

REVIEW ARTICLE

Anesthesia for surgery related to craniosynostosis: a review. Part 1

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Summary

The management of children with craniosynostosis is multidisciplinary and has evolved significantly over the past five decades. The treatment is primarily surgical. The anesthetic challenges continue to be the management of massive blood transfusion and prolonged anesthesia in small children, often further complicated by syndrome-specific issues. This two-part review aims to provide an overview of the anesthetic considerations for these children. This first part describes the syndromes associated with craniosynostosis, the provision of services in the UK, surgical techniques, preoperative issues, and the induction and maintenance of anesthesia. The second part of this review will explore hemorrhage control, the use of blood products, metabolic disturbance, and postoperative issues.

Introduction

One of the most common craniofacial congenital abnormalities requiring surgery is craniosynostosis where there is premature fusion of one or more cranial sutures (Figure 1a). This leads to a failure of normal bone growth perpendicular to the suture. Compensatory growth occurs at other suture sites and results in a characteristic abnormal head shape. The overall incidence of craniosynostosis is one in 3000 live births.

Craniosynostosis occurs as an isolated condition (isolated craniosynostosis) in 80% of cases or as part of a syndrome (syndromic craniosynostosis) in 20% of cases. Isolated craniosynostoses are usually simple, are not associated with other abnormalities and their etiology is nongenetic, the majority probably being caused by intrauterine fetal head constraint.

Syndromes

Syndromic craniosynostoses are usually complex (often more than one suture is affected) and frequently have an identifiable genetic cause. They can be associated

with other facial bony abnormalities, together with extra-cranial features. Both isolated and syndromic craniosynostosis, although predominantly the latter, can lead to raised intracranial pressure (ICP). Raised ICP can occur in 40–70% of syndromic craniosynostoses because of multiple suture fusion. It can be due to hydrocephalus, airway obstruction, the skull being too small for the brain (craniocerebral disproportion) or abnormalities in the venous drainage of the brain. The symptoms of raised pressure include headaches, irritability, seizures, developmental delay, and in extreme circumstances, blindness and death. The treatment is directed at the specific cause and is an integral part of the complex surgical management of syndromic synostosis. Syndromes associated with craniosynostosis are listed in Table 1 and examples of characteristic appearances are shown in Figure 1.

Most syndromic craniosynostoses show autosomal dominant inheritance, although the majority is attributed to new mutations from unaffected parents. Mutations in genes coding for fibroblast growth factor receptors (FGFRs) are responsible for the most common syndromes. Fibroblast growth factors (FGFs)

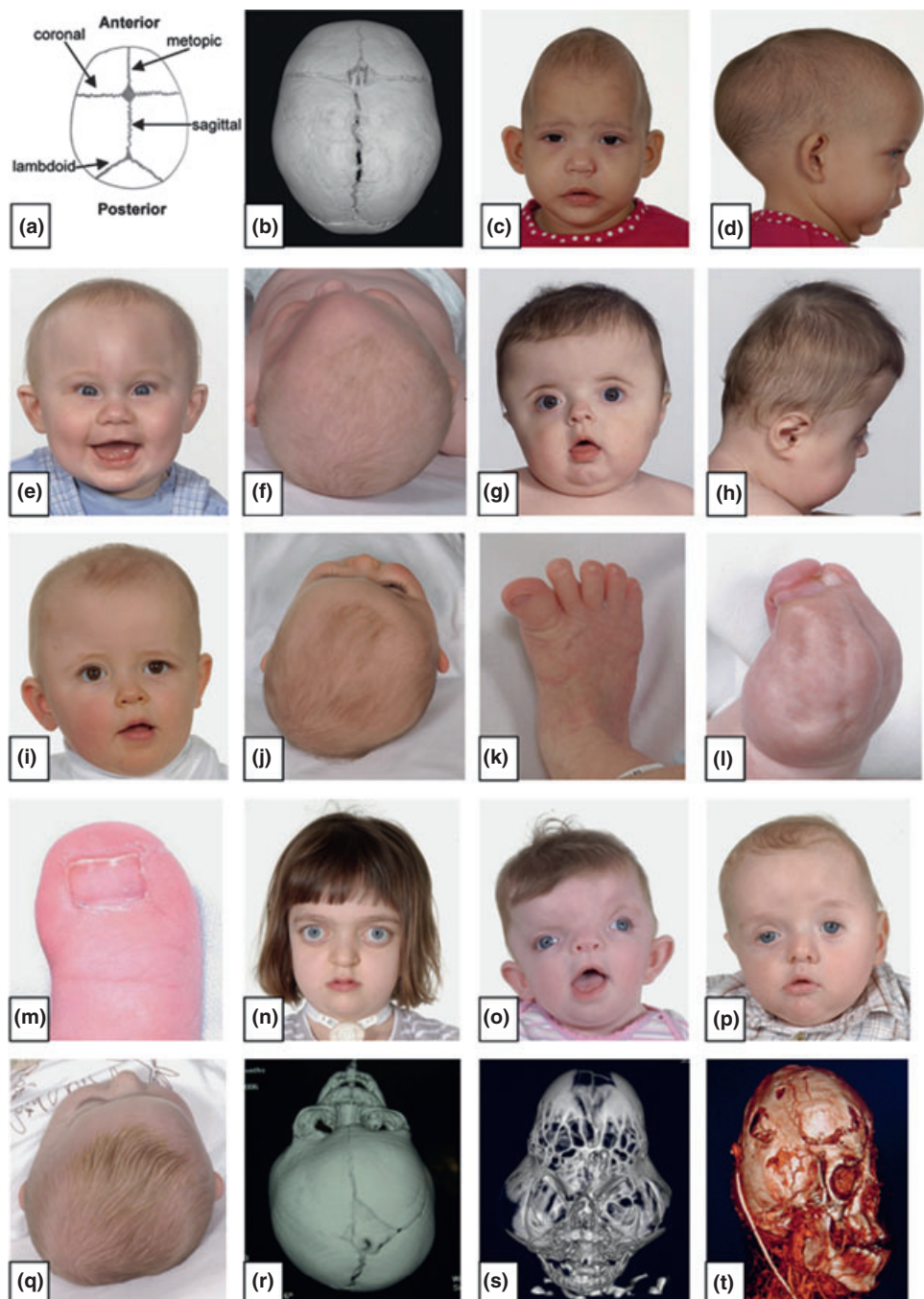


Figure 1 Diagnostic features of craniosynostosis. (a) Schematic diagram showing positions of the major cranial sutures. (b) CT scan (vertex view of skull) showing major sutures; anterior is at top. (c,d) Sagittal synostosis: note long, narrow head. (e,f) Metopic synostosis: note hypotelorism and triangular profile of forehead. (g,h) Bicoronal synostosis: broad, flattened head. (i,j) Right unicoronal synostosis: note flattened brow and anterior position of ear on affected side, deviation of nasal tip and prominent brow on unaffected side. (k–m), Congenital anomalies of feet or hands characteristic of Pfeiffer syndrome (k), Apert syndrome (l) and craniofrontonasal syndrome (m). (n) Crouzonoid facial appearance.

(o) Severe hypertelorism, grooved nasal tip and left unicoronal synostosis in craniofrontonasal syndrome. (p) Ptosis and left unicoronal synostosis in Saethre-Chotzen syndrome. (q) Positional plagiocephaly: prominence on right anteriorly and left posteriorly, with right ear anterior and parallelogram shape to skull. (r) CT reconstruction showing left unicoronal synostosis. (s) CT reconstruction showing cloverleaf skull. (t) CT venogram showing abnormal venous drainage in multisuture syndromic craniosynostosis. See text for further details. (Reproduced with permission from Nature Publishing Group, *European Journal of Human Genetics, Craniosynostosis*, **19**, 369–376; 2011, D Johnson, AOM Wilkie, Figure 2.)

Table 1 Syndromes associated with craniosynostosis

Muenke
Apert
Crouzon
Pfeiffer
Saethre-Chotzen

bind to FGFRs and control the growth and differentiation of various cells. Abnormal interaction of two proteins leads to defective intracellular signaling. For example, in Apert syndrome (one of the more severe forms of the craniosynostosis syndromes), the FGF binds to the abnormal FGFR 2 for a prolonged time, prematurely signaling for immature bone cells to differentiate and cause suture fusion. Apert syndrome occurs in 1 : 65 000 births. In this condition, bicoronal synostosis occurs, leading to brachycephaly with associated large, open anterior and posterior fontanels, which frequently connect. They can frequently be an associated cleft palate. Midface hypoplasia leads to airway problems and obstructive sleep apnea (OSA). Shallow eye sockets (exorbitism) can lead to corneal exposure and potential dislocation of the eyes in extreme circumstances. In addition to the craniofacial features, Apert syndrome can be identified by complex, symmetrical syndactyly, with fusion of at least the central three digits, which may allow antenatal ultrasound diagnosis.

Mutations in the *FGFR 2* gene, located on chromosome 10, are also responsible for Crouzon and Pfeiffer syndromes and lead to a similar facial appearance. In Crouzon syndrome, the hands and feet are essentially normal, whereas in Pfeiffer syndrome, there are typically broad, radially deviated thumbs and great toes. The most severe form of Pfeiffer syndrome can lead to a cloverleaf skull deformity in which all of the cranial sutures are fused (Figure 1s).

A specific mutation in the *FGFR 3* gene is responsible for Muenke syndrome. This is the commonest syndrome and accounts for approximately 30% of all coronal synostosis. The facial features can be fairly mild, although there is an associated low-frequency sensorineural hearing loss. Genetic testing for those with brachycephaly is important for assessing the prognostic outcome of surgery, as the risk of re-operation is much greater for those with Muenke syndrome than those with nonsyndromic coronal craniosynostosis (1).

Other syndromes associated with craniosynostosis include Saethre-Chotzen syndrome (caused by mutations in the *TWIST 1* gene) and craniofrontonasal syndrome (caused by a mutation in the gene encoding ephrin-B1 (*EFNB1*)).

Provision of craniofacial services in the UK

Since 1988, the provision of craniofacial surgery in the UK has been commissioned on a national level by what is currently called the National Specialist Commissioning Team (NSCT). The NSCT is part of the Department of Health and is responsible for funding, managing, and developing 'specialist services'. About 60 highly specialized services are commissioned nationally by NHS Specialized Services. Generally speaking, these are services that affect fewer than 500 people across England or involve services where fewer than 500 highly specialized procedures are undertaken each year.

There are four supraregionally funded designated craniofacial centers in the UK; Oxford Craniofacial Unit, Great Ormond Street Craniofacial Unit, Royal Liverpool Children's Hospital Craniofacial Unit and Birmingham Children's Hospital Craniofacial Unit.

The key to success in craniofacial surgery is in adopting a multidisciplinary approach to the care of patients. The team involved in the care of these patients includes plastic and reconstructive surgeons, pediatric neurosurgeons, maxillofacial surgeons, pediatric anesthetists, orthodontists, orthoptists, speech therapists, geneticists, clinical psychologists, and clinical nurse specialists.

Surgical considerations in craniosynostosis

Timing of surgery

Emergency indications for surgery in craniosynostosis include the following:

1. Need urgently to protect the airway.
2. Need urgently to protect the eyes.
3. Manage acutely or chronically raised ICP.

Elective surgery

The optimal timing of elective surgery in craniosynostosis is controversial. Surgery at an early stage, between 3 and 6 months, has the surgical advantage of the bone being soft and easy to bend and reshape, and at this age, the brain is undergoing rapid growth and thus will drive the growth of the cranial vault. The disadvantages, however, include an increased risk of having to repeat the surgery during youth as a result of ongoing craniocerebral disproportion resulting in craniostenosis. There is also an increased risk to the child because of the smaller blood volume. Surgery performed on children much older can reduce the risks of reoperation, but the bone becomes too thick to remodel and the deformities can become too severe to

correct. In addition, older children lose the ability to ossify small craniectomy defects and may need bone grafting when older 1. In the Oxford Craniofacial Unit, our techniques have developed to allow us to operate on the calvarial vault at around the age of 1-year affording most of the advantages of early operating with fewer of the disadvantages.

Surgical procedures

General principles

Surgery is specific to the synostosis, but some general principles apply. The three principles of elective calvarial surgery are as follows:

1. To prevent progression of the abnormality,
2. To correct the abnormality,
3. To reduce the risk of raised pressure that could occur if surgery is not performed.

Calvarial surgery addresses the fused suture and the restricted calvarial components, together with areas of compensatory overgrowth. Not all three problems are tackled directly by the various surgical techniques, with some techniques resorting to adjunctive therapies, such as helmet remodeling (not performed in the UK). Furthermore, the actual surgery varies between units but the broad categories of treatment are listed below:

Surgery for sagittal synostosis

Extended strip craniectomies

Performed in the first few months of life, this technique comprises excision of the fused suture and limited expansion of adjacent bone. It relies on early, rapid brain growth to drive calvarial remodeling but does not address all aspects of the compensatory calvarial deformity. Critical analyses of isolated strip craniectomies suggest a high restenosis rate and relatively poor resolution of the cephalic index (ratio of the maximum width of the head multiplied by 100 divided by its maximum length) with only 29% returning to normal. This is in comparison with cranial vault remodeling at 66% (2). Few units use sagittal strip craniectomies in isolation (3).

Spring-assisted cranioplasty

The second major form of surgery in sagittal synostosis is spring-assisted cranioplasty. This was developed in the last decade in the quest for more conservative surgery in craniosynostosis (4). This entails performing a sagittal strip craniectomy and placing two springs across the osteotomy defect to gradually separate the biparietal narrowing. The springs are removed under general anesthesia after 6 months. Retrospective

analyses have shown favorable morphological results in sagittal synostosis, but less positive results than with calvarial remodeling procedures. Although the perceived advantages include reduced blood loss and shorter operative time and hospital stay, the technique of spring-assisted cranioplasty has yet to gain universal acceptance (5–7).

Total calvarial remodeling

The mainstay of corrective surgery in sagittal synostosis is cranial vault remodeling. This technique addresses not only the fused suture, but also the compensatory calvarial deformities directly. Meticulous surgical technique is vital during this procedure, because of the location of the sagittal venous sinus.

Frontal orbital advancement and remodeling

Frontal orbital advancement and remodeling (FOAR) can be used to remodel the abnormal frontal bone and also advance the supraorbital rims. Advancement and remodeling of the supraorbital bar corrects the superior orbital rim recession and helps to protect the eyes in severe cases of exorbitism (Figure 2).

This technique is fundamental to the surgical correction of metopic and coronal synostosis.

Posterior expansion and remodeling

In cases of severe progressive turricephaly (secondary to bicoronal synostosis) and raised ICP, releasing the

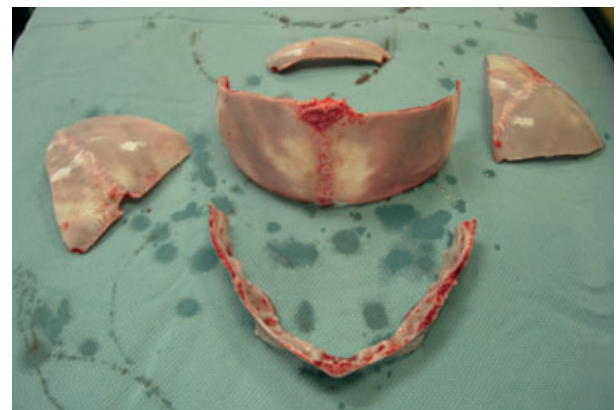


Figure 2 Frontal orbital advancement and remodelling. This shows the supraorbital bar, fused metopic suture and the right and left sides of the trigonocephalic forehead, during an Frontal orbital advancement and remodeling (FOAR) procedure performed on a child with metopic synostosis. The large freestanding panel of bone in the centre of the photograph has been removed from the vertex of the skull and will be remodelled along with the supraorbital bar to make a new forehead.

posterior aspect of the calvarium has gained popularity recently. The released bone is frequently distracted using distractors or springs.

Midface advancement (Le Fort III and monobloc procedures)

One key feature of syndromic synostoses is the additional midfacial hypoplasia. This can be addressed at the time of cranial vault surgery with a monobloc advancement of the frontal bone, supraorbital bar, and midface, or staged at a later date by Le Fort III advancement. In midfacial advancement surgery in children, it is our unit's practice to perform a tracheostomy 2 weeks prior to the midfacial surgery if a rigid external device (RED) frame is planned. The presence of a RED frame (Figure 3) makes conventional laryngoscopy impossible in the event of an airway crisis, although the vertical bar can be removed and the use of a laryngeal mask has been described (8).

Preoperative anesthetic issues of craniofacial synostosis

Airway

A thorough assessment of the airway is necessary to enable careful planning of the anesthetic technique for



Figure 3 Rigid external device (RED) frame. Anterior posterior view of child with Crouzon syndrome, midway through distraction following a monobloc procedure.

craniofacial surgery. In some cases, a previous episode of anesthesia, such as anesthesia for radiological imaging, will provide valuable information about airway management and venous access. The syndromes associated with craniofacial synostosis, such as Apert and Crouzon syndrome, are known to present airway problems. In Apert syndrome, midface hypoplasia and proptosis can make face mask ventilation difficult (9). Small nares and a degree of choanal stenosis cause high resistance to airflow through the nasal route, so these patients are obligate mouth breathers (10). Thus, face mask ventilation with a closed mouth can be challenging but simple airway maneuvers, adjuncts such as an oropharyngeal airway (OPA) or nasopharyngeal airway (NPA) and continuous positive airway pressure (CPAP) are usually effective in relieving the obstruction. A significant proportion of children with Apert syndrome also have fused cervical vertebrae (11). However, intubation via direct laryngoscopy is successful in the majority of cases (12). An important caveat to this is children who have undergone frontofacial advancement. In these patients, intubation may be more difficult as a result of the altered relationships between the maxilla and mandible and reduced temporomandibular joint movement (8).

Owing to the nature of the surgery and the relative inaccessibility of the airway, it is essential to ensure that the endotracheal tube will not be subjected to kinking or compression (for example by use of a reinforced endotracheal tube) and most importantly that it is secured to prevent accidental dislodgement resulting in either endobronchial intubation or accidental extubation. The type of endotracheal tube inserted will vary with different institutions and the nature of the surgery. The options include an oral or nasal intubation, with either a standard or reinforced endotracheal tube. A south-facing Ring-Adair-Elwyn tube can be used successfully for FOAR and nasal cuffed tubes for total calvarial surgery (the issue of cuff displacement exists). Methods to secure the endotracheal tube include adhesive tape, sutures, and wiring.

Respiratory system

A recent study showed respiratory complications in 6.1% of patients with Apert syndrome (13). A history of recent upper respiratory tract infection is a risk factor for intraoperative respiratory complications. Wheezing is the most common respiratory complication, and in some cases, this is sufficiently severe to result in abandonment of the operation. One proposed mechanism for the occurrence of wheeze in this patient group is the lower airway compromise caused by stiff

or vertically fused tracheal rings and the accumulation of secretions which results in monophonic wheezing. This may respond to treatment with tracheal suctioning, deepening of anesthesia and bronchodilator therapy.

Obstructive sleep apnea

Almost 50% of patients with Apert, Crouzon, or Pfeiffer syndromes develop OSA (14) (Figure 4). The obstruction can occur at various levels but midface hypoplasia, causing a distortion in the nasopharyngeal anatomy, is a common feature (15). A timely intervention, such as insertion of a nasopharyngeal airway (NPA), may be indicated early in infancy, and such airways have an established role in the management of upper airway obstruction in these children (16). In a proportion of cases, patients require CPAP. These children are often scheduled for a tracheostomy 1–2 weeks prior to their definitive craniofacial surgery. This allows time for a tract to become established and the tracheostomy ensures a smoother intraoperative and postoperative course. There is debate about the role and indications for tracheostomy in these children with upper airway obstruction, with some centers advocat-

ing insertion of a tracheostomy relatively early on in life and others favoring more conservative management, such as use of an NPA and CPAP. In children with upper airway obstruction without a tracheostomy, the induction of anesthesia can be an eventful period, with possible airway obstruction occurring during induction. Hence, a thorough plan for the management of the airway in these children needs to be determined. In the majority of cases, simple maneuvers such as jaw thrust and insertion of either an oral or nasopharyngeal airway will be sufficient.

In addition to the upper airway obstruction that occurs under anesthesia, it is important to consider the effect of chronic upper airway obstruction on the cardiovascular system and the central nervous system. During sleep, the respiratory obstruction that can develop in children with complex craniosynostosis forms part of a vicious cycle with ICP and cerebral perfusion pressure (CPP). During the active phases of sleep, research has shown that there is an increase in ICP and a subsequent decrease in CPP. These changes have a temporal relationship with upper airway obstruction (17). Recurrent episodes of intermittent reduction in CPP have a negative effect on neurological and cognitive development in the long term.

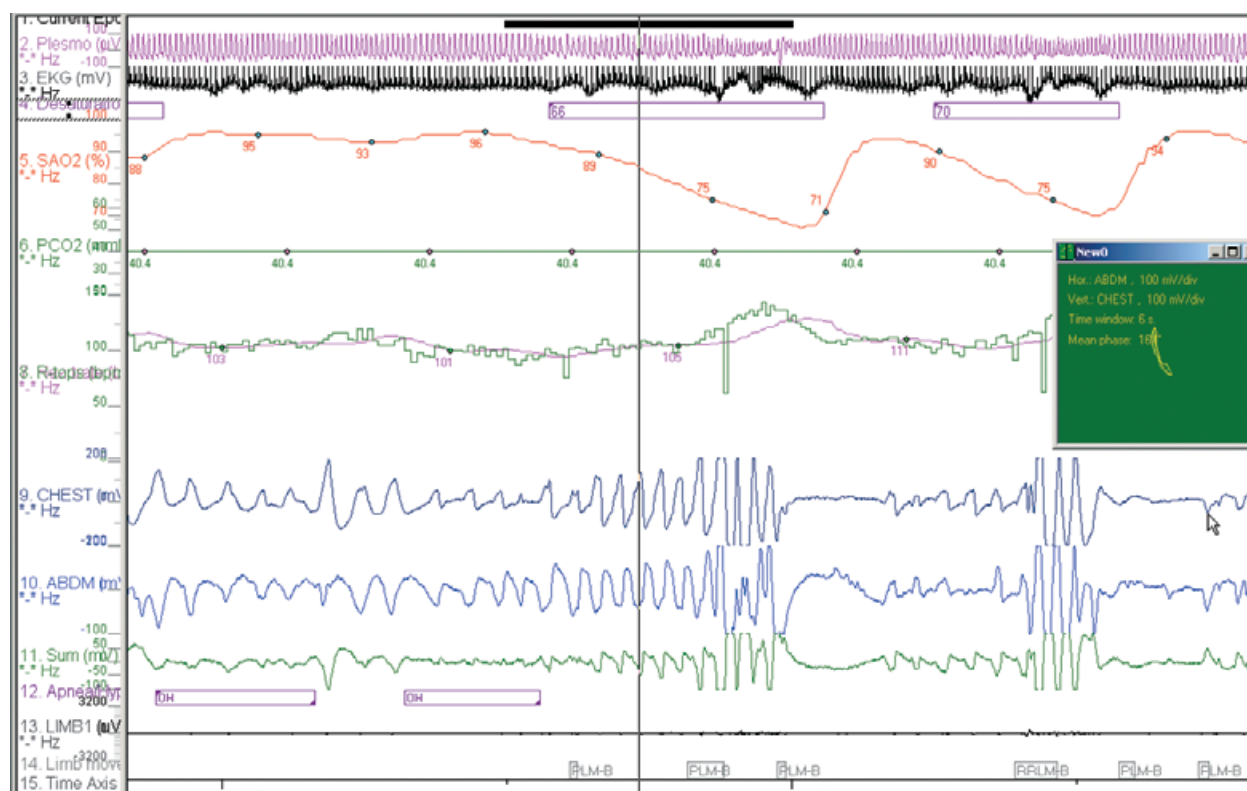


Figure 4 Polysomnograph of child with Crouzon syndrome with severe midface hypoplasia and symptoms of sleep apnea. Shows marked desaturations.

Induction and maintenance of anesthesia

The method of induction of anesthesia is likely to depend upon the individual anesthetist's experience and, to an extent, where applicable, patient and parental preference. The general pro-con debate that exists around intravenous vs gaseous induction in pediatric patients applies to this patient group, such as distress caused by holding a mask over the face and discomfort with intravenous cannulation (18). Specific issues that should be considered in this patient group include the possibility that intravenous access may be difficult in this age-group in general (fat on the dorsum of the hand), in particular in syndromic children, so a gaseous induction may be preferred to optimize conditions for securing intravenous access. The risk of airway issues exist at all inductions of anesthesia, but this risk may be increased with syndromic craniosynostosis, in particular, the risk of upper airway obstruction. For this reason, a gaseous induction with maintenance of spontaneous ventilation is often performed to minimize the risk of sudden loss of airway. An OPA may be needed to improve the quality of the airway. In our experience, it is commonplace to perform an inhalational induction with sevoflurane, ideally with two anesthetists present so that venous access can be obtained swiftly after induction. In certain situations securing intravenous access before, a gaseous induction may be prudent.

Maintenance of anesthesia is likely to be with a volatile agent and oxygen/air mixture [nitrous oxide is discontinued owing to venous air embolism (VAE) risks]. A bolus of fentanyl ($10\text{--}15\text{ }\mu\text{g}\cdot\text{kg}^{-1}$) and a nondepolarizing muscle relaxant is usually administered at the beginning of surgery (some units favor infusions of muscle relaxant) and then, toward the end of surgery, a combination of morphine, intravenous paracetamol, and antiemetics are administered. Other institutions use infusions of remifentanyl perioperatively. Pietrini compared remifentanyl and sevoflurane with remifentanyl and isoflurane in children undergoing surgery for synostosis. He found no difference in hemodynamic parameters and recovery time (19).

Temperature regulation

It is important to commence warm air devices immediately, since induction and line placement can take a long time. Fluid warmers should be used throughout the surgery.

Positioning

Careful positioning is required for optimal surgical access during craniosynostosis surgery and to minimize

the risk of complications. Patients may be supine, prone or in a modified prone position. The modified prone position has also been called the 'sphinx position', as the patient is positioned prone with their head and neck extended so that the chin rests on a support. In a modified prone position (sphinx), hyperextension of the neck may result in spinal cord injury (Figure 5) (20).

Attention must be paid to ensure no direct pressure on the neck, thus minimizing venous pressure and therefore avoiding the potential for both elevated ICP and venous bleeding. Postoperative airway problems may result from macroglossia, secondary to neck flexion compromising venous and lymphatic drainage.

A further method employed to reduce venous bleeding is positioning the patient in a horizontal position (i.e., neutral or no tilt on table) This position represents a balance between control of venous bleeding associated with a head-down position, and the risk of VAE associated with the head-up position (21).

The potential for prolonged duration of surgery necessitates attention to areas at risk of neurovascular compromise caused by prolonged pressure effects. This includes ensuring adequate padding over invasive lines or monitoring leads in direct contact with the skin.

Orbital injury can occur in surgery for both syndromic and nonsyndromic craniosynostosis. Corneal abrasions and irritation from cleaning solutions can be



Figure 5 Sphinx position Lateral view of boy in sphinx position at the end of a total calvarial remodelling procedure for sagittal synostosis. Note the soft horseshoe ring to limit risk of facial pressure sores. Manual headlifts are performed for 15 s every 15 min to relieve pressure areas. It is important to avoid excessive extension of the neck and pressure on the orbits.

minimized by topical lubricant, such as Lacrilube®, and temporary tarsorrhaphy. In children with syndromic synostosis, the orbits are at increased risk because of the associated proptosis. Another mechanism for ophthalmic injury is by direct orbital pressure; such pressure may result in damage to the optic nerve and retinal ischemia resulting in postoperative blindness. An acute presentation of direct orbital pressure occurring during surgery may be a vagally mediated bradycardia, most likely seen in FOAR surgery. With the prone position, the head is placed in a padded support or horseshoe, and the orbits are meticulously checked before commencing surgery. Head lifts are also performed every 15 min. The effects of prone positioning on thoracic compliance are well described (22).

Monitoring

Craniofacial surgery may be associated with sudden cardiovascular changes and rapid blood loss. A central venous catheter and arterial line are mandatory (our preference is to place femoral lines – other institutions favor internal jugular lines). Central venous readings can be unreliable but trends are extremely useful. The arterial line provides essential monitoring of blood pressure and frequent blood sampling. Most centers use end-tidal capnography for detection of VAE.

Neuroanesthesia

Children with craniosynostosis (both syndromic and nonsyndromic) may have raised ICP. Normal reference values for ICP and CPP in children have not been studied. However, an ICP of < 10 mmHg in children is considered normal (23,24). It is generally accepted that an ICP of > 15 mmHg is defined as intracranial hypertension. Many children with complex craniosynostosis will have had ICP monitoring to assist with decisions regarding operative intervention. In cases of raised ICP, giving consideration to CPP at induction and maintenance of anesthesia until craniectomy is performed is necessary. Normal CPP varies with age, and in the absence of published data, consensus opinion describes

a CPP of 40–50 mmHg in infants and small children (23). Accordingly, the anesthetist should attempt to minimize factors that increase ICP, such as hypercapnia and hypoxia, and factors that increase venous pressure, such as the patient's position and coughing.

Venous air embolism is a known complication during surgery for craniosynostosis surgery. Faberowski *et al.* (21) found the incidence of VAE during craniectomy for craniosynostosis to be 82.6%, as detected by precordial Doppler. The median number of VAE events that occurred in this study group was two (range, 0–8). Interestingly, they found that the majority of these episodes were not associated with hemodynamic compromise. Of the episodes of detected VAE, 48.4% had Doppler changes alone. In addition to the Doppler changes, 36% were associated with end-tidal carbon dioxide changes and only 15.6% with hypotension. None suffered cardiovascular collapse. This apparently high incidence of VAE in infants may be due to rapid blood loss causing a decrease in CVP and so the development of a pressure gradient between the right atrium and surgical site favoring the entrainment of air. This means that an episode of hypotension precipitated by blood loss can be immediately followed by a VAE, and so there is potential for the diagnosis of VAE to be missed, and a failure to treat appropriately, such as flooding the surgical field and lowering the head position. The consequences of VAE include hypotension, cardiovascular collapse, and in the presence of a patent foramen ovale (which is present in 50% of children under 5 years old), (25) paradoxical air embolism with neurological sequelae.

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Conflicts of interest

No conflicts of interest declared.

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