






Prognostic and post-surgical updates in the treatment of non-syndromic craniosynostosis: A systematic review

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Introduction: Craniosynostosis represents a rare congenital condition characterized by the premature fusion of one or more cranial sutures. The majority of cases of this disorder are non-syndromic in nature. Objective: This study aims to conduct an analysis and comparison of available surgical techniques, evaluating their respective postoperative outcomes in the treatment of non-syndromic craniosynostosis. The focus lies on assessing functional, aesthetic, and neurological outcomes.

Methods: A systematic review was undertaken, encompassing the search for clinical trials (including randomized trials), systematic reviews, and meta-analyses available online in both Portuguese and English languages. The search terms "prognosis" and "non-syndromic craniosynostosis" were utilized along with the boolean operator "AND". Articles published between 2018 and 2023 were filtered through the Virtual Health Library (VHL) and PubMed platforms, specifically targeting studies presenting prognostic data related to craniosynostosis in pediatric patients up to 12 months of age.

Results: The most favorable prognostic outcomes identified in this investigation were associated with conventional cranioplasty and minimally invasive endoscopic craniectomy techniques. Notably, conventional cranioplasty demonstrated superior intellectual outcomes among patients undergoing this procedure, with an average intelligence quotient of 111.7 ± 13 and academic performance aligning closely with national averages across various domains. Conversely, minimally invasive endoscopic craniectomy exhibited low rates of blood transfusion, complications, and reoperations. **Conclusion:** The findings underscore the superior cognitive prognosis associated with conventional cranioplasty, positioning it as a highly applicable surgical option for addressing craniosynostosis, supported by robust evidence.

Keywords: Non-syndromic, Craniosynostosis, Neurosurgery, Prognosis, Pediatrics

INTRODUCTION

It is estimated that craniosynostosis affects between 1 in every 2,000-2,500 births worldwide, according to 2019 data, with a global total estimated at 84,665 cases, of which approximately 72,857 are classified as non-syndromic. Craniosynostosis is a rare congenital condition characterized by the premature fusion of one or more cranial sutures during fetal development, which can result in issues that persist even after surgical correction, potentially leading to problems with attention, language, information processing, and visuospatial skills [1,2,3].

The early fusion of cranial sutures limits growth perpendicular to the affected suture, leading to cranial deformities and possible specific neurological complications depending on the type of fusion. Among the types of non-syndromic conditions are scaphocephaly, trigonocephaly, brachycephaly, oxycephaly, and plagiocephaly [4,5].

Diagnosis of craniosynostosis is made clinically by examining the shape of the head for asymmetries, and cranial tomography is essential for diagnosis and surgical planning. Once non-syndromic craniosynostosis is confirmed, the indicated treatment is corrective surgical intervention, which aims to correct the deformity resulting from altered growth patterns. Surgical treatment, preferably performed before the age of 1 year, aims to normalize the shape of the skull and prevent intracranial hypertension [5,6].

Our main objective is to investigate and analyze the prognoses associated with non-syndromic craniosynostosis, exploring the clinical and functional outcomes, exposing the current therapeutic interventions available, and the expected results in light of the quality of life perspectives of these patients.



MATERIALS AND METHODS/CASE REPORT /HOW I DO / TECHNICAL NOTE

This study is a systematic review aiming to gather current data on the prognosis of non-syndromic craniosynostosis in children, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) method. The stages post-diagnosis and post-neurosurgical treatment available for this purpose were analyzed. Samples were collected through research in the Virtual Health Library (VHL) and PubMed databases using the terms "prognosis" and "non-syndromic craniosynostosis" with the Boolean operator "AND". The study design is represented in Figure 1.

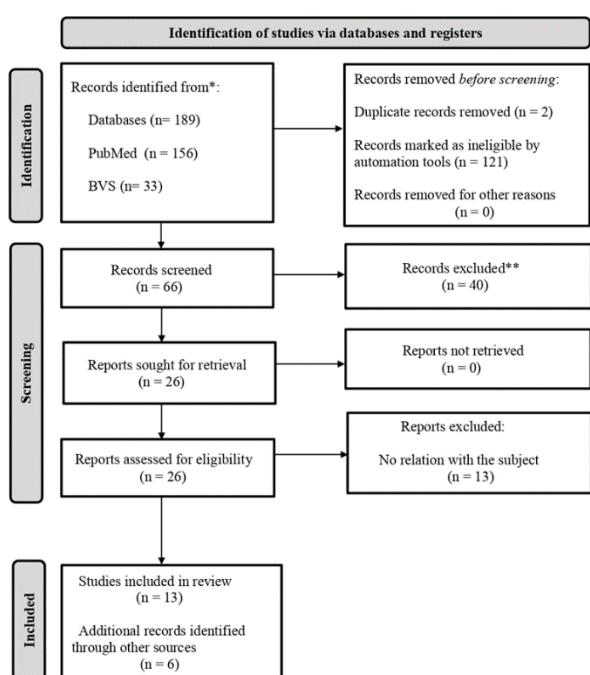


Figure 1- PRISMA flowchart; representative of the criteria for identification, screening, eligibility, and inclusion and exclusion of the systematic review.

Newborns and children up to 12 months of age with non-syndromic craniosynostosis of various types, aiming to evaluate the collected data from pediatric patients post-diagnosis or those who underwent pediatric neurosurgical intervention. There were no limitations based on gender, socioeconomic status, country, or race.

The scientific studies included consisted of clinical trials (including randomized trials), systematic reviews, and meta-analyses available online in full text in Portuguese and English, published between 2018 and 2023, presenting prognoses of craniosynostosis in pediatric patients. Excluded were integrative reviews, descriptive reviews, studies published before 2018, studies in languages other than those specified in the inclusion criteria, studies addressing

syndromic craniosynostosis, and studies involving patients older than 1 year.

RESULTS

Through a literature review, 19 articles were selected, of which 13 provided important results regarding the prognostic updates of non-syndromic craniosynostoses after surgical treatment. The studies utilized included Retrospective, Randomized, Retrospective Observational, Retrospective Cohort, and Case-Control studies. Analyses were conducted by comparing the advantages and disadvantages of the available surgical types for resolving the following categories of craniosynostoses: trigonocephaly, scaphocephaly, oxycephaly, plagiocephaly, and brachycephaly. The sample of patients undergoing various treatments, their types, and outcomes are listed in Table 1 for qualitative analysis. The majority of patients included were children up to 1 year of age.

DISCUSSION

Based on the results, it was observed that the post-surgical prognosis varies depending on the type of craniosynostosis and the type of surgical correction aimed at the cranial vault deformities. This topic generates discussion regarding post-surgical prognoses and complications of the available and current surgical techniques, thus warranting discussion and analysis based on the main scientific evidence.

In two studies, Akai, Takuya et al. 2022 and Gabrick, Kyle S et al. 2020, better prognoses were observed following conventional cranioplasty, which involves remodeling the cranial vault. Patients undergoing this technique showed better cognitive development but with limitations in motor and intellectual functions. Gabrick, Kyle S et al. 2020 demonstrated that patients with metopic craniosynostosis could achieve academic performance scores close to the national average. However, data analysis showed that patients with severe trigonocephaly had significantly lower word-reading performance scores. In the study by Akai Takuya et al. 2022, it was noted that a child with motor delay associated with trigonocephaly and another child with mental delay related to scaphocephaly, both in the non-syndromic group, recovered satisfactory cognitive performance after surgery. Regarding clinical prognosis, Patel, Viren et al. 2020 highlighted in their results the frequent need for blood transfusion in the postoperative period for patients undergoing cranioplasty, as they showed lower hemoglobin values on the first postoperative day (Hgb on POD1) and hemodynamic and neurological decompensation postoperatively [9,13,14].

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Table 1 – Sample of patients undergoing various treatments, their types, and outcome

Author (year)	Study Type	Sample	Type	Type of surgery	Post-surgical results
Abdel-Alim T, et al, 2023 ⁷	Retrospective Study	This study involved 408 patients born between 1991 and 2019, diagnosed with non-syndromic sagittal synostosis and undergoing specific surgical procedures (FBR, ESC, or SAC).	CE	Frontoparietal remodeling (FBR), extended craniotomy (ESC), spring-assisted correction (SAC) – based on three-dimensional (3D) photogrammetry.	The FBR surgery showed more extensive blood loss compared to ESC and SAC. Fifteen patients (five FBR, eight ESC, two SAC) underwent reintervention due to increased intracranial pressure (IICP), skull defect, hematoma, or persistent scaphocephalic head shape.
Agushi R, et al, 2023 ⁸	Retrospective Study	Clinical data from 62 consecutive pediatric patients (ages 3 to 8 months) were obtained from the "Anna Meyer" Children's Hospital database for the period between 2011 and 2022.	CT	Endoscope-assisted craniectomy	92% of the cases had good to excellent surgical outcomes. However, four cases were unsatisfactory, including one with a CSF collection needing repair after two months and another with a wound infection requiring a second surgery.
Akai T, et al, 2022 ⁹	Retrospective Study	The study assessed the long-term prognosis of 51 patients who underwent reconstructive surgery between 1982 and 2015.	CT CE OC PC BC	Conventional reconstructive cranioplasty	At the final follow-up, intellectual outcomes were evaluated. Among 51 patients, 49.0% experienced developmental delay, with no significant difference between syndromic and non-syndromic groups. In non-syndromic patients, those with developmental delay underwent surgery at a significantly later age compared to those without delay ($p = 0.0372$).
Leahthan F, et al, 2019 ¹⁰	Retrospective Study	Preoperative and one-year postoperative computed tomography scans of patients with isolated nonsyndromic unicoronal synostosis treated from 2007 to 2012 at two academic institutions were analyzed.	PC	Endoscopic suturectomy with postoperative helmet therapy	Regression analysis revealed that the type of treatment did not impact the change in pre- and postoperative depth asymmetry. In all patients preoperatively, the synostotic depth was less than the nonsynostotic depth. Postoperatively, two patients from each treatment group exhibited overcorrection (16.7% and 8.7% of patients for advancement and suturectomy, respectively, $P = 0.43$).
Hwang, JH, et al, 2021 ¹¹	Retrospective Study	Among 316 patients with craniosynostosis, 263 (83.2%) were non-syndromic individuals who underwent surgery at the Seoul National University Children's Hospital from 2010 to 2018.	PC CT	Postoperative helmet suturectomy	No signs of increased intracranial pressure or developmental delay were observed. Maximum bleeding was 200 cc, with an average operation time of 140 minutes. No patient required postoperative ICU care, and all were discharged within 4-5 days without complications. Follow-up ranged from

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					12 to 62 months, with helmet use for 6-13 months, determined by aesthetic improvement and patient adherence.
Ha AY, et al, 2020 ¹²	Retrospective Case Control Study	Fifteen patients who underwent endoscopic repair and sixteen patients who underwent open repair between 2006 and 2014 met the inclusion criteria.	CT	Endoscopic craniectomy with postoperative helmet	The endoscopic group, compared to the control group, was significantly younger during surgery (3.3 ± 1.3 months versus 10.4 ± 3.5 months; $P < 0.001$). Additionally, they had shorter operating room time (65 ± 18 minutes versus 389 ± 49 minutes; $P < 0.001$), lower estimated blood loss (52 ± 44 mL versus 378 ± 215 mL; $P < 0.001$), and a reduced need for blood transfusions (7% versus 94%; $P < 0.001$).
Gabrick KS, et al, 2020 ¹³	Randomized study	19 patients who underwent frontoorbital advancement completed a battery of neurodevelopmental assessments evaluating intelligence quotient normalized for age, academic performance, and visuospatial integration.	CT	Conventional cranioplasty	Patients with severe metopic craniosynostosis showed significantly lower performance scores in word reading (95.3 vs. 116 ; $p = 0.039$) and composite reading (98.3 vs. 111.5 ; $p = 0.027$) compared to the moderate group. There was no significant difference between the groups in reading comprehension (101.3 vs. 105.0 ; $p = 0.226$), numerical operations (96.7 vs. 112.3 ; $p = 0.095$), and spelling (90.2 vs. 113.7 ; $p = 0.141$).
Patel V, et al, 2020 ¹⁴	Retrospective cohort	A total of 65 (61.3%) patients underwent spring-mediated cranioplasty and 41 (38.7%) underwent cranial vault remodeling during the period from 2011 to 2018 at a children's hospital in Philadelphia.	CE	Cranial vault remodeling (Conventional cranioplasty) Spring-mediated cranioplasty	Patients undergoing spring-mediated cranioplasty who required postoperative transfusions had greater reductions in preoperative to postoperative Hgb levels (4.1 versus 0.35 g/dL, $P < 0.0004$). Patients undergoing cranial vault remodeling who required postoperative transfusions had lower POD1 Hgb values compared to patients who did not require transfusions (6.6 versus 9.3 g/dL, $P < 0.0002$).
Vaca EE, et al, 2020 ¹⁵	Retrospective Case Control Study	Sixty-six patients underwent surgical treatment for craniosynostosis during the study period.	PC	Conventional cranioplasty Suturectomy with barrel screw fixation	In the univariate analysis, suturectomy with barrel screw fixation ($p < 0.01$) was significantly associated with secondary suture fusion. Postoperative variables included surgical site infection, central nervous system infection, cerebrospinal fluid leakage, duration of last follow-up from initial surgery, cranial index observed at one year or more of follow-up, in the presence or absence of increased intracranial pressure.
Klausin A, et al, 2020 ¹⁶	Prospective Study	Eighty children underwent surgery for nonsyndromic craniosynostosis (trigonocephaly, $n = 30$; plagiocephaly, $n = 10$; scaphocephaly, $n = 38$; brachycephaly, $n = 2$) and were followed up at 3, 6, 12,	CT CE PC BC	Cranioplasty and modulation of frontoorbital advancement (FOA)	Cranioplasty in patients with scaphocephaly resulted in a significant enlargement of both anterior (73.9 ± 3.5 mm) and posterior (132.2 ± 5.2 mm) cranial widths, with no difference compared to the normal population after 1 year. There was improvement in the frontal angle for trigonocephaly correction ($145.9 \pm 3.7^\circ$).

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Riordan CP, et al, 2020 ¹⁷	Retrospective Cohort	Single-center cohort analysis of 500 consecutive babies with craniosynostosis treated by endoscopic suturectomy over a period of 14 years.	CT CE PC BC	Minimally Invasive Endoscopic Craniectomy (ESC)	Was associated with low rates of blood transfusion (6.6%), complications (1.4%), and reoperations (3.0%). Risk factors for transfusion included syndromic craniosynostosis (P = 0.01) and multiple fused sutures (P = 0.02). The median surgical time was 47 minutes, and the hospital length of stay was 1 day. Transfusion and reoperation rates were higher among syndromic patients (both P < 0.001).
ChandlerL, et al, 2020 ¹⁸	Cohort Study	Thirty-six patients with RCV and 39 patients with SAS were evaluated.	CE	Spring-Assisted Strip Craniectomy Cranial Remodeling: Long-Term	There were no statistically significant differences between the RCV and SAS groups (P > 0.05) in any of the BRIEF functional areas. In the BASC-2, only one significant difference was found: the RCV group had fewer symptoms of social withdrawal (47.00 ± 10.27) compared to the SAS group (54.64 ± 10.96), F = 6.79, P = 0.012, Cohen d = 0.688. Both means remained within normal limits.
Runyan CM, et al. 2020 ¹⁹	Retrospective Study	Medical records of 101 patients with isolated sagittal craniosynostosis undergoing sagittal suturectomy were analyzed to compare perioperative outcomes between 2005 and 2018.	CE	Spring-assisted surgery (SAS) Endoscopic surgery	Pre- and postoperative cephalic indices remained unchanged in both groups. However, the placement of springs through a minimally invasive approach required a longer surgical time compared to the open approach, with a mean of 65 minutes versus 53 minutes (P < 0.0001). Conversely, the surgical time for spring removal showed no significant differences, with a mean of 31 minutes in the minimally invasive group versus 29 minutes in the open approach group (P = 0.48).

Legend: CE: Scaphocephaly; CT: Trigenocephaly; PC: Plagiocephaly; BC: Brachiocephaly; OC: Oxycephaly

According to the authors Abdel-Alim Tareq, et al. 2023 and Runyan, Christopher M et al. 2020, spring-mediated cranioplasty is frequently used for isolated sagittal synostosis but has higher incidences of postoperative blood loss and requires longer surgical times for spring insertion. Similarly, frontoparietal remodeling has the same drawbacks but presents even less favorable prognostic conditions compared to spring-mediated cranioplasty, as frontoparietal remodeling involves higher rates of hemorrhage and longer surgical times, in addition to being associated with a prevalence of dural defects. This loss was also observed in the studies by Chandler, Ludmila et al. 2020 and Patel, Viren et al. 2020, which found that patients undergoing spring-mediated cranioplasty who required postoperative transfusions had greater reductions in preoperative to postoperative Hgb compared to conventional cranioplasty, with no issues in cognitive or psychological development [7,14,18,19].

The effects of cranioplasty and frontoorbital advancement (FOA) modulation on different cranial

deformities revealed distinct results according to Klausung, Anne et al. 2020. Notably, patients with scaphocephaly had a significant increase in cranial width, matching the normal population. Conversely, those with trigonocephaly showed improvements in the frontal angle, while those affected by plagiocephaly showed a tendency to recurrence, although with no statistical difference from the normal population. Brachycephalic patients continued to have below-standard cranial volume six months post-procedure. While cranioplasty and FOA modulation can be effective, the maintenance of results may vary depending on the specific type of cranial deformity [16].

As reported by Agushi, Rina et al. 2023 and Ha, Austin Y et al. 2020, endoscope-assisted craniectomy and minimally invasive endoscopic craniectomy demonstrate favorable outcomes in different contexts, especially advantageous in cases of trigonocephaly, with reduced postoperative complications, satisfactory correction of asymmetry, and faster recovery, resulting in lower morbidity in 92% of the cases considered, including one with cerebrospinal fluid

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(CSF) collection Consistently, Riordan, Coleman P et al. 2020 showed that minimally invasive endoscopic craniectomy also presents a good prognosis, characterized by normalization of cranial growth, low need for blood transfusion, reoperation, and other complications, being highly recommended for early correction of isolated sagittal craniosynostosis [8,17,19].

Leathan F. Domeshek et al. 2019 reported data on suturectomy combined with postoperative helmet therapy, observing reduced rates of increased intracranial pressure, hemorrhage, and developmental delay. However, results related to improvement in asymmetry were less significant, and there was no correction of frontal flattening. Notably, the use of the helmet, although dependent on patient adherence, facilitates more effective correction of asymmetries, even though orbital depth asymmetry did not show significant modification after isolated suturectomy. A positive outcome for the surgical technique for coronal-lambdoid suture synostosis was reported in the study by Hwang, Jon Ha et al. 2021, despite some cases showing nasal root and orbital rim deviations, with satisfactory improvement in contralateral occipitotemporal bulging. However, ipsilateral frontal flattening and contralateral parietal bulging improved but were still present in most cases [10,11].

Suturectomy with barrel staving was associated with an unfavorable prognosis, mainly due to secondary suture fusion, potentially causing significant complications, according to Patel, Viren et al. 2020. Additionally, Vaca, Elbert et al. 2020 noted relevant correction of cranial asymmetry postoperatively with the monitored operative variables, which included estimated blood loss, lower intraoperative hemoglobin levels, intraoperative blood transfusion needs, dura mater rupture, while postoperative variables followed were surgical site infection, central nervous system infection, and cerebrospinal fluid leakage [14,15].

CONCLUSION

The studies provided insights into various surgical techniques for treating cranial deformities in non-syndromic craniosynostosis. Conventional cranioplasty showed better cognitive outcomes, while endoscope-assisted and minimally invasive craniectomy were favorable for specific cases like trigonocephaly. Each method has its challenges, emphasizing factors like blood loss and long-term results. Further research is needed to refine techniques, but the studies offer valuable insights for improving outcomes in craniosynostosis patients.

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DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. There was no involvement with the ethics committee, as the article is a systematic review.

Consent to participate

The patients gave consent to use their information and images for research purposes. *Consent for publication*

The patient gave consent to use his information and images for publication.

Conflict of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper

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No.

CONTRIBUTIONS

-Brenda Martins da Silva: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Visualization, Writing – original draft, Writing – review & editing

-Marina Eduarda de Almeida: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Visualization, Writing – original draft, Writing – review & editing

-Caroline Martins Franco: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Visualization, Writing – original draft, Writing – review & editing

-Jéssica Camila Alves Quadros: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing

-Nicollas Nunes Rabelo: Funding acquisition, Project administration, Resources, Software, Supervision, Validation, Visualization, Funding acquisition, Project

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administration, Resources, Software, Supervision, Validation, Visualization

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