A systematic review of endoscopic versus open treatment of craniosynostosis. Part 2: the nonsagittal single sutures

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OBJECTIVE Despite increasing adoption of endoscopic techniques for repair of nonsagittal single-suture craniosynostosis, the efficacy and safety of the procedure relative to established open approaches are unknown. In this systematic review the authors aimed to directly compare open surgical and endoscope-assisted techniques for the treatment of metopic, unilateral coronal, and lambdoid craniosynostosis, with an emphasis on quantitative reported outcomes.

METHODS A literature search was performed in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Relevant articles were identified from 3 electronic databases (MEDLINE, EMBASE, and CENTRAL [Cochrane Central Register of Controlled Trials]) from their inception to August 2017. The quality of methodology and bias risk were assessed using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies.

RESULTS Of 316 screened records, 7 studies were included in a qualitative synthesis of the evidence, of which none were eligible for meta-analysis. These reported on 111 unique patients with metopic, 65 with unilateral coronal, and 12 with lambdoid craniosynostosis. For all suture types, 100 (53%) children underwent endoscope-assisted craniosynostosis surgery and 32 (47%) patients underwent open repair. These studies all suggest that blood loss, transfusion rate, operating time, and length of hospital stay were superior for endoscopically treated children. Although potentially comparable or better cosmetic outcomes are reported, the paucity of evidence and considerable variability in outcomes preclude meaningful conclusions.

CONCLUSIONS Limited data comparing open and endoscopic treatments for metopic, unilateral coronal, and lambdoid synostosis suggest a benefit for endoscopic techniques with respect to blood loss, transfusion, length of stay, and operating time. This report highlights shortcomings in evidence and gaps in knowledge regarding endoscopic repair of nonsagittal single-suture craniosynostosis, emphasizing the need for further matched-control studies.

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KEYWORDS craniosynostosis; endoscopic; nonsagittal suture; craniofacial

ALTHOUGH emerging data from the endoscopic treatment of sagittal synostosis suggest more favorable perioperative outcomes, there is substantially less data to inform decisions for the surgical treatment of nonsagittal single-suture craniosynostosis. Metopic cranio-

synostosis, or trigonocephaly, is often characterized by a triangular anterior cranial vault, bitemporal narrowing with biparietal expansion, or midline forehead ridging. The incidence of metopic synostosis has been estimated to be as high as 1 in 5000 births,²³ and accounts for 10% of

ABBREVIATIONS EBL = estimated blood loss; EPHPP = Effective Public Health Practice Project; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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FIG. 1. PRISMA flowchart for systematic review. Figure is available in color online only.

all craniosynostoses.¹⁵ Unilateral coronal craniosynostosis is the most common cause of synostotic frontal plagiocephaly. It is characterized by frontal and superior orbital retrusion on the fused side, sometimes resulting in strabismus.²⁶ The incidence is estimated to be approximately 66 in 1 million live births.³¹ Lambdoid craniosynostosis is characterized by flattening of the occipital bone, leading to potential cranial vault deformity. Lambdoid suture synostosis is rare, representing 1% to 4% of all cases of craniosynostosis, and occurs once in every 40,000 live births.³⁹

There is still controversy around the cosmetic and neurodevelopmental indications for surgical treatment of craniosynostosis.^{34,45,46} In milder forms, the diagnosis may be difficult and the natural course can be self-limited and self-correcting.⁸ However, because a fused suture may physically limit normal brain development, surgery is often offered to correct the deformity before the age of 1 year.^{1,6,37} Metopic synostosis has shown the greatest correlation with neurodevelopmental delay when compared

to other single-suture synostoses,⁴³ although it is yet unproven if corrective cranioplasty rectifies developmental problems.

The variety of synostosis presentation necessitates a variety of surgical techniques. The operative procedure is often tailored to the severity of the deformity. Open surgery techniques for metopic synostosis include synostectomy,³ the “floating head” cranial vault expansion,²⁸ and fronto-orbital reshaping and expansion with bone grafts.^{2,18} Unilateral coronal synostosis has been treated with open surgical techniques that include forward advancement of the supraorbital bar and correction of the orbital asymmetry.^{2,32} Lambdoid synostosis requires open surgery to release the fused suture and correct the cranial vault. Endoscopic approaches to these 3 suture types include suturectomy, fronto-orbital advancement, or a combination, with helmet therapy to follow surgical treatment.⁴⁸

Since its introduction in 2002, endoscopic treatment for craniosynostosis has been shown to be effective, safe, and inexpensive.^{15,19} This systematic literature review aims to

directly compare open surgical techniques and endoscope-assisted techniques for the treatment of metopic, unilateral coronal, and lambdoid synostosis. A disproportionate number of studies have focused on sagittal synostosis. Given the encouraging outcomes reported, there is greater enthusiasm to further expand indications for endoscopic repair. This review presents the most comprehensive evidence for nonsagittal single-suture craniosynostosis. Given that the data for any one specific nonsagittal suture are limited and variable, the current report evaluates several suture types in the analysis of the newer endoscopic treatments compared to traditional open surgery. We highlight deficiencies in knowledge regarding safety and efficacy of the procedure relative to more established open approaches and discuss future studies to better assess outcomes in this heterogeneous patient population.

Methods

Search Strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and recommendations.^{25,36} A literature search was performed on MEDLINE, EMBASE, and CENTRAL (Cochrane Central Register of Controlled Trials) on August 17, 2017, by a librarian (M.A.). The database searches used keywords (individually and/or in combination) such as “craniosynostosis,” “endoscopic,” and “neuroendoscope” with the appropriate subject headings. The reference lists of retrieved articles were reviewed to identify additional relevant articles. Prior to submission, another search was conducted to include newly published studies.

Study Selection

Retrieved studies were systematically assessed using inclusion and exclusion criteria by 2 reviewers (H.Y. and T.J.A.). Inclusion criteria were 1) diagnosis of metopic, unilateral coronal, or lambdoid craniosynostosis by a plastics surgeon or neurosurgeon; 2) at least 50% of the patient population had isolated metopic, unilateral coronal, or lambdoid craniosynostosis; and 3) cohorts were divided into open surgery and endoscopically assisted surgery. Exclusion criteria for the meta-analysis included 1) lack of quantitative comparison between open surgery and endoscopically assisted surgery; 2) nonhuman subjects; 3) inclusion of patients with syndromic craniosynostosis; and 4) editorials, abstracts, review articles, case reports, and dissertations. When duplicate studies were found, only the most complete reports were included for quantitative assessment.

Data Extraction and Critical Appraisal

All data were extracted from article texts, tables, and figures. Each retrieved article was reviewed by 2 investigators independently (H.Y. and T.J.A.). Authors were contacted when there were missing or incomplete data. The quality of the methodology and the risk of bias across studies were assessed by 1 reviewer (H.Y.) using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies.⁴¹ Measured vari-

TABLE 1. Exclusion of eligible studies

Authors & Year	Excluded	Explanations & Comments
Abbott et al., 2012	Yes	Pts w/ sagittal craniosynostosis only
Arts et al., 2018	No	Analyzed pts w/ metopic craniosynostosis separately
Bonfield et al., 2016	Yes	Pts w/ sagittal craniosynostosis only
Chan et al., 2013	Yes	Includes pts w/ syndromic craniosynostosis; pts w/ metopic craniosynostosis represent 21% of cohort
Dvoracek et al., 2015	Yes	Pts w/ sagittal craniosynostosis only; overlapping pt population suspected
Esparza & Hinojosa, 2008	Yes	Pts w/ sagittal craniosynostosis only
Farber et al., 2017	No	NA
Garber et al., 2017	Yes	Pts w/ sagittal craniosynostosis only
Ghenbot et al., 2015	Yes	Pts w/ sagittal craniosynostosis only
Ghosh et al., 2014	Yes	Pts w/ sagittal craniosynostosis only
Han et al., 2016	Yes	Pts w/ metopic craniosynostosis represent <17% of cohort
Hashim et al., 2014	Yes	Analysis of neuropsychological outcomes only
Keshavarzi et al., 2009	No	NA
Keshavarzi et al., 2010	Yes	Pts w/ metopic craniosynostosis represent 27% of cohort
Kohan et al., 2008	Yes	Case studies of twin pts
Le et al., 2014	Yes	Pts w/ sagittal craniosynostosis only; overlapping pt population suspected
MacKinnon et al., 2009	Yes	Overlapping pt population & data suspected
MacKinnon et al., 2013	No	NA
Nguyen et al., 2015	No	NA
Nowaková et al., 2015	Yes	Translated from Czech; nonquantitative data
Rogers et al., 2015	Yes	Measured outcome is hand preference
Shah et al., 2011	Yes	Pts w/ sagittal craniosynostosis only
Siu et al., 2014	Yes	Case studies of 2 pts w/ unilat coronal craniosynostosis & Down syndrome
Tan et al., 2013	No	NA
Thompson et al., 2018	Yes	Pts w/ metopic craniosynostosis represent 18% of cohort
Vogel et al., 2014	Yes	Pts w/ unilat coronal craniosynostosis only
Yarbrough et al., 2014	Yes	Case series of 5 pts w/ mixed suture types
Zubovic et al., 2015	No	NA

NA = not applicable; pts = patients.

TABLE 2. Demographic characteristics of patients in literature review studies

Authors & Year	City & State or Country	EPHPP Rating	Suture Type	Study Design	No. of Pts	No. of Pts Treated		Mean Age (mos)		% Male		FU (mos)	
						Endo	Open	Endo	Open	Endo	Open	Endo	Open
Arts et al., 2018	Nijmegen, Netherlands	Strong	Metopic	R OS	50	35	15	3.6 ± 1.1	10 ± 2.9	NR		12	
Farber et al., 2017	St. Louis, MO	Weak	Metopic	R OS	26*	13*	13*	NR		NR		12	
Keshavarzi et al., 2009	San Diego, CA	Moderate	Metopic	R OS	33	16	17	4.9	29.5	88	65	>36	
Nguyen et al., 2015	St. Louis, MO	Weak	Metopic	R OS	28	13	15	3.3 ± 0.4	9.5 ± 1.8	70	70	12	
MacKinnon et al., 2013	Boston, MA	Weak	Unilat coronal	R OS	43	21	22	4.0	9.3	NR		23.5	21.5
Tan et al., 2013	Boston, MA	Moderate	Unilat coronal	R OS	22	11	11	2	12	NR		34.5	45.9
Zubovic et al., 2015	St. Louis, MO	Weak	Lambdoid	R OS	12	4	8	5.5	12.8	NR		NR	

Endo = endoscopically assisted surgery; FU = follow-up; NR = not recorded; OS = observational study; R = retrospective.

The mean values are expressed ± SD in studies in which SD was reported.

* These patients considered non-unique because of notable similarities with the Nguyen et al. cohort.

ables included selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop-outs, as well as a global rating, and the tool rates each as “strong,” “moderate,” or “weak.”

Results

Literature Search

The search strategy identified a total of 503 studies (Fig. 1). After removal of 187 duplicate studies, inclusion and exclusion criteria were applied to the titles of the remaining 316 articles. This yielded 28 studies that underwent full-text analysis (Table 1), of which 21 did not meet the inclusion criteria of 1) having more than 50% of patients present with metopic, unilateral coronal, or lambdoid synostosis; and 2) reporting on quantitative results. Two of the studies reported on the same cohort, although analyses were focused on different outcome metrics.^{11,29} Due to a dearth of studies with uniform quantitative data, a meta-analysis could not be conducted.

Cohort Description

The cohort size of the literature review included 111 unique patients with metopic craniosynostosis, 65 patients with unilateral coronal craniosynostosis, and 12 patients

with lambdoid craniosynostosis. Of the 7 studies included, only the patients in the Farber et al.¹¹ cohort were considered non-unique patients because of notable similarities with the cohort in Nguyen et al.²⁹ If these 26 patients, 13 in each group, are not counted separately from the patients in the Nguyen et al. cohort, then 100 (53%) children underwent endoscope-assisted craniosynostosis surgery and 88 (47%) patients underwent open repair (Table 2). The age of the endoscopically treated cohort was generally younger than that of the open cohort (range 2.0–5.5 months and 9.3–29.5 months, respectively).

Perioperative Outcomes

Two studies^{4,20} were able to calculate the mean estimated blood loss (EBL) for patients with metopic craniosynostosis treated with endoscopic (range 39–57 ml) and open surgery (range 190–218 ml); endoscopic procedures were favored (Table 3). Similarly, patients with metopic craniosynostosis benefitted from lower transfusion rates when surgery was done endoscopically (range 17%–62%) compared to open (range 71%–100%) procedures. For patients with metopic craniosynostosis, only Keshavarzi et al.²⁰ demonstrated lower transfusion volumes (91.9 ml vs 184 ml), shorter operating time (1.7 hours vs 2.21 hours), and shorter length of stay in hospital (2.46 days vs 2.76

TABLE 3. Perioperative outcomes of patients in literature review studies

Authors & Year	No. of Pts	Suture Type	Mean EBL (ml)		Mean Transfusion Vol (ml)		% Transfused		Op Time (hrs)		LOS (days)	
			Endo	Open	Endo	Open	Endo	Open	Endo	Open	Endo	Open
Arts et al., 2018	50	Metopic	39 ± 25	218 ± 167	NR		17	100	NR		NR	
	3	Coronal	10	110 ± 85	NR		0	100	NR		NR	
	26	Plagiocephaly	33 ± 25	194 ± 124	NR		0	100	NR		NR	
	6	Multisuture	65 ± 36	207 ± 90	NR		33	100	NR		NR	
Keshavarzi et al., 2009	33	Metopic	56.8	190	91.9	184	62	71	1.68	2.21	2.46	2.76
Zubovic et al., 2015	12	Lambdoid	15	350	NR		0	100	0.98	5.0	NR	

LOS = length of stay.

days) for endoscopic procedures compared to open surgery, although no statistical analysis was performed.

Arts et al.⁴ analyzed patients with coronal sutures, plagiocephaly, and multisutures, and Zubovic et al.⁴⁹ analyzed 12 patients with lambdoid craniosynostosis. Consistently across suture types, endoscopically treated patients had lower mean EBL (range 10–65 ml) compared to patients with open surgery (range 110–350 ml). Analogously, the transfusion rate was consistently lower for endoscopically treated patients (range 0%–33%) compared to patients treated with open surgery (100%). Zubovic et al. also demonstrated that the operating time for endoscopic lambdoid procedures was lower, at 0.98 hours, compared to 5.0 hours for open lambdoid surgery.

Cosmetic Outcomes

Two studies^{11,29} reported on cosmetic outcomes for patients with metopic craniosynostosis (Table 4). The postoperative outcomes do not show a difference with regard to mean frontal width (80 mm vs 81 mm), mean interzygomaticofrontal distance (77.0 mm vs 76.2 mm, $p = 0.68$), mean intercanthal distance (30.3 mm vs 31.0 mm, $p = 0.61$), interfrontal angle (112.5° vs 112.6° , $p = 0.98$), or interzygomaticofrontal distance (109.0° vs 109.8° , $p = 0.73$). These cosmetic outcomes were measured at a minimum of 12 months after the operation.

Tan et al.⁴⁰ analyzed the cosmetic outcomes for unilateral coronal synostosis (Table 4). They determined that there was no difference between endoscopic and open procedures with regard to supraorbital symmetry ($p = 0.054$). The endoscopically treated patients exhibited better facial symmetry in midline deviation ($p = 0.018$) and nasal tip deviation ($p = 0.006$). Zubovic et al.⁴⁹ studied the cosmetic outcomes for unilateral lambdoid synostosis. At 1 year postoperatively, open and endoscopically treated patients were statistically equivalent in all measures (range, $p =$

0.359 to $p = 0.967$), and mean volume asymmetry was significantly improved in both groups.

MacKinnon et al.²⁶ specifically studied the ophthalmic outcomes in children with unilateral coronal synostosis, showing that children treated with fronto-orbital advancement open surgery were more likely to develop amblyopia ($p = 0.0015$) and to receive surgery to correct their strabismus.

These retrospective observational studies were assessed by the EPHPP Quality Assessment Tool to include 4 weak, 2 moderate, and 1 strong study (Table 5). Blinding was either not possible or neglected in the methodology. The data collection and statistical analyses of these studies were rigorous, although the small patient population causes difficulty in finding and adjusting for confounders.

Discussion

In this literature review, we found 4 studies^{4,11,20,29} that support the surgical treatment of metopic synostosis by endoscope-assisted surgery compared with open surgery. Two studies^{26,40} examined unilateral coronal surgery outcomes, and 1 study⁴⁹ evaluated lambdoid synostosis. Based on limited data, endoscopic techniques were associated with better perioperative outcomes. Given the heterogeneity in presentations and procedures, strong conclusions cannot be formulated regarding cosmetic results, although objective indicators of cosmesis were equivocal in the few studies reporting these outcomes.

Two studies^{4,20} demonstrated that endoscopic procedures for patients with metopic craniosynostosis have a lower EBL and lower transfusion volumes, shorter operating time, and shorter hospital stay. These results highlighted, however, the fact that the lower blood loss may only be possible with the availability of appropriate instruments, such as a bone scalpel. Similar trends were reported for unilateral coronal synostosis and lambdoid synostosis.^{4,49}

TABLE 4. Reported cosmetic outcomes comparing endoscopic and open treatment

Authors & Year	No. of Pts		Suture Type	Outcomes	Treatment		p Value
	Endo	Open			Endo	Open	
Farber et al., 2017	13	13	Metopic	Mean frontal width (mm)	80 ± 0.4	81 ± 0.7	0.68
				Z-score	0.0	0.0	
Nguyen et al., 2015	13	15	Metopic	Mean ZF-ZF (mm)	77.0 ± 0.8	76.2 ± 1.8	0.61
				Mean ID (mm)	30.3 ± 0.7	31.0 ± 1.0	0.73
				ZFr-G-ZFI	109.0° ± 1.6°	109.8° ± 2.0°	0.98
				IFA	112.5° ± 1.9°	112.6° ± 2.8°	0.006
Tan et al., 2013	11	11	Unilat coronal	Nasal tip deviation	2.3° ± 1.8°	5.6° ± 3.0°	0.018
				Facial midline deviation	1.4° ± 1.1°	3.6° ± 2.4°	0.054
				Difference btwn lt & rt brow projection (mm)	1.7 ± 0.9	1.0 ± 0.6	0.691
Zubovic et al., 2015	4	8	Lambdoid	PFA	6.4°	6.6°	0.551
				PRA	9.5°	7.9°	0.967
				MCA	3.2°	4.0°	0.359
				Vertical EAM displacement (mm)	-2.3	-2.3	0.459
				Anterior-posterior EAM displacement (mm)	7.8	6.8	

EAM = external acoustic meatus; ID = intercanthal distance; IFA = interfrontal angle; MCA = mastoid cant angle; PFA = posterior fossa deflection angle; PRA = petrous ridge angle; ZF = zygomaticofrontal; ZF-ZF = inter-ZF distance; ZFr-G-ZFI = right ZF–glabella–left ZF angle (i.e., axial bilateral zygomaticofrontal–glabella angle).

TABLE 5. Results of quality assessment of methodology

Authors & Year	Selection Bias	Study Design	Confounders	Blinding	Data Collection Methods	Analyses	Global Rating
Arts et al., 2018	Strong	Moderate	Moderate	Moderate	Moderate	Moderate	Strong
Farber et al., 2017	Weak	Moderate	Weak	Moderate	Moderate	Moderate	Weak
Keshavarzi et al., 2009	Strong	Moderate	Weak	Moderate	Moderate	Moderate	Moderate
Nguyen et al., 2015	Strong	Moderate	Weak	Moderate	Weak	Moderate	Weak
MacKinnon et al., 2013	Moderate	Moderate	Weak	Moderate	Weak	Moderate	Weak
Tan et al., 2013	Strong	Moderate	Weak	Moderate	Strong	Moderate	Moderate
Zubovic et al., 2015	Moderate	Moderate	Weak	Moderate	Weak	Moderate	Weak

Cosmetic outcomes were only reported in 26 patients with metopic craniosynostosis on 1-year postoperative CT scans.^{11,29} Measurements of mean frontal width and interfrontal angle show no significant cosmetic difference between endoscopic and open treatment. Patients with unilateral coronal craniosynostosis seem to benefit more from endoscopic treatment, with better postoperative facial symmetry⁴⁰ and a smaller risk for developing amblyopia or strabismus.²⁶ The analysis of aesthetics is only as rigorous as the metrics available for measurement, which significantly limits the conclusions that could be derived from the literature. Ultimately, how the cosmetic outcomes of endoscopic craniosynostosis repair compare to those of open techniques remains an open question.

In larger studies in which several suture types were studied,^{7,16} the perioperative outcomes also seem to favor endoscopic procedures. Han et al.¹⁶ performed a detailed comparison between endoscopic and open procedures, with only 18.6% of their patients having metopic synostosis. They report similar results for endoscopic surgery: lower EBL ($p < 0.001$), lower transfusion rates ($p < 0.001$), shorter procedure time ($p < 0.001$), and shorter course in hospital ($p < 0.001$). These 4 significant differences are also supported by Chan et al.,⁷ whose cohort included patients with syndromic craniosynostosis, with 19% of their patients having metopic involvement. No studies were found specific to metopic, unilateral coronal, or lambdoid surgical correction that analyzed costs or rates of complication between endoscopic and open procedures.

Given the complex indications for surgery surrounding fused metopic sutures, and the variability of the degree of the deformity, minimally invasive endoscopic approaches may be a preferred option in the future. Although the early literature demonstrates safety and efficacy, a survey of 102 craniofacial surgeons demonstrates that only 19% of surgeons performed endoscopic procedures on mild cases of metopic synostosis.⁴⁸ There has not yet been any analysis of the satisfaction of parents and patients with an extended length of helmet therapy. Furthermore, it is unclear at what ages children are most likely to benefit from one treatment versus another.

Strengths of this study include an extensive search of the current literature, strict adherence to PRISMA guidelines, and quality of evidence analysis by EPHPP protocol. Currently, there is a dearth of literature that directly compares endoscopic and open techniques for the treatment of metopic, unilateral coronal, or lambdoid synostosis. The greatest limitation of this study is the inclusion of several

suture types, although the analysis suggests similar findings. Most of the studies included in this analysis were of weak or moderate quality, consisting of retrospective observational studies; one study was found to be strong. Longitudinal studies with extensive follow-up are required to be able to analyze the long-term cost, neurological sequelae, and cosmetic results.

Conclusions

Endoscope-assisted correction of metopic, unilateral coronal, or lambdoid synostosis shows early benefits over open surgical repair. In 7 studies that directly compared endoscopic and open procedures, there were comparable postoperative cosmetic results and better perioperative outcomes such as less blood loss, shorter operations, and shorter hospital stays. Current evidence in the literature comparing endoscopic and open craniosynostosis repair is mostly of weak to moderate quality. Future large prospective registries or randomized controlled trials are required to study long-term outcomes and to explore multiple sources of heterogeneity.

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Disclosures

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Author Contributions

Conception and design: Yan, Ibrahim. Acquisition of data: Abel, Yan, Anderson. Analysis and interpretation of data: Abel, Yan. Drafting the article: Abel, Yan. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Alotaibi. Administrative/technical/material support: Ibrahim. Study supervision: Yan, Ibrahim.

Supplemental Information

Companion Papers

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