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Midface correction in patients with Crouzon syndrome is Le Fort III distraction osteogenesis with a rigid external distraction device the gold standard?

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ABSTRACT

Introduction: Le Fort III distraction osteogenesis with a rigid external distraction device is a powerful procedure to correct both exorbitism and impaired airways in faciocraniosynostosis. The aim of this study was to investigate treatment effect, perioperative parameters and volumetric outcomes after Le Fort III distraction osteogenesis in patients with Crouzon syndrome in a retrospective study design and to explore potential strengths and weaknesses of this procedure.

Materials and methods: From June 2013 to February 2015, a total of nine children with Crouzon syndrome underwent Le Fort III distraction osteogenesis with a rigid external distraction device (RED device, KLS Martin, Tuttlingen, Germany). Along with perioperative parameters, sleep study reports, traditional cephalometric analysis, three-dimensional imaging and photographs were evaluated for severity of disease and therapeutic effect and structural and functional changes of the upper airway preoperatively, after device removal and one year postoperatively.

Results: Surgery for Le Fort III distraction was performed at a median age of 12.5 years (SD 2.5 months) with an average weight of 43.0 kg (SD 12.9 kg). Mean estimated blood loss was 535.7 ml (SD 128.1 ml), not requiring any red blood cell transfusions. Mean duration of surgery was 240 min (SD 30.6min), average hospital stay eight days (SD 0.5 days) with a planned median ICU stay of 1.7 days (SD 0.4 days) for all patients.

There were a total of five minor complications. Exorbitism and Angle class III malocclusions were corrected in all patients. No patient showed velopharyngeal problems postoperatively. The average amount of distraction was 18.4 mm (14–26 mm). Average length of the distraction period was 18.3 days (SD 0.4 days), with a total distraction plus consolidation time of three months (SD 0.25 months). In two patients, vector correction was performed during distraction. A counterclockwise movement despite vector correction, clinically resulting in an open bite, was observed in one of these two patients. Eight of the nine patients showed a frontal overbite at the end of the distraction period.

Cephalometric analysis revealed a significant increase of Sella-Nasion-Point A angle (SNA) from 76.0° (+/− 2.9; T1) to 86.0° (+/− 3.4; T2) ($p = 0.006$) and growth-related point A-Nasion-point B angle (ANB) from −4.8° (+/−3.7) to 5.7° (+/−4.8) ($p = 0.001$) from preoperatively to device removal and stable results one year postoperatively.

Upper airway structure and respiratory function were improved clinically after the Le Fort III DO treatment in all cases with an average posterior airway space increase from 3199 mm^3 (+/− 229.6 mm^3) to 8917,7 ml (+/−415.1 mm^3) (T1 to T2).

Surgical outcome was judged good to excellent both by patients and families and the craniofacial team.

Conclusion: Le Fort III DO with a rigid external distraction device in patients with Crouzon syndrome is a powerful and reliable surgical procedure that reliably produces a more significant change of appearance than most other single procedures routinely performed by craniofacial surgeons. It effectively treated

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sleep apnea in the affected patients. In our collective, the maxilla remained stable after advancement without any relapse, but there was no subsequent anterior growth on one year follow-up. Careful vector planning was able to avoid frontal open bite in eight patients. Complication rates were acceptably low and patients' functional and esthetic outcome was high.

1. Introduction

Crouzon syndrome is a rare autosomal dominant disorder with a prevalence of 16.5/million births and characterized by faciocraniostenosis due to craniosynostosis (Bannink et al., 2010; Kuroda et al., 2011; Arnaud and Di Rocco, 2012).

Genetic mapping of these syndromes shows that mutations in fibroblast growth factor receptor 2 (FGFR2) are the cause for craniosynostosis in most patients (Hollway et al., 1997).

Reduced intracranial volume associated with intracranial pressure and midfacial hypoplasia are known as the typical pathognomonic symptoms (Kuroda et al., 2011; Arnaud and Di Rocco, 2012) also present in Crouzon syndrome and requiring surgical treatment. Furthermore, there is little anteroposterior midfacial growth overtime without intervention (Wery et al., 2015).

Midfacial hypoplasia presents with several clinical problems, most notably at the level of the airway, orbits, occlusion and facial esthetics with their associated psychosocial problems. Crouzon patients are at high risk for upper airway obstruction and are predisposed for narrowed dimensions of the posterior airway space (PAS).

A high percentage of patients with syndromic craniosynostosis develop OSAS and need airway intervention at some time (Boston and Rutter, 2003; Hoeve et al., 2003; Nout et al., 2008).

The main objectives of surgical treatment in this complex syndromic craniosynostosis remain the prevention of cerebral damage secondary to craniosynostosis and the correction of midface retrusion with the associated problems of exorbitism and upper airways impairment (Fearon, 2001; Bannink et al., 2010; Arnaud and Di Rocco, 2012).

The traditional surgical procedure for correcting midfacial hypoplasia is a Le Fort III (LFIII) osteotomy. While it was first described by Gillies and Harrison in 1949 (Gillies and Harrison, 1950; Warren et al., 2012), it then took 20 more years and refinements by Tessier to be performed on a greater number of adults (Tessier, 1967, 1971). Advances in pediatric esthesia and intensive care treatment allowed for the feasibility of this procedure in children in the 1980s (McCarthy et al., 1984).

In 1993, Cohen et al. first successfully combined LFIII osteotomy with distraction osteogenesis (DO) in a 4-year old boy (Cohen et al., 1995). Since then, several reports have been published dealing with DO on the LFIII level (Polley et al., 1995; Cohen et al., 1997; Britto et al., 1998; Cedars et al., 1999). As experience grew with the technique, research focused on developing new internal and external devices and optimizing DO protocols (Nout et al., 2008).

Although there are both older and more recent reviews on craniofacial distraction osteogenesis in general (Swennen et al., 2001) and in syndromic craniosynostosis (Al-Namnam et al., 2018), the evidence of treatment outcomes in the rare condition of Crouzon syndrome are sparse. Even within the two comprehensive reviews, the total number of Crouzon patients is small and within the reviews, both studies with various different treatment concepts and studies with mixed patient populations (Crouzon, Apert and Pfeiffer syndrome) have been included in the analysis.

In contrast to these reports, the purpose of our study was to evaluate the operative outcome of the uniform treatment concept of LFIII DO with a rigid external distraction device in a homogenous group of patients with Crouzon syndrome.

2. Materials and methods

This monocentric retrospective study was approved by the local Ethics Committee (Ethics number S-237/2009) and carried out according to the Declaration of Helsinki. Written informed consent was obtained from the parents of all patients.

Between June 2013 and July 2015, all children with Crouzon syndrome and faciostenosis, who were treated with a rigid external distraction device for LFIII DO as described by Fearon et al. (Fearon, 2001) at our hospital, were included in the study.

Surgical approach to the facial skeleton was obtained by bicoronal incision and followed by subperiostal dissection to gain access to the orbits. Thereafter, the classic osteotomies (orbital floor, roof and walls, zygoma) were made with separation of the pterygomaxillary junction either from the coronal approach or through a gingivobuccal access. Particular care was put on obtaining clear osteotomy lines. Rowe's forceps were used to mobilize the LFIII segment. The rigid external distraction device (RED device, KLS Martin, Tuttlingen, Germany) was fixed in the established manner by screw fixation of four to five bilateral pins into the parietal bones, taking the quality of the local bone into account. A total of four distraction wires were attached transcutaneously to plates fixed next to both piriform apertures and to two special maxillary retention plates (Fig. 1). All operative procedures were performed by the same surgeon (M.E.).

All patients were hospitalized for seven days regardless of age. Patients were admitted to intensive care unit (ICU) for the first 24–48 h after surgery. DO was initiated one week postoperatively. The rate of distraction was 1 mm/day in two daily activations.

The RED device was activated such that the location of the main vector of force was 50–60% above the occlusal plane as measured from the upper incisal point to the nasion. The direction of the distraction force vector was also maintained parallel to the occlusal plane (Fig. 1).

The duration of DO depended on the desired advancement. During the distraction period, vector modifications took place when necessary. A consolidation period of three months was planned.

Sleep study reports, traditional cephalometric analysis (Figs. 2 and 3), three-dimensional CT imaging/or CBCT (Figs. 4 and 5) and photographs (Figs. 6–8) were reviewed to quantify the degree of severity preoperatively and the effect of the surgical procedure postoperatively (see Fig. 9).

Cephalometric radiographs were obtained at three points of time: preoperatively (T1), at device removal (T2), and at 1-year follow-up (T3). All three radiographs were superimposed at the anterior cranial base and differences of point A and point B on the x- and y-axis were calculated. The x-axis was parallel to the Frankfurt horizontal plane, and the y-axis was perpendicular to x-axis at Sella (S) in this coordinate system.

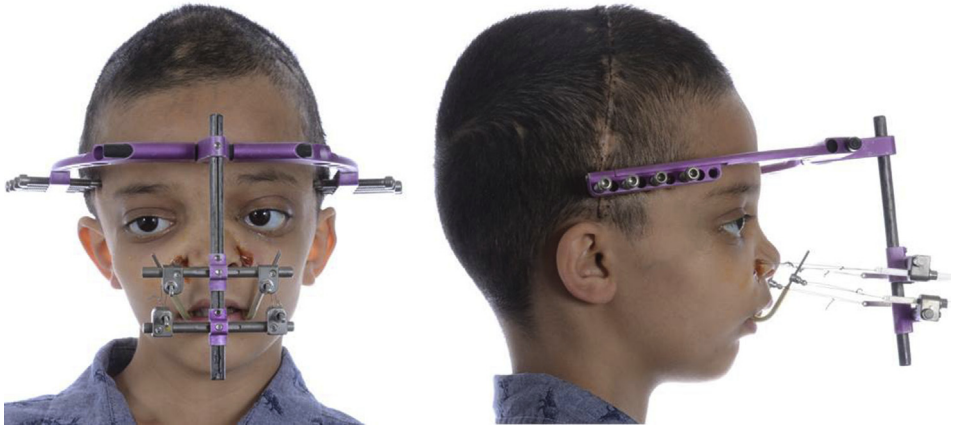

Fig. 1. Patient 1 with RED II distractor during the activation period (fontal view = left picture; lateral view = right picture).

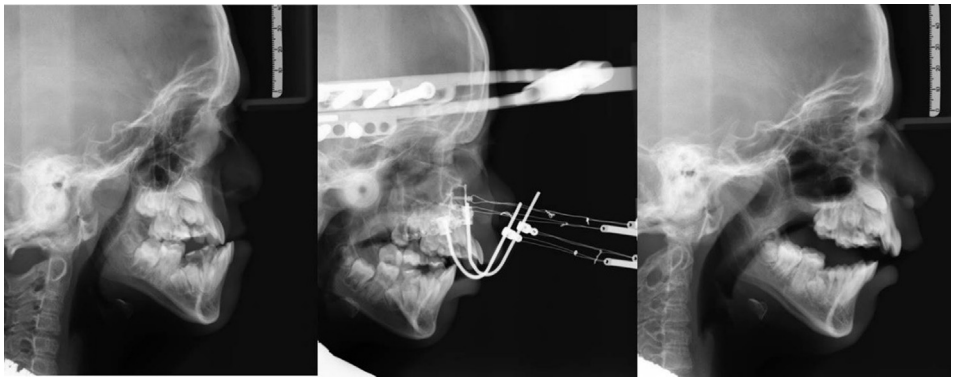

Fig. 2. Lateral cephalometric radiographs of patient 1 at three time intervals: preoperatively (T1), at device removal (T2), and at 1-year follow-up (T3).

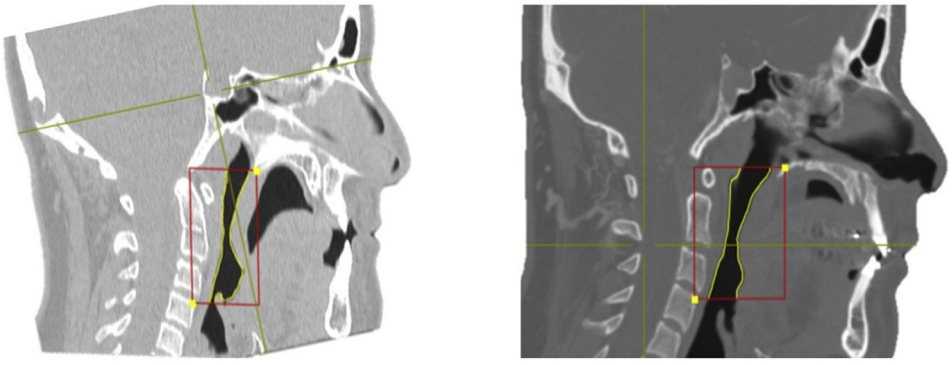

Fig. 3. Lateral view showing the ROI for calculation of the PAS (patient 3).

Paired t tests were used to evaluate stability of postoperative measurements (Sella-Nasion-Point A angle (SNA); Point A-Nasion-Point B Angle (ANB)) (Table 1).

For five patients, three-dimensional CT images or CBCTs were available at two points of time: preoperatively (T1) and at device removal (T2). These images were visualized and analyzed by one investigator (M.B.) using the software iPlan® Cranial (Brainlab, Feldkirchen, Germany) and Sicat Air® (Deutschland). Although three-dimensional imaging was not performed routinely in all patients, some patients required CT imaging for an intracranial shunt. Others presented with conventional radiographs and no additional images were performed to minimize radiation exposure. Patients primarily presenting at our department received CBCT imaging for pre- and postoperative analysis. In these cases, three-dimensional imaging allowed for three-dimensional analysis of midface movement and posterior airway space superior to conventional lateral radiographs.

iPlan® Cranial was used for the measurement of the amount of three-dimensional midface advancement. Sicat Air® was used for the evaluation of upper airway parameters.

After importation to Sicat Air® software, Dicom datasets were oriented based on the following reference planes: Frankfurt horizontal plane (constructed on Po, Orr and Orl), midsagittal plane (perpendicular to Frankfurt horizontal plane, passing through Na

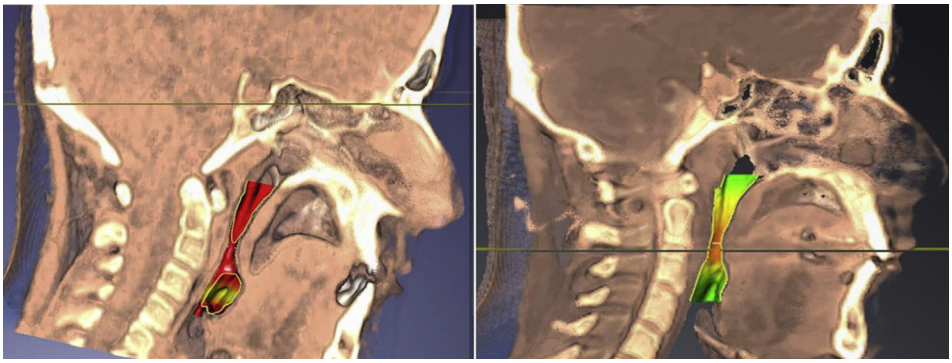

Fig. 4. 3D illustration of the PAS in a (a) pre- (T1) and (b) postoperative dataset (T2) (patient 3).

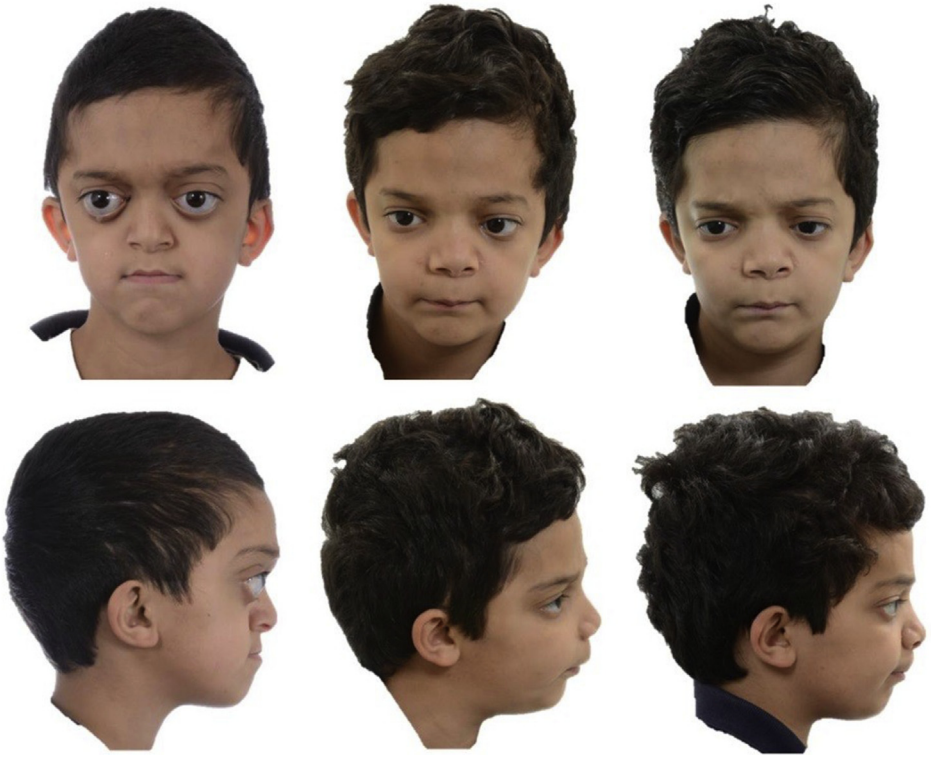

Fig. 5. Patient 1: A 9-year-old boy with Crouzon syndrome seen preoperatively (left), after removing the RED distractor (middle) and 12 months postoperatively (right).

and Ba), and coronal plane (perpendicular to Frankfurt horizontal plane and midsagittal plane).

In the next step, the region of interest (ROI) for the posterior airway space (PAS) segmentation was set (Kim et al., 2010). Two reproducible marker points were placed at the posterior nasal spine and the most anterior cranial point of the fourth vertebral body (Fig. 4). Afterwards, Sicat Air® used an automatic segmentation algorithm computing all air-filled areas within the ROI, clearly demarcating them from bony-tissue and soft-tissue structures, thus processing a volumetric analysis of the defined airways. All PAS volumes were calculated in cubic millimeters (Ristow et al., 2018) (Fig. 5).

Furthermore, sex, weight, age at surgery, complication rate (intra- and postoperatively), duration of surgical procedure (cutting–suture time), hemoglobin values (pre-,-and postoperatively), estimated blood loss, amount of RBC transfusion and length of hospital stay were recorded.

We employed the classification of Whitaker and associates to evaluate the surgical results (Whitaker et al., 1987). The esthetic outcome of surgery was considered “excellent” if both parents and surgeon were satisfied, “good” if only the parents were satisfied and “poor” if both the parents and the physician were not satisfied.

Student t-test was used to compare continuous variables and p-values <0.05 were considered as significant. All statistical analyses were performed using SPSS for Windows version 12.0 (SPSS, Chicago, USA).

3. Results

From June 2013 to February 2015, in this retrospective setting, a total of nine children including six (66.7%) boys and three (33.3%) girls were identified from the medical records with the diagnosis of Crouzon syndrome and underwent LFIII DO with a rigid external distraction device (RED II device/KLS Martin) to treat their craniostenosis at a median age of 12.5 years (SD 2.5 years). Due to standardized digital documentation, complete patient data could be retrieved from all patient files. For five patients, pre- and

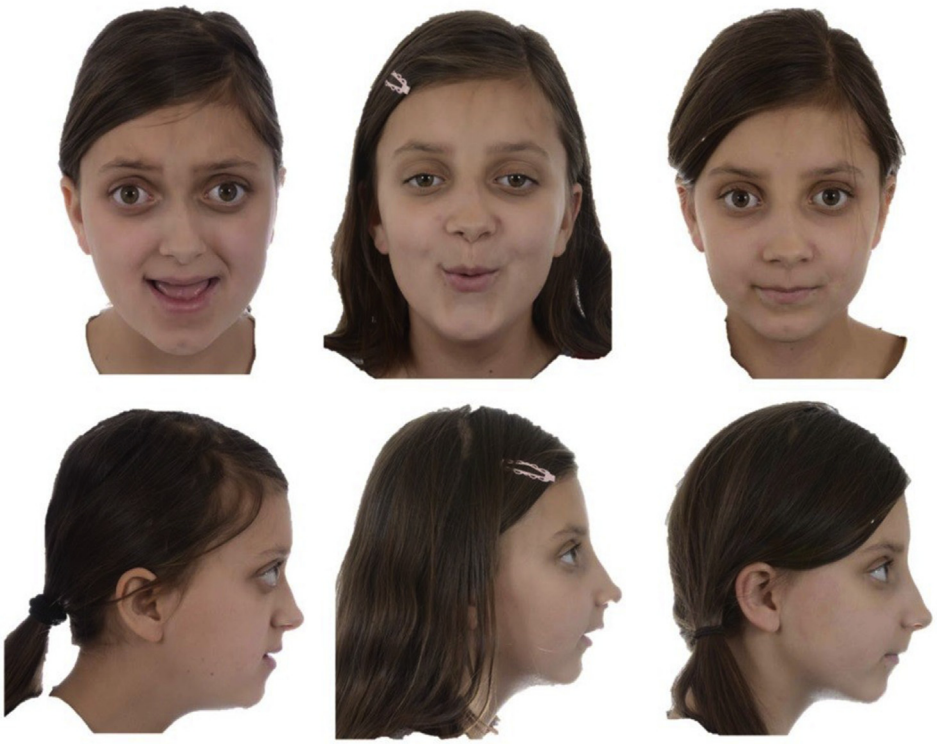

Fig. 6. Patient 2: A 10-year-old girl with Crouzon syndrome seen preoperatively (left), after removing the RED distractor (middle) and 12 months postoperatively (right).

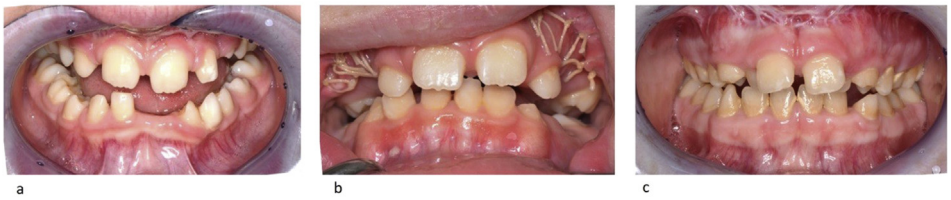

Fig. 7. Definition of occlusal situation after removal of distraction device (a: circular open (patient 4), b: premolar open (patient 5), c. closed (patient 6)).

postoperative CTs or CBCTs were available (Table 2). All of these patients had had craniofacial reconstruction by standardized fronto-orbital advancement in the first year of life as the first part of a two-step approach to correct the faciocraniostenosis. One patient had undergone a previous conventional LFIII osteotomy (patient 3).

All patients in this series tolerated the external devices well. Exorbitism and angle class III malocclusions were corrected in all cases (Figs. 6–8, Figs 10 and 11). Average weight at time of surgery was 43.0 kg (SD 12.9 kg). Mean estimated blood loss was 535.7 ml (SD 128.1 ml). Red blood cell transfusion was not necessary in our study population. Average hemoglobin value was 13.6 mg/dl (SD 0.8 mg/dl) preoperatively and 9.5 mg/dl (SD 0.7 mg/dl) postoperatively. Mean duration of surgery for all patients was 240 min (SD 30.6 min). Average hospital stay was 8 days (SD 0.5 days) with a planned median ICU stay of 1.7 days (SD 0.4 days) for all patients. Average length of distraction period was 18.3 days (SD 0.4 days).

Total duration of distractor period (distraction and consolidation time) was three months (SD 0.25 months). All patients had complete distraction. Detailed patient data is given in Table 2.

No live threatening complications were observed intra- or postoperatively. There were a total of five complications. Three of our patients had an infection in the placement area of the distractor pins (Fig. 11). One patient showed loosening of a distractor pin. In one case the whole external distraction device became loose during the consolidation period and had to be re-fixated operatively. Eight of nine patients had a frontal overbite at the end of the distraction period. Due to an extensive counterclockwise rotation of the midface resulting in a frontal open bite, a vector modification was performed in two patients during the distraction period. Correction was successful in one patient. In the other patient (patient 3), an open bite in the frontal and premolar region was present at the end of the distraction period (Fig. 3a).

Two of our patients suffered from transient problems with mastication postoperatively due to dental arch mismatch in a class II relationship caused by planned overcorrection. Chewing normalized after one year in both patients (Figs. 10 and 11). Eight of nine patients had orthodontic therapy before and during, and all patients had additional orthodontic treatment after LF III DO (Table 2).

No patient in our series showed any velopharyngeal problems postoperatively.

All patients in our series had cephalometric radiographs obtained at our defined measuring points (preoperatively (T1), at device removal (T2), and at one-year follow-up (T3)). The average amount of distraction, as measured by the number of turns made on the distractor, was 18.4 mm (range 14–26 mm).

Cephalometric analysis revealed that the SNA angle increased significantly from 76.0° (+/− 2.9; T1) to 86.0° (+/− 3.4; T2) degrees

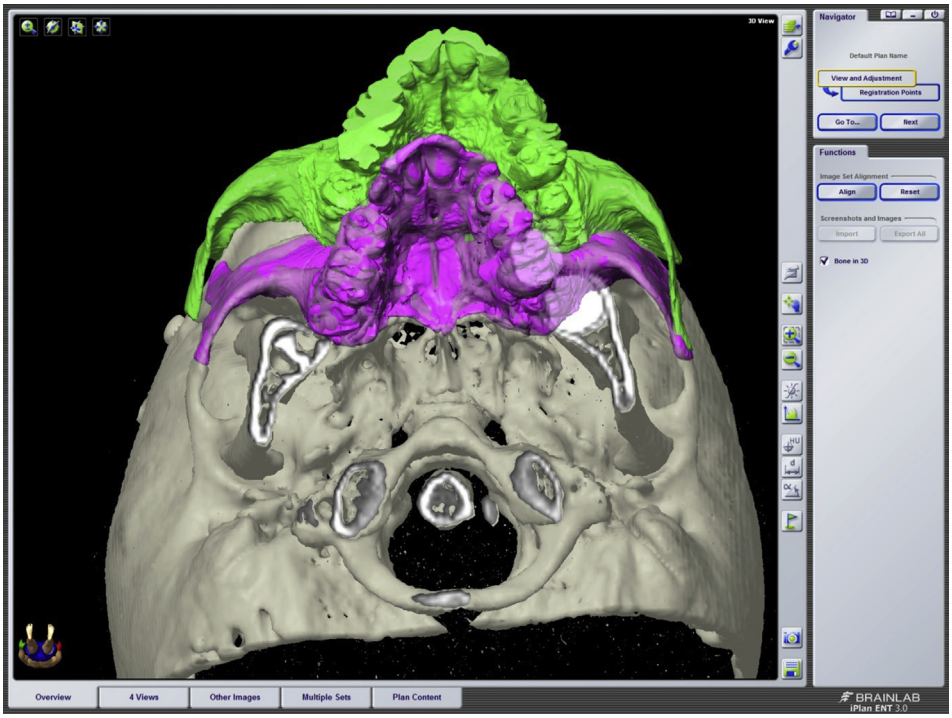

Fig. 8. Demonstration of the distraction distance using iPlan? Cranial in patient 1: preoperatively (T1/purple) and at device removal (T2/green).

($p = 0.006$). The average point ANB angle was corrected from −4.8° (+/−3.7) to 5.7° (+/−4.8) (T1 to T2; $p = 0.001$).

SNA angle was stable in the one year follow up examination (T3). Paired t tests revealed no statistically significant relapse from T2 to T3.

ANB angle decreased from −5.7° (+/−4.8) to 5.1° (+/−3.5) from device removal (T2) to follow-up 1 year postoperatively (T3), however differences were not significant ($p > 0.05$).

Following DO, no additional forward maxillary growth was observed (per lateral cephalogram analysis) up to one year postoperatively (Table 1; Figs. 2 and 3).

Upper airway structure and respiratory function improved clinically after LFIII DO treatment in all cases. In four patients, pre- and postoperative (T1 and T2) CT/or CBCT scans were available to measure the increase of PAS (Fig. 5). The average PAS increased from 3199 mm^3 (+- 229.6 mm^3) to 8917.7 ml (+-415.1mm3) (T1 to T2).

No patient in this series was tracheostomy-dependent before surgery. Seven patients had been suffering from nocturnal snoring without any signs of apnea/OSAS. Snoring disappeared in six patients and decreased in one patient after midface distraction. Two patients with preoperative evidence of OSAS had to be evaluated by overnight polysomnography (PSG). PSG showed that one patient had moderate and a second patient had severe OSAS preoperatively. Both were treated with a nocturnal breathing mask and continuous positive airway pressure (cPAP). Postoperatively, the situation in both patients improved significantly: In the patient with severe OSAS, the respiratory disturbance index (RDI) was reduced from 100 episodes per hour to less than five episodes per hour. In the case of moderate OSAS the respiratory disturbance index (RDI) was reduced from 25 episodes per hour to less than five episodes per hour. Postoperative sleep studies demonstrated that midface distraction with external devices alleviated OSAS in both patients.

According to the classification of Whitaker, seven patients had a Class 1 outcome, with excellent surgical results. Two patients were defined as Class 2 outcome with a good outcome postoperatively. Seven children in this series experienced a very good esthetic correction of their deformities, as judged by both their families and the craniofacial team. In the other two cases, the family was pleased with the outcome, although the craniofacial team still identified mild deficits (good outcome).

4. Discussion

LFIII DO has been described as the treatment of choice for midface advancement by various authors in the literature, especially in younger patients, severe cases and associated syndromic craniosynostosis. With this technique, advancements of more than 30 mm are possible (Shetye et al., 2010; Fearon, 2001, 2005; Xu et al., 2009; Meazzini et al., 2012), while conventional LFIII osteotomy without distraction limits safe and reliable advancement distances to a maximum of 17–20 mm (Toth et al., 1998; Cedars et al., 1999; Saltaji et al., 2014) and may require bone transplants. Ideal treatment age in the literature is between eight and twelve years or after the age of 18 (Shetye et al., 2010; Wery et al., 2015).

Distraction osteogenesis in syndromic patients has replaced conventional LFIII advancement in almost all cases. This is due to the fact that DO allows for greater advancement distances, more stable long-term results (Shetye et al., 2010), less bone gaps and decreased risk of perioperative complications due to gradual soft tissue expansion. Since its introduction in craniomaxillofacial surgery, DO has been utilized for a multitude of indications and has opened up a whole new field of therapeutic options. DO is a versatile and reliable way of bone generation, especially in younger patients. However, well-designed osteotomy lines, correct distractor placement and vector selection are important for treatment success.

In accordance with these recommendations, LFIII DO was considered the best treatment concept for our collective of syndromic Crouzon patients with an average advancement of 18.4 mm and a mean age of 12.5 years.

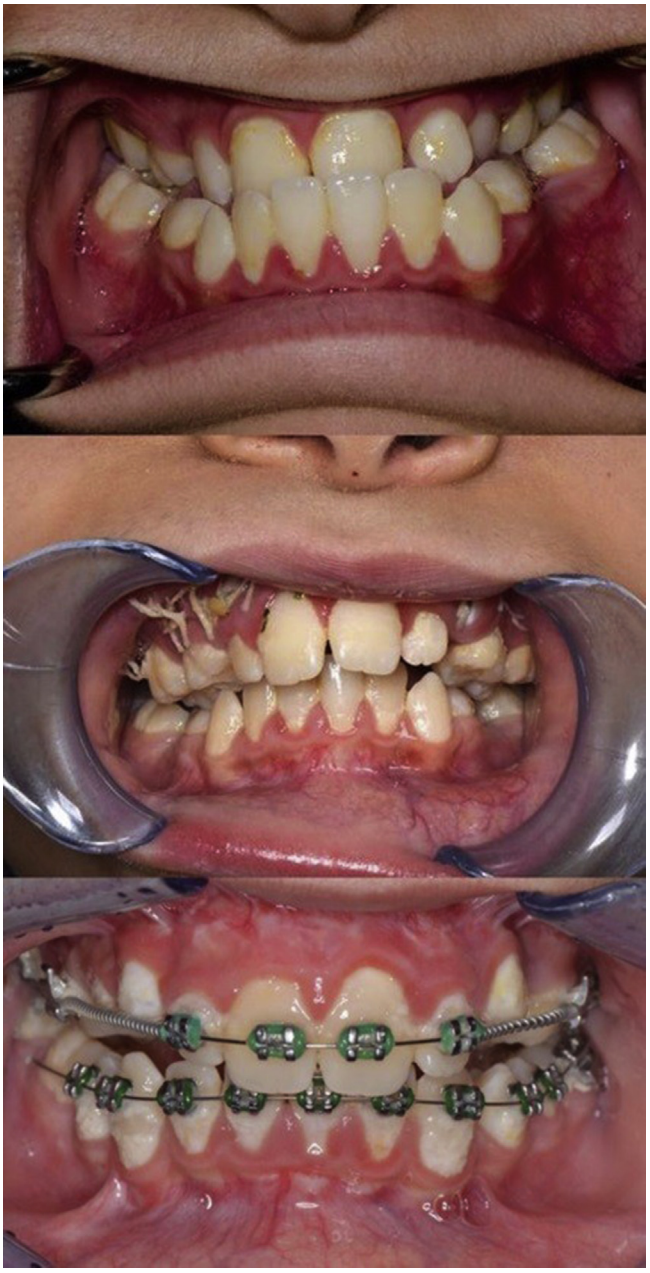

Fig. 9. Dental situation of patient 1 preoperatively (above), after removing the RED distractor (middle) and 12 months postoperatively (below).

On the other hand, adult patients with mild midface hypoplasia may benefit from conventional LFIII osteotomy due to normal occlusion postoperatively, shorter treatment time and the absence of a DO device and associated psychosocial problems (Saltaji et al., 2014).

When performing LFIII DO, a number of challenges and pitfalls have been described:

When performing LFIII DO at a young age, overcompensation of maxillary advancement should be planned to compensate for the lack of maxillary growth postoperatively. This could be confirmed by our analysis with a good maxillary advancement from T0 to T1 but no further maxillary growth thereafter (T1 to T2) and a stable ANB angle in our study population at one year follow up examination without significant relapse of cephalometric measurements on lateral cephalogram analysis.

This is in line with the findings of Shetye et al. comparing the stability of the LFIII versus LFIII-DO procedures and a mild relapse in the LFIII group with excellent stability in the LFIII-DO group, even after relatively greater forward advancements one year postoperatively (Shetye et al., 2010), similar to results by Bradley et al. (2006). The same was true for the five year follow up results of Patel et al. with stable maxillary position after LFIII advancement with distraction, minimal advancement along the *x* axis and more growth along the *y* axis (Patel et al., 2017) and in line with the few other reports on long-term stability with minimal or no relapse of the midface segment after LFIII DO (Fearon, 2005; Lee et al., 2012; Meazzini et al., 2012; Iannetti et al., 2012). One important factor may be that gradually expanding the soft tissue might reduce the elastic forces acting on the maxilla (Fearon, 2005) in contrast to conventional LFIII advancement.

The results of a small heterogeneous cohort of Hu et al. (2017) show less favorable results for Monobloc frontofacial advancement DO compared with LFIII DO with a depressed nose in long-term follow-up especially in very young patients on four year follow-up.

Increased soft tissue tension at the level of the upper midface in comparison to the lower midface during distraction may also contribute to the common phenomenon of counterclockwise rotation of the mandible in LFIII DO (Shetye et al., 2009; Figueroa et al., 2010; Roldan et al., 2011; Bouw et al., 2015) regardless of mode of anchorage (Bouw et al., 2015). However, Lee et al. argue that counterclockwise rotation is due to the main distractor force of external devices and can be overcome by a combination of internal and external distractors (Lee et al., 2012).

In our cohort, we were able to achieve a frontal overbite in eight of nine patients at the end of the distraction period respecting the recommendations of Shetye et al. with a force vector located at 55% (50–60%) of the distance measured from the incisal edge to the nasion and parallel to the occlusal plane (Shetye et al., 2009). In two of our patients, we had to perform a change of vector during the distraction period, which led to successful bite correction in one patient but resulted in a frontal open bite in the other patient nevertheless. As this patient had already undergone a conventional LFIII osteotomy in the past, additional scarring may have been one factor for the failure of sufficient vector correction. Seven of the nine patients did not require any vector correction. In addition, a total of five distractor-related complications (three pin infections, one pin loosening and one distractor loosening and refixation) reflect a relatively high complication rate of external distraction

Table 1
Changes of SNA and ANB angle within the cohort over time (mean and standard deviation).

	Norm value	T1	T2	T3	Δ T1,T2	Δ T1,T3	Δ T2,T3
SNA	81.0° (+/− 3.0)	76° (+/−2.9)	86° (+/−3.4)	85.7° (+/−2.9)	10° (+/−1.9) p = 0.006[a]	9.8°(+/−1.1) p = 0.001[a]	0°(+/−1.2) NS[b]
ANB	2° (+/−2)	−4.8° (+/−3.7)	5.7° (+/−4.8)	5.1° (+/−3.5)	10.4°(+/−1.8) p = 0.001[a]	8.0°(+/−5.3) p = 0.006[a]	−0.1°(+/−1.8) NS[b]

[a] Significant change pre-/postoperatively.
[b] NS = not significant, stable result postoperatively, no significant difference between values at T2 and T3.

Table 2
Patient characteristics; A: general, functional and perioperative data, B: cephalometric and airway space data.

Patient	Sex	Age at surgery	Weight (kg)	Height (m)	BMI	FOA	Snoring pre-op	Tracheostomy preop	Duration of surgery (min)	HB pre-op	HB post-op	Estimated blood loss	hospital stay (days)	RBC-transfusion	intra-op complications
1	m	10.5	27	1.58	13.2	y	y	n	230	13.6	8.8	470	7	n	n
2	f	10.4	26	1.29	15.5	y	y	n	260	13.2	8.3	525	7	n	n
3	f	13.2	46	1.44	22.2	y	OSAS	n	180	15.8	10.8	630	8	n	n
4	m	11.4	60	1.58	24.0	y	y	n	210	13.2	9.5	450	8	n	n
5	m	11	41	1.49	18.5	y	y	n	270	13.3	9.6	330	7	n	n
6	m	14.8	56	1.68	19.8	y	OSAS	n	245	13	10	700	8	n	n
7	m	16.8	48	1.63	18.5	y	y	n	275	13.1	10	730	7	n	n
8	m	9.6	53	1.47	24.5	y	y	n	255	14	9	510	8	n	n
9	f	14.4	30	1.44	14.5	y	y	n	235	13.6	9.8	470	8	n	n

Patient	Distraction period (days)	post-op complications	velopharyngeal problems/ insufficiency	Occlusal situation after removing the distraction device			retention period (months)	CT/CBCT pre-and post	SNA (T1)	SNA (T2)	SNA (T3)	ANB (T1)	ANB (T2)	ANB (T3)	PAS mm2 (T1)	PAS mm2 (T2)
				Frontal region	Premolar region	Molar region										
1	26	local pin infection	n	overbite	Non-occlusion	closed	3,3	y	72	83	83	−2	10	8	3090	9347
2	14	n	n	overbite	Non-occlusion	closed	2,5	n	73	81	81	−3	4	2		
3	16	local pin infection	n	overbite	Non-occlusion	closed	2,9	y	80	92	90	−1	10	8	3541	8456
4	19	n	n	open bite	open bite	closed	3,1	n	76	88	87	−6	7	6		
5	18	distractor refixation	n	overbite	Non-occlusion	closed	3	n	73	83	83	−3	9	8		
6	22	pin loosening	n	overbite	closed	closed	3	n	78	85	87	−11	−3	0		
7	15	local pin infection	n	overbite	closed	closed	3,3	y	75	87	86	−6	6	6	3199	8918
8	15	n	n	overbite	Non-occlusion	closed	3,1	y	79	89	88	−1	9	8	3115	8690
9	21	n	n	overbite	closed	closed	3,2	y	78	86	87	−10	−1	0	3050	9178

devices. Therefore, the benefit of external distraction devices remains questionable. However, pin loosening, distractor loosening and pin infection may also occur in internal devices. Furthermore, due to successful vector correction in one patient, the external distraction device was able to avoid a LeFortI osteotomy procedure at an older age for this patient.

Within the literature, Meling et al. favor the use of external distraction devices due to shorter operating time and the possibility of three-dimensional control (Meling et al., 2011).

Sinha et al. showed good results following internal LFI/II midface distraction, however, their average distraction distance was markedly shorter (13.3 mm) than in our cohort (Sinha et al., 2011).

In their description of an intraoral device, Burstein et al. again discuss two potential downsides of internal devices: the limited amount of distraction compared to external devices and the potential for traditional orthognathic surgery at skeletal maturity due to lack of vector correction (Burstein et al., 2015). The same is true for the cohort of Nakajima et al. who showed successful application of an internal device but reported the problem of frontal open bites at the end of the distraction period (Nakajima et al., 2012) and the results of Satoh et al. with internal distraction resulting in a frontal open bite in all of their exemplary cases (Satoh et al., 2006).

The study by Riediger and Poukens shows the successful application of delicate internal devices in LFIII DO, however, they do not present occlusal results in their cohort and the only presented case shows a Class III occlusion at the end of the distraction period (Riediger and Poukens, 2003).

In their review of distraction osteogenesis in syndromic craniosynostosis, Al-Namnam et al. found a high rate of counterclockwise rotation following LFIII DO with external devices in comparison to internal devices (Al-Namnam et al., 2018). However, with a closer look at their analysis, only a few results on occlusal outcome are given in the cited publications using internal devices. Furthermore, the example of our cohort shows that taking this movement into account when planning the distraction vector can overcome this tendency in most cases. In addition, they found that greater advancements are feasible with internal devices (Al-Namnam et al., 2018). This again does not correspond with the results of our cohort where distraction distances identical to their analysis of internal devices were achieved.

Latency period and rate of distraction of our study population were comparable to most published studies. Saltaji and colleagues published a systematic review in 2014 about the results in LFIII DO versus the conventional LFIII osteotomy in correction of syndromic midfacial hypoplasia (Saltaji et al., 2014). In this publication, the general latency period was 5 days (range 2–7), with a rate of distraction of 1 mm/day, except for the study by Hopper et al., in which patients younger than 6 years underwent a distraction rate of 1.5/day (Hopper et al., 2010).

In most studies, consolidation period ranged from 4 to 12 weeks (Saltaji et al., 2014). With respect to LFIII DO, the study by Arnaud et al. proposed that a short consolidation period might contribute to incomplete ossification and persistent elasticity of the soft tissue and hence an increased risk of relapse. They highlighted the importance of adequate consolidation periods to help prevent relapse (Arnaud et al., 2007; Lee et al., 2012). We are in line with Arnaud et al. and prefer a consolidation period of 10–12 weeks.

In contrast to these studies, Hopper et al. reported relative stability in the maxilla in all patients, regardless of the consolidation duration (Hopper et al., 2010). The clearly conflicting conclusions might have resulted from differences in the "pterygomaxillary osteotomy bone formation" or, possibly, the small number of patients in the latter study. Ergo, association between stability and consolidation period could not be confirmed (Saltaji et al., 2014).

It has also been postulated that both LFIII and LFIII DO relapse might be related to inadequate postoperative fixation or palatal scarring that has occurred from previous operations (Kapucu et al., 1996; Meazzini et al., 2005).

However, not all studies have confirmed that it plays a key role in postoperative relapse after LFIII DO.

No live-threatening complications were observed intra- or postoperatively in our series of nine Crouzon patients. There were a total of five complications. Three of our patients had an infection in the area where the distractor pins were placed. One patient showed loosening of a distractor pin. In one case loosening of the whole external distraction device was observed during the consolidation period and operative re-fixation became necessary. With respect to LFIII DO, multiple investigators have reported minor or no postoperative complications.

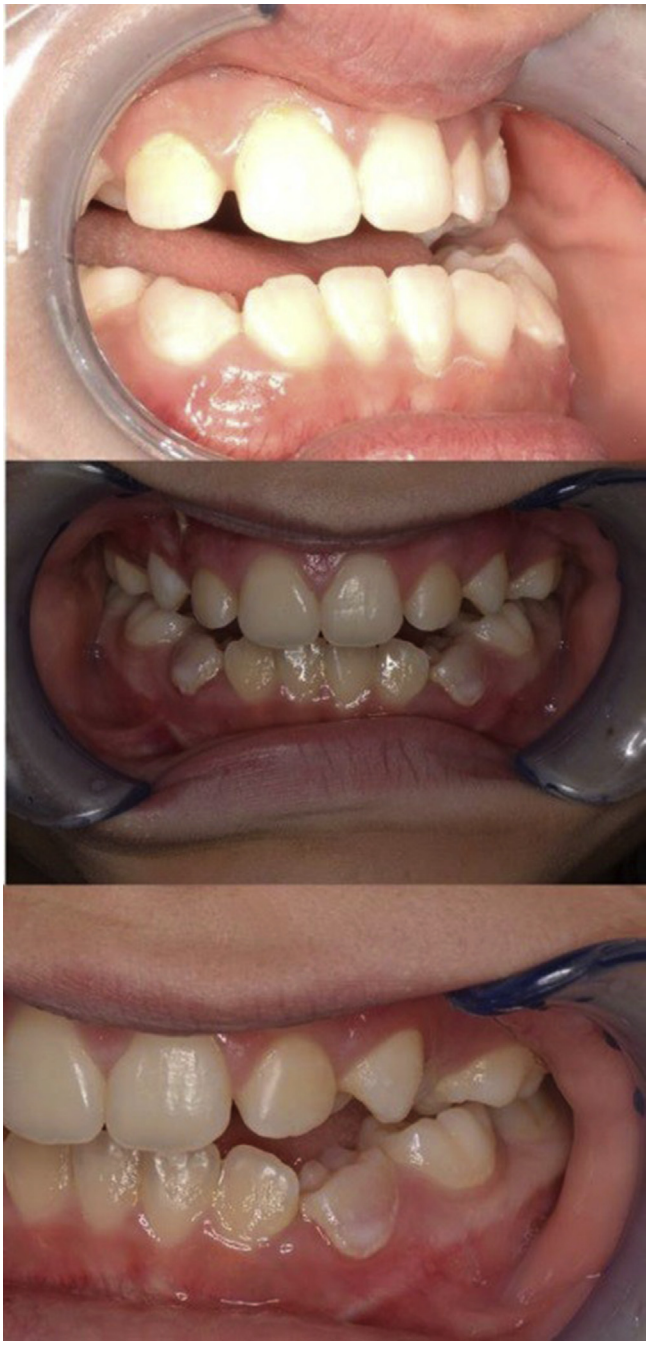

Fig. 10. Dental situation of patient 2 preoperatively (above), after removing the RED distractor (middle) and 12 months postoperatively (below).

However, the LFIII is a high risk operation that can result in complications (Cedars et al., 1999; Ridgway et al., 2011). A number of different and more severe complications can be found in the literature. These complications vary from cerebrospinal fluid leakage to meningitis and infections (Bradley et al., 2006). Other complications reviewed by Nout et al. included cutting the infraorbital nerve, strabismus, ptosis, partial anosmia, zygoma fracture during mobilization, partial exposure of the nasal bone graft, respiratory distress requiring tracheotomy, subgaleal hematoma, cerebrospinal fluid leakage, and visual loss after retro-orbital hemorrhage (Nout et al., 2008; Saltaji et al., 2014).

Swennen et al. reported a number of complications after LFIII DO, including pin loosening, frame migration, traumatic injury,

Fig. 11. Local pin infection during the retention period (patient 3).

intracranial migration of halofixation pins, fracture of the zygomatico-maxillary junction, and intraoperative fragment disjunction (Swennen et al., 2000; Saltaji et al., 2014). Fearon et al. also reported incomplete distraction in three patients and asymmetric advancement in two patients, perhaps related to a "unilateral incomplete downfracture." (Fearon, 2005; Saltaji et al., 2014). All of our patients had complete distraction. We are convinced that clear osteotomy lines and a proper down fracture can avoid incomplete distraction.

After LFIII advancement, there is an increased risk that children may develop velopharyngeal incompetence (Fearon, 2005). No patient in our series showed clinical signs of velopharyngeal problems postoperatively (transient or permanent). In a series of eleven patients who were followed after LFIII using internal distraction, Cedars et al. identified only one patient that had transient velopharyngeal incompetence (Cedars et al., 1999). In a large series of Fearon using RED distractors after a LFIII, only two patients developed transient velopharyngeal incompetence; both spontaneously improved within six weeks without any therapy. Despite an average measured maxillary advancement of just less than 2 cm, no patients in this series developed permanent velopharyngeal incompetence (Fearon, 2005).

At the same time, early surgical intervention of midfacial hypoplasia is indicated to treat OSAS associated with reduced airway space due to a posteriorly positioned midface (Shetye et al., 2010).

Obstructive sleep apnea is common in patients with craniofacial abnormalities, especially in syndromic craniosynostosis like Crouzon syndrome (Ponniah et al., 2008; Witherow et al., 2008; Xu et al., 2009). This may remain undetected in some patients, but nevertheless 50% of patients with syndromic craniosynostosis develop OSAS and need airway intervention at some time (Hoeve et al., 2003; Pijpers et al., 2004). Some severe cases may even need tracheotomy to alleviate airway obstruction. However, tracheotomy has a high complication rate (Moore, 1993; Mahadevan et al., 2007; Xu et al., 2009). No patient in this series was tracheostomy-dependent before surgery. In our collective, two patients had preoperative evidence of OSAS which was significantly alleviated by LFIII DO with a significant improvement of PAS in all patients of the cohort and markedly improved sleep studies postoperatively in the two patients with OSAS in line with the findings of Fearon and Xu (Fearon, 2005; Xu et al., 2009) Furthermore, snoring disappeared in six of our patients and decreased in one patient after midface distraction.

Until now a lot of studies have proven that craniofacial morphology affects the extent of the pharyngeal airway space

(Alves et al., 2008; Park et al., 2010; Stellzig-Eisenhauer and Meyer-Marcotty, 2010). Numerous studies have demonstrated that a combined orthodontic–orthognathic treatment highly influences the upper airway space (Figueroa et al., 1999; Swennen et al., 2000; Fearon, 2001, 2005; Bannink et al., 2010).

In our cohort, we have been able to reproduce these results both clinically and on three-dimensional analysis of posterior airway space. Due to the retrospective analysis of this study, we used all data that had been available from the patient records. However, following these very clear results and results from the literature, it is debatable whether 3D imaging should be performed on a routine basis in these patients or if imaging should be restricted to conventional lateral radiographs. While for a long time, conventional lateral radiographs have been used to plan and follow-up LFIII DO, this modality does not allow for three-dimensional analysis. With regard to the enormous advances in digital three-dimensional analysis, visualization and treatment planning with the possibility of individual planning of osteotomy lines and patient-specific implants and the nature of these rare, complex syndromic cases, we favor three-dimensional CBCT preoperatively and at the end of the distraction period as our gold standard. However, we discuss increased radiation dose critically with the parents.

Aside from functional aspects, LFIII also helps to improve facial morphological features and promotes better psychosocial adaptation during early development. A very important part in the improvement of facial morphological features is the correction of patients' exorbitism and the class III occlusion. We reached this goal and patients' exorbitism and angle class III malocclusions were corrected in all of our cases. All patients showed a significant improvement of the facial morphological features with good to very good esthetic and surgical outcomes according to the Whitaker classification and as judged by the parents and the surgical team, regardless of patient age at operation. The good to very good esthetic results with change of syndromic to non-syndromic appearance are an important argument for early LFIII DO at the age of 8–12 to minimize psychosocial sequelae of stigma before puberty and significantly improve quality of life for Crouzon patients.

5. Conclusion

LFIII DO is a powerful and reliable surgical procedure in Crouzon patients and superior to standard LFIII osteotomy in the growing child in many aspects, and has the ability to produce more significant change of appearance than most other single procedures routinely performed by craniofacial surgeons.

This procedure is indicated for children with Crouzon syndrome and hypoplastic midface. In our collective, the maxilla remained stable after advancement without any relapse, but there was no subsequent anterior growth up to one year postoperatively. The technique effectively improved sleep apnea in all affected patients, and was not associated with any long-term effects on speech or mastication. Complication rates in our series were found to be acceptably low and patients' functional and esthetic outcome was high. Although a frontal overbite could be achieved in eight patients at the end of the distraction and observation period, long term follow-up examinations of our patients will be necessary to evaluate whether LFIII distraction can avoid a second LFIII procedure that is routinely required with the conventional LFIII procedure and the rate of orthognathic surgery in these patients. While there is agreement on the surgical technique, distraction rates and retention period, the potential of further growth reflected by the amount of overcorrection and the use of internal versus external devices are still under debate.

In our cohort, the use of external distraction devices was associated with a relatively high level of minor distractor related complications, while one patient had a benefit from vector correction.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jcms.2018.11.028.

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