Crouzon Syndrome: A Case Series of Craniomaxillofacial Distraction Osteogenesis for Functional Rehabilitation

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Crouzon syndrome (CS) is the most common craniosynostosis syndrome and requires a comprehensive management strategy for the optimization of care and functional rehabilitation. This report presents a case series of 6 pediatric patients diagnosed with CS who were treated with distraction osteogenesis (DO) to treat serious functional issues involving severe orbital proptosis, an obstructed nasopharyngeal airway, and increased intracranial pressure (ICP). Three boys and 3 girls were 8 months to 6 years old at the time of the operation. The mean skeletal advancement was 16.1 mm (range, 10 to 27 mm) with a mean follow-up of 31.7 months (range, 13 to 48 months). Reasonable and successful outcomes were achieved in most patients as evidenced by adequate eye protection, absence of signs and symptoms of increased ICP, and tracheostomy tube decannulation except in 1 patient. Complications were difficult fixation of external stabilizing pins in the distraction device (n = 1) and related to surgery (n = 4). Although DO can be considered very technical and can have potentially serious complications, the technique produces favorable functional and clinical outcomes in treating severe CS.

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More than 100 craniosynostosis syndromes have been described, with an estimated birth prevalence of 1 in 2,000 to 2,500.¹ Syndromic craniosynostoses are estimated to constitute 15% of all craniosynostoses and more than 180 craniosynostosis syndromes have been identified to date, of which approximately 8% of cases are inherited or familial.² Crouzon syndrome (CS) is one of the most common syndromic craniosynostoses related to multiple fibroblast growth factor receptor 2 (FGFR2) mutations and was first reported by Louis Edouard Octave Crouzon in 1912 who described craniofacial dysostosis with the triad of calvarial deformities, facial anomalies, and exophthalmos in a woman and her son.²³

Over the years, conventional craniofacial surgical techniques, such as strip craniectomy, fronto-orbital...
advancement, and Le Fort III procedures, have proved reliable to treat symptomatic syndromic craniosynostosis. However, in severe conditions, large segmental advancement requires the gap to be grafted, stabilized, and closed primarily because inadequate stability secondary to soft tissue restriction and unstable bone segment fixation can cause graft resorption, thus causing relapse and creating less than an ideal long-term outcome.

The introduction of distraction osteogenesis (DO) to craniofacial surgery has provided a reliable surgical alternative in achieving superior segmental advancement compared with conventional techniques in treating functional issues in syndromic craniosynostosis. Apart from obviating an additional bone grafting procedure, the natural process of bone regeneration through gradual traction simultaneously produces new histogenesis, which overcomes the soft tissue limitation.

In cases of severe CS, patients can present with major functional disturbances, namely increased intracranial pressure (ICP), severe exorbitism with the inability to achieve eyelid closure for orbital protection, and serious upper airway obstruction with progressive obstructive sleep apnea (OSA) secondary to a severely hypoplastic maxilla, which eventually might require a tracheostomy to bypass the obstructed airway. As such, the indication for each major surgery in pediatric patients with this condition should be agreed to by the craniofacial team members because the procedure carries substantial mortality and morbidity risks.4

This report presents a case series of pediatric patients with CS who underwent craniofacial DO to manage functional deficiencies, with the focus on surgical indications, choice of device, and the distraction protocol and its associated complications.

Report of Cases

This study was approved by the medical ethics committee of the Faculty of Dentistry of the University of Malaya (Kuala Lumpur, Malaysia; institutional review board reference number DF OS1516/0053[P]) and all participants signed an informed consent agreement.

This report describes 6 pediatric patients with CS (3 boys and 3 girls; age range, 8 months to 6 years). Five patients (patients 1 to 5) presented with increased ICP, severe exorbitism with an inability to achieve eyelid closure, and OSA secondary to a narrow nasopharyngeal space, and 1 patient (patient 6) presented with increased ICP only. All patients underwent a standard craniofacial protocol as routinely practiced in the authors’ multidisciplinary craniofacial clinic, which involved computed tomographic (CT) analysis, fabrication of a 3-dimensional (3D) skull bio-model, and comprehensive assessment from neurosurgeons, maxillofacial surgeons, pediatric ophthalmologists, pediatric otolaryngologists, pediatric respiratory therapists, anesthetists, and clinical genetics. As part of the presurgical workup, the baseplates for the midface internal devices were pre-bent and fixed on a 3D skull bio-model for each patient to allow surgical simulation and vector determination and minimize operating time.

Based on specific functional indications, 5 patients underwent monobloc DO to achieve intracranial decompression, orbital protection, and nasopharyngeal airway relief and 1 patient underwent posterior cranial vault DO to address the isolated increase in ICP.

To treat the 3 functional issues optimally, 4 patients (patients 1 to 4) with severe structural deficiency received a combination of bilateral internal midface devices and a rigid external device (Synthes, Oberdorf, Switzerland) and 1 patient (patient 5) with moderate functional discrepancies received only bilateral internal midface distractors (Synthes). Because patient 6 presented only with signs of a potential progressive increase in ICP, posterior cranial vault expansion was indicated using internal distractors (Synthes).

All procedures were performed through the coronal approach. Before the osteotomy, the internal devices were placed to mark the planned placement site. In patients who underwent monobloc DO, the osteotomy was performed at the fronto-orbital region before completion of the Le Fort III osteotomy and completed through the maxillary tuberosity cut intraorally. Once the midface was separated, the internal devices were fixed and trial activation was performed to ensure correct vector trajectory. For patients receiving an external device, bilateral protective titanium temporal plates were fabricated and placed subperiosteally to prevent temporal bone perforation before the external frame was placed at the end of surgery. Patient 6, who underwent posterior cranial vault expansion, had a similar presurgical workup of the distractor application on his skull bio-model for surgical simulation and vector determination.

All patients were admitted to the pediatric intensive care unit for 3 to 5 days for close monitoring before being transferred to the pediatric ward. The mean latency period was 2.5 days (range, 1 to 3 days). The activation rate was 1 mm per day and the mean skeletal advancement was 16.1 mm (distraction range, 10 to 27 mm), with a mean consolidation period of 24 weeks (12 to 48 weeks). Mean follow-up was 31.7 months (range, 13 to 48 months). Reasonable and successful functional rehabilitation outcomes were documented in most patients as evidenced by the absence of signs and symptoms of increased ICP, ability for eyelid closure to achieve adequate eye protection, tracheostomy tube decannulation, resolved OSA, and an
acceptable facial appearance (Figs 1-6), except in patient 3 who had restricted maxillary movement.

The objective outcomes of 5 patients (patients 1 to 5) who underwent monobloc DO were measured using various parameters from the pre- and postoperative CT scans compared with the respective distraction amount of each case to support favorable functional and clinical outcomes. For patient 6, who underwent posterior vault DO, a marked increase of the intracranial perimeter was found when the pre- and postoperative values were compared (Fig 7). For the assessment of patients 1 to 5, the distance from the sella turcica to the nasion, the distance from the sella turcica to the deepest concavity of the maxilla, and the point between the borders of the orbital floor and the lateral orbital border were measured at the presurgical and post-distraction phases (Fig 8). They were labeled $v(j) = (v_{j1}, v_{j2}, \ldots, v_{jN})$, where $j = 1, 2, 3$ indicates the variables described earlier and $N = 5$ is the total number of patients considered. The variable for the pre- and postsurgical phase were denoted as $v(j)_{pre}$ and $v(j)_{post}$, respectively, and the statistical comparison of these variables was performed using the Wilcoxon signed rank test (IBM SPSS Statistics 24; IBM Corp, Armonk, NY). The null hypothesis ($H_0$) of the test was that there would be no difference in the median of the pre- and postsurgical phases, which can be expressed as $H_0: v(j)_{pre} = v(j)_{post}$. The results presented in Table 1 show non-rejection of the $H_0$ and indicate successful functional rehabilitation outcomes.

Complications were difficult fixation of external stabilizing pins in the distraction device ($n = 1$) and related to surgery ($n = 4$), namely lateral rectus muscle impingement and cerebrospinal fluid (CSF) leak in patient 2, restricted maxillary movement in patient 3, and localized wound infection in patient 6. The management of these complications is comprehensively described in the Discussion section. All data for the DO protocol, complications, and management are presented in Table 2.

**Discussion**

CS is usually diagnosed at birth or during infancy based on a thorough clinical evaluation, the identification of characteristic physical findings, and results from different specialized tests. Nevertheless, an experienced ultrasonographer or obstetrician also can

![Figure 1](Image)


FIGURE 3. A, Preoperative and B, latest postoperative photos of patient 3 (Crouzon syndrome).


FIGURE 5. A, Preoperative and B, latest postoperative photos of patient 5 (Crouzon syndrome).

detect the early evidence of cranial suture fusion during ultrasound or detailed 3D scanning procedures.

The molecular genetic protocol for the diagnosis of CS includes first-line tests of FGFR2 exons IgIIIa and IgIIIc followed by second-line tests of FGFR2 exons 3, 5, 11, and 14 to 17 and FGFR3 Pro250Arg and Ala391Glu as proposed by Wilkie et al.5 Clinically, cranial malformation with shallow orbits and ocular proptosis are diagnostic features of CS.

Plain radiographs and CT scans also can assist in the diagnosis and assessment of CS.6 A copper beaten appearance, enlarged hypophyseal cavity, maxillary hypoplasia, and mandibular prognathism can be visualized on a lateral skull plain radiograph. Brain CT scan can provide a detailed image of diffuse indention of the inner table of the skull and the degree of hydrocephalus. CT scan also can be used for the fabrication of a 3D bio-model for the actual structural evaluation and surgical simulation.

Intracranial evaluation can be performed using plain radiography, CT scanning, or magnetic resonance imaging. Cranial bone thinning or a copper beaten appearance strongly suggests increased ICP. Clinical ophthalmologic assessment and funduscopy are paramount to detect any potential pathologic process of orbital proptosis, and a tonometer can be used to check intraocular pressure. Respiratory issues require nasoendoscopy for the assessment of the nasopharyngeal airway and, if indicated, polysomnography for the diagnosis of OSA.

Increased ICP with hydrocephalus would necessitate ventriculoperitoneal shunting, severe orbital proptosis might indicate temporary tarsorrhaphy, and respiratory difficulty would necessitate a continuous airway pressure device, a nasal stent, or a tracheostomy depending on the severity and the specific anatomic obstruction.

Extent of surgical treatment of the deformities of CS depends on how functionally and severely the patients are affected according to their age. Surgical intervention can be performed as staged or combined to address these functional issues. For example, increased ICP alone can be treated by posterior cranial vault expansion.7,8 Increased ICP with orbital proptosis might require fronto-orbital advancement with or without cranioplasty,9 and increased ICP in
the presence of orbital proptosis and hypoplastic maxilla might require a monobloc as practiced in the authors’ center. Surgery can be performed conventionally or combined with a DO technique, which is indicated for superior structural expansion. Patients with asymptomatic CS can undergo orthodontic treatment with or without orthognathic surgery to correct dental and jaw discrepancies at growth maturation.

The application of DO in treating craniofacial deformity was first reported in 1992. Since then, the benefits of this technique in treating syndromic craniosynostosis as reported in the literature are similar to those in the present study, which include marked improvements in functional parameters involving eye protection, preventing the increase of ICP, and treating airway deficiency. The technique has major advantages, which include producing superior advancement, obviating additional bone grafting, and achieving simultaneous new histogenesis compared with conventional surgical procedures. All patients in the present study had their 3D skull bio-model fabricated to allow surgical simulation and vector determination to optimize the outcome of surgery. The pre-bending of the distractor footplates for the internal device and presurgical simulation proved critical because it contributed to the precision of device fixation and correct segmental movement to ensure a favorable final outcome and decrease operating time.

The selection of devices in the present patients was based on device suitability and functional indications. Increased ICP was assessed by history, presence of signs or symptoms, imaging analysis, and opthalmologic assessment. For the eye, the patients’ ability to achieve eyelid closure was assessed and documented and supplemented with eye examinations that included optic disc condition and cup-to-disc ratio through funduscopy. Airway function was assessed.

**FIGURE 7.** Comparison of the cranial perimeter of patient 6 who underwent posterior vault distraction osteogenesis. A, Preoperative. B, Postoperative.

by history from the guardians, symptoms of OSA, airway endoscopic evaluation, overnight pulse oximetry, and, when indicated, polysomnography.

The combination of internal and external devices provides stable advancement at the central and lateral midface components and the internal device can act as a temporary rigid fixation during the consolidation period after the external frame is removed at the end of the activation phase. Nevertheless, it is vital to comprehensively assess each case before the selection of a device because different distractors can differ in suitability, vector control, and limitations. The external device focuses more on the central component and can be considered to have multiple vectors but might not be suitable for a very young infant and carries the risk of stabilizing pin perforation of a very thin temporal bone surface.15 The internal device is compact and more suitable for small patients but provides only a single vector, thus requiring bilateral fixation, and has been reported to have the disadvantage of central component relapse because it provides only lateral retention.15

The amounts of advancement achieved in the present patients (range, 10 to 28 mm) can be considered substantially superior to the conventional surgical technique and comparable to those of another larger craniofacial DO study.14 The distracted bone space was noted to be filled with new bone (Fig 9). All

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>$P$ Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>$j = 1$ (S-N)</td>
<td>$v(1)_{\text{pre}}$</td>
<td>46.50</td>
<td>53.87</td>
<td>42.50</td>
<td>40.50</td>
<td>58.00</td>
</tr>
<tr>
<td></td>
<td>$v(1)_{\text{post}}$</td>
<td>64.50</td>
<td>65.00</td>
<td>44.50</td>
<td>48.00</td>
<td>59.00</td>
</tr>
<tr>
<td>$j = 2$ (S-A)</td>
<td>$v(2)_{\text{pre}}$</td>
<td>57.00</td>
<td>58.25</td>
<td>50.00</td>
<td>46.00</td>
<td>56.00</td>
</tr>
<tr>
<td></td>
<td>$v(2)_{\text{post}}$</td>
<td>76.50</td>
<td>69.50</td>
<td>53.50</td>
<td>58.00</td>
<td>56.5</td>
</tr>
<tr>
<td>$j = 3$ (Co-O)</td>
<td>$v(3)_{\text{pre}}$</td>
<td>31.00</td>
<td>32.50</td>
<td>33.00</td>
<td>30.00</td>
<td>41.50</td>
</tr>
<tr>
<td></td>
<td>$v(3)_{\text{post}}$</td>
<td>46.50</td>
<td>42.50</td>
<td>42.50</td>
<td>35.00</td>
<td>44.00</td>
</tr>
</tbody>
</table>

Abbreviations: Co-O, point between the borders of the orbital floor and lateral orbital border; S-A, distance from sella turcica to deepest concavity of the maxilla; S-N, distance from sella turcica to nasion; post, postsurgical; pre, presurgical.

* By Wilcoxon signed rank test (2-tailed).
patients achieved a stable clinical outcome (Figs 1-6), with resolved functional discrepancies indicated by the absence of signs and symptoms of increased ICP, the ability to achieve eyelid closure with stable funduscopic findings, and the absence of OSA symptoms after tracheostomy decannulation, indicating adequate nasopharyngeal airway opening, except in 1 patient because of restricted maxillary movement. Findings from the statistical analysis of the pre- and postsurgical data support the clinical outcome in which the desirable segmental advancement is evident (Table 2). Note that the results of the study at this stage are confined to a relatively small sample. Nevertheless, the statistical inference can be considered reliable because of the rare cases of severe CS that require the complex surgical procedure at the authors’ craniofacial center. The authors’ management strategy for functional rehabilitation of patients with CS is presented in Figure 10.

Serious complications arising from craniofacial surgery include mortality, severe blood loss, dural tear, CSF leak, acquired hypernasality, infection, and frontal bone necrosis.4,14,16,17 One patient developed postoperative CSF rhinorrhea for 2 weeks and was conservatively treated with a decreased activation rate, antibiotics, and neurologic monitoring. The same patient also developed an unusual exodeviation of the right eye with associated abduction during the activation phase secondary to direct impingement of the lateral orbital wall on the lateral rectus muscle. The bony impingement was successfully relieved by a lateral bony osteotomy, resulting in resolution of the residual proptosis and free lateral ocular movement.18 The authors also fabricated a customized headgear in a very young patient (patient 4) to allow stable positioning of the temporal stabilizing pins of the external device and prevent potential temporal bone perforations.19

Postoperative long-term stability remains a major concern in the management of syndromic craniosynostosis because minimizing the number of surgeries will benefit patients’ growth and development. Three of 4 patients in the present study after more than 2 years of postoperative follow-up have remained healthy and asymptomatic.5 and 6 expressed satisfaction because his daughter remained on the tracheostomy tube and is currently undergoing nasopharyngeal opening surgery at a later stage. Although further surgical planning is anticipated, especially in those patients with resolved functional discrepancies indicated by the absence of signs and symptoms of increased ICP.

### Table 2. SUMMARY OF DO PROTOCOL AND COMPLICATIONS

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at Operation (yr)</th>
<th>Procedure</th>
<th>Device</th>
<th>Latency (days)</th>
<th>Activation (mm/day)</th>
<th>Advancement (mm)</th>
<th>Consolidation (wk)</th>
<th>Follow-Up (mo)</th>
<th>Complications</th>
<th>Management of Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>Monobloc DO</td>
<td>Ext + Int</td>
<td>2</td>
<td>1</td>
<td>23</td>
<td>21</td>
<td>48</td>
<td>Lateral rectus impingement, CSF leak</td>
<td>Lateral orbital wall box osteotomy, conservative and antibiotic prescription</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>Monobloc DO</td>
<td>Ext + Int</td>
<td>3</td>
<td>1</td>
<td>27</td>
<td>16</td>
<td>48</td>
<td>Restricted movement of maxilla</td>
<td>Secondary osteotomy for pterygomaxillary disjunction</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>Monobloc DO</td>
<td>Ext + Int</td>
<td>1</td>
<td>1</td>
<td>10</td>
<td>48</td>
<td>33</td>
<td>Restricted movement of maxilla</td>
<td>Secondary osteotomy for pterygomaxillary disjunction</td>
</tr>
<tr>
<td>4</td>
<td>8 mo</td>
<td>Monobloc DO</td>
<td>Ext + Int</td>
<td>3</td>
<td>1</td>
<td>11</td>
<td>16</td>
<td>29</td>
<td>loose stabilizing pins</td>
<td>Customized headgear for fixation of external stabilizing pins</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>Monobloc DO</td>
<td>Int</td>
<td>3</td>
<td>1</td>
<td>15</td>
<td>31</td>
<td>19</td>
<td>local wound infection</td>
<td>Wound dressing and antibiotic prescription</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>Posterior cranial vault DO</td>
<td>Int</td>
<td>3</td>
<td>1</td>
<td>11</td>
<td>12</td>
<td>15</td>
<td>local wound infection</td>
<td>Wound dressing and antibiotic prescription</td>
</tr>
</tbody>
</table>

Abbreviations: CSF, cerebrospinal fluid; DO, distraction osteogenesis; Ext, external; Int, internal.

who undergo surgery at a young age, a long-term study by Gwanmesia et al.\textsuperscript{20} showed that the distraction procedure produced long-term stable advancement and functional gains.

In conclusion, the introduction of the DO technique provides a reliable surgical alternative and a predictable outcome in the functional rehabilitation of severe CS. However, its application requires comprehensive...
presurgical planning and carries considerable morbidity risks.

References


