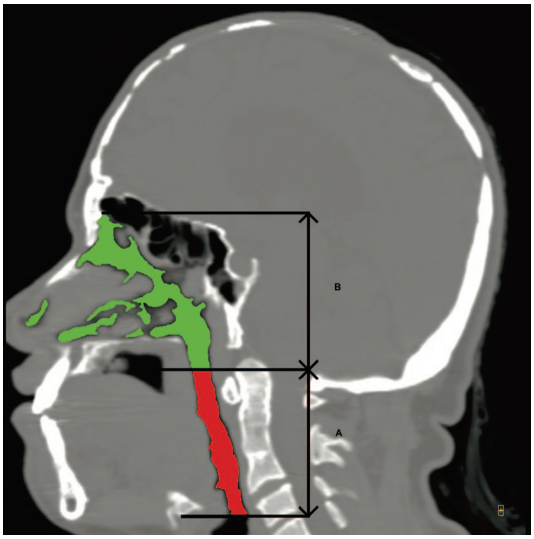

Fig. 2. Computed tomographic scan in midsagittal view. The *three lines* mark the boundaries of compartments A and B. The *upper line* marks the most cranial point of the nasal cavity, the *middle line* runs half the length of the uvula, and the *lower line* marks the most caudal point of the hyoid bone. The part of the airway that represents compartment A is marked in *red*, whereas compartment B is marked in *green*. All paranasal sinuses and the oral cavity were excluded manually.

cavity, was defined to range cranial from compartment A to the most cranial point of the nasal cavity. Separately, both compartments were segmented using a semiautomatic region growing method with a fixed Hounsfield threshold value. The same threshold was used for all data sets. The volume of the segmented compartments was computed preoperatively and postoperatively. By adding the two volumes of compartments A and B, a total volume was calculated preoperatively and postoperatively. To determine the interobserver variability of the volume measurements, a second operator performed the manual masking of 10 randomly selected patients of the study group, independent of the first operator.

The lateral skull radiographs were all traced by hand. On each lateral skull radiograph, the sella (S), roof of orbit (RO), nasion (Na), and A-point (A) were identified. By drawing a line through A parallel to line S-Na and a line through S perpendicular to line S-Na, an intersection was created and labeled J. To determine horizontal advancement, distance J-A was measured on preoperative and postoperative lateral skull radiographs. To determine the vertical advancement, distance S-J was measured preoperatively and postoperatively. As another parameter representing horizontal advancement, the angle between lines S-OR and A-OR was measured preoperatively and postoperatively (Fig. 3). All lateral skull radiographs were traced independently by two operators and the average of the measurements of the operators were used for statistical evaluations. For both volume and advancement, preoperative and postop-

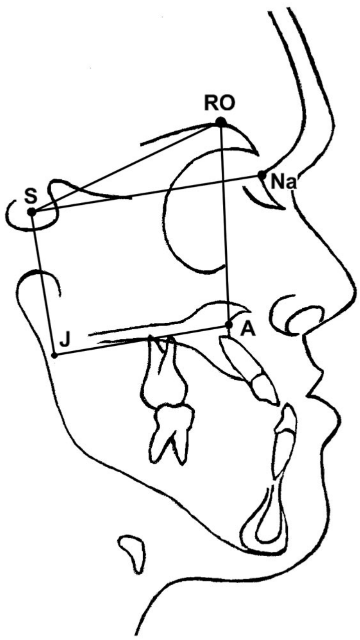

Fig. 3. Cephalogram of a patient with Pfeiffer syndrome. To determine the degree of horizontal advancement, the angle was measured between lines S-RO and RO-A. Also, the horizontal and vertical movement was measured by distance A-J and distance S-J, respectively.

erative data were compared and differences were calculated for each patient.

Statistical Analysis

All data were analyzed using SPSS for Windows XP (version 15.0; SPSS, Inc., Chicago, Ill.). Interobserver reliability was qualified with use of the intraclass correlation coefficient. The paired *t* test was used to compare the preoperative and postoperative computed tomographic data. Concerning the volumetric changes, the mean and SD were calculated for all compartments. Volumetric changes were expressed as percentages of the preoperative airway volumes. Correlation coefficients given are Spearman rank correlations (r_s). In addition, the Spearman rank correlation coefficient was used to evaluate the correlation between the horizontal advancement expressed as degrees and the horizontal advancement expressed as millimeters. To analyze the differences between Apert and Crouzon/Pfeiffer syndromes, independent samples *t* test was conducted to evaluate differences between these two patient groups. A value of $p < 0.05$ (two-tailed) was considered to be statistically significant.

RESULTS

Patient data are summarized in Tables 1 and 2. Interobserver agreement with respect to volume measurements was excellent (intraclass correlation coefficient, >0.99). For the cephalometric analysis of the lateral skull radiographs, the interobserver agreement was moderate (intraclass correlation coefficient, 0.65). The horizontal advancement in degrees correlated with the horizontal advancement in millimeters ($r_s = 0.46$, $p = 0.049$).

Table 1. Overview of Volume Changes According to Compartment and Patient Group*

	Compartment A	Compartment B	Total Volume
Total group	19.7 ± 39.5†	47.8 ± 28.0†	37.4 ± 20.7†
Apert	27.2 ± 36.7†	37.0 ± 22.5†	31.1 ± 13.2†
Crouzon/Pfeiffer	15.2 ± 42.0	54.1 ± 29.7†	41.1 ± 23.8†

*The "compartment" columns represent the changes in postoperative volume compared with the preoperative volume expressed as a percentage.
†Significant result ($p < 0.05$).

Table 2. Overview of Advancement According to Patient Group*

	Degrees	Horizontal Advancement (mm)	Vertical Advancement (mm)
Total group	12.4 ± 5.4	13.2 ± 4.7	6.7 ± 4.6
Apert	9.6 ± 3.4	11.1 ± 4.7	6.4 ± 5.9
Crouzon/Pfeiffer	14.1 ± 5.7	14.5 ± 4.4	6.9 ± 3.7

*The "degrees" column represents the horizontal advancement expressed in degrees.

Total Study Group

Airway volume in compartment A increased with a mean of 20 ± 39.5 percent ($p = 0.044$). Airway volume in compartment B improved with a mean of 48 ± 28.0 percent ($p < 0.001$) and the total volume improved with a mean of 37 ± 20.7 percent ($p < 0.001$) (Fig. 4).

The mean horizontal movement of the midface was 13.2 ± 4.7 mm and 12.4 ± 5.4 degrees. The mean vertical movement was 6.7 ± 4.6 mm.

Both horizontal and vertical movement of the midface measured in millimeters and the volume gain of each compartment did not reveal statistically significant correlations (all $p > 0.48$). In contrast, a significant correlation was found between the horizontal advancement of the midface measured in degrees and the volume gain of compartment B ($r_s = 0.61$, $p = 0.006$).

Postoperative polysomnography showed significant improvement of obstructive sleep apnea

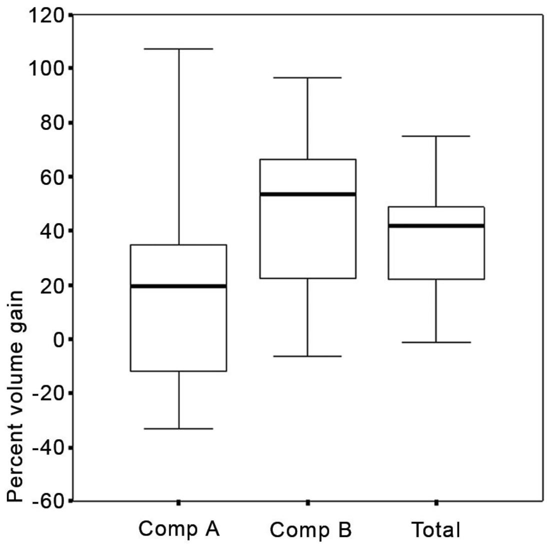

Fig. 4. Box plot of the postoperative volume gains expressed as percentage of the preoperative volumes according to the three compartments in the total patient group. Minimum, maximum, and median values (*bold line*) are visualized. The *box* represents the interquartile range.

in all four patients, with residual mild obstructive sleep apnea in three and absence of breathing difficulties in one.

Apert and Crouzon/Pfeiffer Syndrome

In patients with Apert syndrome, for all three compartments, a significant volume gain was found. On average, airway volume in compartment A increased with 27 ± 36.7 percent (p = 0.009) and in compartment B with 37 ± 22.5 percent (p = 0.012). Total volume increased with 31 ± 13.2 percent (p = 0.003). In Crouzon/Pfeiffer patients, significant postoperative volume gains were restricted to compartment B (54 ± 29.7 percent) (p = 0.002) and total volume (41 ± 23.8 percent) (p = 0.001). When comparing the average volume gains between the Apert and Crouzon/Pfeiffer groups, no significant differences were found (all $p > 0.205$). When correlating the horizontal and vertical movement of the midface to the volumetric airway changes, no significant relation for patients with Apert syndrome was observed. In Crouzon/Pfeiffer patients, a significant positive correlation ($r_s = 0.813$; $p = 0.001$) was found between the horizontal advancement of the midface measured in degrees and the volume gain in compartment B. In contrast, in the Crouzon/Pfeiffer subgroup, no significant correlation was found with respect to volume changes and advancement of the midface expressed in millimeters.

DISCUSSION

Various studies on nonsyndromic patients with class III skeletal deformities have used conventional lateral cephalograms to study airway volume.[2–9] To investigate airway volume following surgery more precisely, segmentation of the airway using computed tomographic data can be performed. An optimal threshold for the air/soft-tissue separation can be defined and used in a region growing algorithm, resulting in three-dimensional airway volumes. Concerning maxillofacial application of airway measurement techniques, effects of bimaxillary, mandibular setback, and mandibular advancement have been evaluated in syndromic and nonsyndromic patients (Table 3).[14,16–18]

Table 3. Overview of Maxillofacial Application of Airway Measurement Techniques in Orthognathic Surgery

Reference	No. of Patients	Evaluation	Technique	Airway Volume
Kawamata et al., 2000[16]	13 (nonsyndromic)	Mandibular setback	Measurements of changes of frontal and lateral width of the pharyngeal airway on CT scans (one-dimensional)	Narrowing of the pharyngeal airway
Degerliyurt et al., 2009[14]	47 (nonsyndromic)	Mandibular setback and maxillary advancement combined with mandibular setback	Measurements of areas on individual CT slices (two-dimensional)	Reduction of oropharynx and hypopharynx after both procedures
Rachmiel et al., 2005[17]	12 (severe hypoplastic mandibles)	Mandibular advancement	Quantification of airway volumes after extraction of a selected area from CT scans (three-dimensional)	Increase of upper airway volume
Perlyn et al., 2002[18]	4 (syndromic)	Mandibular advancement	Quantification of airway volumes after extraction of a selected area from CT scans (three-dimensional)	Increase of the upper airway volume

CT, computed tomographic.

With regard to the Le Fort III advancement in syndromic patients, Xu et al. reported a mean increase of 64 percent in upper airway volume.[15] In the current study, a significant volume gain of the nasopharynx and nasal cavity of 48 percent after Le Fort III advancement was demonstrated (Fig. 5). Unfortunately, only the abstract of this purely Chinese report is available in English. By segmentation of the upper airway, we calculated airway volumes of the complete upper airway. With this method, we were able to analyze the complex anatomy of the complete upper airway in a detailed way with high reproducibility.

Kreiborg et al. conducted a comparative three-dimensional analysis of computed tomographic scans in Apert and Crouzon syndromes.[19] In Apert syndrome, the posterior nasopharyngeal wall seemed to be more curved when compared with the relatively more vertical posterior nasopharyngeal wall in Crouzon patients. In the current study, in both patient groups, a significant overall airway volume gain was found. However, most likely attributable to small patient numbers, no significant differences could be revealed between the two patient groups. Concerning the difficulties with landmark identification on cephalograms in syndromic patients, we chose to use the skull base as a control. Like Kreiborg et al., we evaluated the degree of horizontal advancement after Le Fort III surgery by choosing reproducible, clearly identifiable landmarks.[19] Because the nasion is mobilized during surgery, we also chose to evaluate horizontal advancement by choosing the roof of orbit and sella as stationary reference points. In addition, we used goniometry to verify horizontal advancement. Unfortunately, as interobserver agreement was moderate, landmark identification is difficult in syndromic craniosynostosis patients. More ideally, lateral cephalograms might be extracted from computed tomographic scans and three-dimensional cephalometry could be helpful, but only applicable after validation.[20]

In this study, the correlation between vertical movement and postoperative volume was not significant in the total group or in either subgroup. The three-dimensional visualizations of the segmented airways showed that the shape of the upper airway was remarkably irregular (Fig. 5). This irregularity is probably associated with the complex anatomical variations of the skull base as is frequently observed in syndromic craniosynostosis patients.[19] This may account for an unpredictable change of upper airway volume following midface advancement. Most likely, because of complex anatomy of the airway in these syndromic craniosynostosis patients, clearly, no 1:1 relation between advancement and increase of postoperative airway volume can be assumed. Furthermore, our measurements represent a static reflection of a dynamic environment. Midface advancement does reduce the preexisting airway obstruction in those patients with obstructive sleep apnea through re-

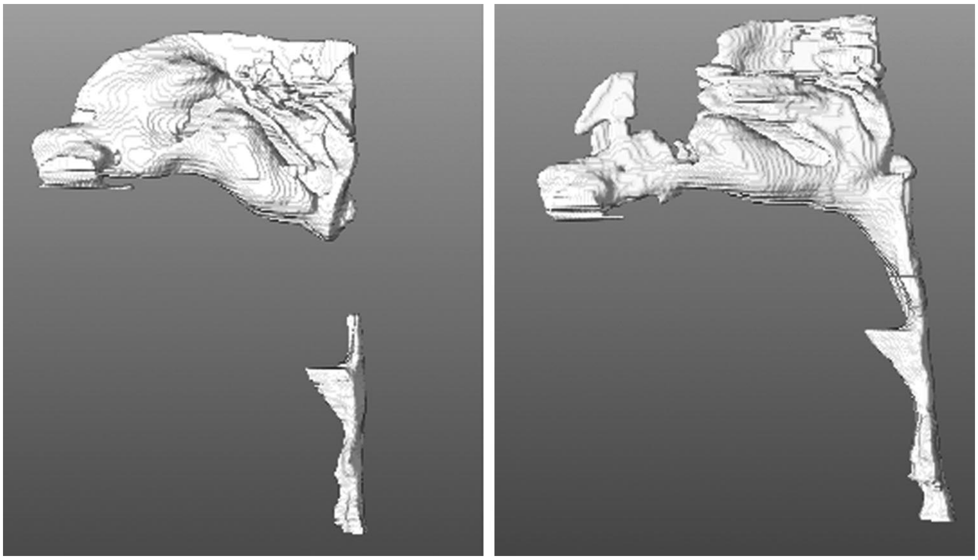

Fig. 5. Example of preoperative (*left*) and postoperative (*right*) airway segmentation of a Crouzon patient, showing evident postoperative volume gain also at the level of the oropharynx and hypopharynx following midface distraction. In this patient, a total collapse of the nasopharyngeal airway in supine position is apparent. Also the fanciful shape of the airway can be observed.

positioning of anatomical structures, which may be more important than pure volume increase of the airways.

The limitations of extrapolating the outcomes of the two-dimensional measurements from lateral radiographs toward possible three-dimensional volume changes have been discussed extensively.[20] The main limitation is lack of understanding and visualization of a three-dimensional problem because of overlapping structures. In syndromic craniosynostosis patients with obstructive sleep apnea, a three-dimensional visualization method would be preferred to provide insight into the complex anatomy of the airway.

A few centers have reported computer-assisted in vivo imaging to evaluate the effect of therapeutic interventions on the upper airway.[17,18,21,22] These reports are more significant for their methodology than their results because of the small number of patients. Several factors may influence the outcomes. First, patients are measured twice with a certain time period in between. In our study group, the mean period between preoperative and postoperative computed tomographic scans was 13 months. Imaginably, some growth might be responsible for a part of the increase in volume of the airway. However, an arrest of midface growth in syndromic craniosynostosis patients is likely to occur.[23] Second, as the airway is covered by a lining mucosa, the thickness of this mucosa may vary depending on the health state of the patient. Third, the manual segmentation process of excluding inactive air-holding cavities can lead to a certain interobserver and intraobserver variability, although analysis of the interobserver variability revealed that the method we used was highly reproducible. However, we advocate standardization of computed tomographic scanning preoperatively and postoperatively with regard to position of the head and health state of the upper airway, thereby minimizing measurement errors.

Currently, research is under way to link the outcome of the volume measurements to the results of polysomnography. Although preliminary, improvement of the obstructive sleep apnea in four patients indicates that a positive influence following midface advancement is expected. By implementing the volume measurements in the treatment protocol, we hope to gain more insight into the pathophysiology of obstructive sleep apnea and contribute to the evolution of treatment options.

CONCLUSIONS

A significant improvement of the upper airway after Le Fort III advancement in syndromic craniosynostosis patients is demonstrated at the level of the nasopharynx/nasal cavity and also, to a lesser extent, at the level of the oropharynx/hypopharynx. No distinct relationship could be observed between advancement and airway volume changes. Postoperative polysomnography showed significant improvement of obstructive sleep apnea in all four patients. Further software development of postprocessing of digital medical imaging data, including three-dimensional cephalometry, together with uniform protocols, probably will improve the computed tomographic volume measurements. This might further unravel the impact of Le Fort III advancement on airway volume and finally the outcomes of the obstructive sleep apnea studies.

Erik Nout, M.D., D.D.S.
Department of Oral and Maxillofacial Surgery
Erasmus Medical Center, Room D-230
Dr Molewaterplein 40
3000 CA Rotterdam, The Netherlands
e.nout@erasmusmc.nl

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