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Craniosynostosis: State of the Art 2019

# Craniosynostosis and ENT

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## ABSTRACT

**Objective.** – The aim of the present study was to review the literature on ENT disorders associated with craniosynostosis (CS), focusing on symptoms, diagnostic work-up, treatment and outcome.

**Methods.** – Publications were retrieved by consulting the PubMed® free search engine of the US National Library of Medicine. The term “craniosynostosis” was combined with the following key-words: ENT, apneas, OSAS, sleep-disordered breathing, tonsillectomy, deafness, hearing loss.

**Results.** – The main ENT disorders associated with CS are upper airway obstruction, chronic otitis and hearing loss. Obstructive sleep apnea-hypopnea syndrome (OSAS) is present in 7% to 67% of children suffering from CS and mainly results from midface stenosis with narrow nasal and rhinopharyngeal cavities. OSAS is diagnosed on polysomnography and airway obstruction levels are determined on wake or drug-induced sleep endoscopy and on CT or MRI. OSAS treatment can be surgical (mainly midface advancement, adenoidectomy and tonsillectomy, tracheostomy) or non-surgical (non-invasive ventilation, nasopharyngeal airway). Hearing impairment is frequently associated with CS. Its main cause is otitis media with effusion (OME) but ossicular malformations and sensorineural hearing loss (SNHL) are sometimes observed. SNHL is mostly found in Muenke syndrome. In view of the frequency and potential severity of these disorders into account, yearly ENT visits are recommended in children presenting with CS.

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## 1. Introduction

Craniosynostosis is defined as the premature fusion of one or more cranial sutures, affecting the development of the skull, face and brain [1]. Its incidence is between 1/2,000 and 1/2,500 live births [2,3]. It can be isolated (non-syndromic craniosynostosis: NSCS) or associated with other malformations, in particular of the face and limbs (syndromic craniosynostosis: SCS). SCS represents 15–40% of cases [1,4,5]. Apert, Crouzon, Pfeiffer, Muenke, Saethre-Chotzen and Carpenter syndromes are the most frequent syndromes [2,6]. Some SCSs are associated with fibroblast growth factor receptor (FGFR) gene mutations, but other gene and chromosomal anomalies may be involved. The aim of the present literature review was to present the incidence, symptoms, diagnostic work-up and treatments of CS-associated ENT disorders.

## 2. Methods

Publications were retrieved by consulting the PubMed® free search engine of the US National Library of Medicine. The term “craniosynostosis” was combined with the following key-words: ENT, apneas, OSAS, sleep-disordered breathing, tonsillectomy, deafness, hearing loss.

## 3. Results

### 3.1. Upper airway obstruction (for a review, see [2])

Sleep-disordered breathing includes OSAS, central apnea, and hypoventilation. The ENT specialist is primarily concerned with OSAS, which consists of prolonged partial or complete intermittent obstruction of the upper airway during sleep. This obstruction impairs both ventilation and sleep quality. In children with CS, OSAS prevalence varies between 7% and 67% [7,8]. This wide range mainly results from the heterogeneity of the diagnostic criteria used in the various published series. In the general pediatric population, OSAS prevalence is lower, ranging between 1.5% and 6% [9].

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Diagnosis of OSAS and the distinction between peripheral and central apnea cannot be based on questionnaires or physical examination, which lack sensitivity and specificity, but requires sleep study [10]. In children, OSAS is defined by an apnea-hypopnea index (AHI)  $\geq 1$ /h. Apnea is a pause in respiration during at least 2 respiratory cycles, and can involve central or peripheral obstructive. Hypopnea is defined as  $\geq 30\%$  reduction in ventilation resulting in a  $\geq 3\%$  decrease in SpO<sub>2</sub> due to partial airway obstruction, or in microarousal. AHI values 1–5, 5–10, and  $>10$  correspond to mild, moderate and severe OSAS, respectively. In teenagers, normal AHI values are poorly defined, and lie somewhere between child and adult values. Sleep studies can measure several additional parameters which help confirm the diagnosis of OSAS and assess its severity: sleep cycles, microarousal index, (number of microarousals per hour), SpO<sub>2</sub> (mean and lowest values, oxygen desaturation index), TcPCO<sub>2</sub> (average and maximum values).

Pediatric OSAS can cause various cognitive (attentional deficit, behavioral disorder, learning difficulties), cardiovascular (hypertension, etc.) and metabolic complications, with significant impact on quality of life. CS-related OSAS is mainly due to hypoplasia of the middle third of the face, with stenosis of the nasal cavities and rhinopharynx (Fig. 1), although it can also be observed in CS forms which are not classically associated with facial straightening, such as Muenke or Saethre-Chotzen syndrome [6]. Since the growth of the lower third of the face is dependent on that of the midface, mandibular hypoplasia is sometimes also present, aggravating the upper airway obstruction (Fig. 1; see also below: possible indications for bimaxillary surgery). CS-related OSAS often seems to stabilize or improve with age [2]. Such favorable spontaneous progression is less frequent in facial middle third hypoplasia. In children with CS, OSAS can induce the usual complications (see above) but may also worsen intracranial pressure elevation [11]. The effect of OSAS on intracranial pressure is mediated by an increase in PCO<sub>2</sub> and blood pressure. CS-associated OSAS can be associated with central apnea, possibly resulting from decreased CSF flow due to narrowing of the craniovertebral junction or to Chiari malformation. The latter is more frequent in Crouzon and Pfeiffer syndromes, due to early closure of the lambdoid suture and of cranial base synchondroses [2]. Several publications suggest that, overall, central apneas are rather rare in CS, even in case of Chiari malformation [12–14].

OSAS treatment depends on the upper airway anomalies found on endoscopy and possibly on CT or MRI. Recently, drug-induced sleep endoscopy (DISE) was found to be a very useful tool for accurate assessment of upper airway obstruction in CS, as in many other cases of OSAS associated with underlying severe comorbidities [15].

Non-surgical options:

- non-invasive ventilation (NIV) is indicated in case of moderate to severe OSAS for which surgical treatment is not indicated or has failed [16,17]. It can be started as of the first weeks of life. Fine adjustment of ventilation pressure is based on the progression of clinical and polysomnographic parameters. Appropriate interfaces are required to decrease the risks of skin injury from pressure sores, eye irritation because of unintentional air leaks, and worsening of facial deformity due to interface pressure on the facial skeleton [18]. Good cooperation of the child and parents is essential for the success of this technique;
- nasopharyngeal airway (NPA) aims is to bypass the nasal and rhinopharyngeal narrowing by positioning the distal end of the tube in the oropharynx. It can be maintained for several weeks to months. Ahmed et al. [19] published a series of 27 patients (mean age: 12.3 months) with CS and moderate ( $n = 17$ ) or severe ( $n = 10$ ) OSAS treated by NPA. Treatment decreased AHI in 26 patients (96%). Under treatment, 3 patients had mild and 24 had moderate

OSAS. NPA was well-tolerated, and the tube could be maintained for more than 6 weeks in 24 patients;

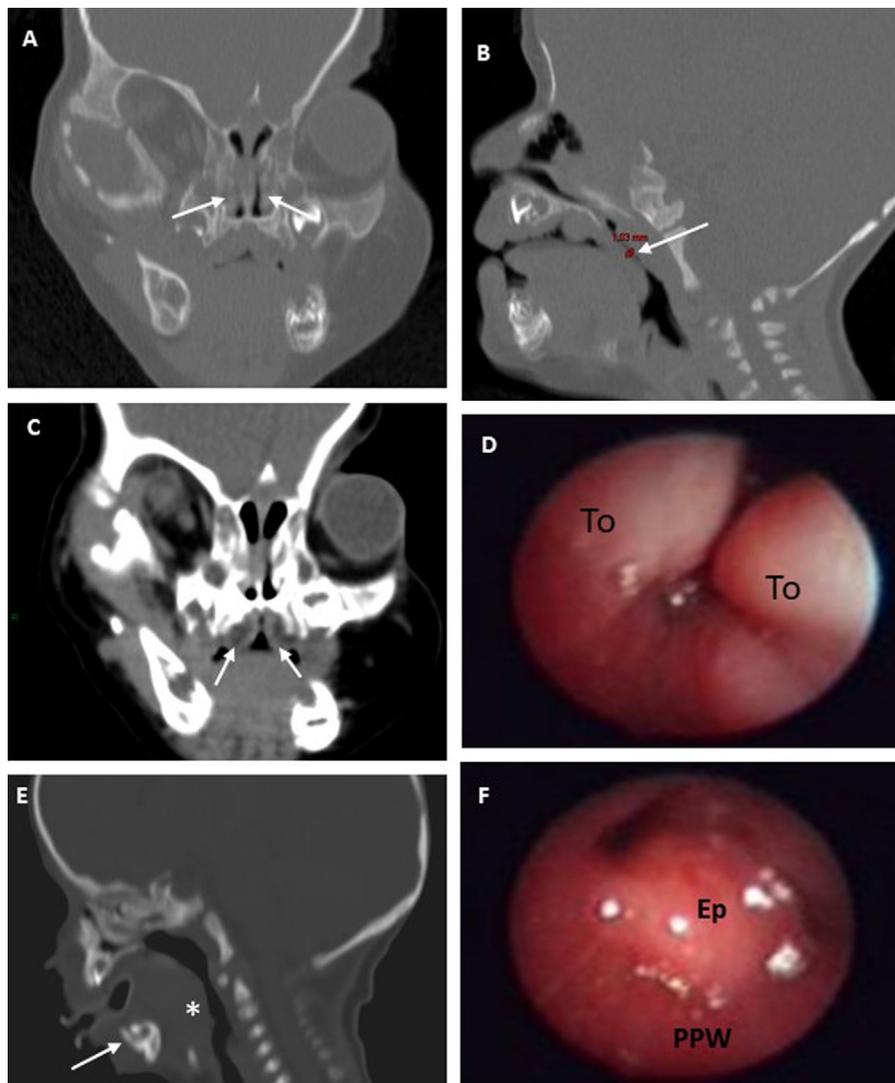
Surgical options:

- tonsillectomy and adenoidectomy (T-A). Hypertrophy of the tonsils and adenoids is extremely frequent in all children between 18 months and 5 years of age, sometimes leading to sleep-disordered breathing and OSAS. Such hypertrophy is not more frequent in CS than in the general pediatric population, but its clinical impact is greater due to narrower pharyngeal cavities. A recent literature review reported that, on average, T-A decrease AHI and desaturation index by 5/h and 8.5/h, respectively [20]. It improved OSAS in 60% of cases, but AHI normalization is rare [2]. It is noteworthy that some studies cited in Saengthong et al.'s review did not find any efficacy for T-A in patients with CS [21]. Adenoidectomy is contraindicated in case of cleft palate, due to risks of postoperative velar insufficiency and hypernasal speech. Tonsillectomy is usually partial (“intracapsular tonsillectomy”), typically using radiofrequency, coblation or microdebrider. The main advantage of intracapsular tonsillectomy is to decrease postoperative pain, and its main drawback is a small risk of symptomatic tonsillar regrowth [22]. The main complications of tonsillectomy are hemorrhage (1–3%), with maximal risk between 10 and 14 days after surgery, transient increase in upper airway obstruction during the first postoperative days, and oropharyngeal pain, which can last up to 2 weeks;
- surgical midface advancement (SMA). Its goals are to improve esthetics, OSAS, dental occlusion and exorbitism. It is mainly indicated in Crouzon, Pfeiffer and Apert syndromes, in which, midfacial hypoplasia is often severe. Since the original description of the Le Fort III technique by Tessier [23], surgical techniques have progressed, including monobloc advancement, distraction osteogenesis and facial bipartition [2,24]. The efficacy of SMA is variable [1,25]. Studies assessing SMA outcomes have had small cohorts (fewer than 20 patients) and rely on heterogeneous subjective and objective criteria. In one retrospective study including 11 patients presenting with CS and moderate to severe OSAS previously treated with NIV or tracheotomy, SMA improved respiratory symptoms in 6 patients, whereas NIV or tracheotomy had to be maintained in 5 patients [24]. In cases of SMA failure, endoscopy showed persistent pharyngeal collapse. Early surgery seems to improve outcome [26]. Simultaneous bimaxillary distraction seems to be a promising technique [27];
- other surgical procedures can be proposed, depending on the results of airway endoscopy and the patient's age: endoscopic supraglottoplasty for laryngomalacia, enlargement of piriform aperture stenosis [28], turbinoplasty or turbinectomy for inferior turbinate hypertrophy, septoplasty for nasal septum deviation, etc.;
- tracheotomy is the last therapeutic option when all other treatments are contraindicated or inefficient.

In conclusion, OSAS is a frequent finding in CS and must be systematically screened for by regular parental interviews, physical examinations performed by an experienced pediatric ENT specialist, and sleep studies. On our opinion, sleep studies should be performed during the first weeks of life, at the age of 3 to 4 years, and whenever symptoms suggestive of sleep apnea are observed. OSAS management strategy depends on the patient's age, CS etiology, associated comorbidities, upper airway imaging, wake endoscopy and possibly drug-induced sleep endoscopy.

### 3.2. Craniosynostosis and hearing loss [29–32]

There are 3 types of hearing loss: conductive (CHL), due to impairment of the vibrations of the tympanic membrane or ossicles, sensorineural (SNHL), due to dysfunction of the inner ear or



**Fig. 1.** Main upper airway obstructive sites in craniostenosis. A. CT-scan, coronal view. 22 month-old child, Pfeiffer syndrome. Notice the narrowness of the nasal cavities (white arrows). B. CT-scan, sagittal view. Same patient as in A. Notice the narrowness of the rhinopharyngeal airway (white arrow). C. CT-scan, coronal view. 18 month-old child. Due to the narrowness of the oropharyngeal cavity, the palatine tonsils are in contact with each other despite their relatively small volume (white arrows). D. Drug-induced sleep endoscopy. Same patient as in C. Severe oropharyngeal obstruction by palatine tonsils (To). Underlying larynx and tongue base are not visible. E. CT-scan, sagittal view. 12 month-old patient, Crouzon syndrome. Insufficient mandibular growth with retrognathia (white arrow) and posterior displacement of the tongue basal (white arrow). F. Drug-induced sleep endoscopy. Same patient as in E. Due to insufficient mandibular growth and retrognathia, the tongue base and the epiglottis (Ep) are in a posterior position. Subsequently, the epiglottis is in contact with the posterior pharyngeal wall (PPW), and the oropharynx is severely obstructed. Underlying vocal folds and upper esophageal end are not visible.

auditory nerve, and mixed (MHL), combining CHL and SNHL. Severity is categorized as mild (20–40 dB), moderate (40–70 dB), severe (70–90 dB) and profound (90–120 dB). In CHL, maximal impairment is 60 dB, and the main etiology is OME, a type of chronic otitis with inflammatory fluid in the middle ear cavities. SNHL and MHL range from mild to profound hearing loss. When hearing loss cannot be cured by surgical or medical treatment, which is often the case in CHL linked with middle ear malformation and in almost all cases of SNHL, treatment consists of hearing rehabilitation and speech therapy. The type of rehabilitation (conventional hearing aid, bone anchored hearing (BAHA), middle ear implant, cochlear implant, brainstem auditory implant) depends on etiology and severity. Hearing impairment is frequent in CS; in a literature review [30], rates in Pfeiffer, Apert, Crouzon and Muenke syndromes were 92%, 80%, 74%, and 61%, respectively. The main etiology of hearing loss in CS is OME. It is favored by the narrowness of the Eustachian tube linked with cranial base malformation, and more rarely by associated cleft palate responsible for insufficient opening of the

Eustachian tube during swallowing and yawning. OME usually induces mild hearing loss, with mild reversible speech anomalies, behavioral disorder and learning difficulties. OME can progress toward other forms of chronic otitis such as tympanic membrane retraction, cholesteatoma (keratinizing squamous epithelium in middle ear cavities) or tympanic perforation. Malformations of the external acoustic meatus or ossicular chain are rarely observed in CS. Stapes ankylosis or dehiscence of the superior semicircular canal (Minor syndrome), both responsible for CHL, have been reported in Apert syndrome. SNHL and MHL are also rare in patients with CS. They can be associated with all syndromes but mostly with Muenke's. In Muenke syndrome, hearing loss predominates in lower frequencies, which is rare in SNHL. In a series of 108 children with CS [29], only 19 (18%) required a hearing aid although 50% had mild to moderate impairment on their better-hearing side. OME, which is the predominant etiology of hearing impairment in CS, can usually be treated by ventilation tube insertion without any need for hearing aids.

#### 4. Conclusions

In view of the frequency and potential severity of respiratory and auditory disorders, yearly ENT visits with wake upper airway endoscopy and hearing tests are recommended in children with CS. Early ENT assessment may be required in case of neonatal respiratory distress. Additional consultations are sometimes necessary if new ENT symptoms appear.

#### Disclosure of interest

The authors declare that they have no competing interest.

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