# Surgical approach of hypertelorbitism in craniofrontonasal dysplasia

## Abordagem cirúrgica do hiperteleorbitismo na displasia craniofrontonasal

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## ABSTRACT

**Objective:** to present our experience in the hypertelorbitism surgical treatment in craniofrontonasal dysplasia. **Methods:** retrospective analysis of craniofrontonasal dysplasia patients operated through orbital box osteotomy or facial bipartition between 1997 and 2015. Surgical data was obtained from medical records, complementary tests, photographs, and clinical interviews. Surgical results were classified based on the need for additional surgery and orbital relapse was calculated. **Results:** seven female patients were included, of whom three (42.86%) underwent orbital box osteotomy and four (57.14%) underwent facial bipartition. There was orbital relapse in average of 3.71±3,73mm. Surgical result according to the need for further surgery was 2.43±0.53. **Conclusion:** surgical approach to hypertelorbitism in craniofrontonasal dysplasia should be individualized, respecting the age at surgery and preferences of patients, parents, and surgeons.

Keywords: Craniofacial Abnormalities. Surgery, Plastic. Maxillary Osteotomy.

## INTRODUCTION

The principles of craniofacial surgery established by the French plastic surgeon Dr. Paul Louis Tessier in the 1960s are among the most relevant milestones of medicine in the 20th century<sup>1</sup>. Among Tessier's remarkable contributions, the art of moving the orbits deserves special attention<sup>1,2</sup>. In his seminal articles, Tessier<sup>3-6</sup> presented the surgical principles for the treatment of orbital hypertelorism (hyperteleorbitism) and demonstrated that it was possible to approach the cranial, nasal and oral cavities in the same surgical intervention, while the orbits and their contents simultaneously moving in all directions.

Hyperteleorbitism is characterized by true lateralization of the entire orbital complex (medial and lateral walls) and is a clinical finding of numerous craniofacial anomalies<sup>7</sup>, especially craniofrontonasal dysplasia, also called craniofrontonasal syndrome (OMIM # 304110), identified in 1979 by Cohen<sup>8</sup> as a subgroup of frontonasal dysplasias (OMIM # 136760). Craniofrontonasal dysplasia is a rare X-linked syndrome, associated with mutations in the EFNB1 gene, which provides instructions for the production of ephrin-B1, a protein important for the normal development of the frontonasal neural crest that originates the face and skull. It displays hyperteleorbitism, often asymmetric, unilateral or bilateral coronal craniosynostosis, among other craniofacial and extracranial deformities. Although its genetics and phenotypes have been addressed in numerous studies<sup>8-11</sup>, guidelines on the specific treatment of hyperteleorbitism are scarce and have been reported almost exclusively in the international context<sup>12-17</sup>.

In previous works, our group<sup>18,19</sup> studied the recurrence of the orbital position after the correction of hyperteleorbitism in different craniofacial deformities. However, to the best of our knowledge, there are no national studies on the intracranial and extracranial surgical approach for the treatment of hyperteleorbitism specifically in patients with craniofrontonasal dysplasia. Therefore, the objective of the present study was to present our experience in the surgical treatment of hyperteleorbitism in craniofrontonasal dysplasia.

#### **METHODS**

This is a retrospective, observational study of patients with craniofrontonasal dysplasia surgically treated at the Institute of Craniofacial Plastic Surgery

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of the SOBRAPAR Hospital between 1997 and 2015. The study was approved by the Ethics in Research Committee of the SOBRAPAR Hospital (002/16) and is in agreement with The Helsinki Declaration of 1975, perfected in 1983.

We included only patients with diagnostic confirmation of craniofrontonasal dysplasia<sup>10,11,17</sup> submitted to craniofacial surgical interventions by the same group of plastic surgeons and with adequate postoperative follow-up. We excluded patients with uncertain diagnosis and/or submitted to major craniofacial surgeries in other services. We obtained demographic and clinical data and information related to surgical interventions through reviews of medical records, photographs, frontal cephalograms, and clinical interviews.

#### Surgical approach

We submitted all patients to facial bipartition or to orbital box osteotomy under general anesthesia with the objective of correcting the hyperteleorbitism. In general, we employed facial bipartition in patients with immature craniofacial skeleton, and orbital box osteotomy, in adults with adequate occlusion. Decisions among surgical approaches were based on the age of the patients, whether or not they had complete dentition, the occlusion aspect and the preferences of patients (or parents) and plastic surgeons.

#### **Orbital box osteotomy**

We used intra and extracranial approaches to make quadrangular orbital osteotomies. We applied a Coronal and gingivobucal sulcus incision to obtain the subperiosteal exposure of the frontal bones, orbits and the middle third of the face. Next, we performed a frontal craniotomy, followed by circumferential orbital osteotomies, taking care to preserve the tendons of the medial cantus. We also osteotomized the zygomaticmaxillary and naso-maxillary pilars. The planned osteotomy of the medial fronto-ethmoidal segment was marked and performed with a reciprocating saw following adequate intracranial midline dissection and frontal lobe retraction. After removal of the median segment, we translocated the orbits medially. We then fixed the nasophrontal processes of the maxilla with steel wires, and the vertical pillars, with titanium plates and screws. Before closure, we raised a pericranial flap and advanced it till the base of the skull on the midline<sup>19</sup>.

#### **Facial bipartition**

For facial bipartition, in addition to the osteotomies described for the orbital box osteotomy, we performed osteotomies of the pterygomaxillary, septal and palatal regions to allow full mobilization of the middle third of the face. After the osteotomies, was proceeded to the craniofacial disjunction with the Rowe de-impacting forceps. In the sequence, was performed a inverted "V" osteotomy in the medial region towards the galli crest, being careful not to to damage the olfactory nerves next to the cribriform plate. This osteotomy was symmetric, for patients with bilateral fusion of the coronal suture, or asymmetric, for individuals with unilateral fusion. We removed the frontal bone, ethmoid bone and nasal septum via intracranial access. Subsequently, we rotated the segments of the hemifaces medially. We then fixed the nasofrontal processes and the lateral portions of the hemifaces to the zygomatic processes with steel wires. We fixed the inferomedial portions of the hemifaces to each other with plates and screws. We placed Autologous bone grafts form the skull cap on the lateral portions of the orbital edges and on the zygomatic arches that were medialized and eventually advanced<sup>19</sup>.

#### **Complementary surgical procedures**

In both techniques, we used different types of locoregional flaps for simultaneous correction of soft tissue deformities. We reconstructed the nose, lips and eyelids as needed. We treated the excess medial skin with Kawamoto ("K") sub-dermal points or resection of the excess frontal skin. All patients underwent transnasal medial cantopexy.

#### **Bone measurements**

We measured the interorbital distance (IOD), which is the transverse distance between the most internal bone portions of the orbital borders, at four different moments: preoperative, intraoperative, recent postoperative (immediately after hospital discharge) and late postoperative (prior to the



**Figure 1.** (Left) Preoperative frontal and basal photographs of a 29-year-old female patient with craniofrontonasal syndrome (unilateral left coronal craniosynostosis, asymmetric hyperteleorbitism, bifid nose, low V-line implantation, low ears implantation, palpebral ptosis, medial epicantic fold and ogival palate). (Right) Postoperative frontal and basal photographs of the patient four years after asymmetric craniofacial bipartition with left orbit elevation. Note the correction of strabismus by the mobilization of the orbits.

preparation of the present study). In the recent and late preoperative and postoperative periods, we performed bone measurements on frontal cephalograms<sup>12,18,19</sup>. In the intraoperative period, we measured the IOD with a pachymeter, before and after the inverted "V" osteotomy<sup>12,18,19</sup>. We classified all patients according to the IOD measured intraoperatively<sup>6</sup>: first degree (mild), IOD > 30 mm and  $\leq$  34mm; Second degree (moderate), IOD>34mm and  $\leq$ 40mm; and third degree (severe), IOD>40mm.

#### **Evaluation of surgical results**

We used the measurements of the recent and late postoperative periods together to define the recurrence of the orbital position after surgery. We defined orbital recurrence as the difference between the measurements of the internal IOD at the postoperative periods<sup>19</sup>. We graded all results of large craniofacial surgical interventions (facial bipartition and orbital box osteotomy) according to the classification system on the need for additional surgery described by Whitaker<sup>20</sup>: category I, does not require surgical revision; category II, requires minor surgical revisions of the craniofacial contour; Category III, requires extensive additional osteotomies (surgical intervention less than the initial/main surgery); and category IV, requires a complete new craniofacial surgical intervention, similar to the initial/main surgery.

#### **Statistical analyzes**

We compiled all information in Excel for Windows (Microsoft Corporation, USA). We used the mean for metric variables and the percentages for categorical variables. We carried out the intragroup and intergroup comparative analyzes (IOD and Whitaker classification) with the Mann-Whitney test and test of equality between two proportions. We performed all analyzes with the Statistical Package for Social Sciences version 20 for Windows (SPSS, Chicago, IL, USA). We considered as significant the values for a 95% confidence interval (p<0.05).

#### RESULTS

We included seven female patients diagnosed with craniofrontonasal dysplasia. The mean patients' age at the time of the craniofacial interventions was 11.86  $\pm$  8.05 years (4-29), being 14.67  $\pm$  12.90 years (4-29) And 10  $\pm$  2 years (7-12) for orbital box osteotomy and facial bipartition procedures, respectively. Three (42.86%) and four (57.14%) patients were classified with mild and moderate hyperteleorbitism, respectively.

Three (42.86%) patients underwent orbital box osteotomy and four (57.14%) underwent facial bipartition (Figures 1 and 2). Patients received a mean of  $3.33 \pm 2.07$  units (1-6) of packed red blood cells during surgery and remained hospitalized for an average of 7.71  $\pm$  3.86 days (6-16). There were two (28.57%) complications related to procedures, infections of surgical sites treated with intravenous antibiotic therapy. There were no deaths or complications such as visual deficit or permanent neurological damage.

Before the interventions, the mean IOD was  $34.43 \pm 3.21 \text{ mm} (30-39)$  as measured with the cephalograms, and  $35.43 \pm 2.7 \text{ mm} (31-39)$  when measured intraoperatively with the pachymeter, just before the osteotomies. The mean reduction in IOD in the recent postoperative period was  $11.14 \pm 4.53 \text{ mm}$ , corresponding to a reduction of  $31.58 \pm 13.14\%$  (19.44-51.61). The mean reduction in IOD in the late postoperative period was  $8.43 \pm 6.80 \text{ mm}$ , which corresponds to a reduction of  $23.29 \pm 17.99\%$  (5.56-43.59) of the IOD initial mean. The mean orbital recurrence was  $3.71 \pm 3.73 \text{ mm}$  (0-10) (Table 1).

The overall mean of the surgical results classified according to the Whitaker need for surgical revision<sup>20</sup> was  $2.43 \pm 0.53$  (between categories II and III) (Table 1). Four (57.14%) and three (42.86%) patients were classified as categories II and III, respectively. All patients have had normal intellectual development and are still in follow up on our service.

#### DISCUSSION

The correction of hyperteleorbitism has been a challenge for plastic surgeons dealing with craniofrontonasal dysplasia<sup>17</sup>, since such patients often have severe and asymmetric hyperteleorbitism<sup>17,21</sup>, therefore requiring a great mobilization of the orbits in three dimensions<sup>18</sup>. Since the first description of craniofrontonasal dysplasia<sup>8</sup>, the surgical treatment of hyperteleorbitism in these patients has been restricted only to reports of isolated cases and to retrospective series in the international context<sup>12-17</sup>. Although there are national publications<sup>18,19,22,23</sup> that address the surgical correction of hyperteleorbitism of several craniofacial deformities together, this is the first Brazilian study that brings the peculiarities of the intracranial and extracranial interventions performed for the treatment of hyperteleorbitism in patients with craniofrontonasal dysplasia.

In the literature, after Tessier<sup>3-6</sup> described the surgical principles of the intra and extracranial approach for the correction of hyperteleorbitism,



Figure 2. (Left) Preoperative frontal and basal photographs of an 11-year-old patient with craniofrontonasal syndrome (bilateral coronal craniosynostosis, symmetrical hyperteleorbitism, bifid nose, low ears implantation, palpebral ptosis, medial epicantic fold and ogival palate). (Right) Postoperative frontal and basal photographs of the patient two years after symmetrical craniofacial bipartition. Note the need of additional soft tissue surgeries.

many adaptations and technical innovations have been published, especially those described by Van der Muelen<sup>24,25</sup>, who modified the box osteomy and created the facial bipartition. The latter comprises the medial rotation of the two hemifaces by means of the intracranial access, associated with successive osteotomies at the pterygomaxillary junction and palatine plates, simultaneously correcting the orbits and the inverted "V" occlusion reported in patients with hyperteleorbitism. In addition, Converse *et al.*<sup>26,27</sup> described the one-stage orbitotomy for the correction of hyperteleorbitism in adult patients, avoiding osteotomies in the palate.

Although there are national reports on the treatment of hyperteleorbitism by extracranial osteotomies<sup>22,23</sup>, the procedures of choice have been

Variables	Orbital box osteotomy (n = 3)	Facial bipartition (n = 4)	p-value	
			(intragroup)	(Intergroup)
Interorbital Distance M ± SD				
Preoperative *	34 ± 3	34.8 ± 3.8		
Early postoperative *	25.7 ± 4.9	23.6 ± 5.7	* *	* * *
Late postoperative *	27.3 ± 6.1	$26.8 \pm 6.6$		
Whitaker Classification $M \pm SD$	2 ± 0	2.75 ± 0.5	-	> 0.05

Table 1. Intra and intergroup (orbital box osteotomy versus facial bipartition) comparative analyses.

PO: postoperatively; M: mean; SD: standard deviation; -: not applicable; \*: bone measurements carried out on frontal cephalograms; \*\*: preoperative < early postoperative = late postoperative period (p < 0.05 for all comparisons, except early postoperative versus late postoperative, with p > 0.05); \*\*\*: p > 0.05 for all intergroup comparisons.

the orbital box osteotomy and facial bipartition<sup>17-19,21</sup>, as both techniques allow the three-dimensional mobilization of the target structures and, therefore, the approach of a broad spectrum of clinical presentation of hyperteleorbitism. In the particular scope of craniofrontonasal dysplasia. Kawamoto et al.<sup>17</sup> considered that facial bipartition enabled a better correction of craniofacial deformity when compared with orbital box osteotomy. It has also been argued that facial bipartition is simpler to perform and does not require osteotomies in the interorbital region that may compromise dental buds and lacrimal pathways<sup>15,17</sup>. It is important that these aspects<sup>15,17</sup> be considered; However, significant rotation of the hemifaces during facial bipartition in adult patients with severe hyperteleorbitism produces a diastema of the central maxillary incisors which may be very difficult to correct orthodontically and potentially require a LeFort I osteotomy<sup>19</sup>. Moreover, in these patients, dental buds are at potential risk during the rigid fixation of the osteotomy segments in the nasomaxillary and zygomaticomaxillary pillars<sup>19</sup>. Based on this, we prefer the orbital box osteotomy for the correction of hyperteleorbitism in adult patients with normal maxillary morphology and acceptable occlusion, while reserving facial bipartition to treat patients with mixed or deciduous dentition<sup>19</sup>. With this surgical approach, we obtained a significant improvement in the craniofacial symmetry of all patients evaluated, there being need of additional surgeries of the craniofacial contour (categories II and III of Whitaker<sup>20</sup>).

The coronal suture fusion pattern (unilateral versus bilateral) determines the clinical characteristics of patients with craniofrontonasal dysplasia<sup>10,11,17</sup>. In addition to hyperteleorbitism, patients with unilateral fusion of the coronal suture also present vertical orbital dystopia, so that the orbit ipsilateral to the fusion is displaced cranially compared with the contralateral orbit<sup>10,11,17</sup>. Therefore, in these situations, the inverted "V" resection should be asymmetrical, the "leg" of the "V" ipsilateral to the coronal suture fusion being vertically planned, and the contralateral leg, horizontally. Total (bilateral) fusions of the coronal suture lead to a facial pattern with greater symmetry, although brachycephalic<sup>10,11,17</sup>, so that the inverted "V" resection can be symmetrical. One can apply this same reasoning to the frontal bone. Patients with unilateral coronal fusion present an asymmetric frontal region (the frontal bone ipsilateral to the fusion is laterally located on the contralateral side, which usually presents with a bone hump or bulging). Thus, we perform the inversion of the bone plate in these situations, so that the bone hump is rotated 180 degrees to be fixed in the depressed frontal region. Such a surgical maneuver allows obtaining of facial symmetry. However, this maneuver is unnecessary in those patients with bilateral fusion of the coronal suture.

Another relevant aspect in the surgical treatment of hyperteleorbitism in craniofrontonasal dysplasia is the manipulation of soft tissues<sup>17</sup>. The medialization of the orbits determines a tissue excess

in the median region, which can be resected in the form of "Z", obeying the principles of Tessier<sup>6</sup>, by means of direct resection without the Z-plasty, or by using the "K" stitches<sup>17,28</sup>. The "K" stitches are named after their creator, Dr. Henry K. Kawamoto, who described the technique to reduce the excess of soft tissues without the need for scars on the frontal region<sup>17,28</sup>. The technique consists in decreasing the thickness of all planes from the forehead to the dermis, but without incision in the epidermis<sup>17,28</sup>. This surgical maneuver, eventually followed by mattress suturing, leads to soft tissue contraction without the need for direct excision, as recommended by the authors<sup>17,28</sup>.

Another important clinical feature is poor positioning of the medial corner, which determines a small skin fold characteristic of craniofrontonasal dysplasia and more easily identified in patients who present unilateral fusion of the coronal suture compared with those with bilateral one. The treatment of this particular deformity is fundamental, since it alleviates the stigma of craniofrontonasal dysplasia. The surgical approach can be performed by means of Z-plasty or by the technique described by Fuente del Campo<sup>29</sup>, which has been routinely used by the UCLA Craniofacial Clinic group<sup>17</sup>.

The literature has reported that selfperception of a deformed face may be present in children less than four years of age<sup>15</sup>. Such children begin to feel different from their peers and lose the motivation to attend environments with other children<sup>18</sup>. As orbital repositioning improves overall facial harmony and allows the acquisition of binocular vision (usually impaired due to hyperteleorbitism)<sup>18</sup>, and early surgery has the potential to attenuate the stigmas and stereotypes faced by children with craniofacial deformities mainly in the school environment<sup>18</sup>, many parents seek specialized centers to resolve the anxiety related to the appearance of their children<sup>18,19</sup>. However, it is important to mention that surgical intervention for the correction of hyperteleorbitism may display recurrence of orbital position and also compromise facial growth, especially when performed in children with an immature craniofacial skeleton<sup>19,21</sup>.

In the literature, analyzes of the 1980s and  $1990s^{12, 30}$  presented mixed results regarding the

relationship between the patients' age and the orbit position recurrence rate. Two recent longitudinal studies<sup>19,21</sup> have evaluated numerous patients with hyperteleorbitism (including patients with craniofrontonasal dysplasia) treated surgically and have shown that age is a determining factor in the rate of orbital position recurrence. In addition, the surgical technique (orbital box osteotomy versus facial bipartition) was not determinant in the rate of recurrence<sup>19</sup> and there is a divergence regarding the effect of the severity of hyperteleorbitism on recurrence<sup>19,21</sup>.

There is evidence that facial growth reaches 90% of the adult size before the age of sixteen<sup>31</sup> and that the permanent upper incisors present eruption typically before the age of eight<sup>19</sup>. Thus, since the presence of permanent dentition may contribute to greater bone stability in the postoperative period and this is an important factor for the choice of surgical technique, we have adopted eight years as the age limit to differentiate patients who have higher or lower potential for continuous growth of the middle third of the face and patients whose state of dentition is less or more mature<sup>19</sup>. By applying this concept, in this study we found rates of orbital recurrence similar to the ones reported in previous studies<sup>18,19,21</sup>.

In this context, while waiting for skeletal maturity to operate hyperteleorbitism is associated with lower relapse rates<sup>19</sup>, other aspects can often determine that interventions be performed in younger patients<sup>19,21</sup>. In fact, multiple factors contribute to the decision on when surgical correction should be performed<sup>19,21</sup>. Among the most relevant are the emotional and psychological responses of both parents and children with hyperteleorbitism<sup>19</sup>. The physical appearance of these children can be shocking, and parents are often anxious to have the surgery performed as early as possible, or before their children reach school age, to try to mitigate the challenges that children may face as they become self-critical and begin to have contact with their peers<sup>19,21</sup>.

Therefore, counseling the parents of patients with hyperteleorbitism to await the maturation of the craniofacial skeleton can be a major challenge and the multidisciplinary approach for family and patients should include a discussion of all of the above issues (intervention age versus outcomes versus potential risks in the short and long terms). If even with this multidisciplinary support the child and parents demonstrate the desire for surgery, it cannot be denied that, in this particular situation, the possibility of recurrence is certainly no more relevant than the desire for positive self-image and recovery of selfesteem, that allow the confrontation of prejudice derived from peers $^{18,19}$ .

According to the presented and discussed surgical results, the approach of these patients should be individualized, respecting, whenever possible, the age and preferences of patients and their parents, as well as the experience of surgeons.

#### RESUMO

**Objetivo:** apresentar nossa experiência no tratamento cirúrgico do hiperteleorbitismo na displasia craniofrontonasal. **Métodos:** análise retrospectiva dos pacientes com displasia craniofrontonasal operados por *orbital box osteotomy* ou por bipartição facial entre os anos de 1997 e 2015. Informações sobre as intervenções cirúrgicas foram obtidas dos prontuários médicos, exames complementares, fotografias e entrevistas clínicas. Os resultados cirúrgicos foram classificados com base na necessidade de cirurgia adicional, e a recidiva orbital foi calculada. **Resultados:** sete pacientes do sexo feminino foram incluídas, três submetidas à *orbital box osteotomy* (42,86%) e quatro (57,14%) à bipartição facial. Houve uma recidiva orbital média de 3,71±3,73mm. A média global dos resultados cirúrgicos de acordo com a necessidade de novas cirurgias foi de 2,43±0,53. **Conclusão:** a abordagem cirúrgica do hiperteleorbitismo na displasia craniofrontonasal deve ser individualizada, respeitando, sempre que possível, a idade e as preferências dos pacientes, seus familiares e cirurgiões.

Descritores: Anormalidades Craniofaciais. Cirurgia Plástica. Olho. Osteotomia.

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