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**Review Article**

# Evaluation, treatment, complications, and prognosis of craniosynostosis

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## ABSTRACT

Craniosynostosis is a congenital craniofacial anomaly that typically presents at birth and affects the skull's shape. It is characterized by the premature fusion of one or more cranial sutures in infants, which can impair brain development and function. While craniosynostosis is considered rare, it has a global prevalence of around three to six cases in 10,000 live births. This review article aims to synthesize the latest developments in diagnostic techniques, treatment strategies, and potential complications for the benefit of healthcare providers, researchers, and affected families. This review commenced on 31 October 2023, following a thorough examination of existing literature. Diverse databases, including PubMed, Web of Science, and Cochrane, were utilized for the literature review. Early diagnosis and evaluation involve a multidisciplinary approach, including clinical assessments, medical history reviews, and advanced imaging techniques like computed tomography (CT) scans and magnetic resonance imaging (MRI). Surgical intervention is the primary treatment option, with the goal of releasing or reshaping the fused sutures to allow for normal skull growth. While open surgical procedures like suturectomy have been prevalent, less invasive methods like minimally invasive endoscopic strip craniectomy are becoming more popular due to reduced complications. Untreated craniosynostosis can lead to complications such as increased intracranial pressure, developmental delays, vision and hearing problems, and psychosocial impacts, emphasizing the importance of timely intervention. However, surgical treatments carry their own risks, necessitating a well-planned and individualized approach. Overall, the prognosis for craniosynostosis is generally positive, and factors such as the specific type of craniosynostosis, the timing of treatment, and the quality of post-operative care all influence outcomes. Prenatal diagnosis and multidisciplinary care have emerged as valuable tools for improving prognosis.

**Keywords:** Craniosynostosis, Evaluation, Treatment, Surgical, Syndromic, Non-syndromic, Complications, Prognosis

## INTRODUCTION

Craniosynostosis is a craniofacial anomaly that usually presents at the time of birth and affects the shape of the skull. This medical condition is characterized by the premature fusion of one or more sutures in an infant's skull, resulting in impairment of brain development and function.[1] In addition to the brain function impairment, increased intracranial pressure (ICP) and respiratory dysfunctionality is also observed in the most severe cases.[2]

Craniosynostosis can be classified into various types based on which sutures are affected, and it may affect one or more sutures simultaneously. Premature fusion of a single suture, usually sagittal, is the most common occurrence, leading to a long and narrow shaping of the skull,[3] followed by coronal, metopic, and lambdoid sutures, illustrated in Figure 1. Complex craniosynostosis is present in individuals where fusion of multiple sutures is observed simultaneously.[3] Craniosynostosis can be divided into two major types based on its causes. Primary craniosynostosis usually occurs due to genetic factors during the developmental stage of embryogenesis.[4] However, secondary craniosynostosis is a result of mechanical stressors such as intrauterine compression of the fetal skull against the maternal pelvis, or metabolic causes like hyperthyroidism, and the effect of teratogens.[4] Another way to differentiate between types of craniosynostosis is based on their syndromic or non-syndromic presence. Syndromic craniosynostosis is generally associated with a few syndromes, such as Crouzon, Saethre-Chotzen, Apert, Pfeiffer, and Muenke syndromes.[5] These cases usually share characteristic syndromic features such as midface hypoplasia, limb anomalies, and exophthalmos.[5] On the contrary, non-syndromic synostosis is not associated with any of the syndromes and, hence, does not present with other morphological abnormalities of the face, trunk, or limbs.[6]

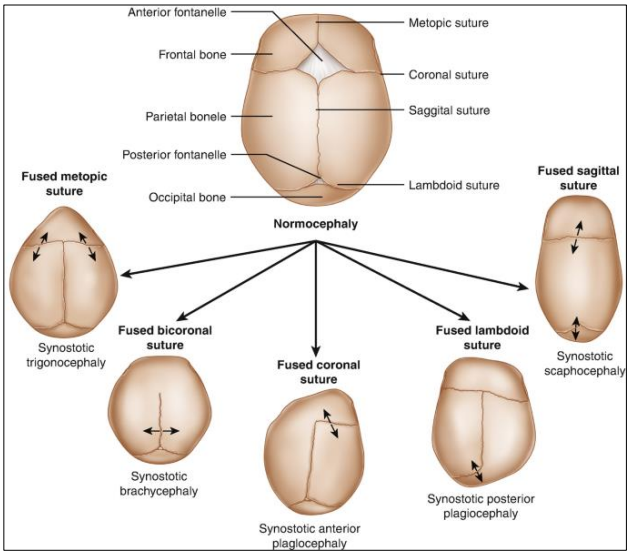


**Figure 1: Types of craniosynostosis.[36]**

The occurrence of craniosynostosis is reported to be rare, but the health implications and associated mortalities make it a significant concern. The global prevalence of craniosynostosis is reported to be around three to six cases in 10,000 live births.[4] In 2019, 84,665 children were born with craniosynostosis around the world, out of which 72,857 (86%) had non syndromic craniosynostosis.[7] A study from the Netherlands reported the prevalence of craniosynostosis to be approximately 7.2 cases per 10,000 live births.[8] Another study from Germany cited the prevalence as being around 4.8 cases per 10,000 live births.[9] An incidence of 5.5 cases per 10,000 live births was recorded in Norway, with an exclusive increase in the non-syndromic cohort, with a 2:1 predominance in the males as compared to the females in the region.[10] Similar prevalence figures were reported in multiple studies from the United States, with 1 case in 2100-2500 live births until 2003.[11,12] The rising cumulative prevalence was identified in both the Netherlands and the USA; however, no obvious cause was underlined in the literature.[8] Approximately 20% of the cases can be attributed to abnormalities in the chromosomes or specific single gene mutations.[3] The most common gene mutations that develop into syndromic craniosynostosis are found in the FGFR2, FGFR3, TWIST1, and EFNB1 gene sites.[3] Non-syndromic synostosis is also often found, with the most probable Pro250Arg mutation in the FGFR3 gene.[3] Usually, the gene inheritance pattern for craniosynostosis is autosomal dominant; however, new mutations were considered a possibility in almost 50% of the cases.[3,13,14] In addition to the chromosomal and gene mutations, environmental factors such as fetal head trauma or constraint, teratogens, antiepileptic drugs, and maternal smoking are also crucial and significant causal factors for craniosynostosis.[13,14] A higher prevalence was reported in Asian countries, especially in the Middle Eastern region. A study from Iran reported that the prevalence of craniosynostosis in Isfahan was estimated to be 16 cases per 10,000 live births.[15]

The study rationale for this review article on craniosynostosis stems from the need to provide a comprehensive assessment of the condition, covering its evaluation, treatment options, potential complications, and long-term prognosis. This review aims to summarize and critically analyze the current state of knowledge on craniosynostosis. It will explore the diagnostic methods and tools used for evaluating different types of craniosynostosis, including imaging techniques and clinical assessments. The article will also delve into the various treatment options available, such as surgical interventions and conservative approaches, and their comparative effectiveness and outcomes. Furthermore, the study will examine the potential complications associated with craniosynostosis, including the risk of increased intracranial pressure, developmental delays, and psychological impacts on patients and families. Finally, the review will assess the long-term prognosis for individuals with craniosynostosis, considering factors like neurocognitive development, quality of life, and the role of early intervention. Understanding the latest advancements in diagnostic techniques, treatment strategies, and potential complications is essential for healthcare providers, researchers, and families affected by craniosynostosis. By synthesizing this information, the review will provide a valuable resource to guide clinical practice and future research in the field.

## METHODS

The research, which began on 31 October 2023, was initiated following an extensive examination of existing

literature. Various databases, such as PubMed, Web of Science, and Cochrane, were employed to carry out this literature review. The search process encompassed the use of a wide array of medical terminology combinations. Additionally, manual searches on Google Scholar were performed to identify pertinent research terms. The primary goal of this literature review revolved around several critical areas, including types of craniosynostosis, evaluation methods, treatment approaches, potential complications, and the long-term effects on health and quality of life. Keywords pertaining to the prognosis of craniosynostosis in infants were also integrated into the search. It is worth noting that the selection of articles for inclusion in this study was guided by multiple criteria, ensuring a comprehensive and robust review process.

## DISCUSSION

Craniosynostosis is typically diagnosed shortly after birth, and treatment often involves surgical interventions to correct the fused sutures. Early diagnosis and intervention are essential in managing craniosynostosis, aiding in the prolonged prognosis of the disorder, as it can help prevent more severe complications and improve the child's long-term outcomes.

### *Evaluation of craniosynostosis*

The evaluation of craniosynostosis typically involves a comprehensive process to diagnose and understand the condition's specifics. The first step is often a clinical assessment conducted by a healthcare provider. They will examine the infant's head shape, looking for signs of abnormal skull growth. Features such as an unusual head shape, ridges along the sutures, or an asymmetric appearance may raise suspicion of craniosynostosis.[16] Moreover, a detailed medical history is essential to understand any risk factors or family history of craniosynostosis.[16] To confirm the diagnosis and assess the extent of craniosynostosis, medical imaging is usually employed.[17] A CT scan provides detailed images of the skull and allows for precise identification of fused sutures, proving to be an excellent diagnostic tool for craniosynostosis.[18] However, clinical features of craniosynostosis are evident, and hence, other imaging techniques such as ultrasounds and magnetic resonance imaging (MRI) can also be used for routine assessment.[19] MRI scans can offer additional information, particularly regarding the brain and intracranial structures.[20] Recent advances in medical imaging has highlighted that quantitative head shape analysis and 3D photography of the skull are precise and objective tools for the identification of skull abnormalities.[21] Similarly, 3D stereophotogrammetry is another tool that avoids the use of radiation and sedation and provides an accurate evaluation of craniosynostosis.[22] In some instances, genetic testing may be recommended, especially when there is a family history of craniosynostosis or when multiple sutures are affected.[23,24] Genetic testing can help identify specific genetic mutations associated with the condition. Moreover, consultations with specialists for both syndromic and non-syndromic craniosynostosis are crucial, to identify and manage associated issues. Pediatric craniofacial specialist, neurosurgeon, ophthalmologist, and psychologist evaluations have proven to be crucial in the management of craniosynostosis.[19] The evaluation process aims to confirm the diagnosis, determine the specific type of craniosynostosis, and assess the extent of cranial involvement. This information is critical for developing an appropriate treatment plan and ensuring the best possible outcomes for the child. Early diagnosis and intervention are essential to managing craniosynostosis effectively.

### *Treatment of craniosynostosis*

The treatment of craniosynostosis typically involves surgical intervention. The specific approach to treatment may vary depending on the type of craniosynostosis, the age of the child, and other individual factors. The primary treatment for craniosynostosis is surgery, which aims to release or reshape the fused sutures.[25] The goals of surgery are to allow for normal skull growth, improve head shape, and prevent potential complications associated with craniosynostosis. Removal of the fused suture, also known as suturectomy or strip craniotomy, has been the most typical surgical way forward for craniosynostosis for decades.[26] These open procedures are predominantly mechanical in nature and include the removal of bony structures, along with reshaping and remodeling of the skull. In addition to open surgical remodeling, spring directed skull growth has also been found to achieve the same purpose. Omega shaped springs are inserted into the space created during the strip craniectomy, which guides the skull into growing in a desired shape. These springs are then removed after 6-8 months through a second surgical operation.[27,28]. However, excessive blood loss and coagulopathy are the most common complications of open surgical management of craniosynostosis, and hence, less invasive treatment options should be preferred.[29] Minimally invasive endoscopic strip craniectomy (ESC) promotes the natural growth of the skull after the removal of the fused suture. As shown in Figure 2, the suture is accessed through a minimal incision and removed using endoscopic visualization.[29] Helmet therapy to redirect the skull growth is then applied, which allows the skull to grow in the traditional way.[29] In addition to these surgical interventions for remodeling the skull, distraction osteogenesis was also reported to be an effective skull remodeling technique for patients with craniosynostosis, having similar outcomes and cost-benefit ratio to craniectomies.[30] Stem cell regeneration has also been explored and found effective in animal studies, however, human interventions and effectiveness are not explored in the literature as of yet.[31] In some cases, mild craniosynostosis may not require surgery, and pharmacological management is also advised.[31] Treatment outcomes for craniosynostosis are generally favorable, especially when the condition is diagnosed and treated

early, however, the specific approach to treatment should be determined on a case-by-case basis.

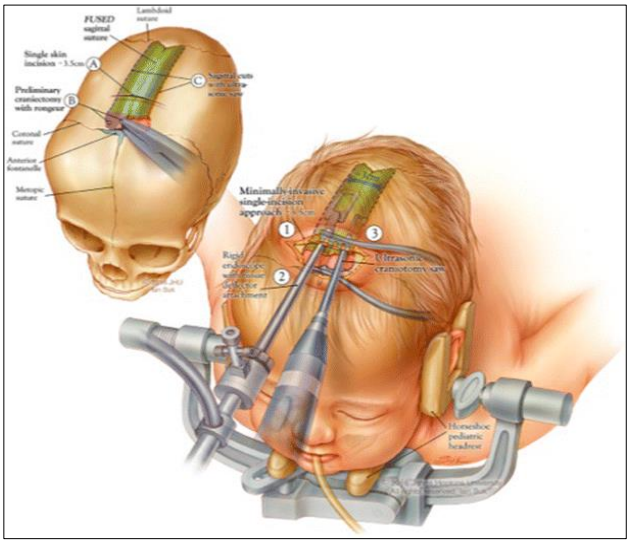

**Figure 2: Minimally invasive endoscopic strip craniectomy (ESC).[37]**

***Complications***

Craniosynostosis, if left untreated, can lead to various complications due to the premature fusion of cranial sutures. The fused sutures restrict the growth of the skull, which can lead to an increase in intracranial pressure. Elevated ICP may result in symptoms such as headaches, vomiting, irritability, and changes in behavior and in severe cases, it can lead to damage to the brain.[3] Children with increased intracranial pressure may experience developmental delays, including delays in speech, motor skills, and cognitive development. In addition to that, vision problems such as strabismus and exophthalmos, hearing loss, dental issues, feeding difficulties, and psychosocial impact may also create a negative advancement in the quality of life of the child.[11] While surgery is the primary treatment for craniosynostosis, it also carries some risks, including infection, bleeding, or the need for further surgical procedures if complications arise.[32] Surgical intervention between the ages of 7-12 months, and concurrent fronto-orbital repair were factors identified by the literature which are associated with surgical complications.[32] Several studies reported that complications from endoscopic surgical repair were distinctively lesser as compared to open repair craniectomies, given that the patient populations are appropriate according to age and morbidity status.[33] It is important to note that with early diagnosis and appropriate treatment, many of these complications can be prevented or minimized. Timely intervention by a multidisciplinary medical team, including pediatric neurosurgeons and craniofacial specialists, is crucial to addressing craniosynostosis and its potential complications effectively.

***Prognosis***

The prognosis of craniosynostosis can be quite favorable, especially when the condition is diagnosed early and treated appropriately. The outlook largely depends on several factors, including the type of craniosynostosis, the timing of treatment, the individual child's health, and the effectiveness of the surgical and post-operative care.[34] In order to identify and detect craniosynostosis at an early stage, prenatal diagnosis is difficult but essential, especially in such cases where cranial abnormalities are not clinically distinct.[35] Tools like abnormal head biometry and ventriculomegaly can be potential markers for cranial abnormalities in the prenatal period, aiding in early detection and management.[35]

On an average, the overall survival rate of children born with syndromic craniosynostosis was reported to be 79%, and 100% for those infants who had non-syndromic craniosynostosis.[35] The specific type of craniosynostosis also plays a role in the prognosis. For example, single-suture craniosynostosis, such as sagittal or metopic craniosynostosis, often has a better prognosis than complex cases involving multiple sutures.[6] Additionally, the timing of the surgery to repair craniosynostosis is also crucial. Early intervention can result in a more favorable head shape and a lower risk of developmental delays since the increased risk of surgical complications is also found to be associated with late age surgeries.[32]

Comprehensive post-operative care, routine physical therapy, long term follow-up, and psychosocial support are some adjunct factors which positively modify the prognosis of lengthy disorders such as craniosynostosis. In general, with appropriate care and early intervention, most children with craniosynostosis can achieve normal head shape and brain development. While individual experiences may vary, the prognosis for craniosynostosis is often very good, and children can go on to lead healthy, fulfilling lives.

## CONCLUSION

The evaluation of craniosynostosis involves a multidisciplinary approach, combining clinical assessment, medical history, and advanced imaging techniques such as CT scans and MRI. Genetic testing may also be considered, particularly in cases with a family history or multiple affected sutures. Consultations with specialists, including pediatric craniofacial surgeons, neurosurgeons, and other experts, play a crucial role in understanding the condition and planning appropriate treatment strategies. Surgical intervention remains the primary treatment option, aiming to release or reshape the fused sutures to allow for normal skull growth.

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